
Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

Welcome and Introduction

Anne Quinn Young, MPH

Hello everyone and welcome to the Multiple Myeloma Update from the 2008 Annual Meeting of the American Society of Clinical Oncology (ASCO). My name is Anne Quinn Young, MPH, and I'm the Program Director at the Multiple Myeloma Research Foundation (MMRF). The MMRF is pleased to provide this update to patients, caregivers, and healthcare professionals. Healthcare professionals will be interested to know that this is a CME activity cosponsored by the Postgraduate Institute for Medicine and AOI Communications, L.P. I'd also like to thank and acknowledge Celgene Corporation and Millennium Pharmaceuticals, Inc., for providing support for this activity through educational grants.

I have the distinct pleasure of speaking with several of the key speakers and moderators from the multiple myeloma sessions here at ASCO. I'd like to welcome Carol Ann Huff, MD, from the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine in Baltimore, Maryland; S. Vincent Rajkumar, MD, from the Mayo Clinic in Rochester, Minnesota; and Jean-Paul Fermand, MD, from the Hôpital Saint-Louis in Paris, France. Welcome everyone and thank you for joining us today.

Upfront and Induction Therapy

Anne Quinn Young, MPH

I'd like to start with a few questions related to upfront and induction therapy. Dr. Rajkumar, could you update us on the Eastern Cooperative Oncology Group (ECOG) trial E4A03 comparing Revlimid[®] (lenalidomide or len) and low-dose dexamethasone (dex) with lenalidomide and high-dose dexamethasone?

S. Vincent Rajkumar, MD

Sure, Anne, thanks for having me. What I presented today was partly an update from what we previously presented at the American Society of Hematology (ASH) annual meeting, which is that the survival rate was superior at 1 year and 2 years with the low-dose dexamethasone and lenalidomide compared with the high-dose dexamethasone [plus lenalidomide] arm. As we pointed out, although the response rate was higher, 79% versus 69% with the high-dose arm having the higher response rate, it did not translate into a better overall survival (OS) at 1 year and 2 years at least on this trial.

The second question that came up at ASH was that the low-dose dexamethasone arm had surprisingly high 1-year and 2-year survival rates of 96% and 88%, respectively. And the question was whether this was the effect of the therapy itself or whether the fact that a lot of patients went on to transplant played a role.

So we did a landmark analysis at 4 months of therapy, at which point 431 of the 445 patients were alive. We found that 255 patients did not go off therapy but rather stayed on therapy. On the other hand, the remaining patients went off therapy at 4 cycles. About half the people who went off therapy went on to transplant, and the remaining half either stopped therapy or went on to other alternative measures.

So we looked at the survival of these 3 cohorts of people. The first cohort, people who took 4 cycles and stopped therapy, had a 2-year survival only in the range of 70%. People who took 4 cycles of therapy and went on to a transplant had an extremely good 2-year survival rate of 93%.

If you look at the people who stayed on primary therapy, that result was different between the high-dose dex arm and the low-dose dex arm. The low-dose dex arm did extraordinarily well. They had the same 93% survival rate at 2 years as the stem cell transplant arm did. The high-dose dex arm was about 5 to 6 points lower than that.

We then compared the transplant cohort to the people who stayed on primary therapy with lenalidomide and low-dose dexamethasone; and the 2 groups appeared comparable, although the transplant group appeared to be younger by about 10 years, median age of 58 or 59 compared with a median age of 66 in those who stayed on therapy.

And then, we did another analysis in which we made a worst-case scenario looking only at patients who went to transplant versus all the rest in terms of the len/low-dose dex, and we confirmed that the 2-year survival rate continued to stay the same as it was in the intent-to-treat (ITT) analysis in the original trial.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

So our conclusions were: 1) The lenalidomide/low-dose dex arm was an excellent regimen for induction and transplant and gave a high 2-year survival rate for that group; 2) It also seemed to suggest that those patients staying on primary lenalidomide and low-dose dex had a good survival outcome at 2 years. This raises the hypothesis that perhaps in the era of novel drugs, we should really compare strategies with novel therapy versus transplant. There was a good discussion in which we clarified, and the discussant also agreed, that this trial is not proof of the principle that low-dose dexamethasone without transplant is the way to go; but rather, it provides us the opportunity to test it in the future in a randomized trial. Such trials are being planned, and we will find out in the near future the best strategy for treating newly diagnosed myeloma.

Anne Quinn Young, MPH

Dr. Huff, during your session yesterday, Paul Richardson, MD, from Dana-Farber Cancer Institute presented updated results from a phase I/II trial combining lenalidomide, Velcade® (bortezomib), and dexamethasone for the treatment of newly diagnosed myeloma patients. Can you tell us about the results?

Carol Ann Huff, MD

Sure, thank you again for inviting me. Dr. Richardson presented results from the phase I/II trial of lenalidomide, bortezomib, and dexamethasone in patients with newly diagnosed myeloma. He presented the data from the phase I component in which they determined the maximally tolerated dose (MTD), which was, in fact, one of the primary objectives of that phase of the trial, and determined that lenalidomide at 25 mg for 2 weeks in conjunction with standard-dose bortezomib, 1.3 mg/m² on the days 1, 4, 8, and 11 and dexamethasone at 20 mg on the day of and day after each bortezomib dose, was the optimal dose.

They then expanded that to a phase II trial and enrolled a total of 35 patients in phase II. So they presented updated data on a total of 68 patients and, in fact, found very high response rates with complete response (CR) or near complete response (nCR) in 36% of patients; and greater than 70% of patients had a very good partial response (VGPR). In fact, in their phase II component, all patients had some level of response, indicating a very high response rate with this regimen. The trial was designed to look at response rate and not at survival, so there are no survival data available from this, but it is a very promising regimen that will be examined in subsequent studies.

I think the other very interesting thing is the incidence of peripheral neuropathy (PN) was actually quite low in this trial, with less than 10% of patients having grade 3 peripheral neuropathy. So it was a well tolerated regimen.

Anne Quinn Young, MPH

During that session, Dr. Palumbo presented some interesting data on the use of bortezomib plus pegylated liposomal doxorubicin and dexamethasone (PAD) as induction therapy prior to autologous stem cell transplant, followed by lenalidomide and prednisone as consolidation and lenalidomide as maintenance. What were the key findings from that study?

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

Carol Ann Huff, MD

So, again, another regimen and trial looking at upfront induction therapy, this in conjunction with an intermediate-dose transplant protocol using melphalan at 100 (MEL100) in a tandem transplant approach; and they achieved a complete response in about 20% of patients and a very good partial response in about 40% of patients. Responses continued to improve following transplantation and were even higher following the addition of maintenance therapy. There has yet, however, to be a survival difference. So, the projected overall 2-year survival rate was about 90% with an event-free survival (EFS) rate of about 80%. They then compared their results to what has historically been observed with tandem melphalan transplants but not to melphalan, prednisone, and thalidomide (MPT), which they had studied in other trials. They indicated that MEL100 with tandem transplant was a better approach than MPT, although it's not clear whether that's the optimal comparator for that.

Anne Quinn Young, MPH

There were also 2 other trials looking at bortezomib-based regimens as induction therapy. Jean-Luc Harousseau, MD, presented updated data from the phase III IFM 2005/01 trial comparing bortezomib and dex with vincristine-adriamycin-dexamethasone (VAD) for induction. And then Craig B. Reeder, MD, presented some interesting early results using CyBorD as induction therapy. Can you talk a little bit about those 2 trials?

Carol Ann Huff, MD

Certainly, so in Dr. Harousseau's update, he presented data looking at different inductions with bortezomib-dexamethasone versus VAD followed by transplantation in patients with newly diagnosed myeloma and found that patients who received the bortezomib-based inductions had higher response rates than patients who received the VAD-based inductions, both before transplant and after transplant. Interestingly, however, there was no difference in overall survival at the 18-month assessment. Perhaps it's too early to see whether such a difference will occur, but there was no difference between the 2 groups in overall survival or in progression-free survival (PFS) at 18 months. They did note that about 50% of the patients who had the VAD induction needed a second transplant and only about 25% of the patients who received the bortezomib induction needed a second transplant. These results were based on their predefined criteria specifying that patients in less than a very good partial response following the first transplant would go on to receive a second transplant.

Upfront and Induction Therapy: Discussion

Anne Quinn Young, MPH

So now I'd just like to open up a few questions for discussion to hear the different perspectives, particularly U.S. versus international, about some of the issues that were just discussed in the abstracts related to upfront and induction therapy. First, Dr. Fermand, is there a new standard of care for newly diagnosed patients eligible for stem cell transplantation, in your opinion?

Jean-Paul Fermand, MD

First, thank you for the invitation. In France and in most European countries at the moment, bortezomib, thalidomide, and lenalidomide are not registered, and cannot be officially used in induction. So the official standard of care is VAD. However, there is, in France at least, an agreement; and usually the health authority authorizes us to use either bortezomib or thalidomide in this setting as an induction regimen before high-dose therapy. And there is at present, a move to increasingly use either bortezomib-dex or thalidomide-dex as the first step, as the induction therapy before high-dose therapy. For high-dose therapy by itself, the standard of care remains high-dose melphalan, 200 mg/m² (MEL200). After that, for patients in complete remission in Europe, we usually do not perform a second high-dose treatment. For patients who haven't achieved a complete remission, the standard of care is to perform a second high-dose treatment. However, there is a tendency to replace this second high-dose sequence with new agents such as thalidomide or bortezomib used as a consolidation therapy or maintenance treatment—that is, for patients who are candidates for high-dose therapy.

Anne Quinn Young, MPH

Dr. Huff or Dr. Rajkumar, what are your thoughts?

Carol Ann Huff, MD

So, I actually think we can't answer this question at this point in time. I think that there are many exciting regimens that have been studied—lenalidomide, low-dose dexamethasone in the ECOG trial that Dr. Rajkumar led. We have the preliminary and early data looking at lenalidomide, bortezomib, and dexamethasone and other bortezomib-based approaches. And, unfortunately, we don't have any trials comparing them against each other. So, I don't think that I could make a statement that there is one standard of care for upfront therapy in patients with newly diagnosed myeloma, pretransplant.

S. Vincent Rajkumar, MD

I'd agree with that. I think you get a standard of care only when you have a regimen that clearly improves overall survival such as they have shown with the nontransplant trials. But in the transplant setting, we don't have such a thing. I must highlight the important trials that we do have. We have a Southwest Oncology Group (SWOG) trial that is ready to open, which is going to compare lenalidomide and low-dose dex (Rd) with bortezomib, lenalidomide, and low-dose dex (VRd) in transplant-eligible patients. Patients will then collect stem cells, and then they are expected to continue therapy on that trial.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

The other trial is an ECOG trial which is comparing bortezomib and dex (Vd) with bortezomib, lenalidomide, and dex (VRd). So although there's no head-to-head comparison of bortezomib/dex and len/dex, this would be indirectly something that would answer that question.

And then there is a third trial, which is sponsored by Millennium Pharmaceuticals, Inc., that compares 3 different regimens. Right now there are 2 arms, but we are planning to add a third arm. One arm would be bortezomib/lenalidomide/dex, the regimen that Dr. Richardson showed, which is the experimental arm in the 2 cooperative group trials. That's 1 arm. The other arm is adding Cytosan[®] (cyclophosphamide) to that. So it'll be a 4-drug combination.

And then the third arm is cyclophosphamide-bortezomib-dex that Dr. Reeder presented; it produced an excellent CR rate and a good response rate. So we're going to have this 3-arm trial as well.

So I just think that we better not say that there is a standard of care, rather we just encourage patients to enter clinical trials and figure this out later.

Anne Quinn Young, MPH

So at the meeting, there weren't data specifically looking at regimens for patients who aren't candidates for stem cell transplant; but with the integration of some of the newer agents like bortezomib and lenalidomide, do you think that the standard of care is changing in that population?

Jean-Paul Femand, MD

In Europe, our current standard of care is melphalan/prednisone plus thalidomide (MPT), according to the results of the randomized trials that were reported by the Intergroup Francais du Myelome (IFM); and this combination has been approved. It has marketing availability in France and in Europe since April. So it's our current standard of care.

However, as you know, the results of the VISTA trial are impressive, at least in terms of response rates. And in my view, I guess that this combination will be approved in Europe, maybe at the end of this year or at the beginning of next year. So at that time we'll have to choose. In addition, we are beginning a large randomized trial in all of France, Vincent knows this trial well, which is going to compare MP plus thalidomide with lenalidomide and low-dose dex during a limited period of time, 18 months or until a relapse occurs.

Carol Ann Huff, MD

So actually, I mean we've had, you know, nice data coming out of Europe looking at MPT being superior to melphalan and prednisone (MP) and the VISTA trial data that's coming out showing superiority of melphalan-prednisone-bortezomib (MPV or VMP) to melphalan and prednisone.

I think the question again comes down to which is the optimal regimen, and I don't think we have the answer to that question. We do also have the data from the ECOG trial showing that the survival benefit for lenalidomide and dexamethasone was greatest in those over the age of 65. And so I think some of the upcoming trials are not going to answer this question entirely. But looking at melphalan/prednisone/thalidomide versus lenalidomide/low-dose dexamethasone either for 18 months or indefinitely will help answer a piece of that question, but won't actually answer

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

the question of which of the regimens is ultimately superior. But one of the wonderful things is that we actually have regimens that have been proven in trials to be superior for our patients who are not transplant candidates with near doubling of survival in that population. So it's a marked improvement.

S. Vincent Rajkumar, MD

We say the same thing. You know, we have all these regimens that we think are great, MPT and VMP for the elderly patients, but we'd rather patients enter clinical trials. So one is the trial here. I want to draw attention to another trial which is an ECOG trial that's just been activated. It's comparing MPT with MP plus lenalidomide (MPR). And, again, so we have trials for the transplant population; and we have trials for the nontransplant population. And hopefully, patients are better off entering one of these trials. In the absence of trials, our group thinks that either MPT or VMP are reasonable for elderly patients who are not transplant candidates.

Jean-Paul Fermand, MD

May I add something about the induction regimen prior to high-dose therapy? I think we should compare the whole treatment, not only the induction regimen. This one is better than the other one, etc. Of course, unfortunately, neither one will cure patients. So we need to have a complete view of the treatment and maybe dex/thalidomide frontline will be better using high-dose melphalan plus bortezomib and then a consolidation step using lenalidomide. Putting all the drugs together at the beginning may not be sufficient, because at the relapse we will not have any effective alternatives.

S. Vincent Rajkumar, MD

That's absolutely true. One of the reasons we are using these short-term endpoints is because we have a problem accruing patients to trials which are a little bit more complicated. And we've traditionally in the U.S. accrued to these very long follow-up trials slowly. So we've taken it upon ourselves to maybe do smaller trials and answer questions, but maybe in the future, like we are doing now with your IFM trial, we are collaborating with you, so that hopefully we can accrue to a very big trial by collaboration between the United States and Europe.

Anne Quinn Young, MPH

Talking a little bit about the current and future role of transplant, I think that perhaps a few years ago with the advent of newer agents like bortezomib and lenalidomide, there might have been some thinking that stem cell transplant may not have the same value or use, or may be used later on, but what we're seeing is some interesting data integrating some of these novel agents with stem cell transplant. What are your views in terms of the role for stem cell transplant right now?

Jean-Paul Fermand, MD

In my opinion, high-dose therapy and autotransplantation remains at the moment the standard of care for young patients, I mean younger than 65 years of age, without pronounced renal impairment or other comorbidities. But, indeed, this strategy should be improved by introducing novel agents. This was part of our previous discussion. So, we are on the way toward designing a novel, new generation high-dose therapy regimen. And in France, this strategy is challenged by

new generation standard-dose therapy (SDT) regimens also incorporating the new agents, and I think we should also design the best new generation standard-dose treatment and, in my view, these both should be compared in well designed, randomized studies. And I guess the next step in terms of randomized trials, should be this kind of comparison: new generation autologous stem cell transplant (ASCT) regimen versus new generation SDT regimen.

S. Vincent Rajkumar, MD

So I agree transplant is the standard of care, and we certainly want patients to collect stem cells early if they're transplant eligible. But I'm not sure that transplant early is the standard of care. I think early or delayed is a patient preference issue, and many factors come into play. Even institutions such as the Mayo Clinic, who advocate that it's probably better for early transplant, do something different. I mean we are transplanting 30% to 40% of our patients; and 60% to 70% of patients are opting for delayed transplant, which you have shown is equal in overall survival. I don't think that the advent of new drugs is going to change that. We may have to test it, but so far there are not data that I have seen that early transplant is superior in overall survival to delayed transplant. There's no trial like that. So in the absence of a trial, it's actually the onus to show that doing the transplant early is the way to go.

So having said that, I think our group feels for many other reasons, not overall survival, that early transplant is preferable. For example, if the patient is elderly, we may not be able to do a delayed transplant. If the patient wants a double transplant or may need a double transplant, we have to do it early. If the patient's insurance won't cover stem cell collection and storage, we have to do it early. If the patient says, "I want to just get it over with" as opposed to, "I don't want to hear about transplant," then you would do it early as well. So a lot depends on patient and institutional preference. You would agree?

Jean-Paul Fermand, MD

Yes. Yes. We haven't the insurance issue in Europe, fortunately, in my opinion, but I agree. When I was speaking of optimizing the new generation of standard-dose treatments, I was thinking of using transplantation as a salvage treatment, as a rescue treatment incorporating this approach.

S. Vincent Rajkumar, MD

What do you do at Johns Hopkins?

Carol Ann Huff, MD

We do transplants in our patients initially, typically when we have a clinical trial that's open, testing a new modality. For example, we have a trial open now looking at harvesting bone marrow from patients who have myeloma, and then expanding a population of marrow-infiltrating lymphocytes *ex vivo*, treating them, transplanting them, and reinfusing them.

More and more of our patients opt for a delayed transplant, as opposed to an upfront transplant. And, again, based on the trials that have been done, there doesn't appear to be a difference in survival; and I haven't seen data that would compel me that patients are doing themselves a disservice by delaying a transplant. And so many patients prefer to continue on, or use their

induction therapy, see how long their remission might be, and use a transplant at salvage at that point in time.

I think that there's certainly intrigue at the idea that you might not have to do transplants at this point in time, but we do not have data that support that decision in this process. And so until such data become available, the data we have supports transplantation at some point in time for patients who are eligible.

Anne Quinn Young, MPH

There have been some data presented about the collection and mobilization of stem cells following different induction therapies. What are your thoughts on the data and even personal experience in terms of some of these newer combinations and the impact they may have on the collection and mobilization of stem cells for an immediate or future transplant?

S. Vincent Rajkumar, MD

Anne, we just had a meeting this morning trying to see if we could look at all the data together and come to some kind of consensus. By and large, the data suggest that with any kind of regimen you use there is a certain failure rate. The failure rate to collect adequate stem cells with growth factor alone is in the range of 5% to 10%. That's kind of felt to be the baseline failure rate, and that failure rate is roughly 2% to 5% if you use growth factor plus cyclophosphamide.

Almost all the investigators universally felt that the failure rates using growth factor alone seemed to be higher if you used lenalidomide-based induction regimens. This effect was not seen by investigators who routinely used growth factor plus cyclophosphamide for mobilization. More people here used growth factor plus AMD-3100 for mobilization.

So the final conclusion was that, as in other induction regimens, we prefer to collect stem cells early in the disease course, say 4 to 6 cycles of therapy. We prefer to give a break of about 3 weeks or so from the last dose of any drugs such as lenalidomide to the time you start collection. And if you were using lenalidomide as an induction therapy and you really don't want to anticipate any failures and you want to do it as planned, then growth factor plus cyclophosphamide may be the way to go, in which case the failure rate was extremely low, similar to non-lenalidomide-containing inductions.

On the other hand, if you use growth factor alone, you have to be prepared for a certain failure rate, which may make you have to go back and do the collection. The collection failure rate seemed to be at least somewhat related to the age of the patient. The older the patient, the greater the number of regimens that they had received, or the longer the therapy, there was a trend toward more difficulty in collecting stem cells. This was true with all inductions, but more so with lenalidomide and dexamethasone.

Also in the French Harousseau trial, there was a slight effect of bortezomib, not as much as lenalidomide. VAD seemed to have the highest collection ability. Bortezomib had somewhat diminished effect on stem cells. But most people felt that once you collect, you know, patients grafted and did well, fine. It was the collection stage.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

The second point is sometimes there is a drop in the number of stem cells, but it's still enough to do 2 transplants. So that also needs to be kept in mind.

And one final point, there were data presented on what the mechanism might be. And what eventually came out was that there was no evidence to suggest a toxic effect of lenalidomide on stem cells, but rather an effect by which stem cells were simply not mobilized from the marrow with growth factor alone and that you needed to give either AMD-3100 or cyclophosphamide in a subset of patients to get these cells to come out.

Jean-Paul Fermand, MD

I agree. However, there is also an issue depending on the drug. The alkylating agents, particularly melphalan, are well known to impair the capacity to collect autologous blood stem cells. And that may be, in my view, the point that we don't know about yet with lenalidomide and bortezomib from this point of view. In addition, the number of collected stem cells is, obviously, critical for performing the high-dose treatment, but the quality also may be. In terms of a patient who received a long period of treatment with an alkylating agent, you can collect stem cells, but if the patient lives a long time, you will observe a secondary or myeloid dysplastic syndrome.

S. Vincent Rajkumar, MD

I agree. I mean we are all dealing with drugs that have been used in the newly diagnosed setting for only 2 to 3 years. So certainly I agree that we need long-term follow-up to make sure that these drugs are safe for long-term use. We just have no idea.

One of the reasons why we prefer the new drugs is that if you look at the old regimens, and I'm really very passionate about this. If you look at the old regimens like dexamethasone, the mortality rate in the first 4 months is 10%. In the French trial as well as in the ECOG trial, as well as in the thalidomide/dex versus dex/placebo International MM-003 trial, thalidomide/dex itself had a 7% to 10% mortality rate in the first 4 months. With the new regimens, whether it's bortezomib/dex, bortezomib/thal/dex, or lenalidomide/low-dose dex, you hardly have anybody dying in the first 4 months. So while there may be an effect on a subset of patients long term, the mortality rate is totally different in the first 2 to 3 years now with the new regimens compared to the old ones. So I think we are taking a risk, but there's a defined benefit that we are getting.

Jean-Paul Fermand, MD

When designing our future randomized trials comparing new generation high-dose regimens with new generation standard-dose regimens and comparing early versus late transplant, we should integrate a point which is, in my view, very important, namely the patient's quality of life.

And in my analysis, we suggest introducing the Time Without Symptoms and Toxicities, the so-called TWiST, the time on therapy, and its impact, as an indicator. It's not a perfect indicator, but it is an indicator of this very important parameter in a disease which, unfortunately, we are still not able to cure.

S. Vincent Rajkumar, MD

Can I comment on that? We are doing that for all of the future ECOG trials, the cooperative group trials. There's a score that we have developed for myeloma patients that looks at myeloma-

Multiple Myeloma Update

from the 44th Annual Meeting

of the American Society of Clinical Oncology (ASCO)



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specific quality of life indicators as well as the traditional quality of life indicators that other people have used for various other cancer trials. And this was developed with input from myeloma patients. It's incorporated into the 2 ECOG trials that are currently open, and I agree, that you need the quality of life measurements.

Treating Relapsed/Refractory Disease

Anne Quinn Young, MPH

Drs. Hussein and Richardson presented data that looked at the long-term use of lenalidomide in patients with relapsed/refractory disease. Can you tell us a little bit about the results from these trials?

S. Vincent Rajkumar, MD

Sure. Dr. Hussein's abstract first. He presented long-term results from the single-agent trial of lenalidomide in relapsed/refractory myeloma. This was the MM-014 trial. It's a multicenter trial that enrolled about 222 patients with relapsed/refractory multiple myeloma. I think the most important findings were that, as a single agent, the drug had a 30% response rate. And on average, the responses lasted about 1 year. I think it speaks to the activity of this drug, but also the other point is that sometimes we see patients in today's arena where we are combining all these drugs. We do sometimes see patients who are frail, or patients who have very indolent relapse, who can sometimes be salvaged with just a single agent with minimal side effects, and this trial provides evidence of that.

I think another interesting thing that the trial showed was that the overall survival of this population was 2 years, and that's remarkable because in relapsed/refractory myeloma achieving a 2-year median overall survival for such a heavily pretreated regimen is not possible without active new drugs. This doesn't reflect just on lenalidomide. I think it's the fact that patients had salvage therapy with other active drugs including bortezomib. But it tells us that with new agents, I think the survival of multiple myeloma has certainly improved.

This is really even more illustrated by the study that Dr. Richardson presented on behalf of several colleagues. It was a randomized trial looking at 2 different dosing schedules of lenalidomide, 15 mg twice daily schedule and a 30 mg once daily schedule. Over 100 patients were enrolled in this trial.

The focus of the abstract was on long-term responders. It was interesting, about 10% of these patients, 15 patients total, had been on therapy with lenalidomide plus or minus dex for over 4 years. It was striking that you could have really prolonged benefit from just 1 or 2 agents such as lenalidomide and dexamethasone in a subset of patients in the relapsed/refractory setting as it was in this trial.

The second point that I thought was interesting was that 2 patients who stayed on for 4 years were patients whose best response was just stable disease (SD). And I've always thought that you need to get a partial response (PR), otherwise the drug is useless. And here he's showing, actually not 2 patients, 4 patients who had stable disease as their best response, who went on for 4 plus years with that same status. And they went into the trial with relapsed/refractory disease. So I think this makes us feel like we may want to reevaluate some of the response criteria we use; but I'm thinking that both these trials show that we are in good times in terms of myeloma with the new drugs that we're getting.

Anne Quinn Young, MPH

There were also some data looking at the use of combination therapy, some of these novel agents, in patients who are relapsed and refractory but who also have impaired renal function. One was Donna Weber, MD, looking at the effect of using lenalidomide plus dexamethasone while Joan Bladé, MD, was looking at pegylated liposomal doxorubicin in combination with bortezomib. What were your thoughts on these data?

S. Vincent Rajkumar, MD

The lenalidomide study that Dr. Weber presented was actually a combination of papers that Dr. Weber and Meletios-Athanassios Dimopoulos, MD, have already published in *The New England Journal of Medicine*. They pooled the 2 trials together so they had a total of 682 patients who received either lenalidomide/dex or dex alone.

And then they looked to see how the patients with varying degrees of renal function did on these trials. You must remember that lenalidomide is excreted by the kidneys; and, therefore, all these trials excluded patients if they had a creatinine of 2.5 mg/dL or higher. But with 2.5 mg/dL creatinine, you can still get pretty low renal function based on creatinine clearance. So they had a subset of people, small subset, about 16 patients who had lenalidomide and dex even though their creatinine clearance was less than 30 mL/min.

So they looked at people who had creatinine clearance less than 30 mL/min versus 30 mL/min to 50 mL/min versus 50 mL/min to 80 mL/min and then more than 80 mL/min. And what they found was that, regardless of renal function, the response rates generally tended to be good. Although I think in the lowest creatinine clearance, the response rate was 50%, and in the other groups, it was about 60%. Patients tended to have slightly more myelosuppression as the renal function worsened, particularly thrombocytopenia, which is not surprising given that they might be having some drug accumulation. And the other interesting finding was that in about 80% of the patients who had borderline renal function, renal function improved on therapy.

The thing that needs to be done is we know bortezomib and thalidomide can be used in patients with very severe renal failure, even patients who have dialysis. That's not been shown with lenalidomide. And so the future trials should look at patients with particularly severe renal function problems to define the dose that is appropriate for them, mainly because all our myeloma patients are eventually going to need all these drugs. And many of them go into renal failure as a result of the disease. So it's not possible to deny lenalidomide for patients with renal failure, but it's our job to find the right dose for that group.

We had another trial. This one was by Dr. Bladé, and this was also a retrospective analysis of a previously published randomized trial. The trial in question is the one with bortezomib versus bortezomib plus pegylated doxorubicin. And what Dr. Bladé did was to go back to the trial and look at patients who had renal impairment on the study to see how they did on this trial. We know bortezomib can be safely given in renal failure, and the question was whether the combination would perform well.

So they had 193 of the 322 patients who had renal impairment. And what they found was that just as in the parent trial, the overall time-to-progression (TTP) was about 3 months superior with

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

combination treatment compared with single-agent bortezomib. And you had the same kind of difference in the renal failure population as well. Renal failure improved in the patients who responded to therapy. There were slightly more side effects (anemia, GI side effects) in the renal impairment group; but I think this trial showed that bortezomib or bortezomib plus pegylated doxorubicin can be safely given in patients with renal impairment.

Just as we saw with the previous trial, this trial also excluded patients with creatinine clearance less than 30 mL/min. So it applies to these people with moderate renal function, but in those with severe renal dysfunction, we still need to look at the combination. We know bortezomib can be used, but for combinations you need more data for the more severely impaired patients.

Anne Quinn Young, MPH

Kenneth C. Anderson, MD, also presented a poster looking at the results of a phase II study combining lenalidomide, bortezomib, and dexamethasone for relapsed/refractory patients. What were the results of that study?

S. Vincent Rajkumar, MD

This was the study that preceded the one that Carol discussed for newly diagnosed myeloma. Dr. Richardson and Dr. Anderson have looked at this combination of lenalidomide, bortezomib, and dex driven to some degree by their preclinical studies that combining the 2 drugs will overcome resistance.

So they use bortezomib-resistant cells and they would show that by adding lenalidomide you get a significant cell kill. So they went ahead and did this relapsed/refractory trial. The trial is pretty mature now, and they presented updated results. A total of 43 patients were treated with this 3-drug combination. Importantly, two thirds of the patients had previously received bortezomib; and they had an impressive partial response rate of 55%. In fact, one third of the patients had a complete or very good partial response with this regimen.

I think this is an important trial, not just for the relapsed/refractory population but also because they have then translated it to the newly diagnosed setting. And as you remember what I said about the new trials, many of the new trials are actually using this regimen as the experimental arm now. So I think it's an important contribution to the myeloma patients and to the literature.

Anne Quinn Young, MPH

And then, finally, there were some presentations on some newer agents, those in phase I and phase II in relapsed and refractory populations. Could you discuss some of those?

S. Vincent Rajkumar, MD

Sure. I think one abstract that was presented at the clinical science symposium by Selina Chen-Kiang, PhD, this was not a clinical trial; but it was a preclinical study where she was targeting Cdk4 and Cdk6. Cdk4 interacts with cyclin D1 and Cdk6 interacts with cyclin D2. What she used was a drug called PD 0332991, and she found that by using it as a single agent there was some activity, but when used in combination with bortezomib, there was significant synergy. So this is a good candidate for phase I and phase II clinical trials, and there's a trial that's already in progress with this regimen. The interesting thing that we have to keep in mind is that myeloma in general is

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

a disease where cyclin D1 or D2 or D3 is overexpressed in almost all types of myeloma, and so targeting cyclin D1 and D2 is important and I think, a good preclinical bench-to-bedside type of translation.

The other drug that was interesting was Zolinza[®] (vorinostat), which is a histone deacetylase inhibitor, and a phase III trial is already being developed. So Ashraf Z. Badros, MD, ChB, presented the phase I/II results of this drug in combination with bortezomib; and they treated 23 patients. I guess this combination is going into phase III because they found 3 patients with bortezomib-refractory disease who achieved a partial response to the combination of bortezomib plus vorinostat. So they think it's a strong enough signal to invest the resources into doing the phase III testing. I think that's another good target and another good combination that's worth keeping in mind for the future.

The third one is an old target. We've all known that interleukin-6 (IL-6) is an important growth factor for myeloma cells and that targeting IL-6 with a monoclonal antibody would be a great idea. It has been tried in the past, but not with a humanized antibody. But now, this new trial that was reported by Peter M. Voorhees, MD, is using CNTO 328, which is a chimeric monoclonal antibody. It's a humanized one they're using in combination with dexamethasone. So the trial design was to use anti-IL-6 antibody alone. If the patients had progressive disease or they had no response after 2 cycles, dex was added.

There were 14 patients treated, and it was well tolerated, but so far they haven't seen any responses with the single agent alone. So I think even though IL-6 we know intuitively is a great target, we still need more work to find out if this strategy will work.

Anne Quinn Young, MPH

So, in general, this meeting really didn't have a lot of data on novel agents earlier in clinical trials – phase I, phase II. So for those combinations under study where there weren't data presented here, which ones are of particular interest to you? Are there certain therapies or combinations that are exciting to you?

Jean-Paul Fermand, MD

I was impressed by the presentation by Dr. Chen-Kiang. I think this approach, although preclinical as Vincent said, is a very clever one. It's very interesting. In myeloma cells as an accelerator of the cell cycle, namely the overexpression of cyclin D, any cyclin D, and blocking this accelerator is a very interesting approach not only to try to kill the cell but, more importantly, in my view, to overcome drug resistance. If I can make the comparison, it's like a car, the motor of which is turning very rapidly, even though the car does not move. And you first slow down the motor and then try to block the machine, to destroy the machine. I think we have here a very interesting approach.

Carol Ann Huff, MD

So I would agree with that. I also think that the histone deacetylase inhibitors are quite interesting and some of the more selective ones, beyond what we see with vorinostat, are interesting, as well as all of the other pathways that people are identifying both in the myeloma stromal cells as well as in the plasma cells and even in the myeloma stem cell compartment.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

S. Vincent Rajkumar, MD

The one that I am excited about is CC-4047, which is an analog of thalidomide and lenalidomide. We are doing a phase II trial, and so far the trial is proceeding really well. We've finished treating the first cohort of patients, and we are expanding the trial to treat an additional 30 patients. So I'm hoping results will come out at ASH this year.

Of course, all of us are very interested in new proteasome inhibitors. There are various proteasome inhibitors from many companies being developed. The one I'm familiar with is carfilzomib (PR-171), which the Multiple Myeloma Research Consortium (MMRC) has worked on in clinical trials and is showing very good activity already, and we are moving ahead with more definitive trials with that drug. So I think the new proteasome inhibitors as a class will be very useful.

Jean-Paul Fermand, MD

Can I add something about the combination of bortezomib plus lenalidomide plus dexamethasone from a European point of view? This combination carries a very important issue, namely the cost. And I think it should be demonstrated as having a huge advantage over other combinations to be registered and so on and to be largely used, at least in our countries.

Genetics/Prognostic Factors

Anne Quinn Young, MPH

There was also a lot of discussion at the meeting, and, Dr. Rajkumar, you brought up the importance and prognostic value of achieving say at least a partial response (PR) if not a complete response (CR) or very good PR. What are your thoughts on the importance of achieving, say, some minimal threshold as well as your thoughts on whether you think CR really is a surrogate or could be a surrogate for overall survival?

Carol Ann Huff, MD

Well, I think Vincent did a wonderful job in his discussion summarizing the data, which actually we believe quite strongly too, and that is that there are certainly trials that do correlate complete response with survival; but there are other situations in which a complete response does not correlate with overall survival. And I believe we need to be cautious in striving so hard to achieve complete response because really, ultimately, what we're aiming for is overall survival for our patients and overall survival such that myeloma is not the disease that they pass away from. And so I think responses are important, but going for the absolute highest complete response rate probably isn't, at least in the way we currently define complete remission, our optimal goal.

Jean-Paul Fermand, MD

I fully agree. CR, the achievement of CR as a surrogate marker, in my view has been overestimated during the last few years. There are many contra-examples, as you said, and at the individual level, we've all known patients who achieve only a partial remission; Vincent told us about one. Conversely, there are situations in which the patient achieves an excellent complete remission very quickly but then relapses very rapidly. For example, in patients with the t(4;14); it's nearly always, unfortunately, the case.

So for a series of patients, it does add value; but at the individual level, it's only a surrogate marker; and we need to improve our definition for the several types of, several subgroups of the disease with specific impact on outcome.

S. Vincent Rajkumar, MD

Yes, and I think you've said the same thing that I strongly agree with. That is, we are sometimes forgetting what is maybe a prognostic or a risk marker where patients who respond very well to therapy tend to do well and interpret that to mean that, therefore, I'm going to now treat to get that endpoint, which is a totally different interpretation. And you can sometimes hurt patients because overall survival in my mind is a composite endpoint. It is a balance between toxicity on the one hand and efficacy on the other hand. If you're not careful, it could go in the opposite direction. And there are, I think, in terms of a general goal of therapy, achieving a stable plateau phase has been always for a long time that's when we would say, "Okay, we've achieved a good response."

If the patient is symptom free and in a good plateau phase, with many of the present regimens we'd probably have a good response in many patients. I don't feel the need to push that further because then that's where the problem can happen. If a CR happens, well and good.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

Anne Quinn Young, MPH

At this meeting there was some discussion about genetics and the definition and importance of a group of high-risk patients, and our knowledge in this area and the data continue to evolve. What are your thoughts on first, the definition of high risk, what the prognostic implications are, and potentially how to treat these patients?

S. Vincent Rajkumar, MD

You know, the definition of high risk varies according to various institutions. In general, one could say that a patient categorized as International Staging System 3 is a high-risk patient; but yet, those types of risk factors based on variables such as β_2 -microglobulin may not give you the true really high-risk patients.

At Mayo and in many other centers, certain cytogenetic abnormalities seem to carry particular consequences. These include the chromosome rearrangements t(4;14), t(14;16), and 17p minus. On conventional cytogenetics, the finding of hypodiploidy or deletion 13 also carries risk. If any one of these factors are present, patients have not done as well with an approach of induction followed by transplant.

Now with the new agents, we are seeing, for example, in the VISTA trial and even in trials done like the APEX trial, high-risk cytogenetic features may be overcome by bortezomib. There was a study by Nizar Bahlis, MD, from the lenalidomide relapse trial showing that some of these cytogenetics may be overcome by lenalidomide. So this area is changing now, so we may have to redefine our high-risk definition based on these new drugs that we have available.

Jean-Paul Fermand, MD

I fully agree. We have identified high-risk markers, and we need now to reassess their prognostic value in the context of the new regimens. In addition, and in my view, the study that was presented by Hervé Avet-Loiseau, MD, is a very important one. We have a lot of work to do to improve the identification of the high-risk patients through standard prognostic markers. But my feeling is that going into the molecular lesions of the plasma cells is a much more fruitful approach to identify these groups of patients and different groups of patients and to identify new lesions using the new molecular approaches. And Dr. Avet-Loiseau and others in this meeting open very important avenues to better define the different subgroups of the disease.

S. Vincent Rajkumar, MD

Yes, I was very impressed with the new technique using the single nucleotide polymorphisms (SNPs) and using SNP arrays to look for copy number changes. And they found that increased amplification of chromosome 1 was a poor-prognostic marker, wasn't it? And they found that chromosome arm 12p deletion was—

Jean-Paul Fermand, MD

It's a new marker.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

S. Vincent Rajkumar, MD

These are new markers.

Carol Ann Huff, MD

And actually, on multivariate analysis, it was the chromosome arm 12p deletion, addition of chromosome 5, and β_2 -microglobulin that came out as significant; and the chromosome arm 1q amplification actually did not hold significance in multivariate analysis. So I think that those are very interesting to understand what the genetic changes are at those loci to help us better understand the disease and potentially even develop additional targets.

I think the other point I would make is that it's intriguing that the data with the VISTA trial and others suggest that these features such as t(4;14) and chromosome arm 17p may not be poor prognostic factors, and whether that overcomes the difference that we've actually seen in these patients not benefiting from autologous transplantations. Perhaps, in fact, as time goes on, we will find that those patients actually do better. But time will tell.

Multiple Myeloma Update

from the 44th Annual Meeting

of the American Society of Clinical Oncology (ASCO)



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Closing Remarks

Anne Quinn Young, MPH

Well thank you so much. It's been a pleasure. The information that you've provided will undoubtedly be very helpful to those who weren't able to be here live at the meeting and hear the presentations firsthand. Thank you.

References

- Anguiano A, Tuchman SA, Perez B, Salter KH, Redman RC, Zhan F, et al. Gene expression profiles defining molecular subtypes, coupled with signatures of tumor biology and chemotherapy sensitivity provide a novel therapeutic approach to multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8501.
- Anderson KC, Jagannath S, Jakubowiak A, Lonial S, Raje N, Schlossman R, et al. Phase II study of lenalidomide (Len), bortezomib (Bz), and dexamethasone (Dex) in patients (pts) with relapsed or relapsed and refractory multiple myeloma (MM). *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8545.
- Avet-Loiseau H, Munshi N, Li C, Magrangeas F, Gouraud W, Charbonnel C, et al. Use of high-density SNP-array analysis to identify novel chromosomal abnormalities that predict survival in multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8522.
- Badros AZ, Philip S, Niesvizky R, Goloubeva O, Harris C, Zweibel J, et al. Phase I trial of vorinostat plus bortezomib (bort) in relapsed/refractory multiple myeloma (mm) patients (pts). *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8548.
- Blade J, Sonneveld P, San Miguel J, Sutherland H, Hajek R, Nagler A, et al. The effect of pegylated liposomal doxorubicin plus bortezomib in multiple myeloma patients with renal insufficiency. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8562.
- Bryant B, Danaee H, Lichter D, Shaughnessy, Jr. JD, Bergsagel PL, Sonneveld P, et al. High-resolution assessment of chromosomal gains and losses in multiple myeloma tumors from bortezomib clinical trials. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8570.
- Chen-Kiang S, Di Liberto M, Louie T, Liang J, Jayabalan DS, Ely S, et al. Targeting Cdk4/6 in combination therapy of chemoresistant multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8503.
- Cook RJ, Vogl D, Mangan PA, Cunningham K, Luger S, Porter DL, et al. Lenalidomide and stem cell collection in patients with multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8547.
- Harousseau JL, Mathiot C, Attal M, Marit G, Caillot D, Hullin C, et al. Bortezomib/dexamethasone versus VAD as induction prior to autologous stem cell transplantation (ASCT) in previously untreated multiple myeloma (MM): Updated data from IFM 2005/01 trial. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8505.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

Hussein MA, Richardson PG, Jagannath S, Singhal S, Bensinger W, Knight R, et al. Final analysis of MM-014: Single-agent lenalidomide in patients with relapsed and refractory multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8524.

Jagannath S, Richardson PG, Zeldenrust S, Alsina M, Wride K, Zeldis JB, et al. Long-term responses observed with lenalidomide therapy for patients with relapsed or refractory multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8525.

Kapoor P, Snozek C, Colby CL, Larson DR, Katzmann JA, Witzig TE, et al. Incorporation of the plasma cell labeling index into the international staging system of multiple myeloma: Impact on prognostic value. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8591.

Ngo TB, Felthaus J, Ihorst G, Engelhardt M, Wäsch R. Monitoring bortezomib therapy in multiple myeloma: Screening of cyclin D1 overexpression as a potential prognostic marker for response to treatment. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8614.

Niesvizky R, Stern J, Manco M, Mark T, Schuster MW, Shore TB, et al. Effect of bortezomib, cyclophosphamide, and filgrastim on complete remission rates and CD34+ stem cell collections in multiple myeloma (MM). *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8587.

Ortega MM, Cunha AF, Albuquerque DM, Costa GL, Sagarra AF, De Souza CA, et al. New overexpressed genes related to cell proliferation stimulation and apoptosis inhibition of plasma cells of multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8598.

Palumbo AP, Falco P, Corradini P, Crippa C, Patriarca F, Rossini F, et al. Bortezomib, pegylated-liposomal-doxorubicin and dexamethasone (PAD) as induction therapy prior to reduced intensity autologous stem cell transplant (ASCT) followed by lenalidomide and prednisone (LP) as consolidation and lenalidomide alone as maintenance. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8518.

Paripati H, Stewart AK, Fonseca R, Dueck AC, Slack JL, Reeder CB, et al. Impact of lenalidomide therapy on stem cell mobilization in myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8543.

Multiple Myeloma Update

from the 44th Annual Meeting
of the American Society of Clinical Oncology (ASCO)



TRANSCRIPT

Rajkumar SV, Jacobus S, Callander N, Fonseca R, Vesole D, Williams MV, et al. Randomized trial of lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone in newly diagnosed myeloma (E4A03), a trial coordinated by the Eastern Cooperative Oncology Group: Analysis of response, survival, and outcome with primary therapy and with stem cell transplantation. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8504.

Reeder CB, Stewart AK, Hentz JG, Bergsagel PL, Pirooz NA, Fonseca R, et al. Efficacy of induction with CyBorD in newly diagnosed multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8517.

Richardson PG, Lonial S, Jakubowiak A, Jagannath S, Raje N, Avigan D, et al. Safety and efficacy of lenalidomide (Len), bortezomib (Bz), and dexamethasone (Dex) in patients (pts) with newly diagnosed multiple myeloma (MM): A phase I/II study. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8520.

Voorhees PM, Manges RF, Sonneveld P, Somlo G, Jagannath S, Zweegman S, et al. Phase II study evaluating the efficacy and safety of CNT0328 in combination with dexamethasone for patients with relapsed/refractory multiple myeloma (MM). *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8593.

Wang M, Giralt S, Handy B, Feng L, Delasalle K, Wang J, et al. Complete remission and survival in multiple myeloma. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8523.

Weber DM, Spencer A, Wang M, Chen C, Attal M, Niesvizky R, et al. The efficacy and safety of lenalidomide plus dexamethasone in relapsed or refractory multiple myeloma patients with impaired renal function. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8542.

Zonder JA, Crowley JJ, Bolejack V, Hussein MA, Moore DF, Whittenberger BF, et al. A randomized Southwest Oncology Group study comparing dexamethasone (D) to lenalidomide + dexamethasone (LD) as treatment of newly -diagnosed multiple myeloma (NDMM): Impact of cytogenetic abnormalities on efficacy of LD, and updated overall study results. *The American Society of Clinical Oncology 44th Annual Meeting*. May 30–June 3, 2008. Abstract 8521.