

WELCOME AND INTRODUCTION

Operator

Greetings, and welcome to the "Myeloma – Update on Treatment From the American Society of Hematology (ASH®) Annual Meeting" telephone and Web education program. It is now my pleasure to introduce your moderator, Lizette Figueroa-Rivera, MA.

[Slide 1 – Welcome and Introductions]

Lizette Figueroa-Rivera, MA

Thank you and hello everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. William Bensinger for sharing his time and expertise with us today. We have over 1,100 people participating from across the United States and several countries around the world, including Andorra, Barbados, Canada, Indonesia, Ireland, Italy, Peru, and the United Kingdom.

Before we begin, I'd like to introduce The Leukemia & Lymphoma Society's President and CEO, Dr. Louis J. DeGennaro, who will share a few words. Dr. Lou, please go ahead.

Louis J. DeGennaro, PhD

Thank you, Lizette. I'd like to add my welcome to the patients, caregivers, and healthcare professionals attending today's program. The Leukemia & Lymphoma Society exists to find cures and to ensure access to treatment for blood cancer patients. Our vision is a world without blood cancer. For more than 60 years, LLS has helped pioneer innovations such as targeted therapies and immunotherapies that have improved survival rates and the quality of life for many blood cancer patients. To date, we have invested over one billion dollars in research to advance therapies and to save lives. Until there is a cure, LLS will continue to fund promising research from bench to bedside.

In addition, as this program demonstrates, we are the leading source of free blood cancer information, education and support, and we assist patients near their homes through our 58 chapters spread across the US and Canada.

Finally, LLS also acts as the voice for all blood cancer patients. We advocate for patients, survivors and their families, helping them navigate cancer treatment and ensuring that they have access to quality, affordable and coordinated care.

We're very, very fortunate today to have as our presenter Dr. William Bensinger, one of the nation's leading experts in myeloma. We appreciate his dedication to supporting our mission and his commitment to caring for patients living with blood cancers. I'd like to personally thank him for providing us today with important information on myeloma.

Now, I'll turn the program back to Lizette.

Lizette Figueroa-Rivera, MA

Thank you, Dr. Lou.

Lizette Figueroa-Rivera, MA

We would like to acknowledge and thank Bristol-Myers Squibb, Celgene Corporation, Takeda Oncology, and Onyx Pharmaceuticals, an Amgen subsidiary, for support for this program.

[Slide 2 – William Bensinger, MD]

I am now pleased to introduce Dr. William Bensinger, Director of the Autologous Bone Marrow Transplant program at Seattle Cancer Care Alliance (SCCA) and member of the Clinical Research Division at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

On behalf of The Leukemia & Lymphoma Society, thank you for volunteering your time and expertise.

Dr. Bensinger, I'm now privileged to turn the program over to you.

PRESENTATION

William Bensinger, MD

Thank you very much, Lizette. It's a pleasure to be here today and, hopefully, provide you with more in-depth information all about multiple myeloma (MM).

[Slide 3 – Disclosures]

This slide shows my disclosures. I do consulting services for a number of pharmaceutical companies that are developing new drugs in myeloma and have active research programs testing many of these new drugs.

[Slide 4 – Etiology of Multiple Myeloma (MM)]

Multiple myeloma (MM) is a cancer that involves a normal cell called the plasma cell. The exact cause and how these plasma cells become cancerous are unknown, but it's thought to be a multistep process involving changes to the genetic structure of the cells. When enough damage occurs, these cells begin to grow in an uncontrolled fashion, which is the hallmark of cancer. These cells typically remain in the bone marrow, at least in the early stages of the disease, frequently produce monoclonal proteins (M protein) that appear in the blood or urine, and change the microenvironment in the bone marrow by altering the signaling that occurs with cells that support the myeloma cells and continue to support their growth.

[Slide 5 – Epidemiology of MM]

This is not a very common disease. Only about 95,000 people in the US have this. It is only about one percent of all cancers and about 10 percent of blood cancers. The incidence does appear to be increasing. There are about 24,000 new cases diagnosed currently in the US. There are about 11,000 deaths per year. The five-year survival for the period from 2004 to 2010 was slightly less than 50 percent. This is increasing, however, and more recent data suggest survivals in excess of 50 percent. There are patients who now live 10 years or more with this disease. It's a disease largely of older patients with the median age of 69 years. Only a tiny percent of patients are younger than 45 years of age: 3.8 percent. It's more common in blacks compared to whites and more frequent in men compared to women.

[Slide 6 – Spectrum of Clinical Manifestations of MM]

When these MM cells propagate and fill up the bone marrow, they secrete monoclonal proteins that can affect kidney function, may affect nerve function, and lead to immunodeficiency because there is actually a depression in normal levels of antibodies in this disease, and patients are more frequently prone to infection. The marrow infiltration can cause bone damage with attendant hypercalcemia or high calcium levels and destroys bone structure with attendant bone pain and actual spontaneous breaks in some patients. Patients also frequently become anemic because, as the marrow fills up with these abnormal cells, there is less space for growth and development of normal red cells.

[Slide 7 – Clinical Presentation]

The clinical presentation can vary, but frequently bone pain, fatigue, weight loss, paresthesias, kidney problems with kidney failure, and in some cases spinal cord compression with paralysis can occur, and back pain is a common symptom. But about 20 percent of patients may have no symptoms at the time of diagnosis. In the laboratory, we look for these elevated levels of monoclonal proteins we call paraproteins. Patients are anemic, as I said, and have low hemoglobin, high calcium levels, low albumin, and then certain markers such as beta-2 microglobulin (B2M) can be elevated or C-reactive protein (CRP). About 20 percent of patients will have abnormal kidney function with an elevated creatinine. X-rays may reveal holes in the bones that we refer to as lytic lesions, or there can be a general demineralization of the bone leading to osteoporosis, but fractures can occur because of the weakening of the bone. It's not uncommon to have patients develop compression fractures in their spine with actual loss of height. The bone marrow shows increased numbers of these abnormal plasma cells.

[Slide 8 – Initial Diagnostic Evaluation]

As far as initial diagnostic evaluation, we test the blood looking at the complete blood count, checking for anemia and other levels of blood cells. We check kidney function and electrolytes, lactate dehydrogenase (LDH), which can be elevated in some patients with this disease, and calcium and albumin levels. We check serum free light chains, which are the small components of the monoclonal proteins. These are just the component pieces called light chains. We measure quantitative immunoglobulins to look for immunodeficiency and then certain markers, as I mentioned, like beta-2 microglobulin.

The monoclonal protein is tested with a technique called protein electrophoresis; either serum protein electrophoresis (SPEP) or urine protein electrophoresis (UPEP) and then immunofixation will tell us more about the specific type of protein. In the urine, we measure the excretion of these abnormal proteins, usually light chains, by running electrophoresis and measuring 24-hour urine.

In the bone marrow, we measure the amount of plasma cells, and we look with special cytogenetic analysis for abnormal changes in the gene structure that have significant prognosis. The gold standard among X-rays is the skeletal survey, but, increasingly, we're using magnetic resonance imaging (MRI) or positron emission tomography (PET) scans or routine computed tomography (CT) scans. These frequently will reveal abnormalities before they appear in the skeletal survey.

[Slide 9 – Hallmark of MM]

Now, just to show you in multiple myeloma, this is what a normal protein electrophoresis looks like with that high peak at one end measuring albumin, and then the gamma region at the other end, or the gamma globulins, which are the antibodies. When you develop multiple myeloma, however, this

William Bensinger, MD

monoclonal protein develops typically in the gamma region, and that is what we look for and what we measure in this disease.

[Slide 10 – Diagnostic Criteria for Symptomatic MM]

For symptomatic myeloma, the acronym that's been used is called CRAB criteria, which stands for Calcium elevation, Renal or kidney failure, Anemia, and Bone lesions. I prefer to use the acronym adding an "i" for CRABi, which includes frequent infections that can also occur in this disease. These are the diagnostic criteria for symptomatic myeloma and generally indicate the need for treatment. Patients who don't have any of these features are considered to have asymptomatic myeloma. Until recently, the standard of care was not to treat patients with asymptomatic or smoldering myeloma. This is changing, however.

There is a recent paper that suggested that patients with certain high-risk features, who are likely to progress quickly to symptomatic disease within two years, may benefit from a combination of lenalidomide and dexamethasone (dex). In addition, there is a reclassification proposal that's been made by the International Myeloma Foundation (IMF) that includes a couple of extra features, including a very high level of plasma cells in the bone marrow—greater than 50 percent—a very high elevated free light chain, or lesions seen by a PET scan or CT scan. These are patients who would normally be asymptomatic, but they're being reclassified according to this proposal to have symptomatic myeloma, and the IMF is recommending that patients receive early treatment if they have any of these three additional features even though they may not meet the CRABi criteria.

[Slide 11 – International Staging System for MM]

There's also an International Staging System. This is useful because it gives prognostic information about the aggressiveness of the disease. The International Staging System relies on a beta-2 microglobulin and serum albumin level. As you can see [on Slide 11], the median survival ranges from two and a half years to over five years depending on your Stage I, Stage II or Stage III.

[Slide 12 – Impact of Genetic Abnormalities on Prognosis in MM]

Additionally, however, we're recognizing genetic abnormalities that are seen in the abnormal myeloma cells on a bone marrow exam. Some of these such as hyperdiploidy, which means an excess number of chromosomes, a deletion 13 by itself, or the (11;14) translocation, either have a favorable prognosis or no significant prognosis. But about 20 percent of patients will have certain genetic abnormalities, such as a (14;16), (4;14), deletion 17 or a combination of them. These patients have a more aggressive disease and typically will respond to treatment but tend to relapse much more quickly and require more aggressive therapy to manage their disease.

[Slide 13 – Myeloma Treatment: A Historical Perspective]

Historically, before the 1950s, there wasn't much to treat myeloma. Urethane was used commonly, but it was proven to be no better than a placebo consisting of Coca-Cola. But melphalan was developed in the '50s along with corticosteroids in the '60s, and then combination therapies were first used with melphalan–prednisone (MP) or other drugs. However, these treatments, while they worked in some patients, did not appear to affect overall survival. The big changes occurred in the '80s when the autologous stem cell transplant was used and ultimately proven to be effective therapy for disease and because it improved overall survival in patients who underwent a transplant. Then in the '90s, things really began to change with the introduction of the new drugs or what we call novel agents.

[Slide 14 – Managing Myeloma: The Components]

Overall, in terms of managing myeloma, we make a distinction between patients who are considered eligible for transplant and patients who are transplant ineligible. Generally, this is a combination of age and performance status. If patients are relatively young, generally 70 years or less, and have good performance status—do not have significant heart or lung disease—they're eligible for autologous transplant. For patients who are older or patients who simply don't want to consider a transplant, these patients generally receive induction therapy or initial therapy followed by consolidation and maintenance therapy. Increasingly, we're using the concept of maintenance or continued therapy as a way to control the disease. For patients who are transplant ineligible, there was a recent paper suggesting that continuous treatment with lenalidomide and dexamethasone was better than a fixed, defined period of treatment with lenalidomide and dexamethasone.

But generally for patients who are transplant eligible, initial therapy is used followed by autologous transplant as a form of consolidation to improve the response. Sometimes additional cycles of therapy are given post-transplant and then maintenance therapy may be used again to control the disease. At some point, patients will relapse and require retreatment with additional drugs. Supportive care measures are an important component of the treatment. Drugs such as bisphosphonates, either zoledronate (Zometa®) or pamidronate (Aredia®), can be used to control or prevent bone fractures. Erythropoietins can be used for the anemia or other growth factors to control neutropenia. These are important components of supportive care, and I'll have more to say about that later on.

[Slide 15 – Goals of Therapy]

The goals of therapy are essentially to control the disease activity in myeloma and improve the disease-related symptoms—bone damage, pain and fractures, lowering a high calcium which can affect kidney function and lead to symptoms such as weakness, anemia which also causes weakness or fatigue and may even develop into shortness of breath in severe cases, as I mentioned the kidney problems, and then to reduce frequent infections. We found mostly that it's useful for patients to achieve a remission because remissions are associated with more durable disease control and, in many studies, patients who achieve remission live longer than patients who don't. At the same time, we want to minimize the treatment-related symptoms because many of these drugs have side effects, and I'll go over some of those a little bit later on in the talk.

[Slide 16 – Current Status of Treatment for MM]

Currently, the therapy has become better thanks to the combinations of new drugs and the use of autologous transplant. Many patients now can survive 10 years or more with this disease. Keep in mind that 15 years ago, the median survival in this disease was three years and almost no one survived 10 years or more, but now it's common, with the new drugs and with the use of autologous transplant.

Cure is still an elusive goal for the majority of patients and, thus, the concept of continuous therapy or maintenance therapy has become more important as a way to forestall a recurrence of the disease. In addition, the treatment is constantly changing. We have many new drugs and new classes of drugs that are under development, and I'll have more to say about that in a few minutes.

[Slide 17 – Drugs for MM]

These are the drugs that currently are used for the treatment of myeloma. The time-honored ones have been steroids, either dexamethasone or prednisone, and alkylating agents. The first one was

William Bensinger, MD

melphalan but cyclophosphamide has become a very important one and bendamustine is an old drug that was fairly recently approved in the US and is also useful for some patients.

Vincristine, the vinca alkaloid, is not used much anymore. It was part of an old combination known as VAD (vincristine–Adriamycin® [doxorubicin]–dexamethasone) and really has fallen out of favor due to studies showing superior outcomes with newer drugs.

Anthracyclines such as doxorubicin or a pegylated form of doxorubicin are useful.

The two new classes of drugs that have really changed the landscape and the treatment of myeloma are the so-called IMiDs, or immunomodulatory drugs, of which thalidomide (Thalomid®) was the first-in-class and lenalidomide has become an important one. More recently, pomalidomide (Pomalyst®) is a third in its class of drugs.

The proteasome inhibitors, the first-in-class was bortezomib (Velcade®). This was a very important drug that was developed. Then, more recently a new generation, carfilzomib [Kyprolis®], has become approved by the U.S. Food and Drug Administration (FDA) and is widely used for the treatment of multiple myeloma.

[Slide 18 – Initial Treatment]

For the initial treatment, there are a variety of combinations that are used. Transplant candidates typically use combinations of bortezomib with dexamethasone and add either thalidomide or lenalidomide. Doublets of bortezomib and dexamethasone can be used or lenalidomide and dexamethasone. Bortezomib–Doxil® (doxorubicin) and dexamethasone are used or combinations with cyclophosphamide can be used.

Older combinations, such as thalidomide–dexamethasone or VAD, are only rarely used and have really been shown to be inferior to the combinations shown above.

For nontransplant candidates, especially in Europe but less so in the US, combinations of melphalan–prednisone with either thalidomide–lenalidomide or bortezomib are frequently used. We tend to avoid melphalan for transplant candidates because it can damage the marrow as part of the initial treatment and may make it more difficult to collect and harvest stem cells.

More commonly used combinations are the lenalidomide–dexamethasone combination for nontransplant candidates or combinations of bortezomib–dexamethasone–cyclophosphamide–lenalidomide or sometimes thalidomide can be used as well.

[Slide 19 – Measuring Treatment Response]

In terms of how to measure treatment response, we typically refer to remissions, which could either be a complete remission (CR) or a partial remission (PR). A CR is the same as calling a patient a complete response. A complete response occurs when there's no sign of the monoclonal protein in the blood or urine. If you look in the bone marrow, you see a normal number of plasma cells, only five percent, which is the normal value, and then no evidence of disease progression or new lesions on a skeletal survey.

William Bensinger, MD

We also refer to a very good partial response (VGPR), which is a 90 percent reduction in the monoclonal protein with only a tiny amount of urinary protein, and then a PR which includes a 50 percent reduction in the M protein in the blood but a 90 percent reduction in the urine.

There is also a classification called a near CR (nCR), which is the same as the above but with a very sensitive test called immunofixation. The test is still positive for nCR patients. These are important because achieving a CR or an nCR or even a VGPR have been associated with prolonged survival compared to patients who get a lesser response.

[Slide 20 – You Need Good Combinations]

This slide just shows some of the responses that we see with the combinations. I mentioned VAD (vincristine–doxorubicin [Adriamycin]–dexamethasone) and thalidomide–dexamethasone (TD), which are infrequently used over here. These overall response rates are in the 50 to 60 percent range with only a minority of patients achieving a CR. But the newer combinations with lenalidomide–dexamethasone or bortezomib with Doxil or combinations with bortezomib–thalidomide or lenalidomide or sometimes CyBorD, which is cyclophosphamide–bortezomib–dex, and even the newer combination with carfilzomib–lenalidomide–dex produce responses, overall responses in the 80 to nearly 100 percent range and up to 40 to 50 percent of patients achieve major responses, complete responses. So, you need good combinations to get rapid control of your disease and to relieve symptoms.

[Slide 21 – Autologous Stem Cell Transplantation]

But following that, for eligible patients, autologous transplant is commonly used. It's considered important therapy for eligible patients with multiple myeloma because of these high rates of CR and VGPR, and these correlate with survival. The disease control is better and nearly all the trials have looked at it, but some trials that have looked at timing of transplant have not always shown survival benefits. What I mean by that is, you can get equivalent survival with a transplant either done initially as therapy or used later in the course of the disease as a form of second-line treatment.

Autologous transplant is safe and has a very low mortality. There's no donor limitation. It does appear to not work as well if you are in that 20 percent group of patients with high-risk features. It's still not curative for the majority of patients, although probably about 10 percent to perhaps 15 percent of patients may enjoy long-term disease control with an autologous stem cell transplant.

[Slide 22 – Indications for Hematopoietic Stem Cell Transplants in the US, 2011]

Now, these are the most recent data; as you can see, they're a few years old from the Center for International Bone Marrow Transplant Registry (CIBMTR). This is a US registry looking at transplant numbers for various diseases. As you can see, multiple myeloma, by far, exceeds all the other disease indications in terms of transplant. That's because of the value of trials that have shown benefit. Most of these are autologous transplant. A small number of allogeneic (allo) transplants are done. These may be useful for some of the high-risk patients but are still considered investigational for the majority of patients that have this.

[Slide 23 – ASCT Improves Major Responses After Traditional or Novel Induction]

This is just a smattering of trials looking at various induction combinations under the regimens and the numbers of patients. As you can see, many of these trials included large numbers of patients, anywhere between 450 and 700 patients or more. They used induction with these various therapies

William Bensinger, MD

followed by stem cell transplant. This is just to show that if you look at the major response, that is a near CR, and you look at the percent of patients who achieve this level after induction, following transplant in every case, autologous transplant improves the percentage of patients who achieve a near CR. So in all of these cases, regardless of the induction regimen, autologous transplant improves the response rate and ultimately should improve the outcomes for patients who are transplanted.

[Slide 24 – Updates from ASH 2014]

Now, a little bit about some of the things at ASH. Carfilzomib is one of the newly approved drugs for multiple myeloma. It has been on the market about two years. Combinations were reported at ASH using carfilzomib–cyclophosphamide and dexamethasone for induction therapy.

This first abstract [Slide 24, ASH 2014 Abstract #4739] showed a combination using the standard two times a week carfilzomib with weekly cyclophosphamide and weekly dexamethasone for up to six cycles. Twenty-eight patients who are considered transplant-eligible, median age of 65, were treated. A dose as high as 56 milligrams per meter squared (mg/m^2) was given with a high response rate, 91 percent, two CRs but 10 VGPRs, so major responses, and only a single patient discontinued for progressive disease.

In another study [Slide 24, ASH 2014 Abstract #175], they looked at weekly carfilzomib–cyclophosphamide–dex. These patients only received it once a week instead of twice a week with the drug looking at a more convenient schedule. These were 30 patients. They were older patients who were not considered transplant eligible, median age of 74, and they got up to nine cycles of therapy and maintenance. Their response rate was similar, 86 percent, with 25 percent CR, and the dose given and tolerated was up to 70 milligrams per meter squared. Thirteen percent of patients had to discontinue this either due to toxicity or progression of disease.

A large study looked at a combination of lenalidomide and dexamethasone with or without the addition of carfilzomib in the relapsed setting. So, this was an international trial with nearly 800 patients who had a median of two prior treatments and a median age of 64 years. This compared CRD, the combination of carfilzomib–lenalidomide–dexamethasone, with just lenalidomide–dexamethasone alone. As you can see [Slide 24, ASH 2014 Abstract #79], the overall response rate was substantially better: 87 percent versus 67 percent. The CR was substantially better, 32 percent versus nine percent, and duration of response that was eight months longer and a duration of treatment that was eight months longer. The progression-free survival (PFS) was 26 months versus 18 months or eight months longer with the three-drug combination. So, this is perhaps a new standard for a relatively early relapse after initial treatment for MM.

[Slide 25 – Novel Agents Under Development]

There are a number of new drugs that are under development. We have several oral proteasome inhibitors, including marizomib (NPI-0052), oprozomib (ONX 0912), and ixazomib (MLN9708). These are drugs, oral forms of the bortezomib and carfilzomib that look very promising.

The most exciting area of work that I'll talk about in a minute at ASH was the monoclonal antibodies (mAbs). Two in particular that identify a protein on the majority of myeloma cells known as CD38 are daratumumab and another drug that only has a number, SAR650984. Both of these are highly active in multiple myeloma and really may be a game changer in terms of treatment. We've never had a

William Bensinger, MD

monoclonal antibody that was available for the treatment of myeloma that was approved yet. The first-in-class will be elotuzumab, which may be the first to reach approval; this trial has finished accrual but the analysis is still ongoing. But these two new drugs have substantial single-agent activity and will likely work even better in combination that I'll show you in a minute.

There are also efforts to combine antibodies with immunotoxins adding a small molecule that carries a poison pill, if you will, into the cell to destroy the myeloma cell. There are also several combinations of small-molecule protease inhibitor mix (PIM) inhibitors or phosphoinositide (PI)3-kinase inhibitors and then histone deacetylase (HDAC) inhibitors, which have been in a number of trials but have yet to really show significant benefits. A recently reported combination with panobinostat added about four months to the progression-free survival when it was combined with bortezomib and dex.

[Slide 26 – Updates from ASH 2014]

Now at ASH, as I mentioned, the CD38 antibodies looked very promising. One study [Slide 26, ASH 2014 Abstract #83] combined the SAR650984 in combination with lenalidomide–dex in a relapsed or refractory myeloma population. Let me point out this is a very heavily pretreated population—31 patients, a median of seven prior therapies, and 84 percent were resistant to either thalidomide–lenalidomide or pomalidomide. So, the combination of this antibody with len–dex, the overall response rate was 58 percent with a nine-month duration of response. Pretty remarkable for this heavily pretreated group.

Daratumumab, the other CD38 antibody, has been also combined with lenalidomide and dexamethasone but in a much less heavily pretreated group. Only three prior therapies and this specifically excluded lenalidomide-resistant or -intolerant patients. So, in contrast to this trial, this trial [Slide 26, ASH 2014 Abstract #84] eliminated these patients from entering. Their overall response rate was higher, as you might expect, in a more sensitive, less heavily treated population. But, again, the combinations of these antibodies with the IMiDs and dex look very promising. I think you're going to see a lot more of this in years to come.

[Slide 27 – Individualizing Care]

Now, in terms of treatment, it's important to individualize care. I've mentioned age. Of course, older patients in general are not considered for transplant. Melphalan is more commonly used, especially in Europe. If you have high-risk cytogenetics, you're more likely to receive combinations of drugs, including the proteasome inhibitors. If you have abnormal kidney function, certain drugs have to be dose adjusted before they can be used, such as lenalidomide; so, you have to take that into consideration. Convenience is an issue. If you have to come into the clinic twice a week and you live an hour away, that may be very difficult for you, so maybe oral drugs may be a better option. Your ability to tolerate the treatment based on your blood counts and your bone marrow reserve may be important. Your ability to tolerate steroids may be important. If you're a diabetic and prone to high blood sugars, corticosteroids can drastically elevate blood sugars and may limit your ability to tolerate the drug. It's important to consider prior therapy because if you've just come off a drug that was no longer working, it may not make sense to add another drug to that or continue with that same drug. It may be time for a drug change. Ultimately, it's important to consider what your preference is for treatment. How can you receive treatment to control your symptoms and yet tolerate the treatment and minimize the disruption to your life?

[Slide 28 – Role of Clinical Trials]

Clinical trials are extraordinarily important and they're critical to the successes that we've made in the treatment of myeloma. All of the new drugs, all of them—thalidomide, lenalidomide, pomalidomide, bortezomib, carfilzomib, pegylated doxorubicin, or Doxil—all of these drugs were approved as the result of patient participation in clinical trials. It's critical for the further development of these drugs for the drugs that are not yet approved. Daratumumab, the SAR650984, elotuzumab, the oral proteasome inhibitors, and any of the other new drugs, they're only going to succeed by patient participation. Patients can often benefit themselves by participating in these trials because they're able to gain access to these drugs at an earlier point when they wouldn't widely be available commercially.

[Slide 29 – Multiple Issues Affect Quality of Life]

If you have MM, there are multiple things that affect your quality of life.

There are disease-related problems: anemia which can result in fatigue or even shortness of breath; bone-related problems: fractures, bone pain, high calcium levels; kidney problems, kidney failure, even sometimes patients require dialysis; immunosuppression which can result in frequent infections; or nervous system problems, neuropathy, peripheral neuropathy, or even paralysis from cord compression can result.

But there are also treatment-related problems. Neuropathy can develop in several of the drugs that we use, most commonly bortezomib and thalidomide; blood clots can develop if you use the IMiDs; kidney function can be affected by the use of bisphosphonates; and osteonecrosis of the jaw, or ONJ as it's called, can develop with bisphosphonates, the bone agents, or even the antibody that's used for this purpose, denosumab [Xgeva®].

[Slide 30 – Managing Disease-Related Symptoms]

Now, how do you manage these symptoms? Well, in terms of anemia, transfusions may be beneficial, sometimes growth factors such as erythropoietins that can stimulate blood cell production, but often just treatment of the disease can improve anemia. As I mentioned earlier, as the marrow fills up with these abnormal plasma cells, anemia develops because there's less space for red cell development. With effective treatment, you clear out the bone marrow space and the red cells will recover on their own and anemia can improve.

Bone disease can be treated with bisphosphonates, or if a surgical intervention is needed, vertebroplasty or other surgeries. Sometimes radiotherapy is useful for lesions that may be leading to affecting the nervous system or causing severe pain.

Kidney function can be managed with hydration, controlling the calcium level, and, again, treating the disease; if you have a patient who has kidney dysfunction on the basis of high levels of light chain production, if you lower those light chain levels, the kidney function will improve.

Patients who are immunosuppressed may require prophylactic antibiotics to prevent infection. Or in patients who have frequent infections, the prophylactic use of immunoglobulin may be helpful.

For the nervous system, you avoid drugs that worsen the neuropathy or use these drugs in altered doses or radiation therapy for spinal cord compression symptoms.

[Slide 31 – Managing Treatment-Related Side Effects]

As for managing the treatment-related effects, I mentioned with neuropathy you can adjust the dose, the frequency, or the route of bortezomib. You may benefit by switching to carfilzomib which doesn't cause much in the way of peripheral neuropathy. But for patients who have existing neuropathy, gabapentin (Neurontin®) or vitamins or certain amino acids are sometimes helpful for control of the symptoms.

For blood clots, it's important to use prophylactic measures such as aspirin, warfarin, or the low-molecular-weight heparins can be used. For infections, I mentioned the prophylactic antibiotics but antivirals are important. For example, in patients treated with the proteasome inhibitors, there is a higher incidence of shingles reactivation, so it's important to take drugs like acyclovir (Zovirax®) or valacyclovir (Valtrex®) to prevent the recurrence of shingles.

Kidney function can be improved by hydration and close monitoring while on bisphosphonates. ONJ, or osteonecrosis of the jaw, can be managed with good oral hygiene and avoiding dental extractions or tooth surgery while you're on bisphosphonates. Hyperglycemia can be managed by reducing or avoiding steroids. In some patients who absolutely require steroids, it may be necessary to use insulin.

[Slide 32 – Communicating With Your Health Care Team]

In terms of your treatment, it's very important to involve all the members of your team. This includes your medical oncologist but also any radiation therapist that may be involved in your care, or if you require some surgery, your orthopedist.

We are frequently using advanced practice providers, nurse practitioners, or physicians' assistants. These individuals have extensive and specific experience in managing patients with MM and managing symptoms related to the disease. But the nurses, the pharmacist, the dietitian, the physical therapist, and the social worker are all part of your team and can help you deal with specifics and issues related to your care.

Often, patients will only see a nurse when they're getting treatment and see a physician or physician's assistant once a month or even less. So, if you're having symptoms such as the onset of peripheral neuropathy, it's very important to mention these symptoms to your nurses. It doesn't mean that your therapy will be stopped, but your therapy can be modified and this will improve your symptoms and allow you to continue with your care. It really is important to involve all these people during your treatment.

[Slide 33 – Resources for Help and Information]

Finally, there are a number of resources that you can turn to for help. This program, sponsored by The Leukemia & Lymphoma Society, is very important, but there are some societies dealing specifically with myeloma. There's a newsletter, the *Myeloma Beacon*, two international research foundations, the International Myeloma Foundation (IMF) and the Multiple Myeloma Research Foundation (MMRF), and there is another recent foundation called Multiple Myeloma Opportunities for Research & Education (MMORE), which all deal with educational aspects and are all willing to help patients with multiple myeloma.

With that, I'm going to stop and entertain any questions from the audience.

QUESTION & ANSWER SESSION

[Slide 34 – Question & Answer Session]

Lizette Figueroa-Rivera, MA

Thank you so much, Dr. Bensinger, for your very clear and informative presentation. It is time for the question-and-answer portion of our program.

We'll take the first question from our Web audience. Jennifer asks, "Are there any advances or progress in treating high-risk myeloma with a 17p deletion?"

William Bensinger, MD

There is some modest progress for high-risk myeloma. There was a large trial known as the HOVON (Hemato-Oncology Foundation for Adults in the Netherlands) trial, which was a Dutch-German collaboration, in which patients with myeloma newly diagnosed received a combination of bortezomib (Velcade®)–Adriamycin® (doxorubicin) and dexamethasone (VAD) induction or received induction with the old VAD-type regimen. These patients went on to have a single or tandem autologous transplant, and the patients who received bortezomib induction had bortezomib as a maintenance therapy after that for one year. The patients who received VAD induction only received thalidomide (Thalomid®) and interferon treatment as their maintenance therapy. The group that got bortezomib had a much better outcome, but when they looked among the patients with the 17p deletion, they also had an improved outcome if they received the bortezomib induction and maintenance regimen compared to the patients who received a VAD-based regimen. They did better than the patients who received VAD, but they still did not do quite as well as the patients who did not have the 17p deletion. So, it looked as though bortezomib could partially overcome the negative effect of the 17p deletion.

Lizette Figueroa-Rivera, MA

Thank you. We'll take the next question from the telephone audience please, Operator.

Operator

This question comes from Marguerite, calling from California. Please state your question.

Marguerite

Doctor, thank you very much for this wonderful conference and knowledge. I'm a survivor since 2005. I had Revlimid® (lenalidomide) and dex treatment in 2005. My question would be, what new drug may I take, because I notice the terrible side effects now: the numbness of my legs; my liver's damaged; I get very, very tired. The toxicity is going through my system. My platelets are low in white. I'm going to talk to my oncologist, of course, but I think I need to change my treatment or just stay on dex and maybe increase it. I only take three a week, but maybe I can increase that to help. What is your suggestion? I'm going to be 77.

William Bensinger, MD

Whether it's time to change treatment and what to do about it will depend on a number of factors. It sounds as though you are having a lot of different side effects that may or may not be related to the combination of Revlimid and dexamethasone. But, importantly, it's worth considering what your disease status is. If your disease is in a remission, that is if you don't have much measurable disease, it may even be possible to go off therapy entirely for a while to see if your symptoms improve.

William Bensinger, MD

On the other hand, if this combination is just barely controlling your disease, then it would be worth considering switching to something else. As I mentioned earlier, pomalidomide (Pomalyst®) is a newly approved drug for myeloma and may be a good alternative. But the specifics of whether it's right for you depend on a lot of factors.

Lizette Figueroa-Rivera, MA

Thank you for that question, Marguerite. The next question, doctor, is from our Web audience. We actually have Debbie, Dorothy, and Maureen asking about smoldering myeloma. Debbie asks, "Has the practice changed from not treating smoldering myeloma to treating patients early with smoldering myeloma? Does this increase the time the patient remains disease-free?"

William Bensinger, MD

This is a very good question. In general, I would say that the approach to smoldering myeloma is changing. We recognize that there are groups of patients with smoldering myeloma who have a very high risk of progressing to symptomatic disease within one to two years. Among those characteristics are patients who have a high level of plasma cell involvement in their bone marrow, patients who have discrete lesions identified by a PET (positron emission tomography) scan or by CT (computed tomography) scan, and patients who have high elevated levels of free light chains. There is some evidence that these high-risk patients do benefit from early therapy, but only one single study, and a relatively small study, shows this benefit.

Having said that, as I mentioned earlier, the International Myeloma Foundation (IMF) is changing the criteria for what they consider to be symptomatic myeloma, and they're including some of these high-risk characteristics such as the advanced degree of bone marrow involvement and the use of elevated free light chains. Those patients under their proposal are now classified as no longer having asymptomatic myeloma but have active disease, and they're recommending treatment for those patients. So this is evolving, but at the present time we only have limited evidence that early treatment will improve the outcomes for these patients.

Lizette Figueroa-Rivera, MA

Thank you, doctor, and we'll take the next question from the telephone audience please.

Operator

Thank you. This question comes from MaryAnn, calling from Oregon. Please state your question.

MaryAnn

Yes, I've had a stem cell transplant, and I had it in 2013. I'm just on acyclovir, and I do have pains in my back and neuropathy in my feet. I'm not sure if that makes any difference, if I should be on something else. My levels have been good, but I just need to know with the stem cell transplant if I'm going to have to need another one.

William Bensinger, MD

Well it's difficult, from this information, for me to tell that. I think what you need, really, and this applies to any patient who has had a stem cell transplant, you probably need a complete reevaluation of your myeloma, perhaps another bone marrow blood and urine testing, as well as some scans to see if your back pain is related to active myeloma or if this could be old compression fractures from previous damage to your back.

William Bensinger, MD

It's important to determine if your symptoms currently are related to active disease or just residual from prior treatment or prior disease activity. Then, a decision can be made about whether it is appropriate to start therapy.

Lizette Figueroa-Rivera, MA

Thank you so much for that question, MaryAnn. We'll take the next question from the Web audience. Marsha asks, "If the conditions are right, what is your opinion about using previously harvested and stored cells for a second transplant?"

William Bensinger, MD

Second stem cell transplants can be very useful. In general, studies that have looked at this have found that patients who achieve at least two years of disease control with their initial transplant will benefit from a second transplant performed at a time of disease recurrence. On the other hand, these studies have shown that if your length of remission is a year or less, it's generally not of value to perform a second transplant. That's generally the algorithm that we have used here in Seattle.

Lizette Figueroa-Rivera, MA

We'll take the next question from the phone audience.

Operator

The next question comes from Pat calling from Pennsylvania. Please state your question.

Pat

Thank you, doctor, for your presentation. I was diagnosed third stage in 2005 and had a transplant in 2006. I am now in remission, and what I want to know is, what is the likelihood of cancer developing in other areas after a patient has multiple myeloma? I am experiencing lumps in my breast, but my oncologist says that these are not cancerous.

William Bensinger, MD

Well, there is a slightly elevated risk of second cancers in patients with multiple myeloma who have had a stem cell transplant. The risk of blood cancers is generally about 2.5 percent, but another two to three percent of patients will develop solid tumors such as breast cancer or other types of cancers. The most common cancers that develop are skin cancers; but if you're worried about this, I think close follow-up from your physician is a good idea. I assume you've already had mammograms, but if not, this is something to consider. Then, if any of these areas in your breasts look suspicious, a biopsy or an ultrasound may be indicated to further define this. But there is, overall, a small risk of second cancers in patients with myeloma.

Lizette Figueroa-Rivera, MA

Thank you, Pat, for your question. Doctor, we'll take the next question from the Web audience. Both Michelle and Herman are inquiring about maintenance therapy, and both inquire as to the importance of maintenance therapy for myeloma, as well as how long maintenance therapy should last.

William Bensinger, MD

Maintenance therapy is increasingly used because, as I mentioned, this disease, while treatable, does not appear to be curable for most patients. Maintenance is used as a way of extending the length of remission and disease control. The best studies have been done to date with the use of

William Bensinger, MD

lenalidomide. Two large trials have been reported, one in the United States and one by the French. These trials both showed that the use of lenalidomide, or Revlimid, after stem cell transplant roughly doubled the length of disease control from about two years to almost four years, and both studies showed essentially the same effect.

Only the US study, though, showed a difference in overall survival. The French study has not shown any differences in survival to date, so there is some controversy about that because some would argue that if it doesn't improve your survival to get maintenance, you may do just as well to get lenalidomide use at the time your disease recurs and have the same benefit.

Those trials do show benefit, though, in length of disease control. There is a cost for this. The drug is quite expensive. It does cause low blood counts with a slight increased risk of infection and it does slightly increase the risk of second blood cancers from about 2.5 percent to about 4.5 percent. Bortezomib has also been used as a form of maintenance, and as I mentioned, in the HOVON trial, did show benefit.

Unfortunately, that trial used bortezomib for both induction and maintenance, so it was hard to separate the effect of the maintenance component. Was it the bortezomib maintenance that shows the benefit or is it the combination of bortezomib upfront followed by maintenance? So, it's a little harder to sort that out. There are some trials in progress using bortezomib, however, that should shed some light on that.

Lizette Figueroa-Rivera, MA

Thank you, Dr. Bensinger, and I know that you did mention the cost of medications. I just wanted to let everybody on the line know that we do have an Information Resource Center that has Information Specialists who can help you with finding financial assistance programs, including our Copay Assistance Program for myeloma patients. You can contact an Information Specialist at 1-800-955-4572.

Thank you. We'll take the next question from the phone audience.

Operator

This question comes from Deborah calling from New Mexico. Please go ahead.

Deborah

Yes, I have had Revlimid (lenalidomide) treatment with and without dexamethasone, and I'm currently on thalidomide (Thalomid®) with dexamethasone treatments. I wonder if you could comment whether the thalidomide is more effective than Revlimid or what. Thank you.

William Bensinger, MD

Well, thalidomide was the first of the immunomodulatory drugs to be developed, and so it's the oldest of the three drugs. It can be very effective in the control of myeloma and is definitely a useful drug for some patients. It is associated with more side effects that patients find uncomfortable. The main one is peripheral neuropathy, and patients frequently develop neuropathy and sleepiness and fatigue while they're on thalidomide, such that they're unable to continue with the drug.

William Bensinger, MD

However, for patients who do not have major problems with those symptoms, this can be a very effective drug. Is it better than lenalidomide? It's hard to say it's better. I think in selected patients it can be just as good.

One other advantage of thalidomide is that it doesn't cause a lowering of the blood counts the way lenalidomide, or Revlimid, does. So, it may be very useful for patients that have poor marrow reserve and can't tolerate Revlimid.

Lizette Figueroa-Rivera, MA

The next question from the Web comes from both Marianna and Mallory, and they're asking if there are any updates on the Mayo Clinic trial using genetically enhanced measles vaccine to treat myeloma.

William Bensinger, MD

I get asked that question a lot. There were only a couple of patients on that trial, and one of them had a rather dramatic response. I know the trial is ongoing, but there were no updates at the ASH 2014 meeting, and I'm unaware of any more recent reports of how patients have done on that trial.

Lizette Figueroa-Rivera, MA

We'll take the next question from the telephone audience, please.

Operator

This question comes from Brenda calling from Florida. Please state your question.

Brenda (Caretaker John)

Yes, this is Brenda's caretaker, John. The question I have is, as a doctor went through many, many, many types of drugs and many, many, many treatment variations, etc., what would be his combination recommendation for the patient or caregiver to try to understand what other options could make most sense for any given patient, whether it is my patient or whatever? Just trying to understand the available options.

William Bensinger, MD

It's very difficult to give you specifics about what drug combination is best. There are relatively few studies that have compared one combination head to head with another combination. So, all of these drug combinations that I showed have shown utility, but there isn't any one study that shows that one is better than the other.

With regard to what's best for a particular patient, that's going to depend on a number of factors that I mentioned earlier, or I mentioned at the end of my talk, looking at a lot of patient-related factors—patients who have perhaps diabetes, or patients that have preexisting conditions such as neuropathy. So, the best combination is going to depend on individual factors for the patient. The best thing to do is to sit down with your doctor and review those things on an individual basis. I just can't give you this kind of advice over the phone.

Lizette Figueroa-Rivera, MA

Also, The Leukemia & Lymphoma's Information Specialists at the Information Resource Center can also help you formulate questions so that you can go back to the physician and have questions that

Lizette Figueroa-Rivera, MA

can help you know more about the diagnosis, as well as the treatment options. If you do have access to the Internet, we also have questions listed on our website under www.LLS.org/whattoask that is a guide of different questions that can open up different conversations with your doctor. Thank you so much for that question. It's very important.

We'll take the next question from the Web. Mary asks, "Are there clinical trials being conducted for enhancing T cells to fight multiple myeloma?"

William Bensinger, MD

There are a limited number of trials that are looking at engineered T cells. This is something of which I think there's great promise. There have been dramatic results reported in acute lymphoblastic leukemia (ALL), but there are relatively few studies that are looking at engineered T cells at the current time. The two places that I know are doing limited trials are the University of Pennsylvania and the University of Maryland, and they do have two trials ongoing for specific patient populations. This is something that is definitely going to expand in the coming months, and you're going to see many more trials open up in this area.

Lizette Figueroa-Rivera, MA

Thank you, and we'll take the next question from the telephone audience.

Operator

This question comes from Fred, calling from Oregon. Please state your question.

Fred

Good afternoon. I hear a lot about maintenance improvement. Do you ever figure about 100 percent cure for this problem?

William Bensinger, MD

Unfortunately, we are nowhere close to 100 percent cure for multiple myeloma. There is, perhaps, 10 or 15 percent of patients who enjoy long-term disease control after autologous transplant. Some or many of these 10 to 15 percent may be cured, but the majority of patients are going to relapse.

Maintenance therapy, in general, is not a cure for this disease. It's a way to control the disease and extend the length of remission so that patients have more quality time to do what they want to do with their life.

Lizette Figueroa-Rivera, MA

The next question comes from the Web. Penny asks, "If there are any complementary therapies that you support for adjunctive care for patients."

William Bensinger, MD

That's a pretty vague question, so I am not sure how to answer that. I think it is helpful for certain types of vitamins for patients who have neuropathies. As far as complementary things, I mentioned bisphosphonates for bone control or immunoglobulins for patients with infection. But I am not sure what exactly is meant by the term complementary therapies.

Lizette Figueroa-Rivera, MA

Sure. We'll take the next question from the telephone audience please.

Operator

This question comes from Jackie, calling from Washington. Please state your question.

Jackie

Hello. A year ago there was a great guy from MD Anderson giving a similar summary of ASH. In one of the question-and-answer sessions he said that there is a developed protocol, not a trial, that is administered at MD Anderson, and I guess maybe other places, for bone control. It gets away from the problems of bisphosphonates. What I think he called it was a conjugated parathyroid injection. Can you speak to that?

William Bensinger, MD

Unfortunately, I can't. I'm not aware of that study, and I really do not know anything about it. I am sorry.

Lizette Figueroa-Rivera, MA

Thank you, Jackie. You can also call our Information Resource Center, and we can try to find that information for you.

We could take the next question from the Web audience. Richard asks, "What is the effectiveness of oral medication versus injection or infusion, as well as the outlook for immunotherapy in myeloma?"

William Bensinger, MD

Well, there are combinations of oral agents, as well as intravenous (IV) or subcutaneous (sub-Q) agents. Generally speaking, among the approved drugs, the proteasome inhibitors require injections. The immunomodulatory drugs are oral agents. They are both effective. There is not any indication that one may be more effective than the other. With regard to immunotherapies, I mentioned briefly allogeneic transplants that can be helpful for some high-risk patients but are still considered investigational. The other immunotherapy that is rapidly moving forward, I mentioned, are the monoclonal antibodies. This is an immune therapy because it uses antibodies to target the myeloma cells. These are going to be very promising treatments that are likely to lead to approval within the next few years.

We also talked in an earlier question about the development of T-cell therapies, the chimeric antigen receptor (CAR) T cells. These are just in their infancy. They've shown remarkable results in acute lymphoblastic leukemia, but there are only very early and few studies in multiple myeloma. But there will be more forthcoming.

Lizette Figueroa-Rivera, MA

We'll take the next question from the telephone audience please.

Operator

This question comes from Janet, calling from California. Please state your question.

Janet

Yes. I'm currently in the clinical trial with high-risk patients with elotuzumab and Revlimid–Velcade–dexamethasone (RVD) and happy to say I did get a complete remission. My question is, I'm currently on maintenance with Zometa® (zoledronic acid), and we've had some questions among patients whether Zometa is better than Aredia® (pamidronate) or vice versa as far as the risk for osteonecrosis of the jaw (ONJ).

William Bensinger, MD

The risk with both Zometa and Aredia are quite similar for ONJ. It's about three to 3.5 percent risk of ONJ, and there doesn't seem to be a major difference between the two drugs.

Janet

Okay. Thank you.

Lizette Figueroa-Rivera, MA

We'll take the next question from the Web. Loretta asks, "Should a clinical trial patient get the flu shot?"

William Bensinger, MD

I actually recommend that all of my patients get a flu shot. While not everyone will respond adequately to the flu shot, it is safe to get the shot. To the extent you get any kind of antibody response, it's going to give you some level of protection.

Now, one thing you need to be careful is you don't want to get the live flu vaccine. That is generally the vaccine called FluMist (quadrivalent), which is an intranasal spray that's given. That is a live vaccine, and you shouldn't get that. But the actual injection is a killed vaccine. It's not going to cause any illness by itself. To the extent it gives some limited immunity, it'll help you.

Lizette Figueroa-Rivera, MA

Thank you so much for that clarification. I know that we do get that question in our Information Resource Center. Doctor, I know that you asked for clarification for the complementary therapies question. Penny was able to write in, and she says, "Do you support the complementary therapies such as oncology massage, Reiki, Healing Touch, and reflexology for help with symptoms and side effects?"

William Bensinger, MD

I think all of those modalities are helpful because they can often help the patient relax or alleviate some of the skeletal or muscle-related problems associated with the disease or treatment. So, I support all of those regimens for patients with myeloma.

Lizette Figueroa-Rivera, MA

Great. Thank you. We'll take the next question from the phone operator.

Operator

This question comes from Danielle, calling from Montana. Please state your question.

Danielle

Yes, I was diagnosed in 2000 and had a tandem stem cell transplant. I have been very fortunate to be very healthy since. But in December I'm showing some low signs of a recurrence that showed up in the blood, skeletal scan, CT scan, and bone marrow, but there was not a significant indication in the PET scan. So, they are saying that maybe I should just do nothing at this time. I'm a little bit uncomfortable with that. But seeing the possible side effects of the drugs that may be given, would it be better to kind of wait or to try and attack it now?

William Bensinger, MD

Well, whether to start treatment will depend on a lot of factors. I'm assuming that, from what you've told me, you've got some level of protein in your blood that's shown up. I don't know whether a bone marrow was done showing a recurrence. If you have some areas in your bones that show bone destruction, however, and that's new, I think that would be an indication for treatment rather than just watching it. But if you don't have any bone destruction, if your calcium level is normal, if you only have a slight elevation in your protein level, it may be entirely appropriate to defer treatment and simply watch things at this time. You're lucky in that your treatment and transplant was really before many of the new drugs that are now available were in use, and so you're going to do very well with any treatment that is used at this time.

Lizette Figueroa-Rivera, MA

The next question from the Web is from MaryBeth, and MaryBeth asks, "What is the importance of medication adherence when on maintenance therapy post-transplant? Do the studies consider the degree of medication adherence?"

William Bensinger, MD

The studies that have looked at this generally have determined that patients should be taking at least 80 percent of their prescribed medication to benefit from this, and that as the compliance falls below 80 percent, there's less of a benefit. So, in general, it's a good idea to stay on the drug that you're prescribed as best you can.

Lizette Figueroa-Rivera, MA

We'll take the next question from the phone audience.

Operator

Thank you, this question comes from Joanne, calling from New York. Please state your question.

Joanne

Hello, doctor, and thank you. I recently had a cell transplant in September, and we are now just going to start Revlimid at a low dose. My concern or question is we started Revlimid when I was diagnosed in January. We did it January and February, and the numbers went up instead of down; so we switched to IV chemotherapy. So now I'm worried about starting Revlimid again, and the doctor seems to think a low dose will be fine.

William Bensinger, MD

Yes, I understand your concern. I think that it is not really known after a stem cell transplant how beneficial low-dose Revlimid will be. I'm certain you'll tolerate the drug well, but I think, depending on what your reevaluation numbers show, you're just going to have to give it a try and see what happens. If you've got a low level of protein in your blood and the Revlimid doesn't change that at all,

William Bensinger, MD

then it's giving you disease control, or if it goes down, that's even better. On the other hand, if you're on the drug and your protein level starts to rise, I think it's clear that it's not going to benefit you. But I think you're just going to have to try it and see. I don't think you can predict how you're going to do on this drug at this point in time, based on the initial treatment.

Lizette Figueroa-Rivera, MA

The next question from the Web comes from Michelle. She asks, "Is there a certain therapy recommendation for preventing blood clots for patients with multiple myeloma, and gives two examples of possibly Xarelto® (rivaroxaban) or Coumadin® (warfarin)."

William Bensinger, MD

The drugs that have been most commonly used are low-dose aspirin, warfarin therapy, or low-molecular-weight heparin. The newer antithrombotic agents, such as Xarelto, have not been systematically studied. There is probably no reason why these drugs should not be as effective as some of the other agents, but there just haven't been any trials of them in patients with myeloma.

Lizette Figueroa-Rivera, MA

The next question we'll take from the phone audience please.

Operator

This question comes from Dorothy, calling from Ohio. Please state your question.

Dorothy

Yes, it was partially answered earlier. I've been smoldering since 2010, and I was just wondering, I mean I'm just waiting. But is there anything that can be done or I can do that's going to help me? I just feel lost sitting, waiting. It's like a time bomb.

William Bensinger, MD

Well, again, it's going to depend on the specifics of your disease. If a bone marrow doesn't show extensive involvement with myeloma, if your protein levels are low, if scans don't show any bone disease or any hot spots that light up, your best bet may be just to wait because half of the patients with smoldering myeloma will never develop symptomatic disease. If you're in that group of patients that doesn't develop symptomatic disease, you can avoid ever needing treatment.

Lizette Figueroa-Rivera, MA

The next question is from the Web, and Paul asks, "For a patient on dialysis due to kidney failure, resulting from myeloma and who also has amyloidosis, is a kidney transplant recommended?"

William Bensinger, MD

That is, of course, a difficult question. I think that if the patient's myeloma can be controlled, and you can get what I would call a remission or near remission of the myeloma, one would expect the amyloidosis to also be controlled. So, it may be possible at that point to do a kidney transplant and restore kidney function and not have a great risk of recurrence of amyloid to destroy the kidney, as long as the myeloma is controlled. So, I think in selected cases, it would be possible to do a kidney transplant.

Lizette Figueroa-Rivera, MA

The next question is from the telephone audience.

Operator

Thank you, this question comes from Linda calling from Florida. Please state your question.

Linda

Hey there, I'm not sure I understand the chart, but on the hallmark of multiple myeloma [Slide 9], does this say that you can identify the myeloma based on the albumin and the M-protein levels in the urine?

William Bensinger, MD

Patients with myeloma frequently will have monoclonal protein in their urine that is detectable. It's one of the components of making a diagnosis of the disease, but it's not the only thing you look for. You need to look at the bone marrow, and you need to look at other parameters such as bone lesions on X-rays.

Lizette Figueroa-Rivera, MA

The next question is from the Web. It's from Joseph. It says, "Even though the exact cause of the disease is unknown, what has been identified, if anything, that increases risk of developing the disease, such as race, ethnicity, lifestyle, genetics, or environmental exposure?"

William Bensinger, MD

The disease is twice as common in black men as opposed to white men. It's more common in men than women: 60/40 percent. There are certain occupations that have an increased risk. For example, firemen have twice the risk of developing myeloma as the general population. Certain activities, people who've worked in the nuclear industry where they may have radiation exposure are at increased risk of developing myeloma. But other than those general factors, there is no specific item that says a patient's going to get myeloma.

Lizette Figueroa-Rivera, MA

Our last question from the Web is from Peter, and he asks, "Have you seen any patients who remain in remission indefinitely?" Peter has been in remission for 10 years now. Or he wants to know does the disease always return at some point?

William Bensinger, MD

I have a number of patients who have remained in remission for prolonged periods of time, quite a number of patients who are 10 years or more after autologous transplant. I also have patients who've undergone donor or allogeneic transplants. The longest patient I have is surviving now more than 25 years. She was transplanted when she was in her early 40s for multiple myeloma. Actually, she had a more aggressive disease, plasma cell leukemia, and she's now been in a remission for 25 years. She was transplanted from her brother.

Lizette Figueroa-Rivera, MA

That's very good to know; and I'm glad, Peter, to hear that you're doing so well.

CLOSING REMARKS

[Slide 35 – The Leukemia & Lymphoma Society (LLS) offers]

Lizette Figueroa-Rivera, MA

Thank you, doctor, and thank all of you for all of your questions. We hope this information will assist you and your family in your next steps. Just as a reminder, The Leukemia & Lymphoma Society offers online chats for patients with myeloma and chats for young adults as well as caregivers. These chats are moderated by oncology social workers and do provide forums for patients and caregivers to share experiences and support each other. For information on how to participate, please review the flyer in your packet or you can go online to www.LLS.org/chat.

If you weren't able to get your question answered today, please call The Leukemia & Lymphoma Society's Information Resource Center at 1-800-955-4572. Information Specialists are available to speak with you from 9 AM to 9 PM Eastern Time, or reach us by email at infocenter@LLS.org. We can provide information about treatment, including clinical trials or answer other questions you may have about support, including questions about financial assistance for treatment.

Please help me thank Dr. Bensinger for volunteering his time with us today. On behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us. Goodbye, and we wish you well.