Joining us today to talk a little bit about multiple myeloma. I am new for Barnwell, the myeloma doctors here at Yale and we will be talking about three different topics, each about 15 minutes long and then will have 15 minutes of discussion Q&A.

So I will be talking about understanding myeloma come my colleague, Doctor Sabrina Browning will be talking about myeloma come my colleague, Doctor Sabrina Browning will be talking about.

More specific.

About the new treatments out there for multiple myeloma and or.

Really excellent physician assistant.
Tara Anderson will be talking about Texas cities of certain drugs and then we'll have our the rest of our team join us for the question and answer and doctor Terry Parker and Doctor Natalia will parts so. With that we will start our Session.

Alright. So my goal for the next 15 minutes is to give you some insights into understanding what is multiple myeloma and some general principles of how we think about treatment for multiple myeloma.
I have no disclosures.

I'd like to start by talking about the bone marrow, which is where my llama lips, now the bone marrow, is a spongy part of the bone, and it’s in charge of making some important cells in our body.

It makes red blood cells, which carry oxygen and give us energy.

It makes platelets which prevent bleeding and it makes white blood cells which help fight infections.

Now, one of the white blood cells is called plasma cells, and these plasma cells help our
bodies fight infection by making antibodies and antibodies are proteins that bind to foreign substances, for example, like a bacterial infection, and it helps kill it and clear it from the body. Now, under normal circumstances we have a small amount of these plasma cells in the bone marrow, roughly 5% or so, and they make a variety of antibodies. So uhm, no antibody is like the other. Now, if one of these plasma cells is now becoming cancerous, it’s abnormal normal.
It’s able to replicate itself and make a clone out of itself, and in doing that it over crowds the bone marrow with too many of these abnormal plasma cells and they no longer make variety of antibodies, but rather they make a lot of 1 type of antibody. And this antibody can be one of the common antibodies that are found in our bodies, most commonly, IgG IGA is often also seen and more rarely IG M and IG D Now a part of...
that protein is called the light chain, and it’s either Kappa or Lambda. So a monoclonal protein can be identified, for example, is an IgG Lambda and IGA Kappa, and that is that that clone for that individual. So how does multiple myeloma affect the body? How does it make someone feel? I’m gonna talk about some of the common manifestations of multiple myeloma, but I want you to remember that not all of these are found in every person. OK, so the first thing is high calcium level.
and I put this. See for that here and sometimes high calcium levels. It’s not that bad. It’s not going to make anyone feel anything differently, but if it’s very high it can make someone feel unwelcome cause confusion. You can cause some Constipation or abdominal discomfort. So I put the picture there to just to signify that the next is represented by the letter R. So are standing for renal, another word for renal is kidney, so my Loma cells and the proteins that
they produce can cause damage to the kidneys.

Next, a four anemia, so that’s low red blood cell count and therefore you have less oxygen going around. People feel tired in this situation. They’re not able to do. Their daily activities. And lastly, be standing for bone pain or bone lesions, and a lesion is any kind of abnormality seen in the bones. And so in myeloma you can have either holes in the bones and this can make
the bones weaker and you can have fractures which can cause pain, but sometimes more rarely we see actually accumulation of these abnormal plasma cells forming a ball or a mass and this can be within the bone or outside of the bone and we call these plasmacytomas.

So you can see the CRA beat spells crab and this is the famous crab criteria or crab symptoms that we often talk about. Or you might have read. Now the definition of myeloma has changed over time for many many years. Basically, yes, you had to have these abnormal plasma cells,
but you had to have met one at least one of the crab criteria that we just talked about.

Things changed in 2014. The criteria changed and now we have slim crepe.

How did we get slim?

So to really understand why and how Slim came about, we have to go back and understand the precursor, the condition that comes before multiple myeloma called this the precursor states myeloma. We know that all patients who have
myeloma before they developed in myeloma had these abnormal plasma cells exist within a small quantity and it didn’t cause any trouble so you wouldn’t know you had them unless you actually go and look for them. The majority of patients with MGUS actually don’t progress to myeloma, but some. Do you move on to the next step and the next step is what we called smoldering myeloma. Now smoldering myeloma and us both don’t have any crab criteria. What we called the precursor states,
but the difference between them is smoldering element has more plasma cells as you can see here. If you go by the correct by, the technical definition should have more than 10% plasma cells in the bone marrow. But what does this mean to the person right? How does that affect you? Uhm, well, the risk of progression to myeloma is slightly higher in the smoldering group, where we have a 10% average risk of progression to myeloma. Compared to 1% in the US population.
Now looking at the Group of smolder malama little bit more closely, yes, we have a very well. Defined, you know, definition for this, but the folks in this group are quite diverse and not everyone is the same, so we have. Patients here that actually behave their disease behaves more like M Gus, and they never progress to multiple myeloma. On the other hand, we have patients who behave more like myeloma, and they actually progressed to those crab symptoms fairly soon after the diagnosis of small drink.
So many researchers in the community of myeloma have focused their attention to this group of patients trying to figure out who really should be in the myeloma group. And that’s where this slim criteria. That’s why they identified three important qualities. Come in, that’s. Here so S stands. But sorry, three important qualities that that predicts the rapid progression to multiple myeloma. 1S stands for 60% or more plasma cells within the bone marrow. Li stands for a light chain ratio.
00:08:18.116 --> 00:08:20.530 over 100 and M stands for MRI,
NOTE Confidence: 0.99112105
00:08:20.530 --> 00:08:22.260 showing more than one lesion,
NOTE Confidence: 0.99112105
00:08:22.260 --> 00:08:25.012 and this is important ’cause we used to
NOTE Confidence: 0.99112105
00:08:25.012 --> 00:08:28.140 just use X rays to look for these lesions.
NOTE Confidence: 0.99112105
00:08:28.140 --> 00:08:29.870 These holes in the bones.
NOTE Confidence: 0.99112105
00:08:29.870 --> 00:08:32.723 Now we know this is not enough and we
NOTE Confidence: 0.99112105
00:08:32.723 --> 00:08:35.878 need to use more advanced imaging for
NOTE Confidence: 0.99112105
00:08:35.878 --> 00:08:38.480 these particular patients to identify.
NOTE Confidence: 0.99112105
00:08:38.480 --> 00:08:41.130 No lesions that would move
NOTE Confidence: 0.99112105
00:08:41.130 --> 00:08:43.780 you into the myeloma category.
NOTE Confidence: 0.99112105
00:08:43.780 --> 00:08:46.705 So now that we have no diagnosis of myeloma,
NOTE Confidence: 0.99112105
00:08:46.710 --> 00:08:47.914 what do we do?
NOTE Confidence: 0.99112105
00:08:47.914 --> 00:08:49.720 When is our goal for treatment
NOTE Confidence: 0.99112105
00:08:49.791 --> 00:08:50.928 for this disease?
NOTE Confidence: 0.99112105
00:08:50.930 --> 00:08:52.981 So anyone that has myeloma has a
NOTE Confidence: 0.99112105
00:08:52.981 --> 00:08:55.159 certain amount of disease at diagnosis.
What we called the disease burden, and we measured this through one of the blood. So we look for that M protein. The bone marrow looked the amount of plasma cells in the bone marrow, and thirdly imaging, right? So we look at the amount of bone disease, but we also look for these. The solid form of myeloma. The PLASMACYTOMAS, which is important to know. And. Yeah, my goal is to kill as many plasma
00:09:21.243 --> 00:09:24.379 cells as we can to get these deep
NOTE Confidence: 0.99112105
00:09:24.379 --> 00:09:26.960 responses and to keep people in
NOTE Confidence: 0.99112105
00:09:26.960 --> 00:09:29.516 response for as long as possible.
NOTE Confidence: 0.99112105
00:09:29.520 --> 00:09:31.698 Unfortunately, this you know some point.
NOTE Confidence: 0.99112105
00:09:31.700 --> 00:09:33.520 The disease does come back.
NOTE Confidence: 0.99112105
00:09:33.520 --> 00:09:35.998 We do not think myeloma is a
curable disease at this time.
NOTE Confidence: 0.99112105
00:09:35.998 --> 00:09:37.889 So when the disease comes back,
NOTE Confidence: 0.99112105
00:09:37.890 --> 00:09:40.080 we do have other treatments and
NOTE Confidence: 0.99112105
00:09:40.080 --> 00:09:42.348 we bring the disease back down
NOTE Confidence: 0.99112105
00:09:42.348 --> 00:09:44.613 and this pattern goes on and on.
NOTE Confidence: 0.98517895
00:09:49.920 --> 00:09:52.580 I want to take just a few minutes to talk
NOTE Confidence: 0.98517895
00:09:52.650 --> 00:09:55.120 about response assessment for myeloma.
NOTE Confidence: 0.98517895
00:09:55.120 --> 00:09:56.420 How we assess the response?
NOTE Confidence: 0.98517895
00:09:56.420 --> 00:09:58.760 So as I mentioned, we look at the blood.
NOTE Confidence: 0.98517895
00:09:58.760 --> 00:10:00.060 We look at this protein.
We also look at the bone marrow to look at how many plasma cells are there. So once we start treatment we measure the lab because it’s very easy to look at blood work and we see how the protein falls. If you’ve had a 50% reduction, we call this a partial response. Uhm, if you’ve had disappearance of this protein and then when you look at the bone marrow, you don’t find any of these abnormal plasma cells when you look with your eyes. It’s then we call this a complete response, which is great. Nowadays we actually have even more
sophisticated tests that look at really microscopic level of disease looking at the DNA of the plasma cells, and if we don’t find this DNA in the bone marrow’s. We call this the deepest response. Call it minimal residual disease, negativity murdy negative negativity and you might have heard about this. This measurement and I just wanted to bring it up here so people understand what this really is and what are we looking at. And we do this in clinic and it’s also been investigating clinical trials and this is a very important point.
So how do we get these deep responses? How do we choose initial therapy initial therapy in my limits called induction. OK, so we’re lucky we have a lot of different drugs and they’re very effective at killing plasma cells, and they’ve been used in induction. I categorized them here under different colors and shapes to signify that each group represents a drug that acts a little bit different in how it kills my llama, and we like to combine the drugs in these different groups. To get the best responses as we can. And I’d say for the most part,
we really and think that combining proteasome inhibitors.

Juicy down here, along with Imids, a module to her drugs and steroids as being very effective and one of the most commonly used treatments has been Velcade REVLIMID index method zone. I think one of the more recent advances is adding daratumumab, the monoclonal antibody to this regiment, and this is also been shown to have very very great responses, and so you know on one hand the coin one side of the coin I’m telling you about. Obviously want very effective treatment,
but we also want to look at the other side and how this dream is affecting the individual right.

So these drugs have toxicities have side effects we want to make sure that the patient the individual can tolerate it. So just to give you an example from someone with kidney disease which you can have with my Loma doesn’t tolerate limit very well.

So in this case we might use cytoxan instead. You know some folks you know four or even three drug books might be. Too difficult, and in that situation we use two drugs,
so the bottom line is we want a very effective treatment that will be well tolerated, and that’s how we choose our induction treatment.

Initial therapy doesn’t stop with induction, as many of you know, we have several cycles of induction, but then we move on to different treatments.

So for some folks we do recommend high doses of chemotherapy and stem cell transplant, and that’s again to deepen the responses and prolong the time you stay in response. But this is.

Cancer treatment with significant side effects and that recovery time
so it’s not meant for everyone.

It is something to decide on individual basis.

Regardless, if you get a transplant or not, after induction you move onto maintenance and maintenance is really you know what it stands for.

It’s meant to maintain the disease and are good levels so it doesn’t come up, but meant to be well tolerated so you can continue this for years.

So often we use one drug or maybe 2 for some situations, or the disease might behave a little bit more aggressively and we continue.
this for as long as we can.

As I mentioned,

at some point the disease does come back and we do need to think about different treatments.

So how do we decide treatment at relapse?

Well, we choose a different combination.

Again, we’d like to choose combinations from different classes of drugs here,

so I added a few to my list to my treatment menu.

Here we have palm list, which is the 2nd generation of the relevant.

That meant we also have other other monoclonal antibodies, like below,
and we basically choose something you have not had before. Often we use pomalidomide as the second it you include pummel, admired in the combination. Second treatment, and then if you need a third or fourth treatment, we’re very lucky that our treatment menu is growing and is continuing to grow. So we have selling X or we have a blunt wrap. We have now male flap. And most recently, the cartee avec ma. And least, but not.

Sorry,

last but not least clinical trials,
00:15:08.990 --> 00:15:11.657 so we have an assortment of clinical 
NOTE Confidence: 0.98690903
00:15:11.657 --> 00:15:15.000 trials where it gives opportunity to try new, 
NOTE Confidence: 0.98690903
00:15:15.000 --> 00:15:16.604 very possibly very effective 
NOTE Confidence: 0.98690903
00:15:16.604 --> 00:15:17.807 treatment for myeloma. 
NOTE Confidence: 0.98690903
00:15:17.810 --> 00:15:20.421 So with that I’d like to conclude 
NOTE Confidence: 0.98690903
00:15:20.421 --> 00:15:23.312 my section of the talk and move 
NOTE Confidence: 0.98690903
00:15:23.312 --> 00:15:25.427 on to doctor Sabrina Browning. 
NOTE Confidence: 0.98690903
00:15:25.430 --> 00:15:27.872 He will talk about the details 
NOTE Confidence: 0.98690903
00:15:27.872 --> 00:15:30.345 of these newer agents that we 
NOTE Confidence: 0.98690903
00:15:30.345 --> 00:15:32.245 have for to treat myeloma. 
NOTE Confidence: 0.9597568
00:15:46.870 --> 00:15:49.102 Great, OK, so good evening everyone 
NOTE Confidence: 0.9597568
00:15:49.102 --> 00:15:51.678 and thank you again for joining us. 
NOTE Confidence: 0.9597568
00:15:51.680 --> 00:15:53.804 Come again. My name is Sabrina 
NOTE Confidence: 0.9597568
00:15:53.804 --> 00:15:55.750 Browning as Doctor Barr stated. 
NOTE Confidence: 0.9597568
00:15:55.750 --> 00:15:58.684 I am one of the doctors in our multiple 
NOTE Confidence: 0.9597568
00:15:58.684 --> 00:16:01.300 myeloma gammopathy program here at Yale.
So in this next part of our discussion, I will review recent advances in the treatment of multiple myeloma and specifically will focus on the newly approved medications for patients. Either that have relapsed so with recurrence of their disease or refractory. They’re not responding to their current treatment. And I have no disclosures to report. So fortunately, as a result of the introduction of new medications and combinations of my Loma agents, as stated by Doctor Bar over the last few decades,
there has been significant improvement both in prognosis and quality of life.

For those letter living with multiple myeloma, the major classes of medications used in myeloma, as touched upon by Doctor Bar, which may be familiar to you or listed here, and they include the immunomodulatory agents or imids proteasome inhibitors, or Pi monoclonal antibodies. Alkylating agents and the histone release inhibitor referred to as put in a panobinostat. These medications have been or are currently being studied as a part of.
00:17:11.082 --> 00:17:12.897 are targeting earlier in disease

00:17:12.897 --> 00:17:14.630 course as Doctor Barr mentioned,

00:17:14.630 --> 00:17:19.498 our treatment going myeloma is really

00:17:19.498 --> 00:17:21.590 to achieve what we refer to as deep or

00:17:21.590 --> 00:17:23.546 maximum responses to therapy that are

00:17:23.550 --> 00:17:25.692 And while we won’t review this

00:17:25.692 --> 00:17:27.120 agent in detail today,

00:17:27.120 --> 00:17:29.058 I’ve signaled Isatuximab in the chart

00:17:29.058 --> 00:17:31.178 here as a more recently approved

00:17:31.178 --> 00:17:33.452 antibody that targets a protein known

00:17:33.452 --> 00:17:36.405 as CD 38 found on immune cells and

00:17:36.405 --> 00:17:38.556 myeloma cells and isatuximab is now

00:17:38.556 --> 00:17:40.734 approved for use in combination with.

00:17:40.740 --> 00:17:42.116 Both pomalidomide and dexamethasone,
as well as with carfilzomib

and dexamethasone,

and is being studied further

in additional clinical trials.

So what has remained a challenge

and an area where improvements are essential is the treatment of individuals with myeloma who have received multiple lines of therapy,

particularly those who are no longer showing response to the P eyes or proteasome inhibitors.

The imids immunomodulatory agents or the monoclonal antibodies and this is referred to as a triple,

reclass refractory disease,
and as you can see here, in addition to isatuximab, there have been four other agents approved over the last two years for the treatment of individuals with Relapsed or refractory myeloma and this really presents great opportunities and promise for our myeloma patients. And so we’ll review each of these medications and in more detail, and we’ll have time at the end of our discussion for any questions that come up. So firstly is selinexor which is a small molecule that binds and blocks exportin one and export one is a
protein that’s found on myeloma cells
that can promote the growth of tumor
by removing proteins from the myeloma
cells that are meant to suppress the tumor.
However, if you see here in the figure on the right when selinexor, which is also referred to as selective inhibitor of nuclear export or sign, is bound to this exportin. One.
The tumor suppressors can accumulate in the nucleus of the cell and the body then can eliminate tumor cells while preserving normal cells. Selinexor is the first drug in this
NOTE Confidence: 0.9749668
00:19:14.119 --> 00:19:16.135 class of medications and is being
NOTE Confidence: 0.9749668
00:19:16.135 --> 00:19:18.326 studied in other blood cancers as well.
NOTE Confidence: 0.9749668
00:19:18.330 --> 00:19:19.455 In multiple myeloma,
NOTE Confidence: 0.9749668
00:19:19.455 --> 00:19:21.705 selinexor is approved as an oral
NOTE Confidence: 0.9749668
00:19:21.705 --> 00:19:23.897 pill at a dose of 80 milligrams,
NOTE Confidence: 0.9749668
00:19:23.900 --> 00:19:26.357 taken twice per week with the steroid
NOTE Confidence: 0.9749668
00:19:26.357 --> 00:19:28.216 dexamethasone and this is for
NOTE Confidence: 0.9749668
00:19:28.216 --> 00:19:30.061 individuals with relapsed or refractory
NOTE Confidence: 0.9749668
00:19:30.061 --> 00:19:32.161 myeloma who have received at least
NOTE Confidence: 0.9749668
00:19:32.161 --> 00:19:34.331 four prior lines of therapy and are
NOTE Confidence: 0.9749668
00:19:34.340 --> 00:19:36.335 no longer responding to at least two
NOTE Confidence: 0.9749668
00:19:36.335 --> 00:19:38.509 of the pies previously discussed.
NOTE Confidence: 0.9749668
00:19:38.510 --> 00:19:41.294 At least two images and an anti CD.
NOTE Confidence: 0.9749668
00:19:41.300 --> 00:19:42.628 38 monoclonal antibody selinexor
NOTE Confidence: 0.9749668
00:19:42.628 --> 00:19:45.052 is also approved at a dose of
NOTE Confidence: 0.9749668
00:19:45.052 --> 00:19:47.278 100 milligrams once per week with
NOTE Confidence: 0.9749668
00:19:47.278 --> 00:19:48.391 Bortezomib and dexamethasone.
NOTE Confidence: 0.9749668
00:19:48.400 --> 00:19:49.094 For patients,
NOTE Confidence: 0.9749668
00:19:49.094 --> 00:19:51.176 again with three lobster refractory myeloma.
NOTE Confidence: 0.9749668
00:19:51.180 --> 00:19:52.164 But this time,
NOTE Confidence: 0.9749668
00:19:52.164 --> 00:19:54.460 those who have received only at least
NOTE Confidence: 0.9749668
00:19:54.524 --> 00:19:56.946 one prior line of therapy and these
NOTE Confidence: 0.9749668
00:19:56.946 --> 00:19:59.497 approvals are based on the storm and
NOTE Confidence: 0.9749668
00:20:01.168 --> 00:20:04.108 Boston clinical trials, respectively,
NOTE Confidence: 0.9749668
00:20:04.110 --> 00:20:06.564 So the storm clinical trial evaluated
NOTE Confidence: 0.9749668
00:20:06.564 --> 00:20:09.566 122 patients in the US in Europe
NOTE Confidence: 0.9749668
00:20:09.566 --> 00:20:11.716 who had this triple refractory
NOTE Confidence: 0.9749668
00:20:11.716 --> 00:20:13.755 multiple myeloma that I mentioned
NOTE Confidence: 0.9749668
00:20:13.755 --> 00:20:16.317 and had received a median of seven
NOTE Confidence: 0.9749668
00:20:16.320 --> 00:20:18.276 lines of prior treatment.
These individuals were given oral selinexor, 80 milligrams and dexamethasone 20 milligrams, both twice a week, and 26% of these patients achieved what doctor bar defined as a partial response or more than 50% improvement in their monoclonal protein. And while 30 and end of this group, 39% of patients had at least a minimal response and responses overtime in those patients who did have at least a partial response or seen in the figure here at the left, the median duration of the response or the.
median time that the response lasted was about 4.4 months.

And then the second trial with Selinexor is the multicenter phase three Boston trial, which looked at 402 myeloma patients.

That were treated with one to three prior lines of therapy, and these patients were randomly assigned to get either selling X or 100 milligrams once per week combined with Bortezomib and dexamethasone. The proteasome inhibitor and dexamethasone alone and what’s shown here in the figure on the right is that the patients who received selinexor, so they sell an extra group,
had a longer time without disease.

Progression at a median of 13.9 months when compared to the group who only got Bortezomib and dexamethasone.

Where the progression at the time without progression was about 9.5 months.

The more common side effects observed with selinexor in both of these clinical trials and in practice include fatigue, gastrointestinal symptoms such as nausea, infections, and low blood counts. Thrombocytopenia or low platelet count in particular, was seen in 73% of patients and storm, although in the Boston trial,
even though patients had low platelet counts, they did not have significant bleeding events or complications with bleeding. Notably, the use of anti-nausea medication, so medications to try to prevent naushe is really important with one specific approach that has been used by our group and others is to give a medication called olanzapine or Zyprexa daily. With treatment to try and prevent the onset of significant naushe. Side effects from selinexor do appear to improve as after initial treatment or as treatment continues.
and they can be well managed with supportive care and are reversible. If this selinexor is stopped, the next agent will discuss is Bill Lanthanum Alpha Dowtin, which is a medication made up of an antibody that’s attached to a drug that’s toxic or can kill myeloma cells and as seen in the figure here on the right, it binds what’s referred to as B cell maturation antigen ORB may, which is a protein on the surface of myeloma cells that overexpressed. So there’s more than than in normal cells, and this allows for delivery.
of mpid open into the cells.

Resulting in interruption or stopping of cell division and myeloma cell death.

Blanton on methadone and also improves or enhances the body’s own immune spot response are the immunes ability to fight off myeloma cells.

Blanton AB is approved as a single agent, a single medication at a dose of 2.5 milligrams per kilogram, which is administered through intravenous infusion. Once every three weeks, and this again is approved for patients with relapsed or refractory.

Hi Wilma,
who have received at least four prior therapies including Apiai, Imid and an anti CD. This is based off effectiveness that was shown in the dream two study. So the dream two trial evaluated this first anti BCMA antibody drug conjugate in 196 patients with relapsed or refractory myeloma who had received at least three lines of treatment prior and were refractory or were no longer responding to the. Again, the three categories of medications we talked about frequently, the P,
imid or immunomodulatory agent and an anti CD 38 monoclonal antibody and these patients studies were rent studied.

End of my story.

See if either a 2.5 milligram per kilogram dose of Balanta map or 3.4 milligrams per kilogram, and this was given intravenous, the overall response rate in the dose that’s recommended, which is the 2.5 milligrams per kilogram, was 31%, and 60% of these patients who responded had at least a very good partial response,
which is an improvement in the monoclonal protein of more than 90%. Overall response rate was also 38.5% in the population of patients who had higher risk genetic features to their myeloma. And in this population is often a harder to treat, with the median time to response for Balanta map was 1.4 months, and 73% of those patients achieved a response. Having it maintained at least for six months at the time that
this clinical trial was reported.

A major category of side effects with Balanta map or the eye disorders that are listed here and observed in 77% of patients in this clinical trial and mainly the side effects in regards to eye symptoms are related to changes that happen in the cornea, which is the very front part of our I and these changes are known as keratopathy and the reported frequently within mostly the first two treatment cycles and they may require either. A reduction in dose or holding of the treatment.
Learning about these eye symptoms has prompted a requirement for patients with angle antiknock ticket. Regular eye exams for close monitoring and also it’s recommended that individuals on this medication use a lubricant. Eye drops regularly and avoid contact lenses. Other potential side effects associated with Blanton Mabor listed here. They include allergic, type or infusion related reactions, infections, and low blood cell counts. So Next up is melphan Fluphenazine mid or malfouf in and this again.
00:26:41.902 --> 00:26:44.140 is a first in class medication.

NOTE Confidence: 0.9699676

00:26:44.140 --> 00:26:46.828 It’s a peptide which is a short chain

NOTE Confidence: 0.9699676

00:26:46.828 --> 00:26:49.161 of amino acids and it’s combined

NOTE Confidence: 0.9699676

00:26:49.161 --> 00:26:51.531 with or conjugated to an alkyl

NOTE Confidence: 0.9699676

00:26:51.607 --> 00:26:54.109 later drug similar to the melphalan

NOTE Confidence: 0.9699676

00:26:54.109 --> 00:26:56.179 that we had discussed previously.

NOTE Confidence: 0.9699676

00:26:56.179 --> 00:27:00.912 And what happens is this medication

NOTE Confidence: 0.9699676

00:27:00.912 --> 00:27:01.986 can rapidly enter and be released

NOTE Confidence: 0.9699676

00:27:01.990 --> 00:27:03.151 into myeloma cells,

NOTE Confidence: 0.9699676

00:27:01.990 --> 00:27:03.151 causing irreversible damage

NOTE Confidence: 0.9699676

00:27:03.151 --> 00:27:05.473 to the DNA of the tumor.

NOTE Confidence: 0.9699676

00:27:05.480 --> 00:27:07.064 That’s important for two.

NOTE Confidence: 0.9699676

00:27:07.064 --> 00:27:09.044 Or growth and this therefore

NOTE Confidence: 0.9699676

00:27:09.044 --> 00:27:10.430 leads to cell death.

NOTE Confidence: 0.9699676

00:27:10.430 --> 00:27:12.025 Melphalan Fofana Mid is approved

NOTE Confidence: 0.9699676

00:27:12.025 --> 00:27:14.420 at a dose of 40 milligrams.
It is given by intravenous infusion, but once every four weeks and it’s combined with the steroid dexamethasone, which is administered weekly for patients. And again this approval is for patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and are no longer responding to a PPI image and an anti CD. Antibody and this is based off the horizon study melphalan fluphenazine. I’d is a bit unique in that it does require a central catheter for infusion,
such as a port or a pick line.

So the horizon study was a multicenter trial of a total of 157 patients with relapsed or refractory myeloma. Though the approval was really based on a smaller group of patients in the study who had received at least four prior lines of treatment and were considered or triple class refractory refractory. In this group, the overall response rate was 26% and 9.3% of patients achieved a very good partial response or improvement of more than 90% in their monoclonal protein. The median time to response was 2.1 months,
so it took about 2.1 months for most patients to see a response and the duration of response was about 4.2 months. But 4.2 months there was a 15% overall response rate. In patients with what’s referred to as extramedullary disease or myeloma disease involving tissues and or organs that are outside the bone or bone marrow, which typically is a high risk feature for myeloma. Side effects observed with melphalan included primarily low grade low blood cell counts which were managed appropriately with either reduction.
in doses of the medication or other supportive care given by providers. Fatigue, swelling, and bone and joint inks also occurred. GI symptoms such as nausea and vomiting, were not severe in the clinical trial and there was no hair loss or neuropathy or numbness and tingling in the extremities or legs or arms. That were reported with the use of melphalan flu femmed in this trial. The last therapy we will discuss is the most recently approved and this is the chimeric antigen receptor T cell or what is known.
NOTE Confidence: 0.894865200000001
00:29:35.917 --> 00:29:39.610 as CAR T cell therapy idake.
NOTE Confidence: 0.894865200000001
00:29:39.610 --> 00:29:43.775 Excuse me, I to sell or idake.
NOTE Confidence: 0.894865200000001
00:29:43.780 --> 00:29:46.500 I do sell Vic Loosle ore Ida Salandit,
NOTE Confidence: 0.894865200000001
00:29:46.500 --> 00:29:48.990 the brand name forward is referred
NOTE Confidence: 0.894865200000001
00:29:48.990 --> 00:29:50.650 to as a Beckman.
NOTE Confidence: 0.894865200000001
00:29:50.650 --> 00:29:53.178 And the way that the car T and
NOTE Confidence: 0.894865200000001
00:29:53.178 --> 00:29:55.017 this product in particular works
NOTE Confidence: 0.894865200000001
00:29:55.017 --> 00:29:57.642 is that a patient’s own T cell,
NOTE Confidence: 0.894865200000001
00:29:57.650 --> 00:30:00.450 a type of immune or white blood cell,
NOTE Confidence: 0.894865200000001
00:30:00.450 --> 00:30:02.415 is genetically modified by adding
NOTE Confidence: 0.894865200000001
00:30:02.415 --> 00:30:04.380 the chimeric antigen receptor or
NOTE Confidence: 0.894865200000001
00:30:04.445 --> 00:30:06.829 car that can then bind to the BCMA
NOTE Confidence: 0.894865200000001
00:30:06.829 --> 00:30:08.500 antigen present on myeloma cells.
NOTE Confidence: 0.894865200000001
00:30:08.500 --> 00:30:09.595 As previously discussed,
NOTE Confidence: 0.894865200000001
00:30:09.595 --> 00:30:11.785 there is activation and growth of
NOTE Confidence: 0.894865200000001
these reprogrammed T cells which are then able to find and kill myeloma cells through various mechanisms through a variety of ways including release of cytokines. Which are small proteins? Importantly, which are important in inflammatory responses and signaling to cells. Ida Cell is the first car T approved in patients with relapsed or refractory multiple myeloma, and these patients who are eligible to receive it have received at least four prior lines of therapy, which again include AP and image and
anti CD 38 monoclonal antibody and. This was based off what is known as the Karma trial and with car T cell therapy there are more. Multiple steps which are required including with Ida cell treatment and this includes blood collection or removal of these T cells through a process called a pheresis. This is followed by the manufacturing or the production of the car T cell product and this usually takes about a four week period and patients receive a low dose chemotherapy before I do cell infusion.
00:31:14.760 --> 00:31:16.360 usually over three days.
NOTE Confidence: 0.894865200000001
00:31:16.360 --> 00:31:19.579 And I do cells then administered as an
NOTE Confidence: 0.894865200000001
00:31:19.579 --> 00:31:22.197 infusion over 30 minutes per infusion bag.
NOTE Confidence: 0.894865200000001
00:31:22.200 --> 00:31:22.573 Importantly,
NOTE Confidence: 0.894865200000001
00:31:22.573 --> 00:31:25.184 there is a period of close monitoring
NOTE Confidence: 0.894865200000001
00:31:25.184 --> 00:31:26.949 after receiving Ida sell as well.
NOTE Confidence: 0.9257143
00:31:31.160 --> 00:31:33.162 So the Karma trial was a multi
NOTE Confidence: 0.9257143
00:31:33.162 --> 00:31:35.179 center phase two trial that included
NOTE Confidence: 0.9257143
00:31:35.179 --> 00:31:37.369 patients who had received at least
NOTE Confidence: 0.9257143
00:31:37.369 --> 00:31:39.748 three prior therapies including Apiai,
NOTE Confidence: 0.9257143
00:31:39.750 --> 00:31:42.935 Imid and an anti CD 38 antibody.
NOTE Confidence: 0.9257143
00:31:42.940 --> 00:31:45.052 Patients received I to sell at
NOTE Confidence: 0.9257143
00:31:45.052 --> 00:31:47.312 different dosages and of the 128
NOTE Confidence: 0.9257143
00:31:47.312 --> 00:31:49.277 patients who received this therapy,
NOTE Confidence: 0.9257143
00:31:49.280 --> 00:31:52.264 73% of them had a response with 33%
NOTE Confidence: 0.9257143
00:31:52.270 --> 00:31:54.790 having achieved a complete response or
normalization of their myeloma studies in the blood or urine or better, the responses observed at the various dose levels and in the total group are seen in the figure here with the approved dose for Ida cell now being 300 to 450 * 10 to the six Carty positive. Cells the majority of patients who received the approved dose were free of disease progression for 11.1 months and this increased to 20.2 months in those who had achieved what’s known as a stringent complete response. With where there’s disappearance of the myeloma protein in the blood
in urine and no evidence of myeloma
NOTE Confidence: 0.9257143
and the bone marrow,
NOTE Confidence: 0.9257143
the most common side effects of
NOTE Confidence: 0.9257143
this treatment were low blood cell
NOTE Confidence: 0.9257143
counts and what’s referred to as
cytokine release syndrome,
NOTE Confidence: 0.9257143
or the body’s response to
NOTE Confidence: 0.9257143
this uncontrolled and.
NOTE Confidence: 0.9257143
Really excessive release of these
NOTE Confidence: 0.9257143
proinflammatory cytokines that we
discuss and this can lead to fever,
NOTE Confidence: 0.9257143
low blood pressure,
NOTE Confidence: 0.9257143
fast heart rate and low oxygen levels,
NOTE Confidence: 0.9257143
among other symptoms.
NOTE Confidence: 0.9257143
Cytokine release syndrome occurred
NOTE Confidence: 0.9257143
to some degree in 84% of patients at
a median of one day after infusion. Those severe events were not very common, and cytokine release syndrome was quickly identified due to the close monitoring and appropriately managed depending on its severity. Neurologic side effects occurred less frequently in this study than with other card T agents. So in addition to these newly approved agents, treatment options for patients with multiple myeloma continue to expand, and this is really through the study of new medications and combinations. On this slide, I’ve outlined a sampling.
of our available clinical trials here

at Smilow and Yale Cancer Center,

which, as you can see,

are fortunately available for all time

points in the myeloma disease course.

So we have a study available

for patients with smoldering or

asymptomatic multiple myeloma that

assesses or evaluates the benefit

of adding Derek to map the anti CD

38 monoclonal antibody to previously

studied Lenalidomide for patients

with newly diagnosed multiple myeloma.

We do have an investigator initiated

trial led by Doctor Never Eats that is

evaluating a more complete assessment
00:34:06.351 --> 00:34:08.361 of response in myeloma by looking
00:34:08.361 --> 00:34:10.856 both in the bone marrow and data
00:34:10.856 --> 00:34:13.148 myeloma bone lesions before and after.
00:34:13.150 --> 00:34:15.343 Therapy with carfilzomib,
00:34:15.343 --> 00:34:17.536 Lenalidomide and dexamethasone.
00:34:17.540 --> 00:34:20.291 And for those patients who are to
00:34:20.291 --> 00:34:21.943 receive maintenance therapy after
00:34:21.943 --> 00:34:23.973 undergoing a stem cell transplant
00:34:23.973 --> 00:34:26.726 but still have evidence of a low
00:34:26.726 --> 00:34:28.496 level of residual or remaining
00:34:28.496 --> 00:34:30.538 myeloma disease in the bone marrow,
00:34:30.538 --> 00:34:32.198 or what Doctor Barr defined
00:34:32.198 --> 00:34:34.268 as minimal residual disease,
00:34:34.270 --> 00:34:36.734 we do have a study looking at outcomes
00:34:36.734 --> 00:34:38.900 of adding again daratumumab to
00:34:38.900 --> 00:34:41.068 the treatment.
our standard maintenance regimen.

For many patients, which is Lenalidomide.

And lastly,

we have multiple trials for patients with relapsed or refractory myeloma.

Including an investigator initiated trial looking at quality of life for patients on daratumumab and trials with new medications,

including those that use our patient’s own immune system to fight off the myeloma and so at the conclusion of our talk, we’d be happy to share more information to help answer any questions you may have about our clinical trials.

And thank you again for your time.
I will now turn it over to Tara Anderson.

Alright. One second, see.

OK. Thank you Sabrina. So I’m Tara Anderson. I’m a physician assistant with the myeloma group here and I’ve been here since 2015 and started doing myeloma in 2005 and I’m going to talk about the common side effects with the myeloma therapies. The main therapy since the doctor Browning touched on all of the recent approved drugs and all of those side effects. So I’m going to talk about the main classes of medications that Doctor Barr discussed and.

The general side effects from each class.
Alright, so the different classes of treatment as Doctor Barr discussed in her presentation and then we usually combine as she mentioned, three drugs, or potentially now for drugs and one from each class. So produce some inhibitors, immune modulatory drugs, monoclonal antibodies, and most of our therapies include dexamethasone. I just don’t want to have to put it in all the slides, so you can always refer back to this slide is fatigue.
All of them are transgenic. We know with the imids we always do the Rams program, but all of them should require 2 forms of contraception and. They’re all class D for pregnancy, so and all of the medications that we use can cause rashes. Sometimes we’ll just do an Anna histamine prior to taking the medication, and if the rash is more severe
than we will hold the medication and potentially reduce the dopes. And then all of the treatments also cause decreased blood counts. So with each treatment when you come in for treatment, we check your blood counts to make sure it’s safe to go ahead with treatment. And if it’s not, sometimes we have to hold the medication, and occasionally we have to reduce the dose. And I and sometimes will also use growth factors like NEUPOGEN to stimulate the bone marrow to help reduce some of those cells. And with the reduced blood counts
you can see, I mean a suppression and with all of the treatments that can happen.
So we want to make sure you call for any fevers you know. There’s always somebody here,
so a temperature is considered 100.4 or higher, and then if you get frequent infections,
or hospitalized for several infections, sometimes will talk to you about giving an Ivy called IVIG which is immuno globulin.
Which gives you some of the immunoglobulins that you don’t normally produce. To help protect you.
From getting infections, and we usually do that once a month, so these are the general side effects from all those classes of drugs. And then specifically for the produce some inhibitors which are listed below. I will talk about someone specific just for those, and you can see the dates when these drugs were approved. So I started doing my element 2005 and I can tell you when we started doing it. When I started doing it. The drugs that we use weren't as good as the ones we have now.
of these drugs are pretty well tolerated.
At least we want them to be.
So if you’re not tolerating them well then
definitely reach out to us so we can.
Make it easier for you to tolerate it,
because once you’re started on treatment,
we tend to keep you on therapy for
life and want to make sure we can
keep the disease under control while
maintaining good quality of life.
So proteasome inhibitors in general can
cause gastrointestinal side effects mildly.
Sometimes we hear nausea,
but it can some more than others,
as I'll get two with the oral proteasome inhibitor and they all have a risk of reactivating herpes zoster or shingles, so all patients should be on acyclovir as a prophylaxis. And again, referring to the first slide, all those apply as well. And then both them up or VELCADE. One of the most common side effects we see with that is peripheral neuropathy. We would see it a lot more when we did give Velcade Ivy and we used to give allocate twice a week and now we give it in a subcutaneous form and typically we give it weekly. We see a lot less neuropathy,
but we still see it. So the key is to get a baseline assessment to see if anybody has any numbness or tingling in their hands and feet is typically where we see it at baseline and then to monitor to make sure it’s not getting. Worse, we want to make sure it’s not painful and it’s not interfering with daily functioning like buttoning buttons or holding on to a coffee cup, or those types of things. And if it does then we may have to hold it or lower the dose and most of...
the time in 70% of patients it’s reversible, so the key is to communicate with us when you have the neuropathy so we can, make it better, and then we can also use these medications. Gabapentin, Lyrica or Cymbalta which sometimes. Help with neuropathy? We can also lower blood pressure, so if you’re on blood pressure medication sometimes will have to hold it during the time when you’re getting the VELCADE, and this isn’t really a side effect but just kind of a note that if
we take them in C supplements,

we should hold it because there

is data showing that vitamin C can

interfere with the efficacy of alkane.

Carfilzomib so the main thing

with carfilzomib is the cardiac

toxicities and the key here is also

getting a baseline assessment.

So if you have hypertension to get

it controlled before we get started

with the treatment and then to

also want to make sure the hearts

functioning OK so we'll do an echo.

So an ultrasound of the heart prior to
starting typically and we usually do an EKG and then a BNP as a blood draw. The lab that looks at the nonspecific marker of the stress on the heart. So we monitor that monthly. And then we want you to watch out for any kind of swelling in your legs, shortness of breath. Abdominal distention, because some of those could indicate that the heart isn’t pumping as effectively as it should, so we watch for those. It’s a low percentage, but it does happen so. We monitor those monthly as well.
And because it’s given Ivy, we sometimes see inflammation of the vein or thrombophlebitis, and you can use ice and that should help Tylenol. But if it keeps happening sometimes we recommend to use support and occasionally we can see pulmonary hypertension. So sometimes the shortness of breath may not be due to the heart, but it may be more due to the lungs, so we can usually pick that up on an echo. Or if we can’t figure out what’s going on with the heart,
Sometimes will refer to a pulmonary doctor. And then examine or narrow is the last produce I’m going to have better that was approved and it’s oral. So because it’s oral we see a lot more GI side effects or in the data. And in all the trials they see a lot more jet GI side effects. I think in practice we don’t see as many, but we usually tell you to have Zofran or Imodium on hand just in case, and then obviously if you were to vomit after taking the pill we won’t want you to reach, you know take the pill again ’cause we don’t know. How much was absorbed?
And also reach out to us if that was to happen. You can also see lower extremity swelling with this one. We recommend compression stockings, elevating your legs and sometimes will give you a water pill or lay 6. OK, and the second class of medications that we use in combination or the immunomodulatory drugs or image. So the first one that was approved was the Little Mide approved in 2006, but we were using it earlier and kind of off label,
and we don’t use it as much because it has more toxicities and the other two.

So now we typically start with Lenalidomide or REVLIMID and then after relapse, use POMALYST.

So in general, that emits are putting patients at higher risk of venous thromboembolism.

So we don’t want so blood clot. So we want you to let us know if you had any swelling in your legs or pain and your legs or shortness of breath. And we put you on an aspirin as prophylaxis, typically. Or if you if you’re at high risk have had a thought before,
we usually place you on an oral anticoagulant now. In the past we use Lovenox or Coumadin. And now we have the newer agents which are easier to use the oral anticoagulants. And then I know I brought up the terror that regeneca effects in general, that's why the REMS program but with this one we have to do the Rams paperwork and you have to do the phone surveys and so just a reminder with that way back in the 50s and 60s the limit was used as a sleeping pill for pregnant women and then they had babies that were had deformity. So that’s why the REMS program
is in place with that drug.

00:45:24.510 --> 00:45:26.210 So Speaking of full time,

00:45:28.590 --> 00:45:30.012 see are fatigue, Constipation,

00:45:30.012 --> 00:45:31.218 numbness and tingling.

00:45:34.545 --> 00:45:37.089 we can see a slowed heart rate with it,

00:45:37.090 --> 00:45:40.674 which may be causing some other fatigue.

00:45:40.680 --> 00:45:42.408 We typically used it at lower

00:45:42.408 --> 00:45:44.320 doses when I was using this,

00:45:44.320 --> 00:45:46.434 when there wasn’t much else to use,

00:45:46.440 --> 00:45:48.888 we would use much higher doses and it was

00:45:48.888 --> 00:45:51.290 very difficult to tolerate at that time.

00:45:51.290 --> 00:45:54.994 But with the lower doses we can usually.

00:45:55.000 --> 00:45:57.086 Use it with minimal side effects and

00:45:57.086 --> 00:45:59.238 some of these medications to help so
the same with them with the numbness and tingling in the gabapentin, Lyrica, and Cymbalta.

And the typical things we want you to do if you’re constipated, so Senate police increased water fiber. Those types of things.

And then learn a little made one of them are common side effects as diarrhea, especially the longer you’re on.

It tends to be more of a cumulative effect and we do different things. First, we want to make sure that you’re not having diarrhea from a different cause like infection.
00:46:34.880 --> 00:46:37.155 Or, you know, is it you know,
NOTE Confidence: 0.9766345
00:46:37.160 --> 00:46:39.110 did you develop an intolerance to
NOTE Confidence: 0.9766345
00:46:39.110 --> 00:46:40.750 lactose or something like that?
NOTE Confidence: 0.9766345
00:46:40.750 --> 00:46:42.054 Or high fat foods?
NOTE Confidence: 0.9766345
00:46:42.054 --> 00:46:44.010 So sometimes will alter the diet.
NOTE Confidence: 0.9766345
00:46:44.010 --> 00:46:44.660 Try Imodium,
NOTE Confidence: 0.9766345
00:46:44.660 --> 00:46:46.285 and if those don’t work,
NOTE Confidence: 0.9766345
00:46:46.290 --> 00:46:48.054 sometimes will add a medication called
NOTE Confidence: 0.9766345
00:46:48.054 --> 00:46:50.022 full listed which helps with the
NOTE Confidence: 0.9766345
00:46:50.022 --> 00:46:51.506 diarrhea associated with Lenalidomide.
NOTE Confidence: 0.9766345
00:46:51.510 --> 00:46:53.785 And then I put trash in here,
NOTE Confidence: 0.9766345
00:46:53.790 --> 00:46:56.065 even though we already talked about it,
NOTE Confidence: 0.9766345
00:46:56.070 --> 00:46:58.026 because it’s fairly common with Lenalidomide,
NOTE Confidence: 0.9766345
00:46:58.030 --> 00:46:58.622 and again,
NOTE Confidence: 0.9766345
00:46:58.622 --> 00:47:02.058 a lot of times we have to hold and reduce the
NOTE Confidence: 0.9766345
00:47:02.058 --> 00:47:05.250 dose if the creams and the Anna histamines.
Aren’t controlling the rash?

And then if you second primary malignancies can happen,

this is because people are living longer and doing better with myeloma.

On this for a long time.

And they’ve seen second primary malignancies.

So just a reminder to follow up with

your primary care for routine screenings.

Definitely the benefits of the

Lenalidomide outweigh the

risk of these second primary malignancies,

but it’s still something to be cautious

of and follow up with your primary care.

And then the last images,
00:47:41.910 --> 00:47:42.235 comma,
NOTE Confidence: 0.9766345
00:47:42.235 --> 00:47:44.185 little mid and again rash is
NOTE Confidence: 0.9766345
00:47:44.185 --> 00:47:46.396 fairly common with this one and the
NOTE Confidence: 0.9766345
00:47:46.396 --> 00:47:48.160 only other one we see peripheral
NOTE Confidence: 0.9766345
00:47:48.229 --> 00:47:49.601 neuropathy occasionally with this
NOTE Confidence: 0.9766345
00:47:49.601 --> 00:47:52.310 not as much as with the little mine,
NOTE Confidence: 0.9766345
00:47:52.310 --> 00:47:54.260 but otherwise it’s fairly well tolerated.
NOTE Confidence: 0.9766345
00:47:54.260 --> 00:47:57.176 We don’t usually see as many GI side effects.
NOTE Confidence: 0.9766345
00:47:57.180 --> 00:48:00.212 We tend to see a little bit more
NOTE Confidence: 0.9766345
00:48:00.212 --> 00:48:02.488 cytopenia or low blood counts.
NOTE Confidence: 0.9766345
00:48:02.490 --> 00:48:04.807 Mainly because it’s used later in therapy.
NOTE Confidence: 0.9592045
00:48:07.290 --> 00:48:09.908 OK, and then the last class of
NOTE Confidence: 0.9592045
00:48:09.908 --> 00:48:12.789 medications or the monoclonal antibodies.
NOTE Confidence: 0.9592045
00:48:12.790 --> 00:48:14.188 So there’s three.
NOTE Confidence: 0.9592045
00:48:14.188 --> 00:48:16.984 There are two memebr and illtories
NOTE Confidence: 0.9592045
00:48:16.984 --> 00:48:20.124 map were both approved in 2015 and
then just last year daratumumab was approved subcutaneously and then. It’s a text map, so these have made a big difference and treatment, and they’re fairly well tolerated. And now that we have daratumumab subcutaneous, it’s made a big difference and some other patients that have had Ivy know that the first time we give it. It’s like an all day infusion and then the next is like half a day. So it was a long.
There are long days and now that we can give it subcutaneously, it's a lot shorter. It's about a 10 minute injection. And you only have to stay for a few hours after the first injection. So our main concern with these medications are the infusion related reactions and we typically would only see a reaction with the first injection or first infusion. But as you can see the reactions are fairly common with Dara. I've eaten subq, it's 34 to 48%.
NOTE Confidence: 0.9592045
00:49:26.770 --> 00:49:29.206 Matt is similar to the Dara and
NOTE Confidence: 0.9592045
00:49:29.206 --> 00:49:31.910 the E Lo is only about 10%.
NOTE Confidence: 0.9592045
00:49:31.910 --> 00:49:33.745 So to prevent these infusion
NOTE Confidence: 0.9592045
00:49:33.745 --> 00:49:35.580 reactions we premedicate with Tylenol,
NOTE Confidence: 0.9592045
00:49:35.580 --> 00:49:37.056 Benadryl and dexamethasone and
NOTE Confidence: 0.9592045
00:49:37.056 --> 00:49:39.270 with the first infusion we also
NOTE Confidence: 0.9592045
00:49:39.338 --> 00:49:40.710 give singular for Dara.
NOTE Confidence: 0.9592045
00:49:40.710 --> 00:49:45.129 And we give Pepcid for acid attacks in men.
NOTE Confidence: 0.9592045
00:49:45.130 --> 00:49:46.691 And this and we give this with
NOTE Confidence: 0.9592045
00:49:46.691 --> 00:49:47.916 each infusion the singular we
NOTE Confidence: 0.9592045
00:49:47.916 --> 00:49:49.446 only do with the first infusion,
NOTE Confidence: 0.9592045
00:49:49.450 --> 00:49:52.229 and this tends to reduce the rate.
NOTE Confidence: 0.9592045
00:49:52.230 --> 00:49:54.660 And most of the infusion reactions
NOTE Confidence: 0.9592045
00:49:54.660 --> 00:49:57.089 are very mild. We just stopped.
NOTE Confidence: 0.9592045
00:49:57.089 --> 00:49:59.104 Infusion treat the reaction and
NOTE Confidence: 0.9592045
Then we started at a lower dose. So we just want to make sure you let the nurse know if you notice anything like scratchy throat, cold, nauseous to let the nurse know right away so we can stop the infusion and treat the reaction. And then we also see shingles with monoclonal antibodies. So you need to be on prophylaxis with acyclovir with this one as well, and then the studies that are increased risk rates of an upper respiratory infections. And then the last one is steroids.
00:50:33.600 --> 00:50:34.791 Everyones favorite dexamethasone.

00:50:34.791 --> 00:50:37.934 So this one is probably the hardest to tolerate just because of you know the weight.

00:50:40.390 --> 00:50:41.407 Gain the irritability.

00:50:41.407 --> 00:50:42.763 All these things that happened and trouble sleeping.

00:50:44.310 --> 00:50:46.350 So sometimes will give melatonin or atterax which is a older generation antihistamine and we may have to reduce the dose if there’s lots of side effects, and then you should be following up with an eye doctor ’cause it can cause cataracts.

00:50:48.531 --> 00:50:51.177 antihistamine and we may have to reduce

00:50:51.177 --> 00:50:53.950 the dose if there’s lots of side effects,

00:50:53.950 --> 00:50:57.163 and then you should be following up with an eye doctor ’cause it can cause cataracts.

00:50:57.163 --> 00:51:00.418 eye doctor ’cause it can cause cataracts.

00:51:00.420 --> 00:51:02.810 And primary care under friend

00:51:02.810 --> 00:51:05.210 ’cause you can see steroid

00:51:05.210 --> 00:51:08.140 induced steroid induced diabetes.

NOTE Confidence: 0.97746074

88
Excuse me

So in summary, treatment for myeloma is generally well tolerated now with a lot of a lot better and the like since 2005. Prior to 2005, I think it was, you know, more of the traditional chemotherapy with hair loss, nausea, vomiting, a lot more toxicity. So with the newer generation of all the different classes we have now, that treatment should be pretty well tolerated. So the key is communication. Make sure you let us know if you’re having any side effects.
so we can adjust it and get the best treatment to help improve.
The disease and also we want to get a good baseline assessment to make sure the side effects are coming from the medication. And not something else. So I need a good doctor patient team. Relationship. OK, and then these are just resources for you to look up different side effects and different information. So MRF is a good website and then the multiple myeloma support group meets every the last Tuesday of every month. And then I just put in their
00:52:24.567 --> 00:52:26.200 their phone number and.
NOTE Confidence: 0.98192424
00:52:26.200 --> 00:52:27.444 The contact information if
NOTE Confidence: 0.98192424
00:52:27.444 --> 00:52:28.377 anybody’s interested in.
NOTE Confidence: 0.98192424
00:52:28.380 --> 00:52:30.473 I know it’s zoom now because because
NOTE Confidence: 0.98192424
00:52:30.473 --> 00:52:32.633 of kovit I don’t know if they’re
NOTE Confidence: 0.98192424
00:52:32.633 --> 00:52:36.960 planning to go back to in person, but.
NOTE Confidence: 0.98192424
00:52:36.960 --> 00:52:38.768 That is another place.
NOTE Confidence: 0.98192424
00:52:38.768 --> 00:52:40.610 And that’s it, I think.
NOTE Confidence: 0.9110213
00:53:00.940 --> 00:53:03.523 So thank you to Doctor Barr and
NOTE Confidence: 0.9110213
00:53:03.523 --> 00:53:05.790 Doctor Browning and Terra for this.
NOTE Confidence: 0.9110213
00:53:05.790 --> 00:53:07.282 Great talks and presentations.
NOTE Confidence: 0.9110213
00:53:07.282 --> 00:53:08.028 Very educational.
NOTE Confidence: 0.9110213
00:53:08.030 --> 00:53:10.921 I think we have a few questions
NOTE Confidence: 0.9110213
00:53:10.921 --> 00:53:13.900 in both the chat and the Q&A.
NOTE Confidence: 0.9110213
00:53:13.900 --> 00:53:17.210 And. I believe, UM, the.
NOTE Confidence: 0.9110213
00:53:17.210 --> 00:53:19.664 There’s a few actually discussing whether
00:53:19.664 --> 00:53:22.978 or not these slides would be made available,

00:53:22.980 --> 00:53:25.157 and the video of presentation will be

00:53:25.157 --> 00:53:27.919 posted at the yalecancercenter.org website,

00:53:27.920 --> 00:53:30.935 and a copy of the slides can be requested

00:53:30.935 --> 00:53:34.098 by emailing cancer answers at yale.edu,

00:53:34.100 --> 00:53:37.208 Her Emily, which we can hopefully if

00:53:37.208 --> 00:53:40.194 Emily maybe you could put that in

00:53:40.194 --> 00:53:43.139 the chat box for everyone if they

00:53:43.139 --> 00:53:46.139 were interested in obtaining a copy.

00:53:46.140 --> 00:53:49.244 I think that answers to our questions on

00:53:49.244 --> 00:53:52.288 our chat and one of the first questions

00:53:52.288 --> 00:53:55.184 that we had and that maybe Doctor

00:53:55.184 --> 00:53:57.890 Barkin answer was regarding where a

00:53:57.890 --> 00:54:01.606 Lam Lloyd fit on the spectrum of EM guys,

00:54:01.610 --> 00:54:03.234 to my Lomax, sure.
So that's a very good question. It can fit on any of that spectrum actually. So anytime you have, UM, a cell or plasma cell, even the B cell conflicts of lymphomas. So creating these proteins specifically these light chains they can deposit into organs, and there's no way to predict which which patient or which condition will lead amyloid. It's something about the nature of this protein that leads to the deposition into different organs, and that's what Emily is right? So you can get it.
With us you can get a smoldering and you can get it in the same time that you have myeloma, so this is something we as physicians I think about and UM, no ask you questions that make us, UM, you to screen for these things. Ask you questions that if if it is positive that makes us think we should I look deeper into whether there is amyloid deposition. So it’s a good question.

OK, uh, thanks no Friday. I do believe Emily posted in the chat now where the slides could be.
obtained if he would like her copy.

And we had a few questions.

Then over in the Q&A that whoever wants to tag, take a stab at them regarding the effectiveness of the COVID vaccine for our multiple myeloma patients, and what precautions should someone still be taking either around other vaccinated or unvaccinated individuals? So I don’t know who wants to brave the COVID world.

I can answer that one, so I think it’s obviously a very important question, and I think you know we’re learning more about it as time goes on, you know,
I think studies have suggested that patients myeloma patients on a treatment, and patients with other blood disorders may have less of a response to our available COVID vaccines. Fortunately, the COVID vaccine start at a high level, very high level of effectiveness, and so our recommendation to our myeloma patients is still to get the vaccine, but I think it is important to know that maintaining preventative measures like mask wearing and good hand washing and avoiding sick people.
It’s probably more important in our myeloma patients and the general population, so I would recommend that all my lower patients get the vaccine as soon as possible. If they have not already, but continue to practice measures to try to avoid COVID. And would add to that that there were a couple of recent publications about myeloma patients and their response to the vaccinations. And yes, it is evident that the antibody production may be lower, like 50% of what you might
In healthier population. But there are also very significant cell responses in their immune cells, T cells and some of the T cells and B cell responses. And that’s what provides protection to model of patients after vaccination. Yeah, I think to follow up on that and the group at Mount Sinai published some of their findings just recently. Actually, on the 28th of this month they had looked at 320 individuals and they had looked at 320 individuals who had had the COVID vaccine, 260 of them received either the Pfizer.
the Moderna, so the two dose and what they had shown was about 16%.

Fifteen point. 8% of patients did not mount any detectable antibodies compared to the other 84.

Your dad, but that response was very variable and they did find that patients who had had COVID had a higher immune response.

Tattoo that. OK, and we have some other questions.

I think 2 regarding acyclovir are whether or not an individual could stop acyclovir if they had received the shingles vaccine.
So I don’t know if Terra if you want to address that under side effects.

Yeah sure I meant to say that actually no.

I mean, if you had the shingles vaccine, you still need to stay on acyclovir.

If you’re getting a monoclonal antibody or producing inhibitor, sometimes we will stop the if you’re just on an image for maintenance.

You can stop the acyclovir, but otherwise you need to stay on it regardless of the vaccine.

OK. Uh, we have a few questions coming in and about Carty and transplants.
And so maybe Doctor Power, you can handle some of these. Someone is asking whether or not there’s hospitalization involved with Carty, and if so what is that duration? Yes, so there is hospitalization involved with car T therapy, and that’s really to follow on the side effect. Expected side effects, which are this side that kind of lease which majority of patients do get and then potentially even neurotoxicity. So at least seven days but sometimes longer really depends on how you do. OK, great and another question
that's coming in regarding on stem cell transplant and side effects.

As a questioning at about the malignancies that we should be looking out for following a stem cell transplant and use of REVLIMID maintenance so I don’t know if either Natalia know first Sabrina would like to answer one of that.

I can respond to that.

I can respond to that Terry.

So in the studies with REVLIMID or Lenalidomide maintenance, there was a slight increase in the absolute risk of developing second primary cancers,
and there was approximately 3% absolute increase risk, so the risk is very small, and the types of cancers that were observed or mostly another blood related malignancy or bone marrow malignancy. There were a few cases of non Hodgkin lymphoma, leukemia, myelodysplastic syndrome. These were. Types of bone marrow cancers that developed overtime in among those observed on the trials there. But there were also several solid tumors as well, and this is what we see in our practice.
So the conclusion is that majority of the second primary cancers would be blood related, but overall absolute increased risk of secondary cancers is on the order of two to 3%, so the risk is small and the benefits certainly outweighs benefits. A problem in prolonging survival awhile and maintenance therapy outweighs that risk.

Great thank you Natalia. Does anyone have anything else to add on that? And if not, we'll move on to another question is,
as far as if an individual has a medical officer of undetermined significance for an extended period of time, what is the likelihood to remain at that? I'm guess level versus risk of transformation to myeloma. I can answer that so you know, come with them guys. As I mentioned, the risk of progression is 1% per year, but this is an average and there's actually other markers we look at to assess the risk of M gusts. These are things like elevated light chains. UM, the amount of protein, the monoclonal protein, and I'd say yes, time does give us some information, right?
If someone said M ghosts and everything is completely stable for five years, that is informative. And in actually smaller in world, we know as we. Go, you know, as we follow patients overtime that 10% risk does go down after five years or so. So yes, time is important, but it gives us information about the behavior for disease.
and those were dealing with smoldering myeloma specifically.

If there's anything in individual can do to help prevent the progression of smoldering to multiple myeloma? If so, what does that look like and what treatments are available for small joint individual?

I know Doctor Browning you had mentioned that there are some trials, so would you mind enlightening us on smoldering myeloma?

Sure, absolutely.

So similar to our approach with an MGus.
we want to understand their risk and we do that by looking at a couple of things. The percentage of a plasma cells that are in the bone marrow as well as the size of the protein in the blood and the size of or the amount of free light chains that we see in the blood as well. And patients who fall. Uh, into the intermediate or higher risk category for smoldering myeloma. There has been evidence that earlier treatment with the medication, Lenalidomide has been helpful now.
as occurred.

Doctor Parker stated, there are more trials looking at either additions to Lenalidomide or other combinations of therapies and their effectiveness in preventing progression too. End organ dysfunction in patients who have smoldering myeloma.

So to answer the first question, I don’t think there’s anything in particular that individuals can do, you know, I think when we get this question, can can do you know? maintaining a healthy diet
and physical activity is important.

But really, it depends on kind of the risk of the smoldering myeloma and how it progresses over time.

I think there was a question on the generic Lenalidomide. Yeah, and I think there’s none that are currently available for the United States as an approved use. As you know, the REVLIMID slash Lenalidomide produced by Celgene is currently off the label of the patent, meaning the patent has expired, but unfortunately,
the price of the drug has not been reduced across the world in Europe and Asia.

There are several similar drugs you may call them biosimilars, or the generics of these emit medications. Lenalidomide or pomalidomide, and these are produced in various parts of Europe and Asia. So, for instance, you may hear people using Indian when a little mind and similar drugs and and they appear to be just as effective. I think there were some of the studies coming out of Asia that that showed efficacy that’s kind of equivalent, so. But uhm.
I’m not aware of the approved US use.

OK, and then one more that’s in the chat and then we can go to another one that was submitted ahead of time is do the panelists recommend patients having their cells sequenced or and next generation sequencing done to look for targeted treatment or for personalized medicine? And so maybe we can go around having having each of the panelists answer that question. Sorry, I think that’s a very interesting question and under you know, uh, the right?
it's not something that's routinely done.
NOTE Confidence: 0.93897206
It's not an FDA approved, UM.
NOTE Confidence: 0.93897206
A way to do things,
NOTE Confidence: 0.93897206
but I think it's in the research world.
NOTE Confidence: 0.93897206
I would recommend it.
NOTE Confidence: 0.98434293
Yeah, I would agree with that I.
NOTE Confidence: 0.98434293
I think it's not a part
NOTE Confidence: 0.98434293
of our standard practice,
NOTE Confidence: 0.98434293
but I think there's a lot to learn
NOTE Confidence: 0.98434293
from that and and I agree that no
NOTE Confidence: 0.98434293
incorporation of that into clinical
NOTE Confidence: 0.98434293
trials moving forward is important
NOTE Confidence: 0.98434293
and I think will be enlightening and
NOTE Confidence: 0.98434293
how to best guide our our treatments.
NOTE Confidence: 0.98434293
As you saw, for patients who have
NOTE Confidence: 0.98434293
relapsed or refractory disease,
we now have a whole number of treatments, but understanding the sequencing of what to use first you know is is a challenge. And I think understanding more about you know the specifics of each patient. My Loma may help that. I don’t have money. I don’t have much to add to that. I mean, I think it’s been it’s been around for awhile. Just having it has not been approved but it would be great if we could do that. ’cause there’s so many different presentations of myeloma.
you know, specific patients that have different mutations and things, but I don’t know how far they are like getting this approved.

Great, so it sounds like more to come and then again one last question that was submitted ahead of time which was dealing with solitary plasmacytomas and specifically what is the risk of progression to multiple myeloma with the solitary plasmacytoma? And and so I don’t know if Doctor Bar you wanna take that or doctor Pepper eats.

I’m sorry, can you rephrase the question? Yes, so the question that was submitted was regarding solitary plasma cytoma’s
and risk factors for progression to multiple myeloma. So in some of the largest cohorts out of US and European experience says it was observed that patients who had solitary plasmacytomas either in the bone or in other tissues within the subsequent follow up after initial treatment for the plasmacytoma. Approximately 50% of patients did. Evolved to develop multiple myeloma in the subsequent three to five years of follow up. So I think the close follow-up is recommended with periodic imaging as to what? What are the factors that
01:08:33.820 --> 01:08:35.044 promote that progression?
NOTE Confidence: 0.9749503
01:08:35.050 --> 01:08:37.786 I think the Nordic Group had looked at
NOTE Confidence: 0.9749503
01:08:37.786 --> 01:08:40.776 some of the angiogenesis risk factors and
NOTE Confidence: 0.9749503
01:08:40.776 --> 01:08:44.049 they did not identify many risk factors,
NOTE Confidence: 0.9749503
01:08:44.050 --> 01:08:47.314 but there one of them was the badger,
NOTE Confidence: 0.9749503
01:08:47.320 --> 01:08:50.110 which is the endothelial blood vessel.
NOTE Confidence: 0.9749503
01:08:50.110 --> 01:08:51.182 Type of.
NOTE Confidence: 0.9749503
01:08:51.182 --> 01:08:53.326 Inflammatory or angiogenesis mediator,
NOTE Confidence: 0.9749503
01:08:53.330 --> 01:08:55.420 but it’s not something that
NOTE Confidence: 0.9749503
01:08:55.420 --> 01:08:56.674 we routinely test,
NOTE Confidence: 0.9749503
01:08:56.680 --> 01:09:00.870 and there’s no other easy ways
NOTE Confidence: 0.9749503
01:09:00.870 --> 01:09:03.292 of making that prediction,
NOTE Confidence: 0.9749503
01:09:03.292 --> 01:09:05.423 and so they the mainstay of monitoring
NOTE Confidence: 0.9749503
01:09:05.423 --> 01:09:07.988 would be just periodic surveillance
NOTE Confidence: 0.9749503
01:09:07.990 --> 01:09:10.510 and subsequently at every six month

117
interval with updated blood work,

urine tests all of the usual

myeloma lab tests,

which includes certain protein

electrophoresis like chains and urine,

protein electrophoresis and

and at least an annual.

I think nowadays that will be with one

of the advanced imaging modalities,

like either a PET scan or low dose CT scan,

or alternatively MRI of the

body where it’s available.

Great, thank you.

So those were all of our pre

submitted questions and I don’t see
01:09:46.167 --> 01:09:48.828 any additional ones in the QA or chat.
NOTE Confidence: 0.9610744
01:09:48.830 --> 01:09:51.224 So if anyone has any last minute
NOTE Confidence: 0.9610744
01:09:51.224 --> 01:09:52.930 questions please submit those now.
NOTE Confidence: 0.9610744
01:09:52.930 --> 01:09:55.567 If not but we can wipe things as down
NOTE Confidence: 0.9610744
01:09:55.567 --> 01:09:58.035 and thank you all for your attention
NOTE Confidence: 0.9610744
01:09:58.035 --> 01:10:00.799 and thank you to all the panelists.
NOTE Confidence: 0.98661715
01:10:02.960 --> 01:10:04.690 Thank you very much everybody.
NOTE Confidence: 0.98661715
01:10:04.690 --> 01:10:05.728 Great talks everyone.
NOTE Confidence: 0.98854965