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.
NOTE Confidence: 0.981817
00:00:36.726 --> 00:00:39.600 Tara Anderson will be talking about
NOTE Confidence: 0.981817
00:00:39.674 --> 00:00:41.792 Texas cities of certain drugs and
NOTE Confidence: 0.981817
00:00:41.792 --> 00:00:44.169 then we'll have our the rest of
NOTE Confidence: 0.981817
00:00:44.169 --> 00:00:46.262 our team join us for the question
NOTE Confidence: 0.981817
00:00:46.270 --> 00:00:48.952 and answer and doctor Terry Parker
NOTE Confidence: 0.981817
00:00:48.952 --> 00:00:51.519 and Doctor Natalia will parts so.
NOTE Confidence: 0.981817
00:00:51.520 --> 00:00:54.946 With that we will start our.
NOTE Confidence: 0.981817
00:00:54.950 --> 00:00:57.100 Session.
NOTE Confidence: 0.981817
00:00:57.100 --> 00:00:57.760 2nd.
NOTE Confidence: 0.9911908
00:01:07.200 --> 00:01:10.814 Alright. So my goal for the next
NOTE Confidence: 0.9911908
00:01:10.814 --> 00:01:13.528 15 minutes is to give you some
NOTE Confidence: 0.9911908
00:01:13.528 --> 00:01:15.958 insights into understanding what is
NOTE Confidence: 0.9911908
00:01:15.958 --> 00:01:18.306 multiple myeloma and some general
NOTE Confidence: 0.9911908
00:01:18.306 --> 00:01:20.910 principles of how we think about
NOTE Confidence: 0.9911908
00:01:20.910 --> 00:01:22.580 treatment for multiple myeloma.
NOTE Confidence: 0.989964
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 is what we called the monoclonal protein M spike and protein, all different names for the same thing. 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,
is an IgG Lambda and IGA Kappa, and that is that that clone for that individual. OK, so the first thing is high calcium level OK, not all of these are found in every person. OK, so the first thing is high calcium level OK,
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.

Now the definition of myeloma has changed over time for many many years.
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 M Gus 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 my luma 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. 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 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
cells as we can to get these deep responses and to keep people in response for as long as possible. Unfortunately, this you know some point. The disease does come back. We do not think myeloma is a curable disease at this time. So when the disease comes back, we do have other treatments and we bring the disease back down and this pattern goes on and on. I want to take just a few minutes to talk about response assessment for myeloma. How we assess the response? So as I mentioned, we look at the blood. 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 'cause 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 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,
so we have an assortment of clinical trials where it gives opportunity to try new, very possibly very effective treatment for myeloma.

So with that I'd like to conclude my section of the talk and move on to doctor Sabrina Browning. He will talk about the details of these newer agents that we have for to treat myeloma.

Great, OK, so good evening everyone and thank you again for joining us. Come again. My name is Sabrina Browning as Doctor Barr stated.

I am one of the doctors in our multiple 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 who 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 DSS release inhibitor referred to as put in a panobinostat. These medications have been or are currently being studied as a part of. Combination regimens and many
are targeting earlier in disease course as Doctor Barr mentioned, our treatment going myeloma is really to achieve what we refer to as deep or maximum responses to therapy that are prolonged without disease progression. And while we won’t review this agent in detail today, I’ve signaled Isatuximab in the chart here as a more recently approved antibody that targets a protein known as CD 38 found on immune cells and myeloma cells and isatuximab is now approved for use in combination with. 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 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 and 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
class of medications and is being studied in other blood cancers as well. In multiple myeloma, selinexor is approved as an oral pill at a dose of 80 milligrams, taken twice per week with the steroid dexamethasone and this is for individuals with relapsed or refractory myeloma who have received at least four prior lines of therapy and are no longer responding to at least two of the pies previously discussed. At least two images and an anti CD monoclonal antibody selinexor is also approved at a dose of
100 milligrams once per week with Bortezomib and dexamethasone.

For patients, again with three lobster refractory myeloma. But this time, those who have received only at least one prior line of therapy and these approvals are based on the storm and Boston clinical trials, respectively, which we’ll talk more about. So the storm clinical trial evaluated 122 patients in the US in Europe who had this triple refractory multiple myeloma that I mentioned and had received a median of seven 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 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 selinexor or 100 milligrams once per week combined with Bortezomib, once per week combined with Bortezomib. The proteasome inhibitor and dexamethasone.

The steroid or Bortezomib 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,
NOTE Confidence: 0.98759824
00:21:27.060 --> 00:21:29.100 had a longer time without disease.
NOTE Confidence: 0.98759824
00:21:29.100 --> 00:21:31.438 Progression at a median of 13.9 months
NOTE Confidence: 0.98759824
00:21:31.438 --> 00:21:34.087 when compared to the group who only
NOTE Confidence: 0.98759824
00:21:34.087 --> 00:21:35.667 got Bortezomib and dexamethasone.
NOTE Confidence: 0.98759824
00:21:35.670 --> 00:21:38.184 Where the progression at the time
NOTE Confidence: 0.98759824
00:21:38.184 --> 00:21:40.660 without progression was about 9.5 months.
NOTE Confidence: 0.98759824
00:21:40.660 --> 00:21:43.072 The more common side effects observed
NOTE Confidence: 0.98759824
00:21:43.072 --> 00:21:46.021 with selinexor in both of these clinical
NOTE Confidence: 0.98759824
00:21:46.021 --> 00:21:48.565 trials and in practice include fatigue.
NOTE Confidence: 0.98759824
00:21:48.570 --> 00:21:50.650 Gastrointestinal symptoms such as nausea,
NOTE Confidence: 0.98759824
00:21:50.650 --> 00:21:54.040 infections, and low blood counts.
NOTE Confidence: 0.98759824
00:21:54.040 --> 00:21:55.472 Thrombocytopenia or low platelet
NOTE Confidence: 0.98759824
00:21:55.472 --> 00:21:56.546 count in particular,
NOTE Confidence: 0.98759824
00:21:56.550 --> 00:21:59.430 was seen in 73% of patients and storm,
NOTE Confidence: 0.98759824
00:21:59.430 --> 00:22:01.220 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 nausha is really important with selinexor and 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 nausha, 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.
who have received at least four prior therapies including Apiai, Imid and an anti CD.

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 ant CD 38 monoclonal antibody and these patients studies were rent studied.

End of my story.

See if either a 2.5 milligram 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 a median time to response of 1.4 months, for Balanta map was 1.4 months, with 73% of those patients who achieved a response. Having it maintained at least 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 melphalan 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

00:27:03.151 --> 00:27:05.473 causing irreversible damage
NOTE Confidence: 0.9699676

00:27:05.480 --> 00:27:07.064 to the DNA of the tumor.
NOTE Confidence: 0.9699676

00:27:07.064 --> 00:27:10.430 That’s important for two.
NOTE Confidence: 0.9699676

00:27:10.430 --> 00:27:12.025 leads to cell death.
NOTE Confidence: 0.9699676

00:27:12.025 --> 00:27:14.420 Melphalan Fofana Mid is approved
NOTE Confidence: 0.9699676

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.

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.

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 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 flu. Fenamad 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 one most recently approved and this is the chimeric antigen receptor T cell or what is known
as CAR T cell therapy idake.

Excuse me, I to sell or idake.

I do sell Vic Loosle ore Ida Salandit, the brand name forward is referred to as a Beckman.

And the way that the car T and this product in particular works is that a patient’s own T cell,
a type of immune or white blood cell, is genetically modified by adding the chimeric antigen receptor or car that can then bind to the BCMA antigen present on myeloma cells. As previously discussed, there is activation and growth of
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, including 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 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.
usually over three days.

And I do cells then administered as an infusion over 30 minutes per infusion bag.

Importantly, there is a period of close monitoring after receiving Ida sell as well.

So the Karma trial was a multi center phase two trial that included patients who had received at least three prior therapies including Apiai, Imid and an anti CD 38 antibody.

Patients received I to sell at different dosages and of the 128 patients who received this therapy, 73% of them had a response with 33% 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 $300 \text{ to } 450 \times 10^6$ 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

and the bone marrow,

the most common side effects of

this treatment were low blood cell counts and what’s referred to as cytokine release syndrome, or the body’s response to this uncontrolled and.

Really excessive release of these proinflammatory cytokines that we discuss and this can lead to fever,

low blood pressure,

fast heart rate and low oxygen levels, among other symptoms.

Cytokine release syndrome occurred 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

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
Response in myeloma by looking both in the bone marrow and data myeloma bone lesions before and after. Therapy with carfilzomib, Lenalidomide and dexamethasone. And for those patients who are to receive maintenance therapy after undergoing a stem cell transplant but still have evidence of a low level of residual or remaining myeloma disease in the bone marrow, or what Doctor Barr defined as minimal residual disease, we do have a study looking at outcomes of adding again daratumumab to.
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.

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. The general side effects that are included in all of our treatments, 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.

So what we typically would do for a rash is use a steroid cream.

Or, depending on the how much the rash covers of the body or the symptoms from the rash.

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, sometimes 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. We saw a lot more side effects and most
00:39:00.707 --> 00:39:03.116 of these drugs are pretty well tolerated.

00:39:03.120 --> 00:39:05.087 At least we want them to be.

00:39:05.090 --> 00:39:07.834 So if you’re not tolerating them well then

00:39:07.834 --> 00:39:09.749 definitely reach out to us so we can.

00:39:09.750 --> 00:39:12.470 Make it easier for you to tolerate it,

00:39:12.470 --> 00:39:14.510 because once you’re started on treatment,

00:39:14.510 --> 00:39:16.782 we tend to keep you on therapy for

00:39:16.782 --> 00:39:19.276 life and want to make sure we can

00:39:19.276 --> 00:39:21.472 keep the disease under control while


00:39:25.820 --> 00:39:28.388 So proteasome inhibitors in general can

00:39:28.388 --> 00:39:30.560 cause gastrointestinal side effects mildly.

00:39:30.560 --> 00:39:32.288 Sometimes we hear nausea,

00:39:32.288 --> 00:39:33.582 vomiting, not commonly,

00:39:33.582 --> 00:39:36.599 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.

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 allocate it 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, you know, 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.  
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 monitor it throughout and then we 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, 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?
NOTE Confidence: 0.9375047
00:43:28.380 --> 00:43:30.382 And also reach out to us if
NOTE Confidence: 0.9375047
00:43:30.382 --> 00:43:31.830 that was to happen.
NOTE Confidence: 0.9375047
00:43:31.830 --> 00:43:34.194 You can also see lower extremity
NOTE Confidence: 0.9375047
00:43:34.194 --> 00:43:35.770 swelling with this one.
NOTE Confidence: 0.9375047
00:43:35.770 --> 00:43:37.750 We recommend compression stockings,
NOTE Confidence: 0.9375047
00:43:37.750 --> 00:43:40.225 elevating your legs and sometimes
NOTE Confidence: 0.9375047
00:43:40.225 --> 00:43:42.859 will give you a water pill or lay 6.
NOTE Confidence: 0.97588384
00:43:46.060 --> 00:43:48.426 OK, and the second class of medications
NOTE Confidence: 0.97588384
00:43:48.426 --> 00:43:51.306 that we use in combination or the
NOTE Confidence: 0.97588384
00:43:51.306 --> 00:43:53.098 immunomodulatory drugs or image.
NOTE Confidence: 0.97588384
00:43:53.100 --> 00:43:55.398 So the first one that was
NOTE Confidence: 0.97588384
00:43:55.398 --> 00:43:57.403 approved was the Little Mide
NOTE Confidence: 0.97588384
00:43:57.403 --> 00:43:59.749 and that was approved in 2006,
NOTE Confidence: 0.97588384
00:43:59.750 --> 00:44:01.976 but we were using it earlier
NOTE Confidence: 0.97588384
00:44:01.976 --> 00:44:04.050 and kind of off label,
NOTE Confidence: 0.97588384
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 or 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, 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.

So Speaking of full time, I’d the main side effects that we see are fatigue, Constipation, numbness and tingling. So those are the top three and then also we can see a slowed heart rate with it, which may be causing some other fatigue. We typically used it at lower doses when I was using this, when there wasn’t much else to use, we would use much higher doses and it was very difficult to tolerate at that time. But with the lower doses we can usually use it with minimal side effects and some of these medications to help so
00:45:59.238 --> 00:46:01.489 the same with them with the numbness
NOTE Confidence: 0.97652555
00:46:01.489 --> 00:46:03.479 and tingling in the gabapentin,
NOTE Confidence: 0.97652555
00:46:03.480 --> 00:46:04.752 Lyrica, and Cymbalta.
NOTE Confidence: 0.97652555
00:46:04.752 --> 00:46:07.720 And the typical things we want
NOTE Confidence: 0.97652555
00:46:07.801 --> 00:46:10.267 you to do if you’re constipated,
NOTE Confidence: 0.97652555
00:46:10.270 --> 00:46:13.366 so Senate police increased water fiber.
NOTE Confidence: 0.97652555
NOTE Confidence: 0.9766345
00:46:16.740 --> 00:46:19.233 And then learn a little made one of them
NOTE Confidence: 0.9766345
00:46:19.233 --> 00:46:21.600 are common side effects as diarrhea,
NOTE Confidence: 0.9766345
00:46:21.600 --> 00:46:23.220 especially the longer you’re on.
NOTE Confidence: 0.9766345
00:46:23.220 --> 00:46:25.604 It tends to be more of a cumulative
NOTE Confidence: 0.9766345
00:46:25.604 --> 00:46:27.760 effect and we do different things.
NOTE Confidence: 0.9766345
00:46:27.760 --> 00:46:29.958 First, we want to make sure that
NOTE Confidence: 0.9766345
00:46:29.958 --> 00:46:31.970 you’re not having diarrhea from a,
NOTE Confidence: 0.9766345
00:46:31.970 --> 00:46:34.875 you know a different cause like infection.
NOTE Confidence: 0.9766345
Or, you know, is it you know, did you develop an intolerance to lactose or something like that? Or high fat foods? So sometimes will alter the diet. Try Imodium, and if those don’t work, sometimes will add a medication called full listed which helps with the diarrhea associated with Lenalidomide. And then I put trash in here, even though we already talked about it, because it’s fairly common with Lenalidomide, and again, a lot of times we have to hold and reduce the 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 ilities
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%.
Matt is similar to the Dara and the E Lo is only about 10%. So to prevent these infusion reactions we premedicate with Tylenol, Benadryl and dexamethasone and with the first infusion we also give singular for Dara. And we give Pepcid for acid attacks in men. And most of the infusion reactions are very mild. We just stopped. Infusion treat the reaction and
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.

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 fast, the last one is steroids.
Everyone’s favorite dexamethasone. So this one is probably the hardest to tolerate just because of you know the weight. Gain the irritability. All these things that happened and trouble sleeping. 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. And primary care under friend ‘cause you can see steroid induced diabetes.
Excuse me

So in summary, treatment for myeloma is generally well tolerated now with a lot of better and the like since 2005. Prior to 2005, I think it was, more of the traditional chemotherapy with hair loss, nausea, vomiting, a lot of 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
or not these slides would be made available, and the video of presentation will be posted at the yalecancercenter.org website, and a copy of the slides can be requested by emailing cancer answers at yale.edu. Emily, which we can hopefully if everyone were interested in obtaining a copy. I think that answers to our questions on our chat and one of the first questions that we had and that maybe Doctor Barkin answer was regarding where a Lam Lloyd fit on the spectrum of EM guys, 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.
00:55:15.903 --> 00:55:18.950 obtained if he would like her copy.
NOTE Confidence: 0.9604375
00:55:18.950 --> 00:55:21.386 And we had a few questions.
NOTE Confidence: 0.9604375
00:55:21.390 --> 00:55:23.826 Then over in the Q&A that
NOTE Confidence: 0.9604375
00:55:23.826 --> 00:55:25.450 whoever wants to tag,
NOTE Confidence: 0.9604375
00:55:25.450 --> 00:55:27.977 take a stab at them regarding the
NOTE Confidence: 0.9604375
00:55:27.977 --> 00:55:30.052 effectiveness of the COVID vaccine
NOTE Confidence: 0.9604375
00:55:30.052 --> 00:55:32.347 for our multiple myeloma patients,
NOTE Confidence: 0.9604375
00:55:32.350 --> 00:55:34.400 and what precautions should someone
NOTE Confidence: 0.9604375
00:55:34.400 --> 00:55:37.086 still be taking either around other
NOTE Confidence: 0.9604375
00:55:37.086 --> 00:55:39.358 vaccinated or unvaccinated individuals?
NOTE Confidence: 0.9604375
00:55:39.360 --> 00:55:40.722 So I don’t know who wants
NOTE Confidence: 0.9604375
00:55:40.722 --> 00:55:42.000 to brave the COVID world.
NOTE Confidence: 0.95552003
00:55:42.940 --> 00:55:46.468 I can answer that one, so I think it’s
NOTE Confidence: 0.95552003
00:55:46.468 --> 00:55:48.428 obviously a very important question,
NOTE Confidence: 0.95552003
00:55:48.430 --> 00:55:51.686 and I think you know we’re learning more
NOTE Confidence: 0.95552003
00:55:51.686 --> 00:55:54.700 about it as time goes on, you know,
I think studies have suggested that patients with 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 and I 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
00:57:00.552 --> 00:57:01.980 get in healthier population.
00:57:01.980 --> 00:57:04.056 But there are also very significant
00:57:04.056 --> 00:57:06.270 cell responses in their immune cells,
00:57:06.270 --> 00:57:08.678 T cells and some of the T cells
00:57:08.678 --> 00:57:10.908 and B cell responses and.
00:57:10.910 --> 00:57:12.854 And that’s what provides protection to
00:57:12.854 --> 00:57:14.830 model of patients after vaccination.
00:57:17.960 --> 00:57:19.590 Yeah, I think to follow
00:57:19.590 --> 00:57:21.450 the group
00:57:21.528 --> 00:57:23.818 at Mount Sinai published some
00:57:23.818 --> 00:57:26.108 of their findings just recently.
00:57:26.110 --> 00:57:28.588 Actually, on the 28th of this month
00:57:28.588 --> 00:57:31.383 and they had looked at 320 individuals
00:57:31.383 --> 00:57:33.861 who had had the COVID vaccine,
00:57:33.870 --> 00:57:36.579 260 of them received either the Pfizer,
the Moderna, so the two dose and what they had shown was about 16%.

Fifteen point. Eighty percent of patients did not mount any detectable antibodies compared to the other eighty-four.

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

That. OK, and we have some other questions. I think two regarding acyclovir are whether or not an individual and 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 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, involved with car T therapy, so there is hospitalization 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 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,
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 benefit. 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. If there is no progression. So yes, time is important, but it gives us information about the behavior for disease. Great so I love that line of questions. We did have some questions that had come in before the presentations.
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 M Gus. When we look at somebody with smoldering myeloma,
we want to understand their risk and you know, 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. I think when we get this question, 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 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.

It’s not an FDA approved, UM.

A way to do things,

but I think it’s in the research world.

I would recommend it.

Yeah, I would agree with that I.

I think it’s not a part

of our standard practice,

but I think there’s a lot to learn

from that and I agree that no

incorporation of that into clinical

trials moving forward is important

and I think will be enlightening and

how to best guide our treatments.

As you saw, for patients who have

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 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 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. If we could know how to target different,
01:07:09.420 --> 01:07:10.695 you know, specific patients that
NOTE Confidence: 0.9877601
01:07:10.695 --> 01:07:11.970 have different mutations and things,
NOTE Confidence: 0.9877601
01:07:11.970 --> 01:07:13.580 but I don’t know how far they
NOTE Confidence: 0.9877601
01:07:13.580 --> 01:07:15.030 are like getting this approved.
NOTE Confidence: 0.983915199999999
01:07:20.600 --> 01:07:23.288 Great, so it sounds like more to come
NOTE Confidence: 0.983915199999999
01:07:23.288 --> 01:07:26.081 and then again one last question that
NOTE Confidence: 0.983915199999999
01:07:26.081 --> 01:07:29.225 was submitted ahead of time which was
NOTE Confidence: 0.983915199999999
01:07:29.225 --> 01:07:31.269 dealing with solitary plasmacytomas
NOTE Confidence: 0.983915199999999
01:07:31.269 --> 01:07:34.172 and specifically what is the risk
NOTE Confidence: 0.983915199999999
01:07:34.172 --> 01:07:36.302 of progression to multiple myeloma
NOTE Confidence: 0.983915199999999
01:07:36.302 --> 01:07:38.560 with the solitary plasmacytoma?
NOTE Confidence: 0.983915199999999
01:07:38.560 --> 01:07:42.010 And and so I don’t know if Doctor Bar you
NOTE Confidence: 0.983915199999999
01:07:42.104 --> 01:07:45.310 wanna take that or doctor Pepper eats.
NOTE Confidence: 0.9749503
01:07:49.890 --> 01:07:52.576 I’m sorry, can you rephrase the question?
NOTE Confidence: 0.9749503
01:07:52.576 --> 01:07:55.180 Yes, so the question that was submitted
NOTE Confidence: 0.9749503
01:07:55.245 --> 01:07:57.375 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
promote that progression?

I think the Nordic Group had looked at some of the angiogenesis risk factors and they did not identify many risk factors, but there one of them was the badger, which is the endothelial blood vessel. Type of. Inflammatory or angiogenesis mediator, but it’s not something that we routinely test, and there’s no other easy ways of making that prediction, and so they the mainstay of monitoring would be just periodic surveillance initially at every three months, and subsequently at every six months.
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 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

any additional ones in the QA or chat.

So if anyone has any last minute questions please submit those now.

If not but we can wipe things as down and thank you all for your attention.

and thank you to all the panelists.

Thank you very much everybody.

Great talks everyone.

Thanks for joining. Bye.