**TRANSCRIPT**

## WELCOME AND INTRODUCTION


***Lizette Figueroa-Rivera, MA***

Hello, everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. Philip L. McCarthy for sharing his time and expertise with us today. We have over 1,000 people participating in today's program from across the United States and Canada.

Before we begin, I'd like to introduce Dr. Louis DeGennaro, The Leukemia & Lymphoma Society's President and Chief Executive Officer (CEO), who will share a few words.

***Dr. Louis DeGennaro, PhD***

I'm Dr. Louis DeGennaro, President and CEO of The Leukemia & Lymphoma Society. I'd like to welcome all of the patients, caregivers and healthcare professionals attending the program today.

At The Leukemia & Lymphoma Society, our vision is a world without blood cancers. Since we started in 1949, LLS has invested more than $1.2 billion in breakthrough research to advance life-saving treatments and cures. We've played a pioneering role in funding many of today's most promising advances, including targeted therapies and immunotherapies that have led to increased survival rates and improved the quality of life for many blood cancer patients.

Though LLS is known for funding ground-breaking research, we do so much more. As this program demonstrates, we are the leading source of free blood cancer information, education and support for patients, survivors, caregivers, families and healthcare professionals. We also support blood cancer patients in their local communities through our chapters across the country. And we advocate at the

state and federal level for policies to ensure that patients have access to quality, affordable and coordinated care. We're committed to working tirelessly toward our mission every single day.

Today, you'll have the opportunity to learn from esteemed key opinion leaders. They each have volunteered their time, and we appreciate their dedication to supporting our mission, their commitment to caring for patients living with blood cancers.

Thank you for joining us.

***Lizette Figueroa-Rivera, MA***

We would like to acknowledge and thank Amgen, Celgene and Takeda Oncology for support of this program. Following the presentation, we will take questions from the audience.

**TRANSCRIPT**

## PRESENTATION

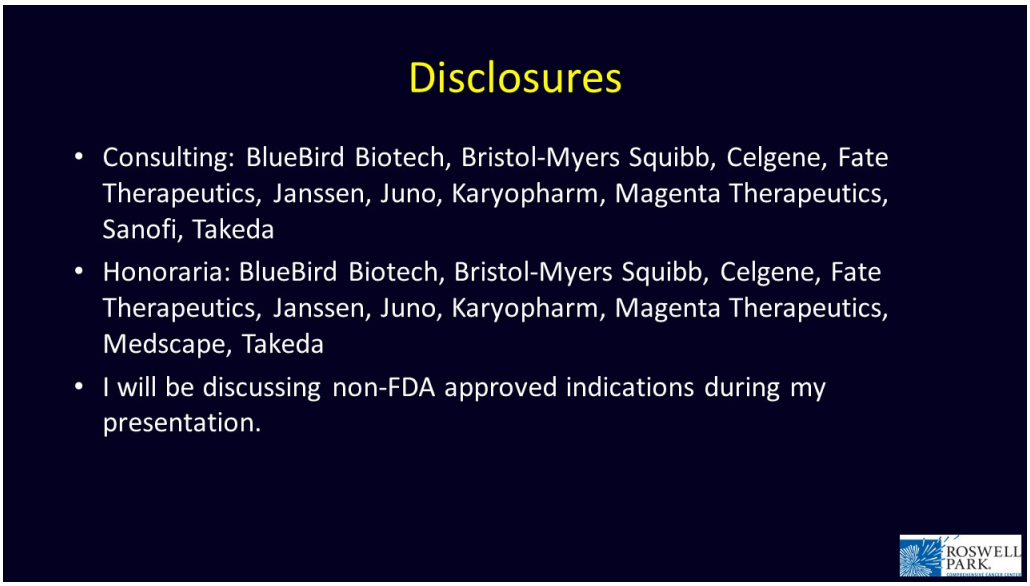
***Lizette Figueroa-Rivera, MA***

I'm now pleased to introduce Dr. Philip L. McCarthy, Professor of Oncology and Internal Medicine and Chief of Transplant and Cellular Therapy Program at Roswell Park Comprehensive Cancer Center SUNY at Buffalo in Buffalo, New York.

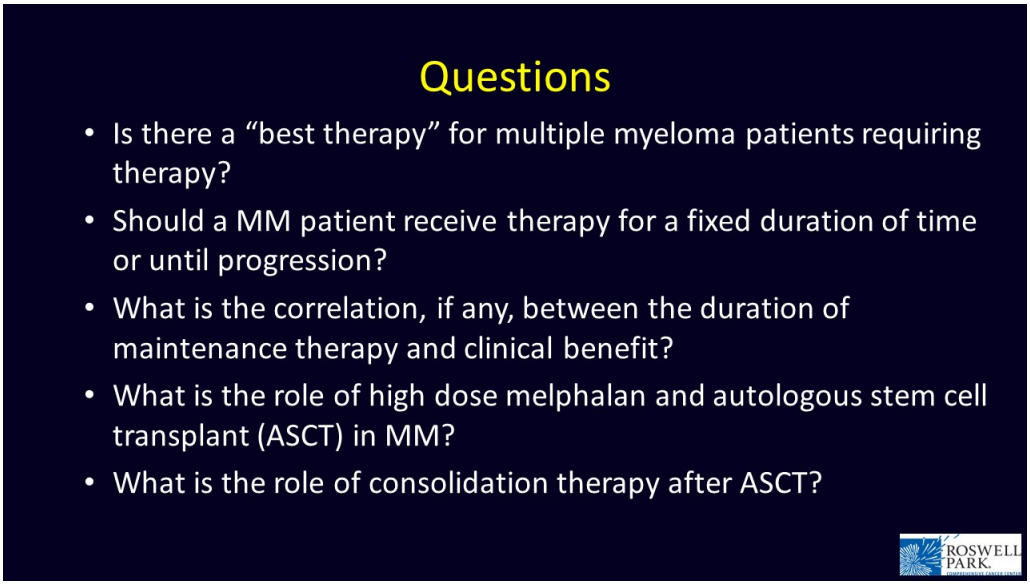
On behalf of The Leukemia & Lymphoma Society, thank you for volunteering your time and expertise with us, Dr. McCarthy. I'm now privileged to turn the program over to you.

***Philip L. McCarthy, MD***

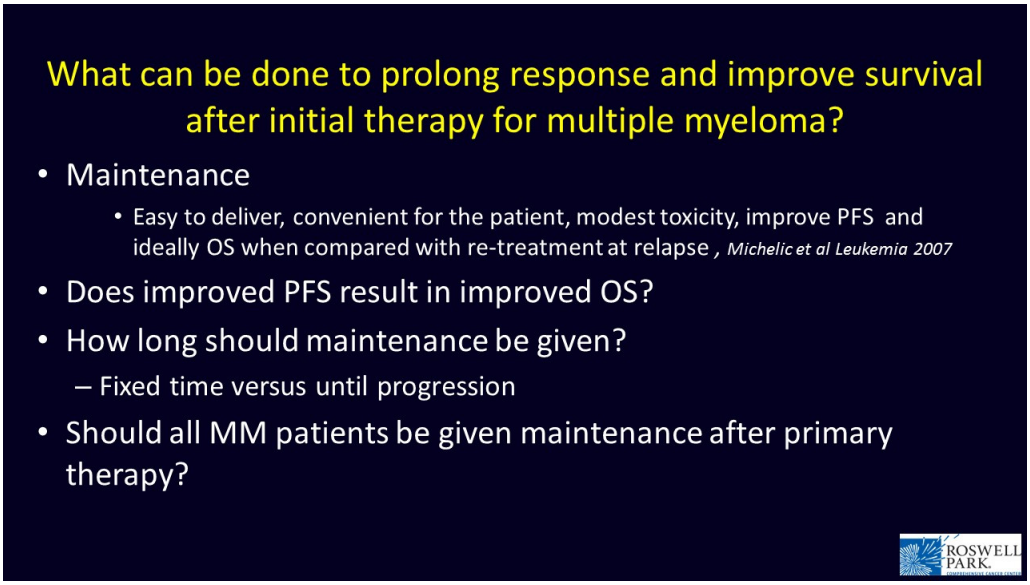
Thank you very much. I really appreciate the opportunity to do this. One thing I should warn you is there are a lot of slides. And I may go fast through some of them, but as was noted, these will all be posted on the Internet and so you'll be able to go back and read them because some of this is background, and I find it's sometimes useful to have background to understand some of the data that I'll be presenting.



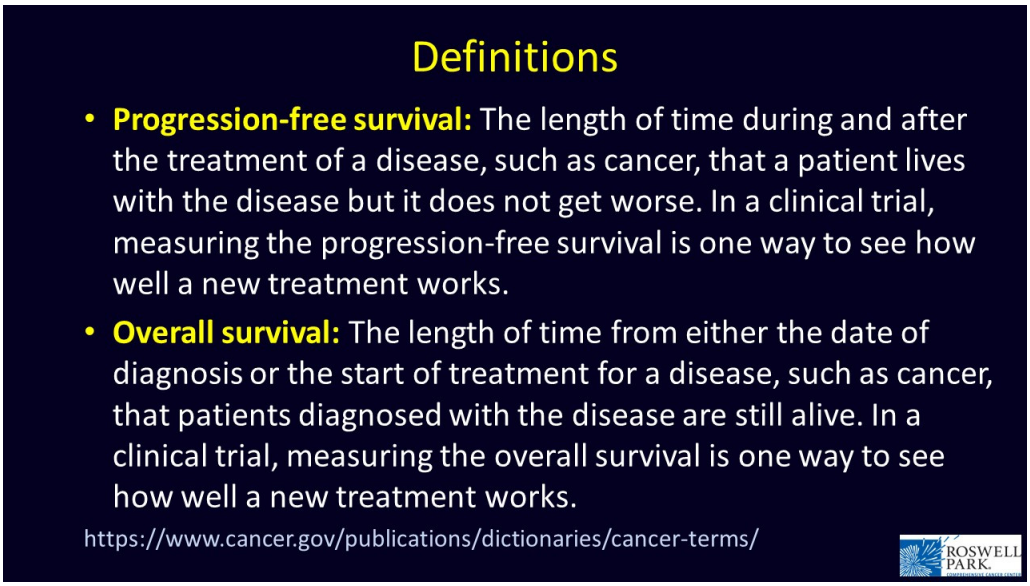

So, these are my disclosures. I'm consulting for these companies' honoraria, and I will be discussing non-FDA approved indications during my presentation, but I'll make sure I let you know that when that happens.




So, we can start with some questions, is there a best therapy for multiple myeloma (MM) patients requiring treatment? And should a patient receive therapy for a fixed duration of time or until progression? So, what is the correlation, if any, between the duration of say maintenance therapy and clinical benefit? What's the role of stem cell transplant in myeloma? And what's the role of consolidation therapy? This would be for upfront patients.



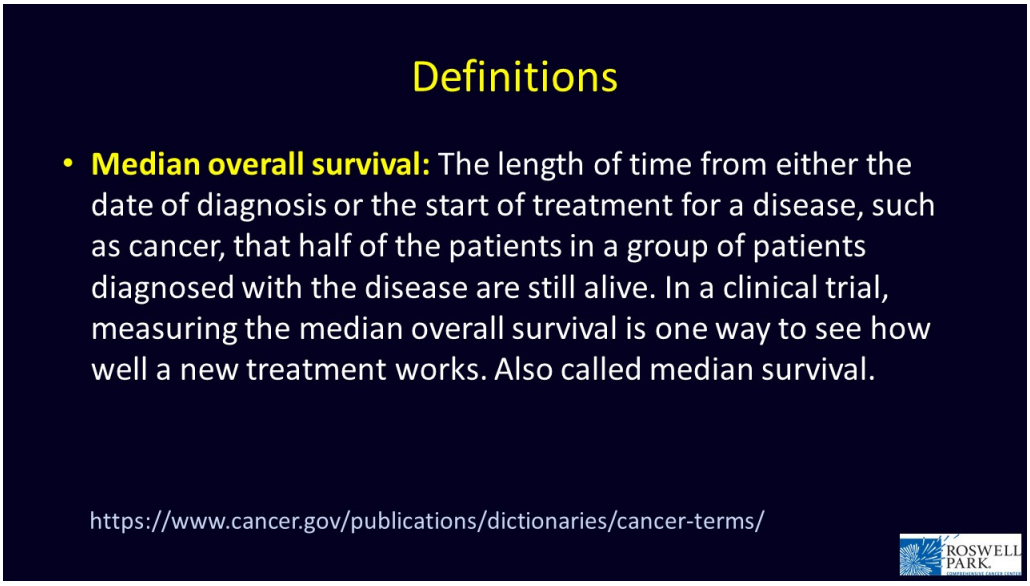

So, what can be done to prolong response? If a patient requires therapy, will we prolong the response and improve survival after initial therapy? So, these are some of the principles for maintenance. It has to be easy to deliver, convenient, minimal toxicity, improve progression-free survival (PFS) and, ideally, overall survival (OS) when compared to retreatment at relapse. And what we really need to know is if you have an improved progression-free survival, will that result in improved overall survival? And for patients getting maintenance, how long should it be given? Is it a fixed time versus until progression? And should all patients get maintenance after primary therapy?



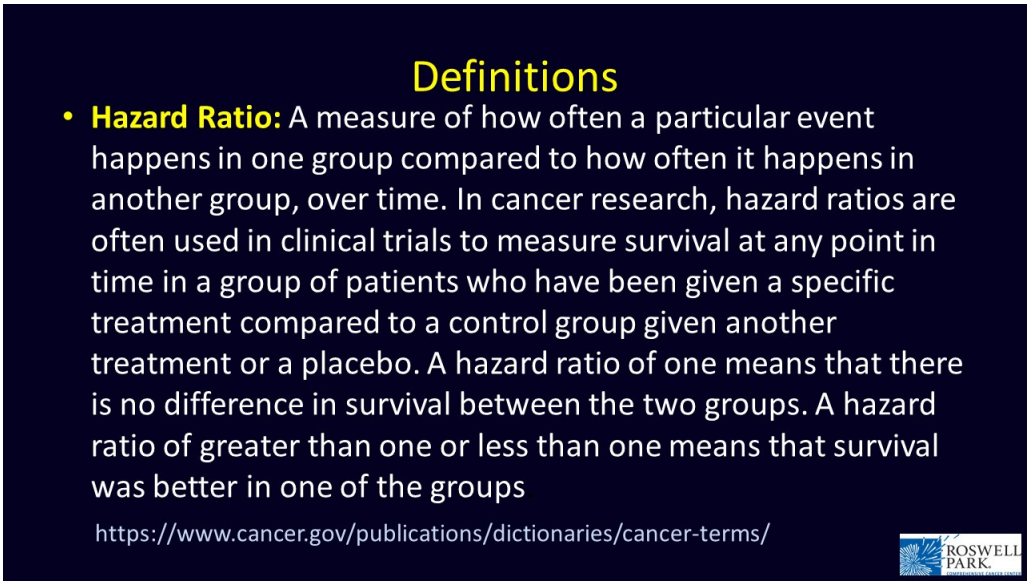

But first I'm going to do some definitions because we use these terms, but I thought it would be useful to have them. And, again, you can go back later on and read them in more detail if you would like.

PFS or progression-free survival is the length of time during and after the treatment of disease, such as cancer, that a patient lives with the disease but does not get worse. And a clinical trial measuring PFS is one way to see how well a new treatment works. So, you can either go into remission and then have progression later on, or you can have just low-level disease. It is stable, but then it starts to come back, and that also fulfills criteria for now the patient has progression.

Overall survival is actual survival, so it's the length of time from either the date of diagnosis or the start of treatment for disease, such as cancer, that patients diagnosed with the disease are still alive. And a clinical trial measuring overall survival is one way to see how well the new treatment works. And this is from *cancer.gov* publications, so you can go on the Web and find this.

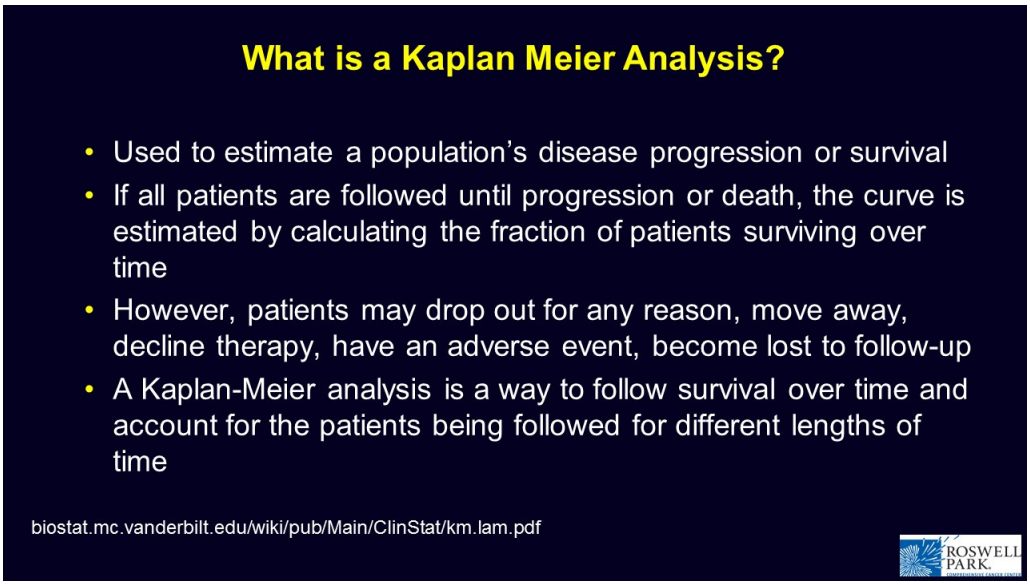



Now another term that people will use is median overall survival, and this is the length of time from either the date of diagnosis or start of therapy that half the patients in a group diagnosed with the disease are still alive. So, if you have 100 patients and 50 have died within three years, the median overall survival is three years. And this is one way to measure how well a new treatment works. We can also do median progression-free survival.

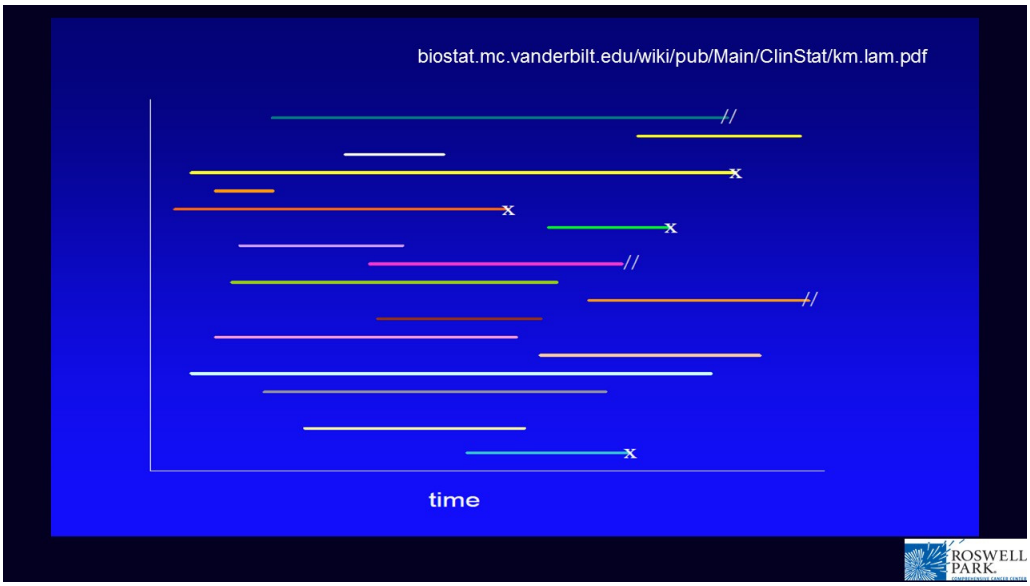



Now a hazard ratio is something else. I won't go over it in great detail, but you'll see a lot of presentations, especially if it's reading a paper or going to a clinical presentation where a hazard ratio will be given. And it's a measure of how often a particular event happens in one group compared to how often it happens in another group over time. So, example, for the control group versus the study group. And in cancer research, hazard ratios are used to measure survival at any point or progression-free survival in a group of patients who've been given a specific treatment compared to a control group. And a hazard ratio of one means they're equivalent. Whereas, if there's a hazard ratio

of greater than one or less than one, that means that one of the groups has a superior survival or progression-free survival.

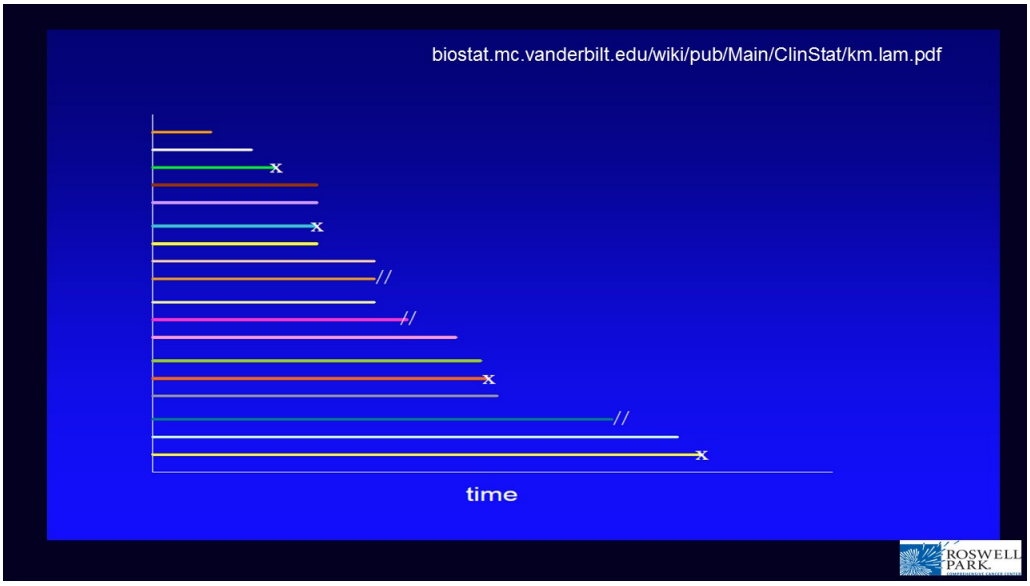



And then, lastly, Kaplan-Meier. Kaplan-Meier were two statisticians, and Kaplan-Meier analysis is used to estimate a population of disease progression or survival. If all patients are followed until progression or death, the curve is estimated by calculating the fraction of patients surviving over time or not having progression over time. However, patients drop out – they move away, they have toxicity. They may decline further therapy, have an adverse event, and so we need to account for dropout. And so, Kaplan-Meier analysis does this in the cancer patients over time. So, this is, simply put, how this is done.

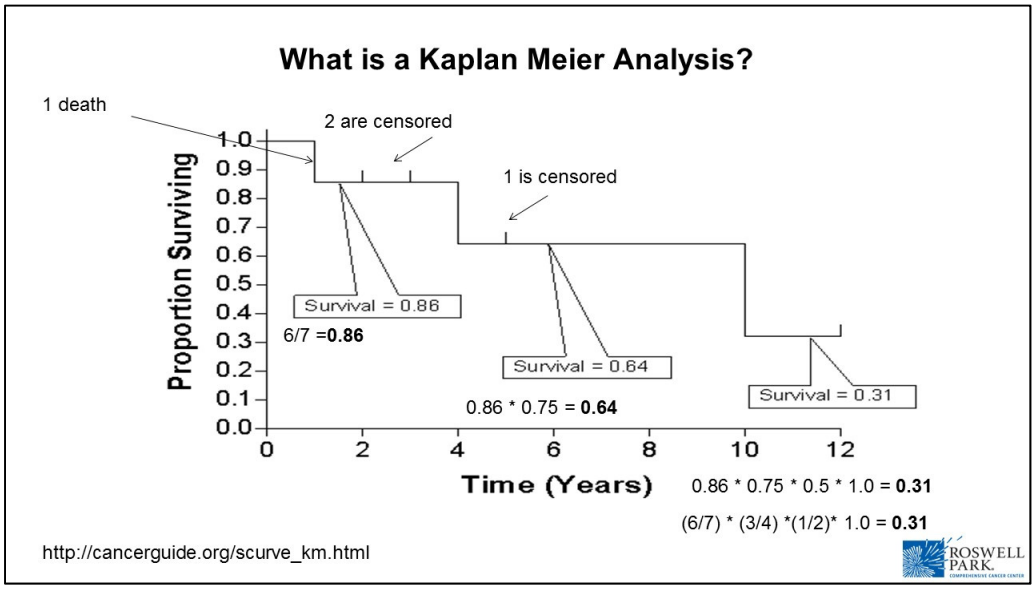



So, you have a group of patients who are all starting therapy on the left at different times. And you can see that the double slash forward is an event. And in this case, we'll say it's an adverse event. The X means that the patient has either had progression or death. And you can see that there's

different lengths of time. Some of these patients, if you look three from the bottom of the gray line, the patient started therapy on the left and is still on therapy but has not reached a timepoint that some of the other patients have because they started a little bit later. So, a Kaplan-Meier curve helps account for this.

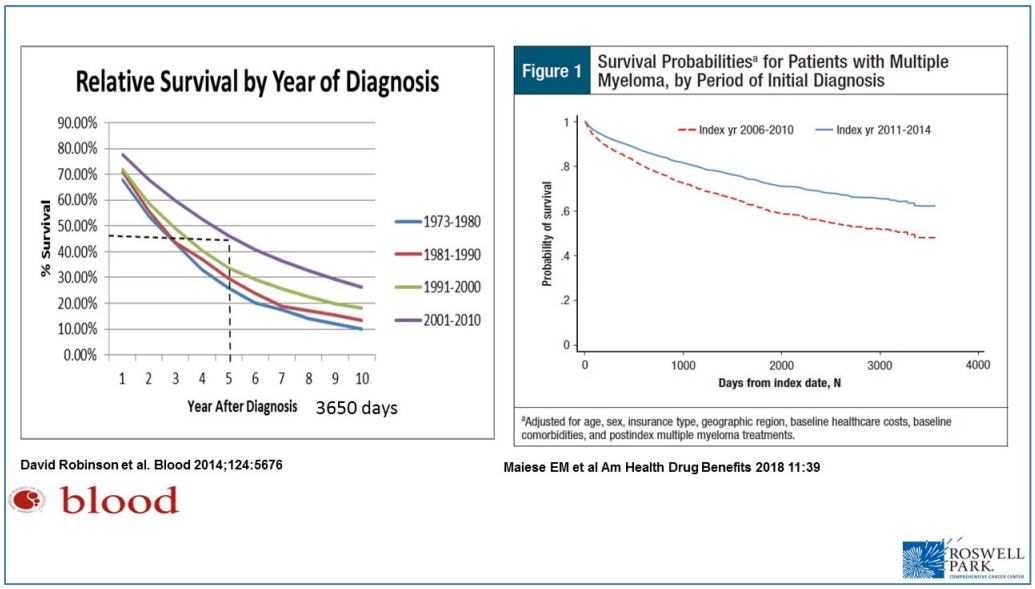



And what happens is the Kaplan-Meier takes all these patients and puts them as if they all started treatment on the same day, so now you can see how they've all lined up. And this allows for an analysis to account for these differences in start times. And you can see it here very simply put a Kaplan-Meier analysis.

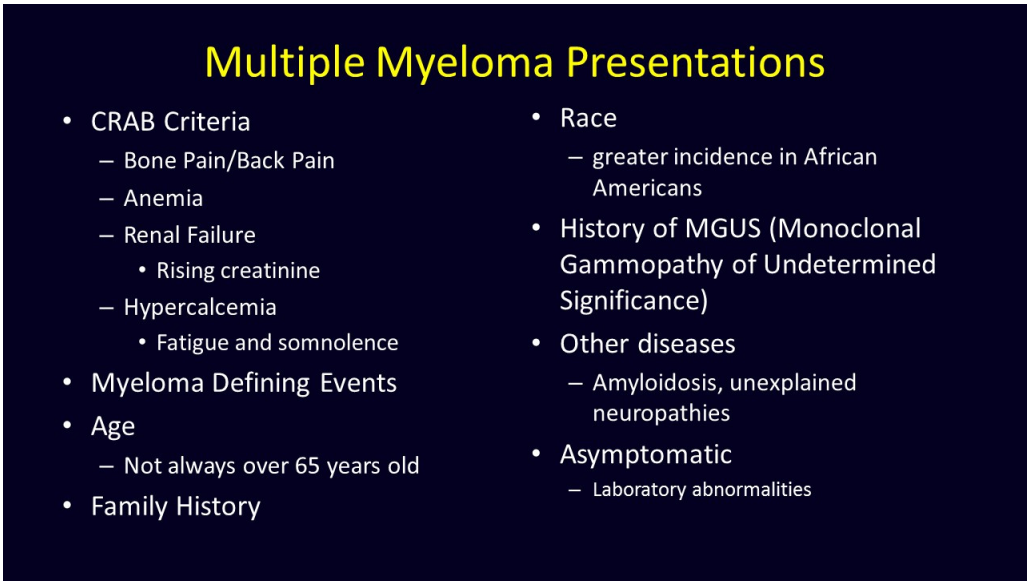



And here you can see on the left where everybody starts at one, you have 100% of patients who are surviving, but then there is a death and it drops down, is a stepdown, and then you can see that they were censoring. These are patients who they've moved away, they had an adverse event. So, you

don't count them as a death, but you have to account for them because they no longer are being considered for an overall survival. And you can see how this steps down over time.



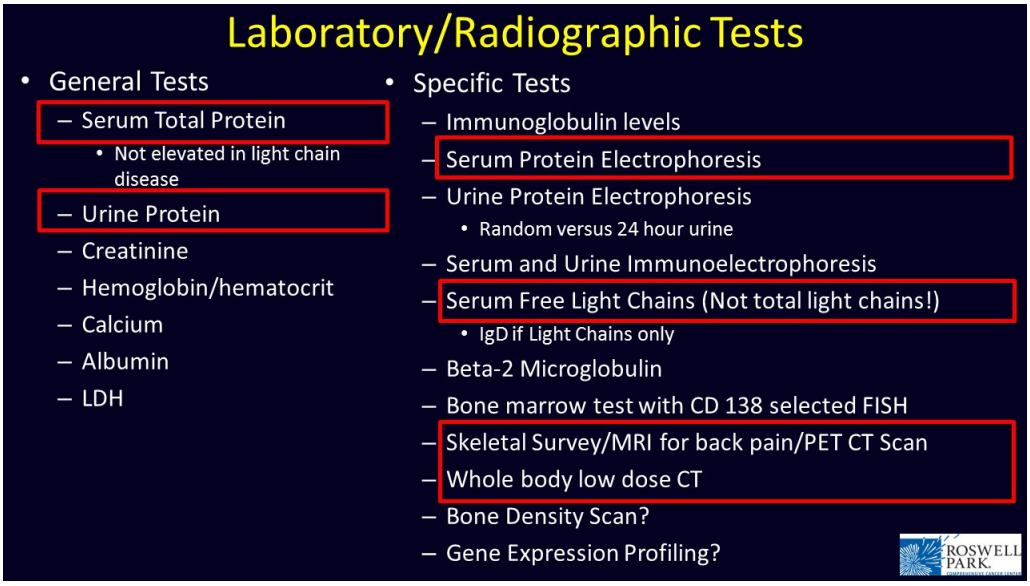

And the reason why it's important to know this is in the next slide these are Kaplan-Meier curves which talks about the survival of myeloma patients over time at different eras. So, if you look at this, this is a slide from David Robinson et al, *Blood* 2014, and you can see here over a ten-year period, if you look in the blue line at the bottom, that's the survival, year of diagnosis from 1973 to 1980. And if you look at the top curve in purple, that's from 2001 to 2010. So, you can see that the median survival has improved over time. It went from in the '80s, the median survival was about three years; now it's over five years. And if you look over on the right-hand side, you can now see going from 2006 to 2010 and then 2011 to 2014 you again see an improvement in overall survival as demonstrated in the Kaplan-Meier curve. So now the median overall survival for transplant-eligible patients is approaching ten years. And that's, obviously, an improvement. We need to do better, but this is how we measure this and, actually, how we show it graphically.



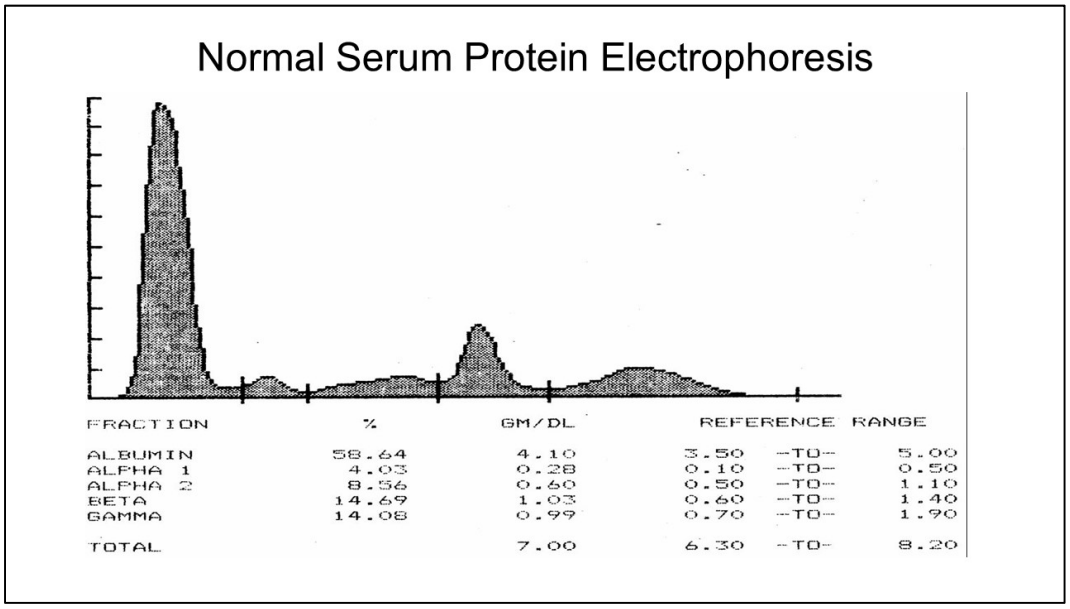

So, now I'm going to turn to myeloma presentations. I'll go through this fairly quickly. I know some of you, unfortunately, have had to experience some of these things. The CRAB criteria, which is high calcium, renal failure, anemia and bone disease. Often myeloma will present with bone pain, anemia, kidney problems or high calcium. And there are things called myeloma-defining events where you will have organ involvement but without some of the other criteria for myeloma. So, for example, kidney problems where the kidney starts spilling protein and the patient's not in renal failure, but the kidneys are leaking protein because of protein infiltration by the plasma cell product in the kidneys.

Age, these are not patients always over the age of 65. The average age is around 70, but there are young patients who get this disease. It can run in families. It's more common in African Americans, we can talk about that later. Most of the time these patients will have a history of monoclonal gammopathy of undetermined significance (MGUS). In other words, small amounts of protein which grow over time. It's just that not all MGUS patients will progress to myeloma but a significant percentage of them will. There are other diseases such as amyloidosis, unexplained neuropathies and then sometimes there are just laboratory abnormalities and the patient has no symptoms at all.

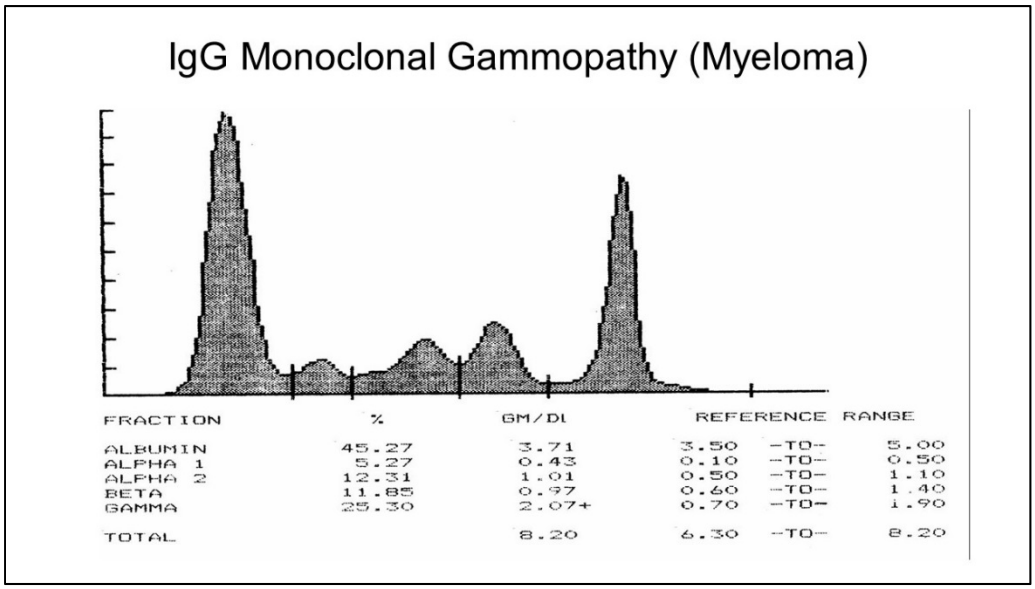
## TRANSCRIPT




These are some of the tests we'll get. You may hear about this from your clinical team. Oftentimes, the referring doctor will send the patient to a hematologist/oncologist for evaluation because they have a high total protein in the serum. However, a high total protein is not seen in patients with light chain only disease. I'll show you that in a little bit. Urine can be checked for protein, kidney function, hemoglobin and hematocrits for anemia, calcium, albumin and LDH (lactate dehydrogenase), which is a marker of cell proliferation. Specific tests are immunoglobulin levels, serum protein electrophoresis (SPEP) – I'll show you a picture of that - urine protein electrophoresis (UPEP), again, looking for protein, and immunoelectrophoresis (IEP), which specifically defines which one. There's something called serum-free light chains (SFLC), which have become very important over the last ten years, beta-2 microglobulin (B2M), a bone marrow test with something called CD138 selected FISH (fluorescence in situ hybridization), and I'll explain to you what FISH is, a skeletal survey which is now really being more an MRI (magnetic resonance imaging) or a PET CT (positron emission tomography computed tomography), and I'll show you why this is important. Sometimes whole body, low-dose CT is done, bone density scan for osteopenia, which myeloma can cause bone loss. And then there is some molecular testing for helping us risk stratify high risk versus low risk.

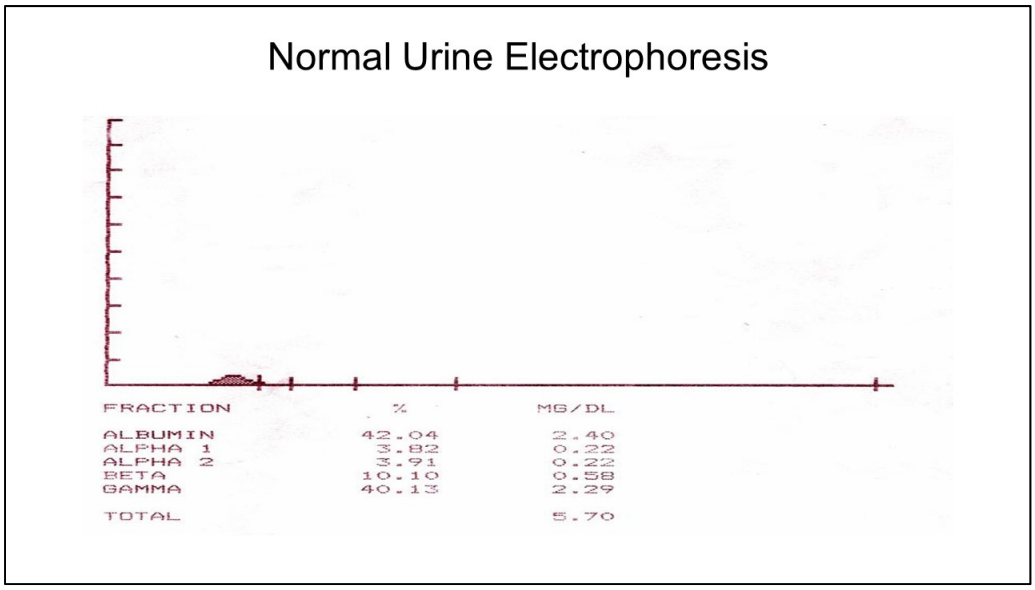



Now this is a serum protein electrophoresis. I don't know if any of you have seen these things. We do this for all our patients. And what this involves is taking a small amount of serum, putting it in a gel and then running an electric current. And then some of the proteins migrate at different points. On the left-hand side is something called albumin that has the highest peak. And then you can see other peaks that go over to the far right. The far right is the gamma region. And, as we do a lot in medicine, instead of saying, "One, two, three, four," we go, "Alpha 1, alpha 2, beta and gamma," because like to do things in Greek. Why do we do that? It's a long history.

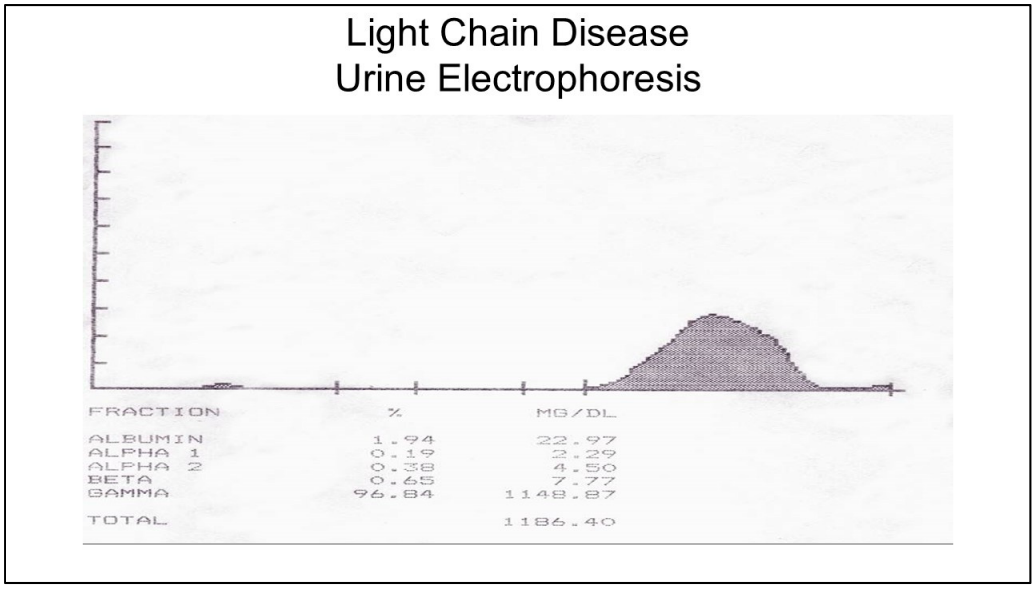



So, if you look, this is a normal pattern. But pay attention to the right-hand side please. You'll see now the albumin on the left, but you'll see this big spike on the right. And this is the monoclonal protein. So, this is an IgG monoclonal gammopathy and this is the patient with myeloma. Why? Because this is a very high peak. Sometimes this peak is a little bit smaller than this and that could be MGUS. But

this is the types of things that the laboratory will send back to the treating physician to help them understand whether or not the patient has the monoclonal gammopathy.




What you'll also see is patients will have a urine electrophoresis. And some of you may have had a 24-hour urine collected. There's the thought that serum-free light chains may be able to replace this, but we still do them on occasion. So, here's a normal one. There's a tiny bit of albumin here on the left.




And now you'll see there's a tiny bit of albumin here on the left, but on the right there's this big, old hill. And that hill is full of light chains. So, this is somebody who has light chain disease where instead of a total immunoglobulin being produced, only a portion of the immunoglobulin is being made and that's called the light chain. And that's being excreted into the urine.

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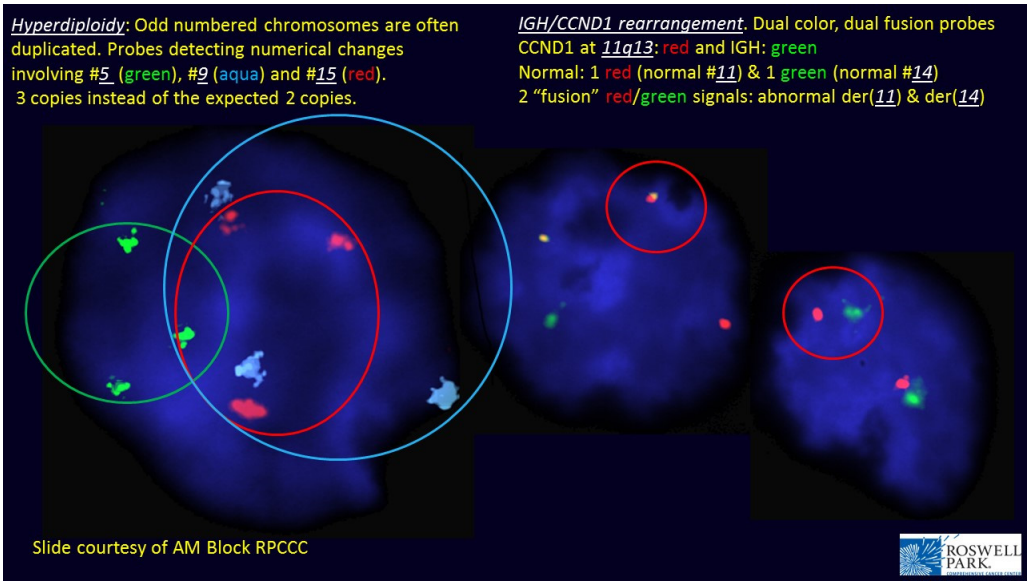


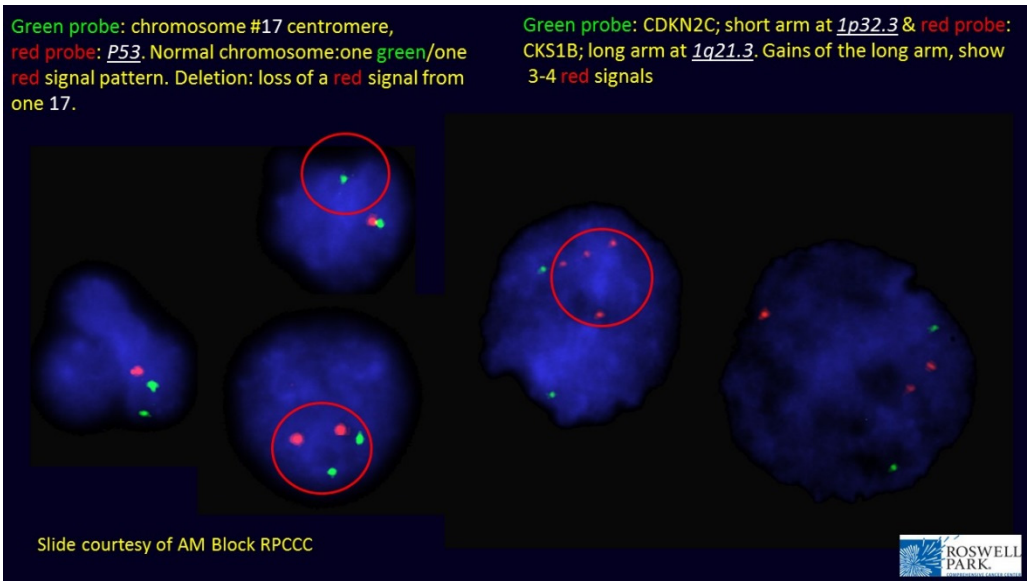

So, I mentioned FISH before. FISH stands for fluorescence in situ hybridization. And what that is the laboratory people take a piece of a known chromosome and they light it up with a color. And so, by lighting it up with a color, it allows to light up a cell to see what the chromosome configuration is. And by CD138 selection, CD138 is on plasma cells. And so, what the laboratory is doing is they're gathering all the plasma cells and then looking at the chromosomes within the plasma cells. In the old days, we used to not do this selection, and we really had, I would say, essentially worthless information. Now that we have this fluorescence in situ hybridization on CD138 cells, we gather a tremendous amount of information.

And what we see here is we have a patient who has something called hyperdiploidy. Normally, you would expect two green chromosomes, but this patient has three. So, this is known as a trisomy and this is chromosome 5 where there were three copies of chromosome 5.

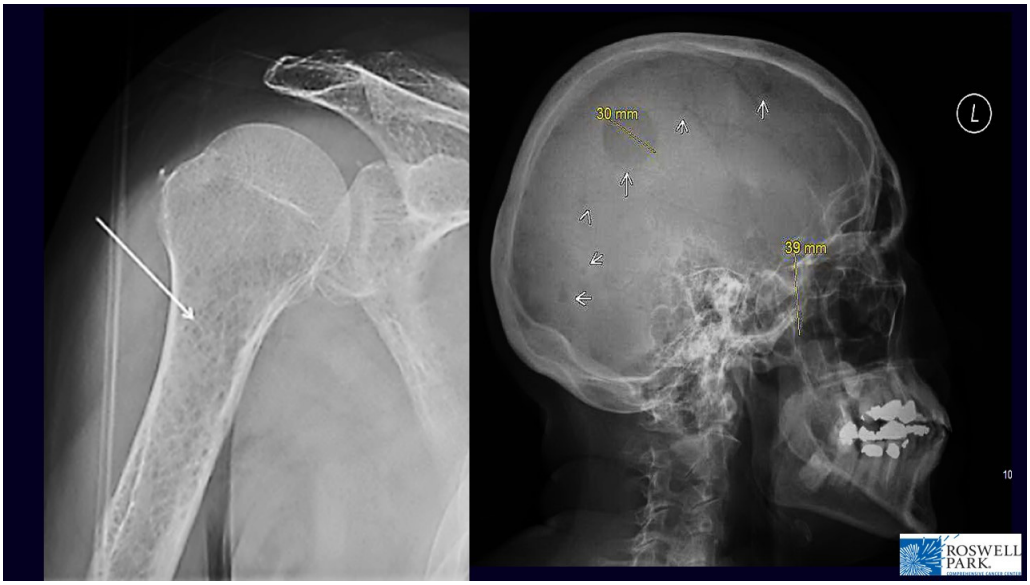
If you look at the next one, now you see three copies of blue, and that's chromosome 9, and three copies of red, and that's chromosome 15. So instead of having two chromosomes, this cell has three. And this is called hyperdiploidy, too many chromosomes, also known as trisomy's where there were three. Disomy would be two. So, this is seen in some myeloma patients' plasma cells.

Now on the right, you'll see something a little different. This is a translocation. So, this is the dual colored, dual fusion probes. There's one at chromosome 11 and then one at chromosome 14. Chromosome 11's in red, chromosome 14 is in green. So, what you would normally see here on the right, you'll see the cell with two green signals, two red signals. And on the left what you see is a green signal and a red signal, but now you see something different, and this is a fusion where the green and the red have come together. A part of chromosome 11 has gone next to chromosome 14 – this is the translocation - and you see this fusion color where it's sort of reddish and yellow. I guess it's brown. So, what you're seeing here now is a translocation here normal and now you're seeing the translocation. So, the laboratory will come back to the clinician and say, "This patient's myeloma has a translocation 11;14." And this is very important for some patients because 11;14 translocations are actually potentially going to be treated with a drug called venetoclax. And I could talk about that later

on. But we're now beginning to use this also to risk stratify because there are certain chromosome abnormalities that are more associated with high-risk or with low-risk disease.

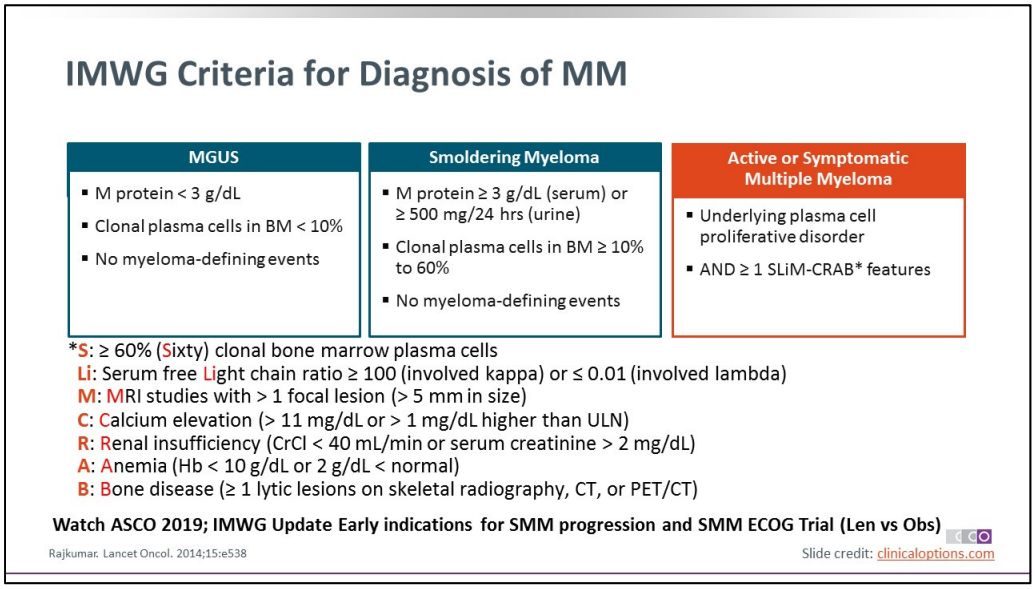



Ah, one more. This is chromosome 17. This is a little bit thought to be more high risk. Here you see a normal, two reds, two greens, but you'll see in this one there's two greens, but it's missing a red. So, what's happening is you've lost a signal and that red signal is one chromosome 17. And you'll see it here. Now you'll see chromosome 1p red pro. And now what you're seeing is a duplication, so instead of seeing two, you're now seeing four. So, this is something that would be considered abnormal, and it's a 1p gain. And if you lose a 1q, you would have a deletion. This is in this case is a 1p reduplication. These are very important because it allows the clinician to (A) track the disease and also, potentially, risk stratify, or consider the patient's risk for recurrence.




Now this is old school. This is a skeletal survey. So, this is an X-ray of a patient's head, and you can see the skull. And you'll see this lucency here, this dark spot. This is a myeloma lesion which has

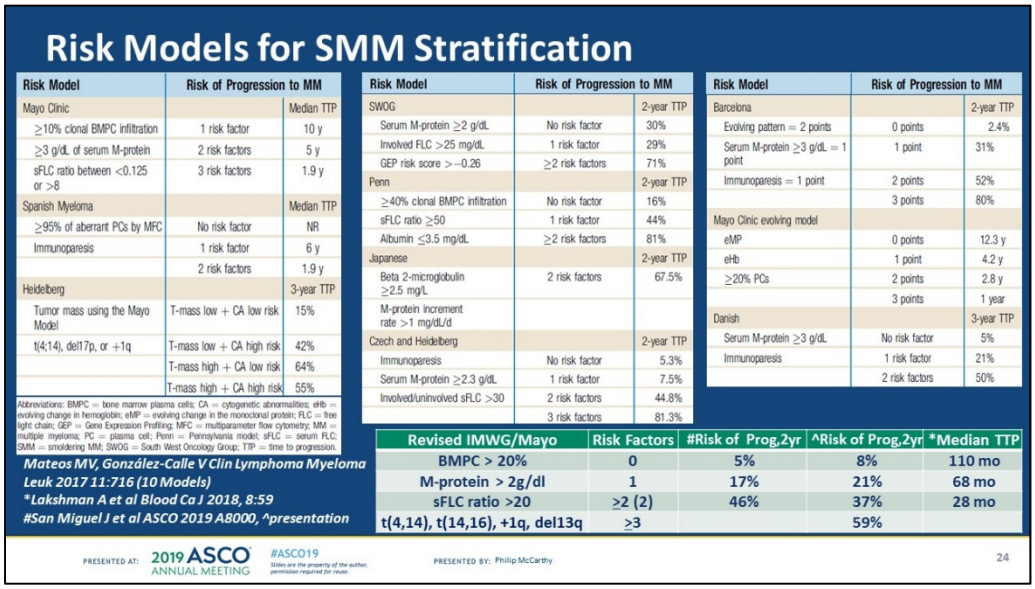
punched a hole in the skull. It won't be in the brain, but it will be in the skull. And you'll see over here in this patient, you'll see this muddled appearance. This is another way the myeloma can present where it is destroying the bone and it looks not quite like Swiss cheese, but it's a muddled appearance where there are small holes in the bone where they myeloma has caused bone destruction. We now are looking more at MRI and PET CT, and these are thought to be better tests for helping us establish the diagnosis and then follow the patient after response.




These are IMWG criteria for the diagnosis of myeloma, the International Myeloma Working Group. Monoclonal gammopathy of undetermined significance, less than 3 grams of protein in the urine and in the blood, small amount of plasma cells that are abnormal in the bone marrow, and no myeloma-defining events, those CRAB criteria.

Smoldering myeloma traditionally has been thought to be greater than 3 grams, a higher amount of protein in the urine, 10 to 60% plasma cells in the bone marrow and no myeloma-defining events. I'll show you some data that suggests that may be changing that was just presented at the last ASCO or American Society of Clinical Oncology meeting.

And then lastly are symptomatic myeloma patients. These are people who have CRAB criteria. There's the thought that slim CRAB – it's Joe Mikhael, MD, Med, FRCPC, FACP, who came up with this – greater than 60% clonal cells, light chain ratio that's very high or very low, depending on which light chain is abnormal, and all MRI studies, magnetic resonance imaging, showing that there is more than one lesion in the marrow.



## Risk Models for SMM Stratification

| Risk Model | Risk of Progression to MM | |
|---|---|---|
| Mayo Clinic | | Median TTP |
| ≥10% clonal BMPC infiltration | 1 risk factor | 10 y |
| ≥3 g/dL of serum M-protein | 2 risk factors | 5 y |
| sFLC ratio between <0.125 or >8 | 3 risk factors | 1.9 y |
| Spanish Myeloma | | Median TTP |
| ≥95% of aberrant PCs by MFC | No risk factor | NR |
| Immunoparesis | 1 risk factor | 6 y |
| | 2 risk factors | 1.9 y |
| Heidelberg | | 3-year TTP |
| Tumor mass using the Mayo Model | T-mass low + CA low risk | 15% |
| t(4;14), del17p, or +1q | T-mass low + CA high risk | 42% |
| | T-mass high + CA low risk | 64% |
| | T-mass high + CA high risk | 55% |

| Risk Model | Risk of Progression to MM | |
|---|---|---|
| SWOG | | 2-year TTP |
| Serum M-protein ≥2 g/dL | No risk factor | 30% |
| Involved FLC >25 mg/dL | 1 risk factor | 29% |
| GEP risk score >−0.26 | ≥2 risk factors | 71% |
| Penn | | 2-year TTP |
| ≥40% clonal BMPC infiltration | No risk factor | 16% |
| sFLC ratio ≥50 | 1 risk factor | 44% |
| Albumin ≤3.5 mg/dL | ≥2 risk factors | 81% |
| Japanese | | 2-year TTP |
| Beta 2-microglobulin ≥2.5 mg/L | 2 risk factors | 67.5% |
| M-protein increment rate >1 mg/dL/d | | |
| Czech and Heidelberg | | 2-year TTP |
| Immunoparesis | No risk factor | 5.3% |
| Serum M-protein ≥2.3 g/dL | 1 risk factor | 7.5% |
| Involved/uninvolved sFLC >30 | 2 risk factors | 44.8% |
| | 3 risk factors | 81.3% |

| Risk Model | Risk of Progression to MM | |
|---|---|---|
| Barcelona | | 2-year TTP |
| Evolving pattern = 2 points | 0 points | 2.4% |
| Serum M-protein ≥3 g/dL = 1 point | 1 point | 31% |
| Immunoparesis = 1 point | 2 points | 52% |
| | 3 points | 80% |
| Mayo Clinic evolving model | | |
| eMP | 0 points | 12.3 y |
| eHb | 1 point | 4.2 y |
| ≥20% PCs | 2 points | 2.8 y |
| | 3 points | 1 year |
| Danish | | 3-year TTP |
| Serum M-protein ≥3 g/dL | No risk factor | 5% |
| Immunoparesis | 1 risk factor | 21% |
| | 2 risk factors | 50% |

Abbreviations: BMPC = bone marrow plasma cells; CA = cytogenetic abnormalities; eHb = evolving change in hemoglobin; eMP = evolving change in the monoclonal protein; FLC = free light chain; GEP = Gene Expression Profiling; MFC = multiparameter flow cytometry; MM = multiple myeloma; PC = plasma cell; Penn = Pennsylvania model; sFLC = serum FLC; SMM = smoldering MM; SWOG = South West Oncology Group; TTP = time to progression.

| Revised IMWG/Mayo | Risk Factors | #Risk of Prog,2yr | ^Risk of Prog,2yr | *Median TTP |
|---|---|---|---|---|
| BMPC > 20% | 0 | 5% | 8% | 110 mo |
| M-protein > 2g/dl | 1 | 17% | 21% | 68 mo |
| sFLC ratio >20 | ≥2 (2) | 46% | 37% | 28 mo |
| t(4,14), t(14,16), +1q, del13q | ≥3 | | 59% | |

*Mateos MV, González-Calle V Clin Lymphoma Myeloma Leuk 2017 11:716 (10 Models)*
**Lakshman A et al Blood Ca J 2018, 8:59*
#San Miguel J et al ASCO 2019 A8000, ^presentation

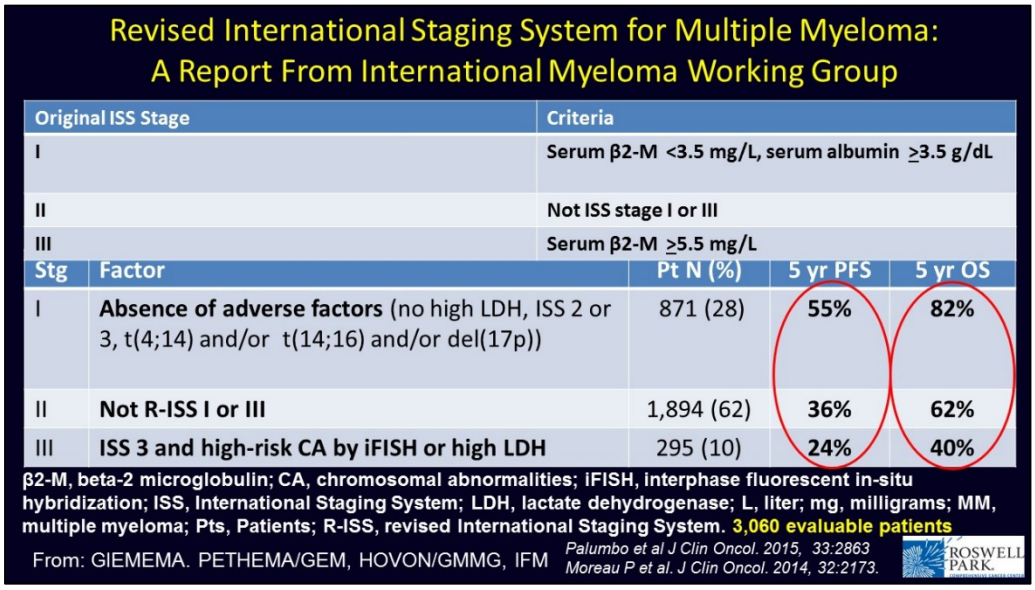
PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19 Slides are the property of the author, permission required for reuse. PRESENTED BY: Philip McCarthy 24

So, I don't expect you to remember all of this. And if you want to go and look, there are at least ten models for risk stratification of smoldering myeloma. And this is a review from Maria V. Mateos, MD, PhD, and one of her colleagues in a journal which you can go look up. The Mayo Group postulated a new risk stratification based on a lower amount of protein, 2 grams per deciliter instead of 3, bone marrow plasma cells of 20% rather than 60%, and a serum-free light chain ratio of greater than 20 rather than 100. And they found that, depending on the number or risk factors, you had a 5, 17 or 46% chance at two years of having full blown multiple myeloma.

Now Dr. Mateos presented data showing that if patients have one of these chromosome abnormalities, you now can change the risk score from 8, 21, 37 to 59%. So, if you have all of these things, including one of these chromosome abnormalities in the bone marrow, you now have a 59% chance of smoldering myeloma turning into full blown myeloma.

So, we're now beginning to try and identify which patients are at higher risk and should receive earlier therapy. It's not quite ready for prime time. There was an ECOG (Eastern Oncology Cooperative Group) trial just presented at ASCO where patients were randomized to receive lenalidomide or observation. And the patients who received lenalidomide had a lower risk of progression to full blown myeloma. We need longer term follow-up to see if this will become the standard of care.

## TRANSCRIPT

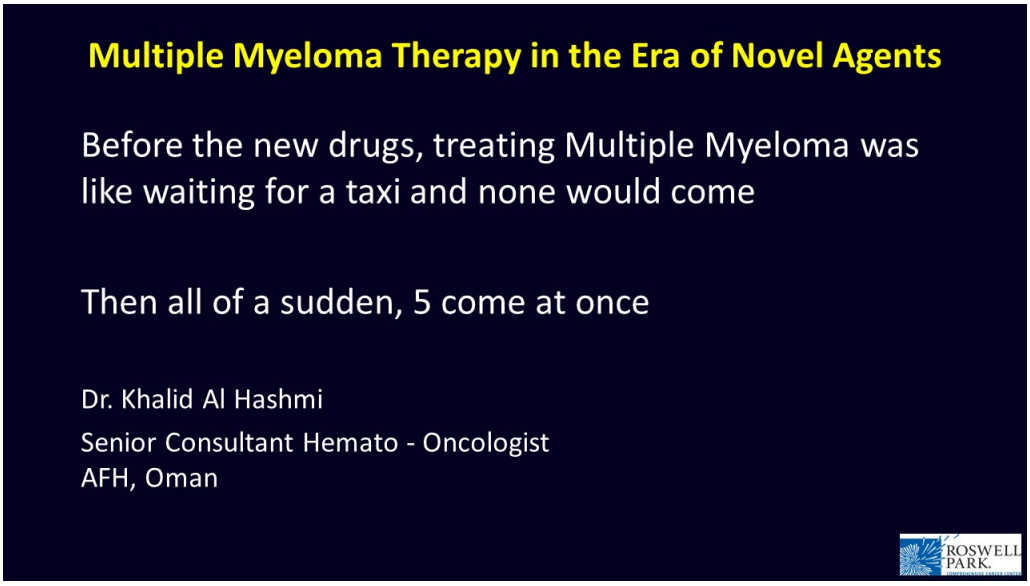



So, this is the revised international scoring system (R-ISS). This is why patients should have a beta-2 microglobulin and an LDH, a bone marrow test and, of course, measurement of blood parameters. The original criteria were based on that beta-2 microglobulin and serum albumin. And the staging went from I to III based on the amount of beta-2 microglobulin and how low or high the albumin was.

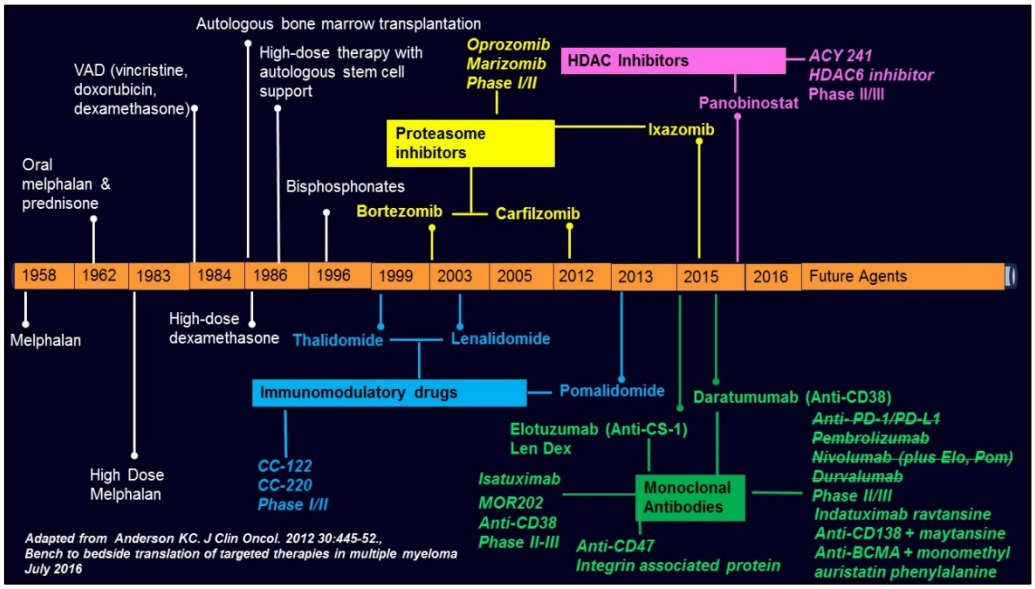
What we see now is we've now incorporated in that lactate dehydrogenase, or LDH, the old ISS scoring system and now these three chromosome abnormalities 4;14, 14;16 translocations or deletion 17p. And what we see is that patients who don't have any of these adverse risk features have a five-year progression-free survival of 55% and overall survival at five years of 82%. Whereas patients who have high burden disease, one of these chromosome abnormalities, or that high LDH, they have a 24% progression-free survival versus a 40% overall survival at five years. And then in between, R-ISS II's, which are neither I nor III and they're at 62%.

So, this is very useful for helping the clinician and the patient understand what the risks are long term for the patient and are also developing new strategies because treatment of R-ISS I, can be very different potentially than an R-ISS III. Right now, we use, essentially, the same therapy, but we're now beginning to develop strategies to help us control disease in these higher-risk patient populations.

## TRANSCRIPT

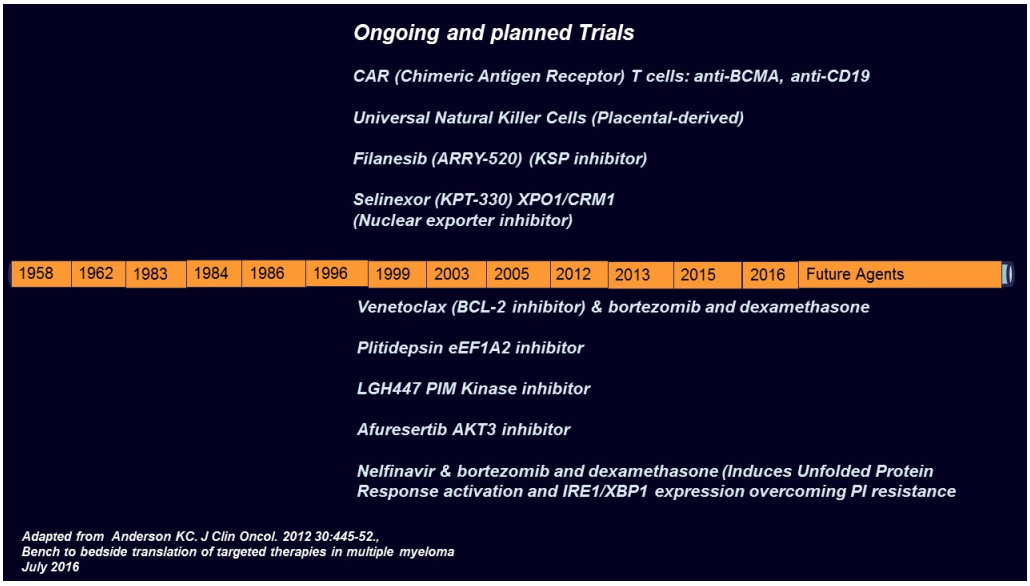



So, I use this little cartoon which I got from a physician from Amman in the Middle East. Before the new drugs, treating multiple myeloma was like waiting for a taxi; none would come. Then all of a sudden, five come at once. And I like to say we now have a good problem in that we have multiple drugs to choose from to treat our patients.

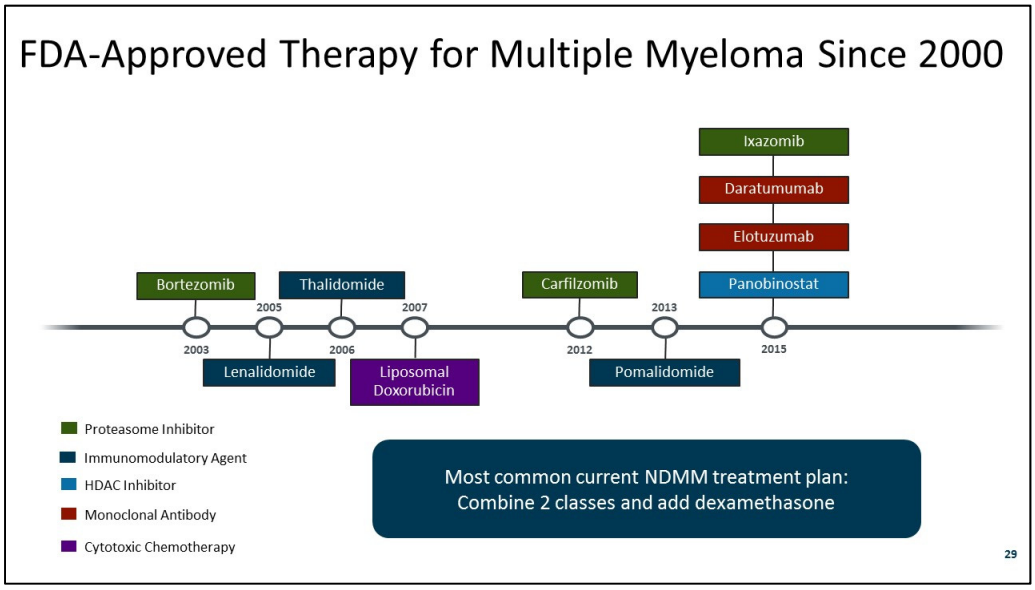



So, this is a timeline. I'm not going to go through it in great detail, but back in the '50s all we had was oral melphalan. Into the '60 was steroids. And then we had the introduction of newer drugs. VID back then stood for vincristine-Adriamycin-dexamethasone. We don't use this anymore. In fact, the V now, as many of you know, stands for Velcade® or bortezomib. Velcade is the brand name; bortezomib is generic. And then we have the introduction of the proteasome inhibitors, the immunomodulatory agents here in blue. Thalidomide technically isn't an IMiD (immunomodulatory drugs) whereas len (lenalidomide) and pom (pomalidomide) are. The HDAC (histone deacetylase) inhibitor, panobinostat, and there's some other HDAC inhibitors being trialed. And then the monoclonal antibodies, big game

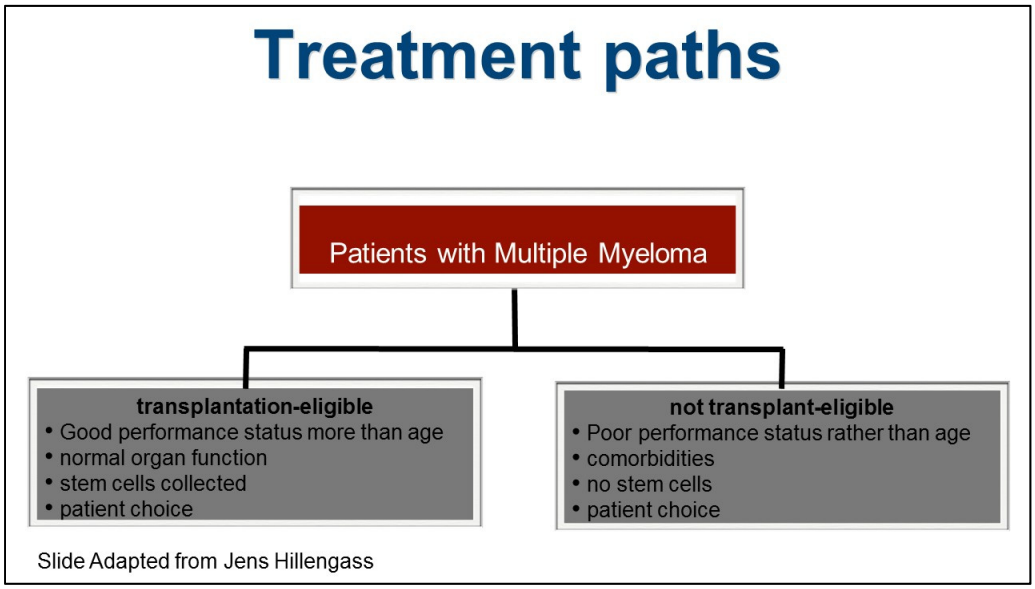
changer. Elotuzumab-daratumumab, which some of you may be very well familiar with. We're testing some new drugs. The checkpoint inhibitors have been put on hold because of toxicity, but there's a variety of new strategies that involve a new target BCMA, B-cell maturation antigen. I'll talk about that a little bit later.



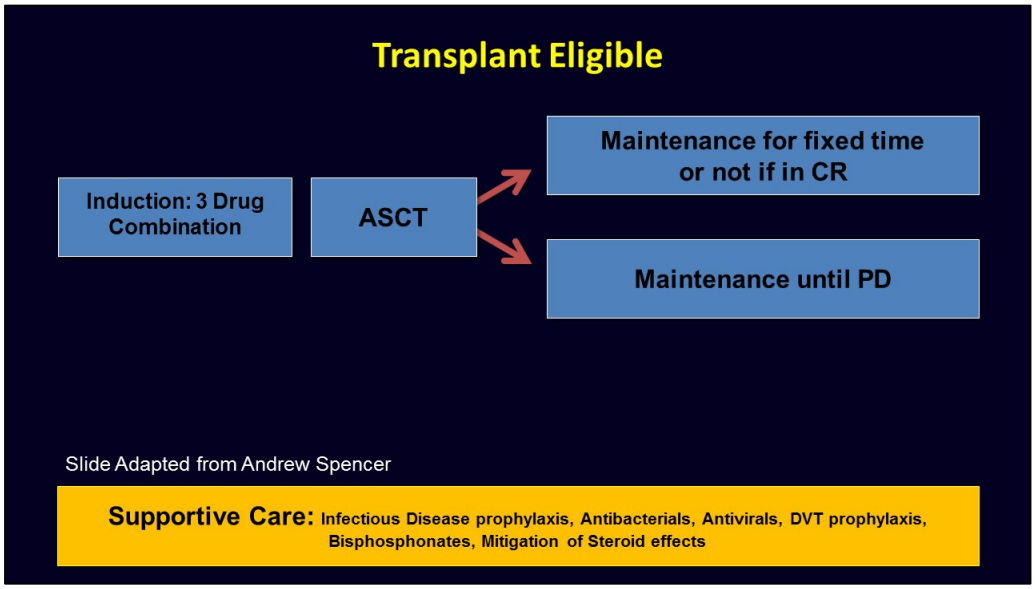

So, these are some of the things that are ongoing. I have some more data showing you about CAR (chimeric antigen receptor) T-cell treatment. There's natural killer (NK) cells that are being utilized. Here's another drug which kinesin spindle poison (KSP), selinexor, which a nuclear exporter inhibitor, venetoclax I mentioned earlier, and these are some other drugs that are being trialed and, hopefully, will be available for our patients in the near future.



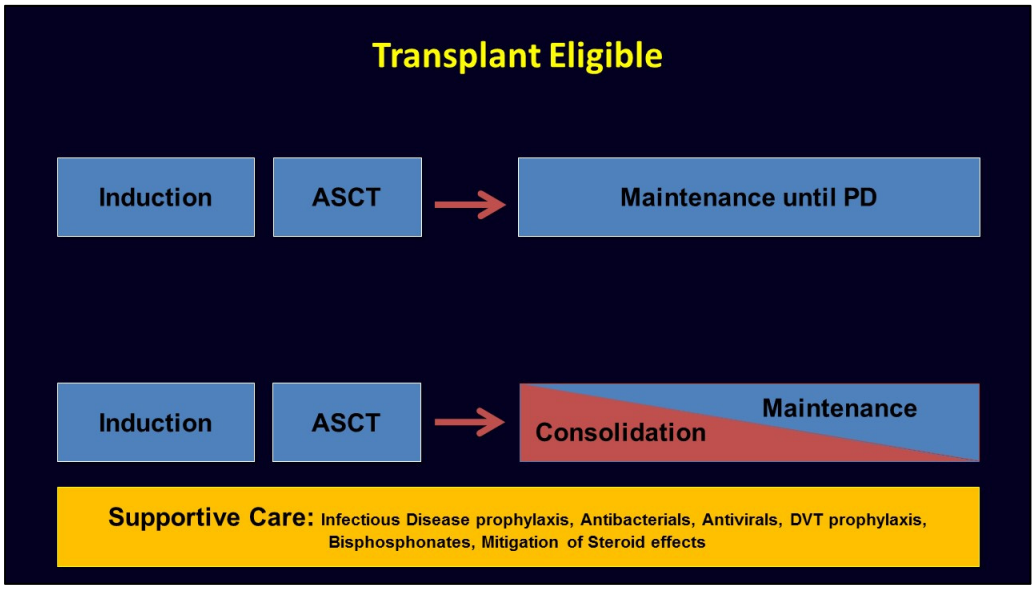

So, this is a different timeline showing the new drugs since 2000 – bortezomib-thalidomide-lenalidomide, liposomal doxorubicin, carfilzomib-pom and then the monoclonals and the HDAC inhibitor.



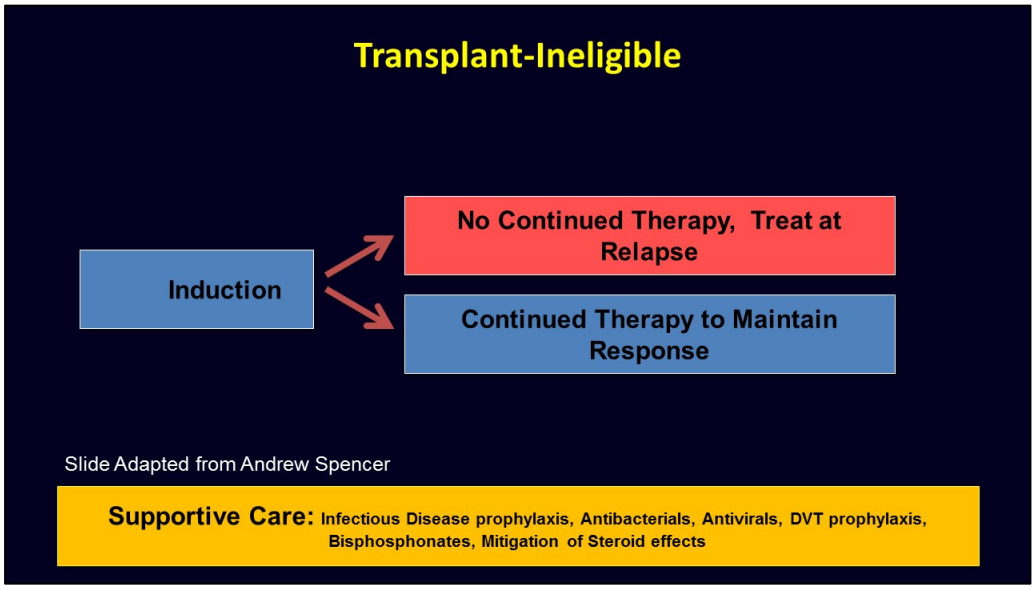

So, treatment paths. We will look at a patient and how we treat based on what they have. Patient who is transplant eligible usually has good performance status, normal organ function. Patient's stem cells are collected, and the patient and the clinician may decide, well, I'll do it later and we could talk about now versus later, versus nontransplant eligible, poor performance status rather than age. Comorbidity – somebody has bad kidney; not so much that, but bad lung and bad cardiac function they may not be a good stem cell transplant candidate. They can't have stem cell collected and there are some patients who'd elect not to do that.



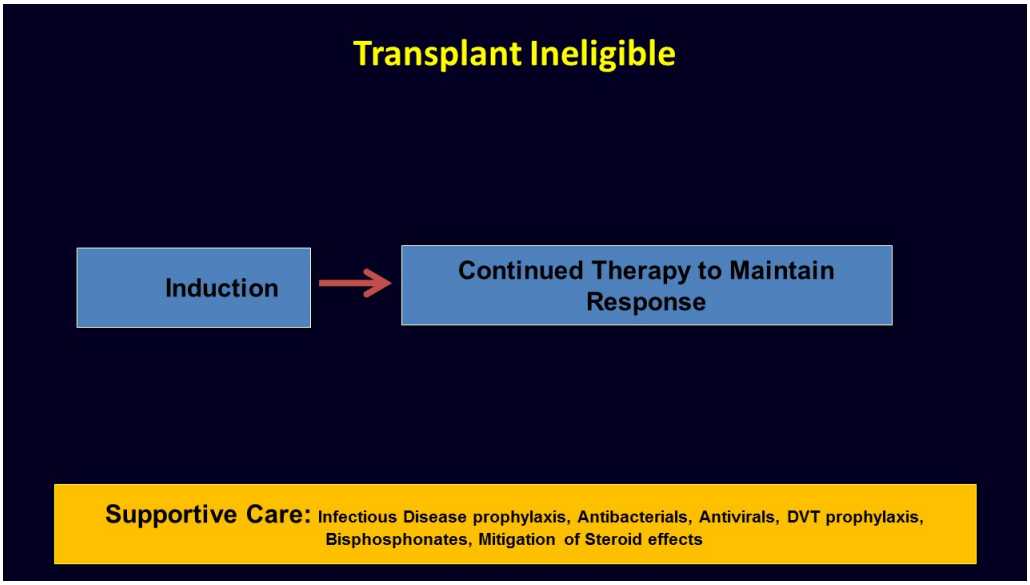

So, this is from Andrew Spencer, MBBS FRACP, FRCPA, DM, from Australia. Often the transplant eligible patients are getting a three-drug combination, a transplant and then maintenance for fixed time or until progression.




I would make the argument that it's until progression. In Europe, consolidation is very popular or for high-risk patients. What's very important is patients should get infectious disease prophylaxis. There's the study from Britain saying that patients could get levofloxacin to prevent infectious problems. Everybody should be getting antivirals to prevent shingles from being too severe. DVT stands for deep vein thrombosis prophylaxis to prevent clots and, in particular, in patients on thalidomide-lenalidomide or pomalidomide. Bisphosphonates and mitigation of steroid effects because dexamethasone, as many of you know, can be postdiabetes and a variety of other things. Bisphosphonates help prevent bone lesions.

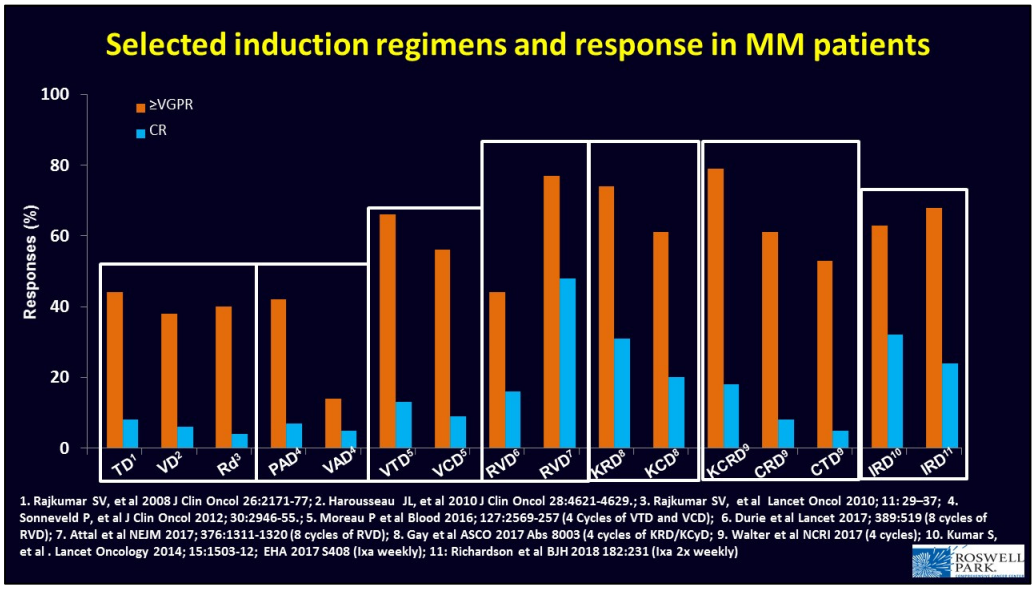



This is for transplant ineligible and induction. It used to be a double. Now there's thoughts of doing a triple, and I'll show you some data on that. And then the issue becomes, continue therapy versus no continued therapy and treating at relapse.




I'd make the argument that now it's continued therapy to maintain response.

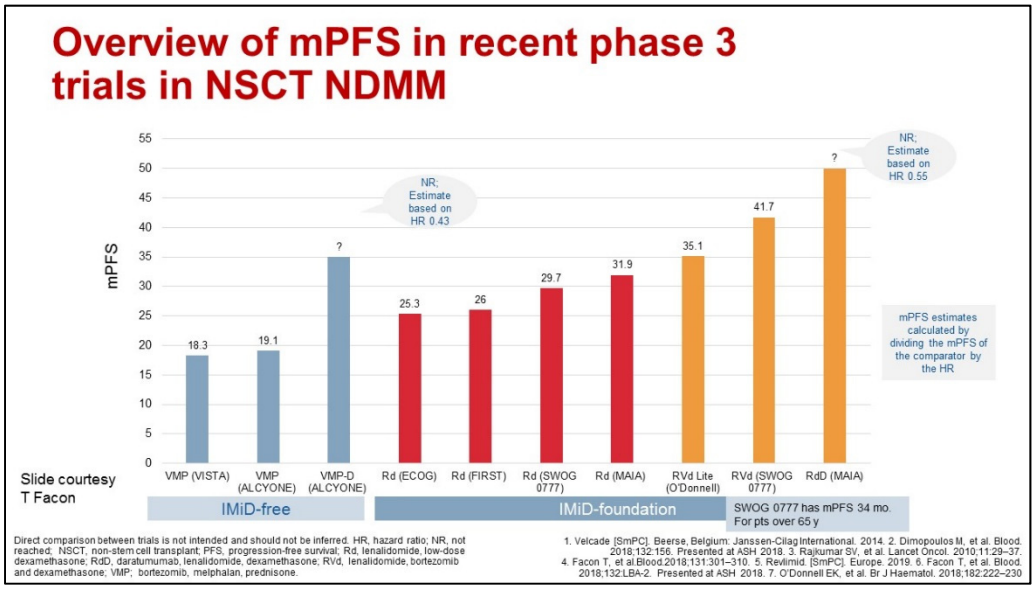
## TRANSCRIPT




So, this I'll go through fairly quickly. These are just showing in orange that are VGPR (very good partial response) and greater, so VGPR means that you've had a 90% reduction in the tumor burden. So, in the old days, we'd have patients getting VGPRs of less than 50%. Only less than 50% of patients were having good responses. The blue are those who are attaining CRs (complete response). You could see they're fairly low.

This is thalidomide-dex (dexamethasone) and bortezomib-dex and lenalidomide-dex. Then you can see here PAD stands for PS-341 because that was what bortezomib's name was before it became commercialized. And I guess they didn't want to call it BAD because that didn't sound good, so it became PAD. So that's PAD with Adriamycin-dex versus the old VAD, which I talked about earlier. And you can see here now with the novel triplets, bortezomib-thalidomide-dex, you're now seeing much higher VGPR rates, a little bit higher CR rates. This one's cyclophosphamide. And now you're seeing lenalidomide-bortezomib-dex. You're seeing much better response rates. These are different timepoints they're measured, that's why there's a bit of a difference there.

This is using carfilzomib-len-dex. This is being studied. Here we are with a quadruplet from the British. This is cyclophosphamide-thalidomide-dex. And this is using ixazomib upfront in a specific study. You'll notice that daratumumab's not here, but there are some studies that are incorporating daratumumab upfront, and I can talk about that a little bit later.

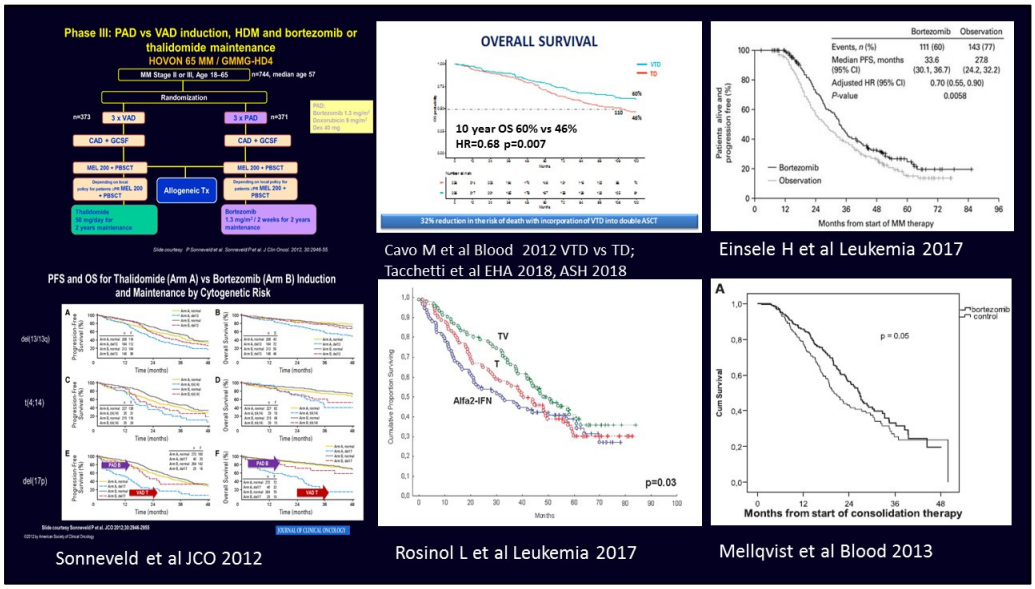



This is looking at nontransplant approaches. Here we are with VMP, bortezomib-melphalan-prednisone, from the Evista trial and then VMP from the ALCYONE trial, which compared VMP versus VMP plus dara (daratumumab). And you can now see there's a bigger difference in the progression-free survival.

This is the old ECOG (Eastern Cooperative Oncology Group) trial looking at len-dex. And then here we are len-dex in the first trial and len-dex in the SWOG (Southwestern Oncology Group) trial which compare. In the first trial, it compared len-dex versus VTD (Velcade (bortezomib)-thalidomide-dexamethasone), and in the SWOG trial, it compared len-dex versus len-dex plus bortezomib over here. So here they are as the two arms. And then you'll see the MAIA trial, which is len-dex, versus len-dex-daratumumab, which is over here on the far right. So, what you're seeing here is that there's an improvement in the medium progression-free survival as novel drugs are being introduced.

This one here, RVD (Revlimid®-Velcade-dexamethasone) LITE, is a phase II trial where you can see now a better response but with an attenuated lenalidomide-bortezomib-dex, to account for the fact this was a frailer patient population. So, the higher these bar goes, the better the responses. And we're seeing over time with newer studies, we're seeing better responses.

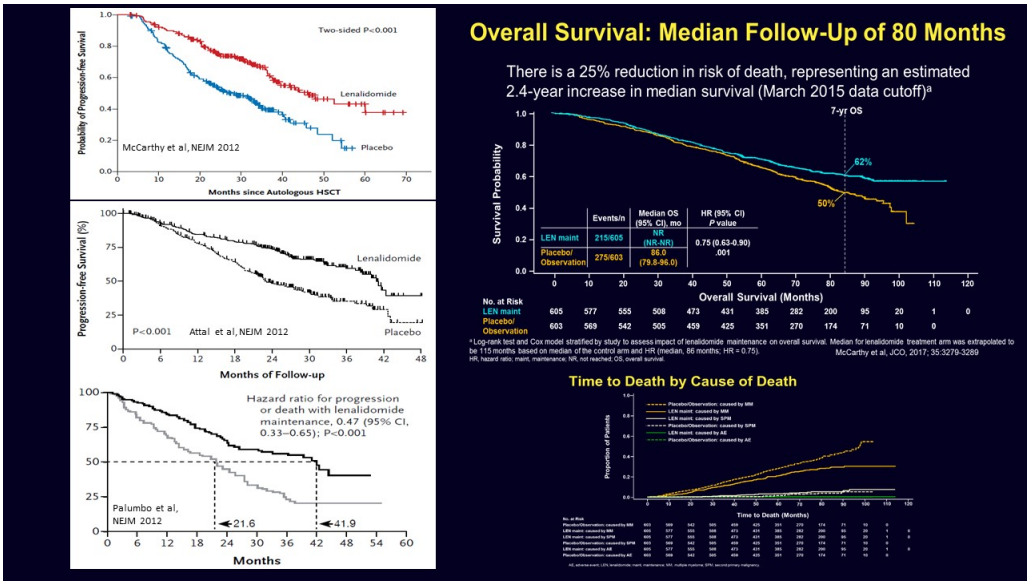
## TRANSCRIPT



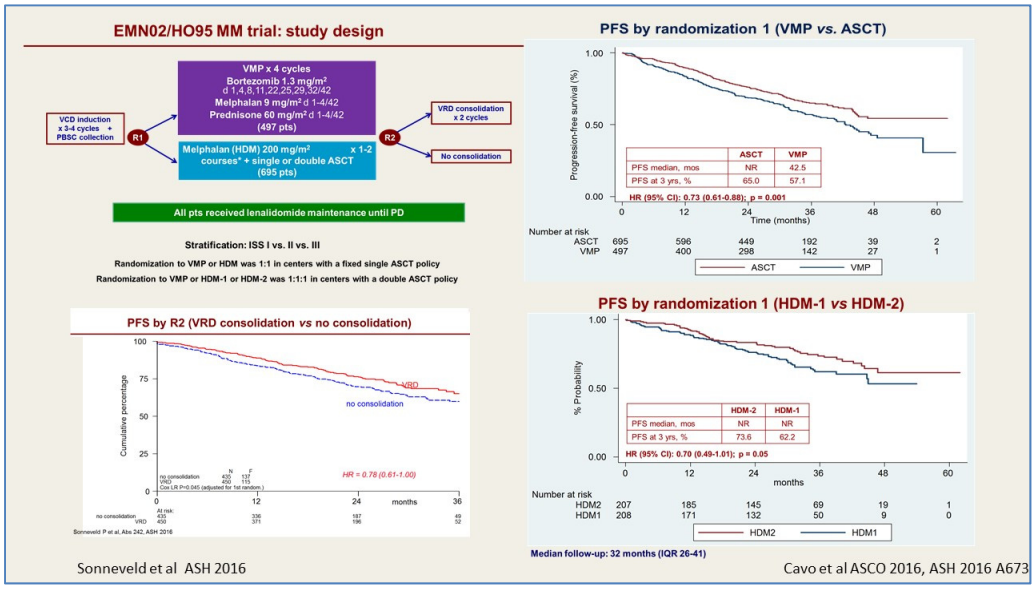

Now this is a very busy slide, and this is just meant to show the concept of bortezomib maintenance consolidation after treatment. And what this showed is that bortezomib was utilized in a Dutch study, Dutch-German study, and they found that the best benefit were those patients who had deletion 17. But they compared it to thalidomide, which is really no longer a standard for maintenance.

Here are two trials from the Nordic and German regions showing that there's a progression-free survival benefit; it's modest. And then the Italians did a study looking at bortezomib-thalidomide-dex versus thalidomide-dex showing the blue curve being better, but it took them almost ten years to find out that there was an overall survival benefit. And this is the Spanish trial looking at thalidomide-bortezomib. So, we're now seeing that this is providing the progression-free and overall survival benefit. The problem is it's hard to tolerate bortezomib long term because of the neuropathy problems.

## TRANSCRIPT

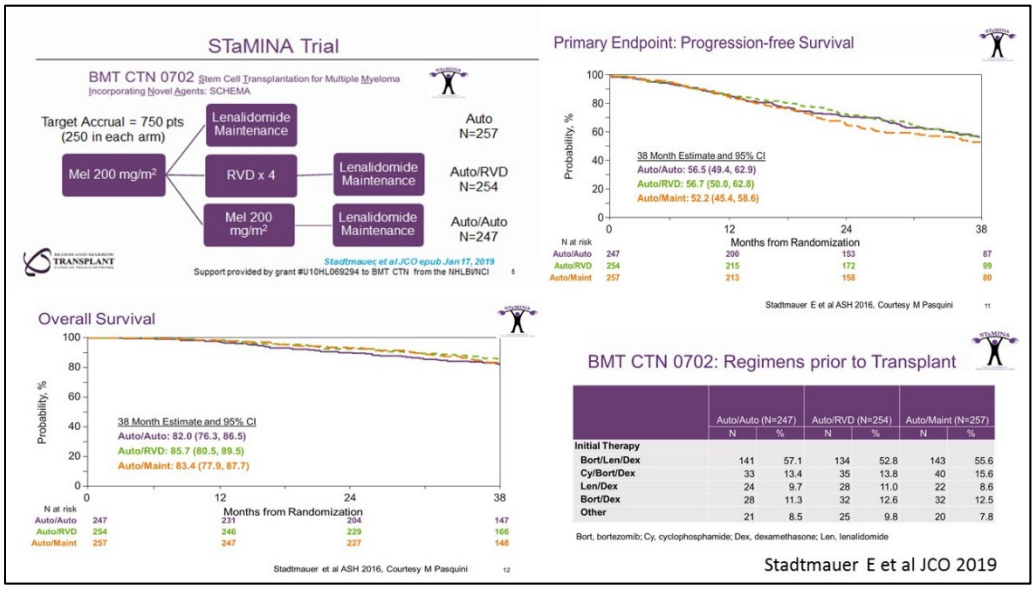



This is a meta-analysis which combined three trials from the CALGB (Cancer and Leukemia Group B) 100 104 from America, from France and from Italy. And we pooled all the data and showed that now with lenalidomide maintenance, we're seeing at seven years 62% of patients are still alive versus 70% who did not receive maintenance. And so, this was what led to the approval of lenalidomide as a maintenance option for patients until progression in those patients who had a transplant. However, there was a second primary malignancy signal, what we see in this bottom right-hand curve. It's a bit hard to see is that patients who got lenalidomide had a higher risk of getting a second cancer, but those who got placebo on the top curve had a high risk of dying of their multiple myeloma. So, thus, there is a risk, but we think the benefit of maintaining the response and keeping the disease from coming back outweighs the risk of the second cancer.

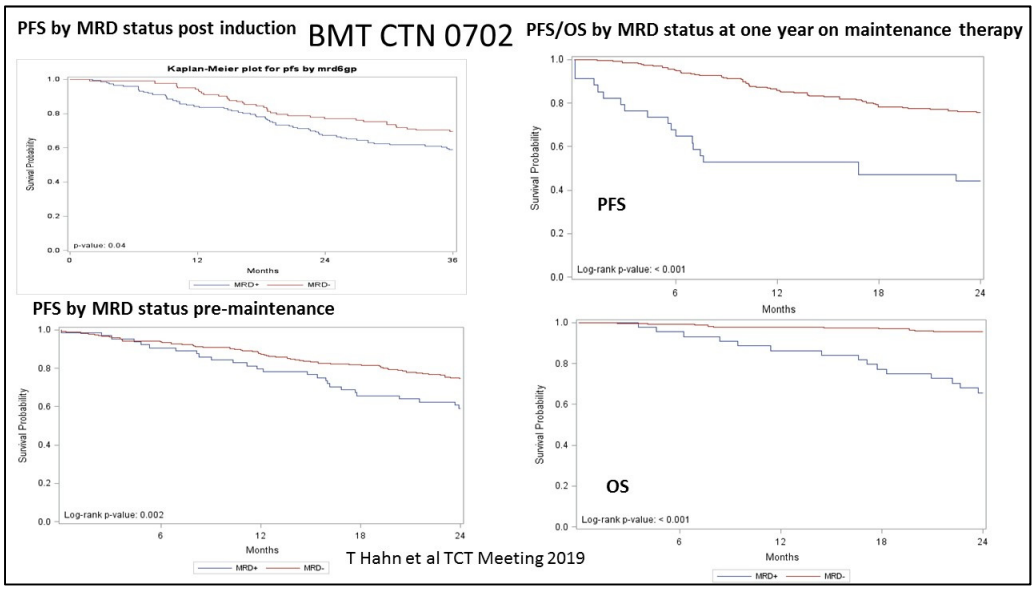



Now this is an EMN02 trial. It's not been published yet. It's looking at chemotherapy with VMP versus high-dose melphalan and then a consolidation question. And what they showed is that those patients

who got a transplant versus VMP had a superior progression-free survival. If they got one transplant versus two – this was done in Europe – certain patients did better if they got two transplants. And those who did a consolidation treatment with bortezomib-len-dex had a better progression-free survival than those who did not get consolidation.

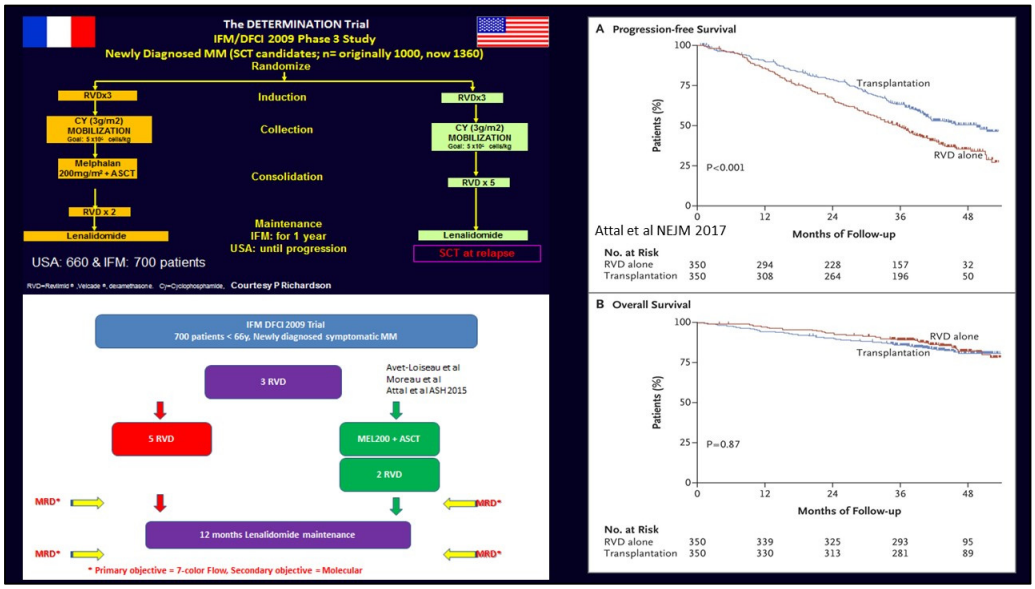



So, we await this paper because in the US we did a very similar study and found completely different results. So, this is a single transplant followed straight by len maintenance versus an RVD consolidation versus a second transplant. All of the arms are followed by len maintenance. And you can see here that progression-free survival is essentially no difference, and this is the overall survival. There were some differences in regimens, but now we have this interesting difference between Europe and America, so at least in the US the current standard is single transplant followed by len maintenance.

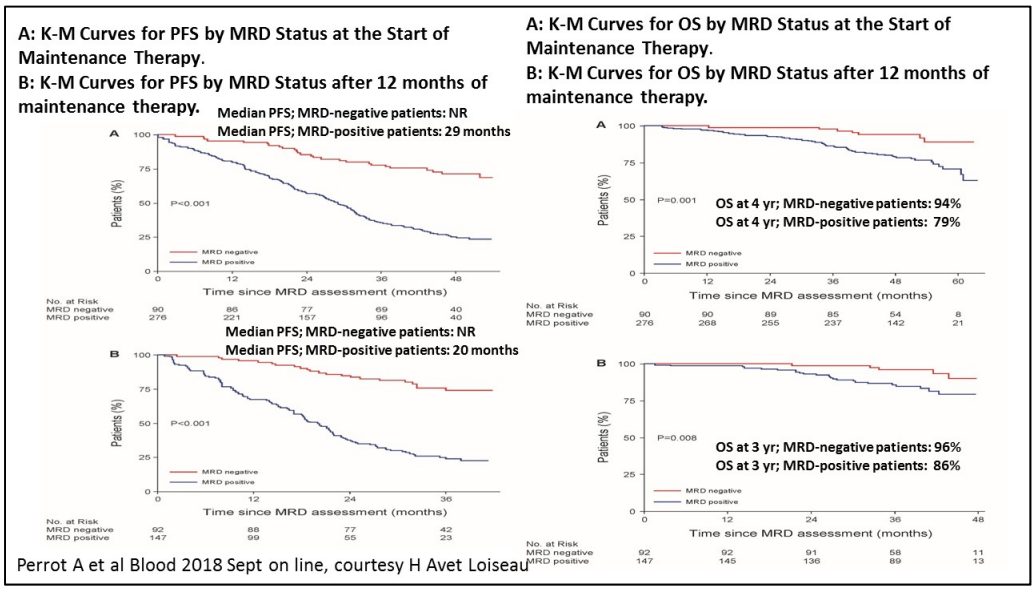



And this is looking at the concept of minimal residual disease (MRD). Some of you may have heard about this in the bone marrow. And this is from that trial that I just showed you, and this showed that patients who are early, their progression-free survival if they had no detectable disease by flow cytometry, in the bone marrow, those who are MRD negative did better than those who were positive in terms of progression-free survival after induction. What we also showed is that after their transplant or their consolidation, depending on the arm, those who are MRD negative did better than those who were positive. But at one year after being on maintenance, those who maintain their MRD negative status in the marrow had a superior progression-free survival than those who were positive and, most importantly, that is superior overall survival. So, we're beginning to see how this is going to become a standard, we think, for determining outcome and it'll probably be used in clinical trials as a randomization point. In somebody who becomes MRD negative, you may randomize them to continuing therapy or stopping treatment. It remains to be determined.

## TRANSCRIPT

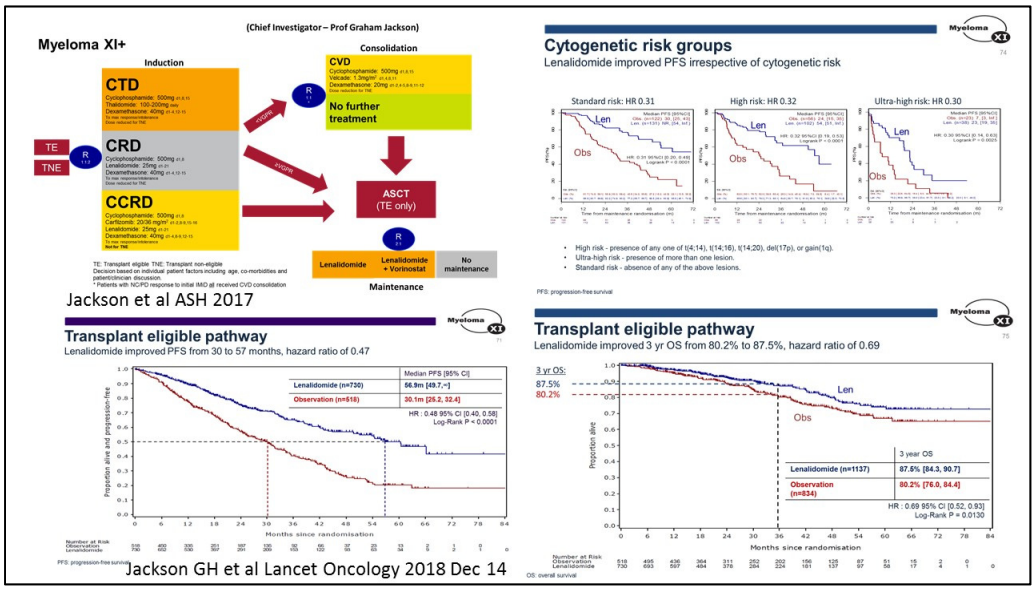



So, this is the part about transplant versus no transplant from France. This is a French-American study. It is chemotherapy, collect stem cells, single transplant, consolidation, len maintenance versus RVD chemotherapy alone followed by len maintenance. The French study looked at maintenance for a year. The US portion is looking at until progression. This is the schema down below. This is the progression-free survival for those who had a transplant. There's about a 14-month benefit in terms of the disease taking longer to come back versus chemotherapy, but you'll see there's no overall survival benefit as of yet. What's also interesting is that here, once the maintenance stops, the rate of progression appears to increase. Again, as I mentioned, the US study is maintenance until progression, so that will be reported separately.



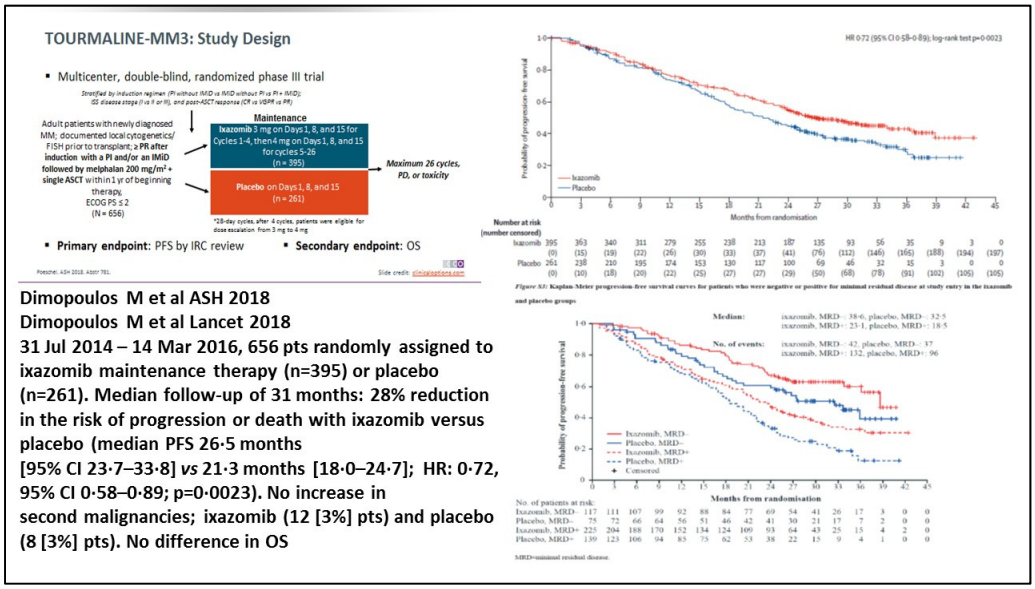

This is their MRD testing, minimal residual disease testing. This is looking at it at the start of maintenance therapy and after 12 months progression-free survival, again, start one year. And here the medium PFS is not reached versus 29 months, not reached versus 20 months. And here on the

right are the Kaplan-Meier curves for overall survival. The top one at the start of maintenance and then the bottom one after 12 months of maintenance. And you can see those patients who had no detectable disease in their marrow – this was by a different technique called next generation sequencing, it's a molecular test – they had a superior survival if they were MRD negative. And this is just the numbers at four years and three years.



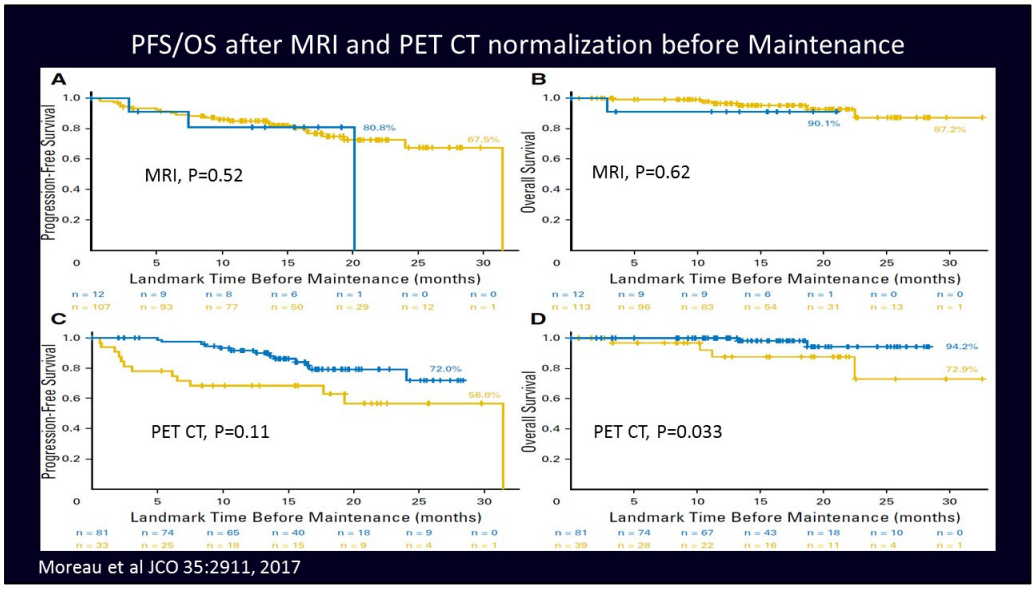

So, this is a British trial. I'm not going to go into the detail because it's transplant, no transplant. But what they showed is that those who got a transplant and then got len maintenance these are the patients the blue curve is the len maintenance. The red curves are those who did not get it; they were observed. And then for the overall survival, there is also an overall survival benefit for those patients who got len. And what they showed is that even in patients who had high-risk cytogenetic features, there was a benefit to receiving len versus no maintenance at all. So, you may hear people say, "Oh you shouldn't get len if you have high-risk features." That's not necessarily true, and this study has actually demonstrated that. It may be that you need to get bortezomib and lenalidomide, but that remains to be proven. I can discuss that later.

## TRANSCRIPT



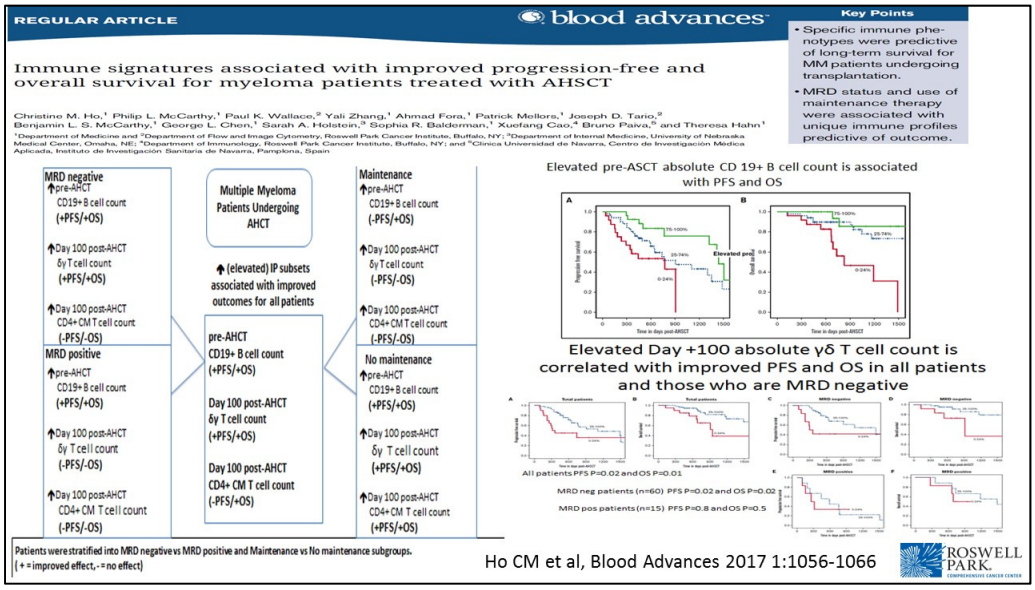

**Dimopoulos M et al ASH 2018**
**Dimopoulos M et al Lancet 2018**
**31 Jul 2014 – 14 Mar 2016, 656 pts randomly assigned to ixazomib maintenance therapy (n=395) or placebo (n=261). Median follow-up of 31 months: 28% reduction in the risk of progression or death with ixazomib versus placebo (median PFS 26·5 months [95% CI 23·7–33·8] *vs* 21·3 months [18·0–24·7]; HR: 0·72, 95% CI 0·58–0·89; p=0·0023). No increase in second malignancies; ixazomib (12 [3%] pts) and placebo (8 [3%] pts). No difference in OS**

This study was just published. This is ixazomib, the oral proteasome inhibitor. Here is the progression-free survival, the ixazomib in red versus the placebo in blue. This is stratifying it by MRD negativity, so that's, again, helping us determine those who got the ixazomib and were MRD negative did the best. And, again, this was just published recently and so remains to be seen if this will become a standard.

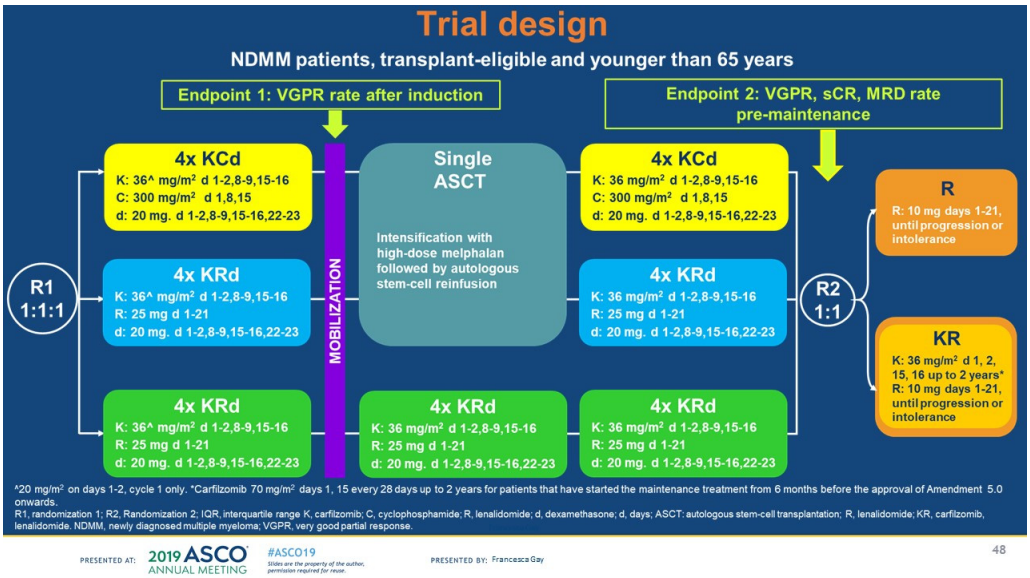



This is looking at imaging. This is from that IFM (Intergroupe Francophone du Myélome), that French study I showed you. And, simply put, those patients who become MRD negative and have a negative PET – in other words, their PET CT normalizes, the disease all goes away on radiographic imaging – have a superior progression-free and overall survival.

## TRANSCRIPT

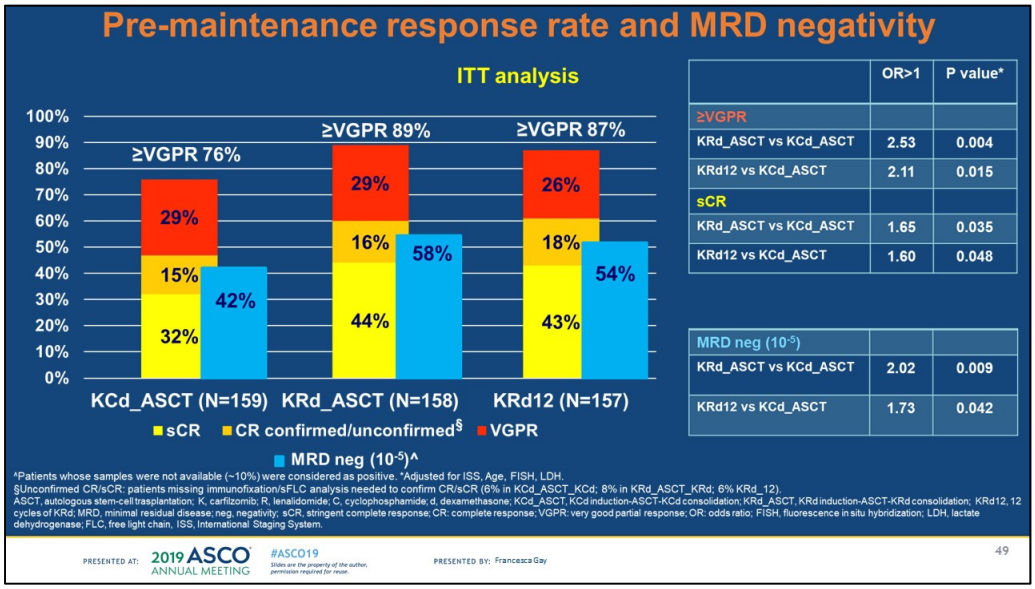


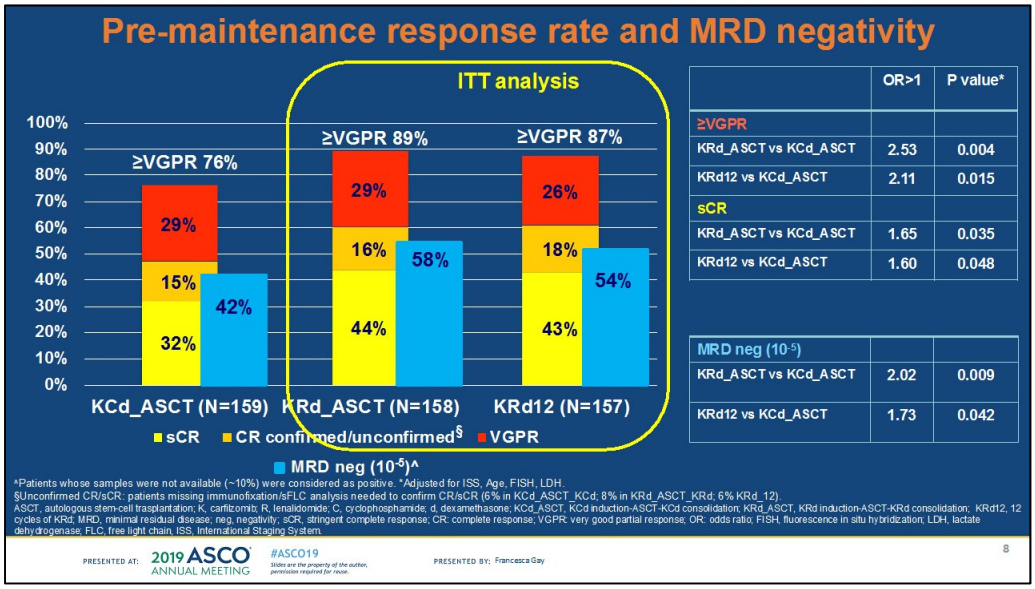

This is our own data. I'm not going to go over it in great detail because in the interest of time. And you can see here that we have found that there's certain subsets, here B cells and patients have lower B cells. They don't do as well in the red curve versus those from the green and the blue. And these are some other cells, subsets called gamma-delta T cells. The bottom line in this is that we're just beginning to scratch the surface about how the immune system will help us control the patient's myeloma long term.




I'm going to wrap up now with this is the KCd (carfilzomib-cyclophosphamide-dexamethasone) trial from the Italians. This was the FORTE trial. It was just presented at ASCO. Three-day induction regimens, a transplant versus continued chemotherapy and consolidation and a randomization to len versus carfilzomib-len for maintenance. Somewhat complicated.

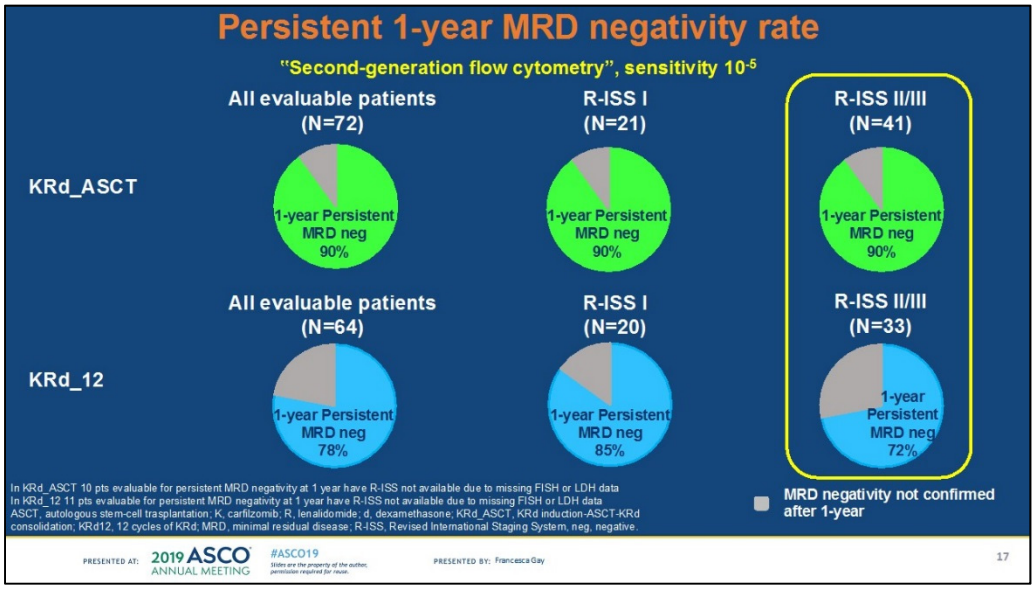
## TRANSCRIPT



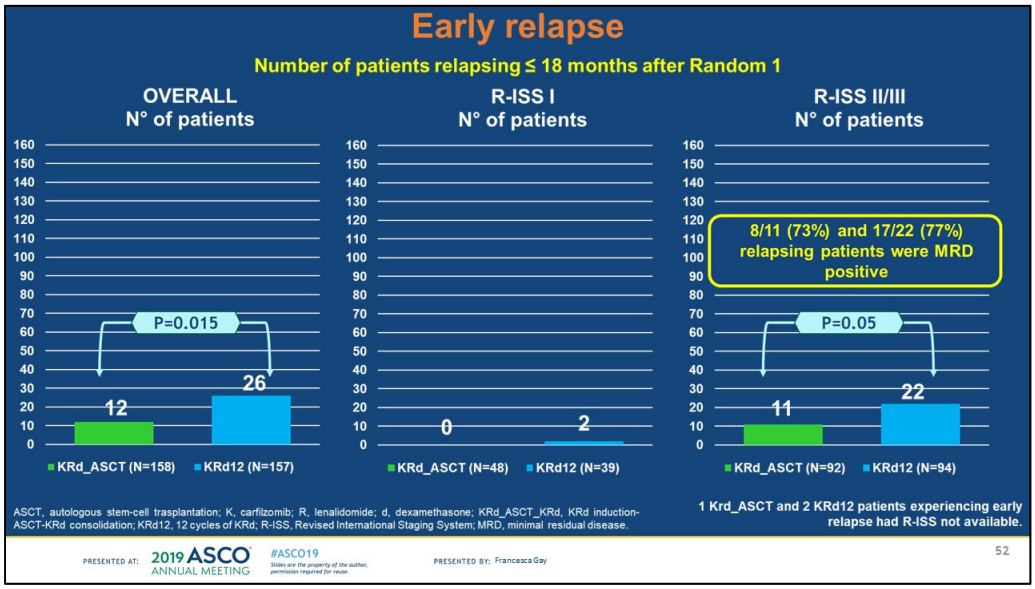




And they've only presented the upfront data which shows that those patients who got a transplant after KRd (Kyprolis (carfilzomib)-(Revlimid) lenalidomide-dexamethasone) as opposed to KCd had a better response rate, and, in particular in blue, had a higher MRD negative rate, including those who got chemotherapy only.

## TRANSCRIPT

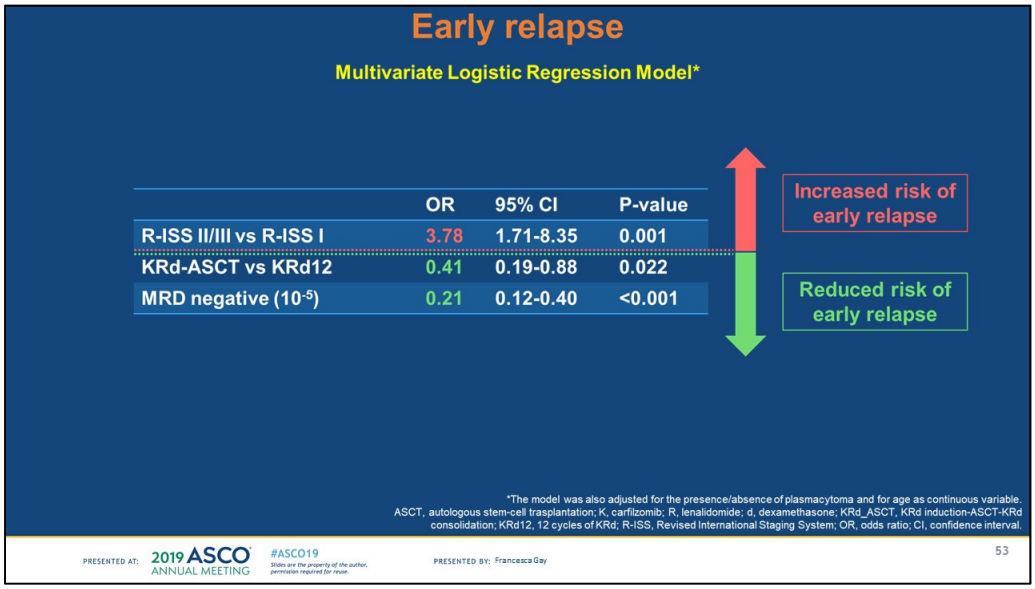



But what they also showed, and it's a little bit complicated slide, but if you look on the far right, those who got a transplant in green had a higher rate of MRD negativity at one year than those who got chemotherapy only for 12 cycles listed below in blue.

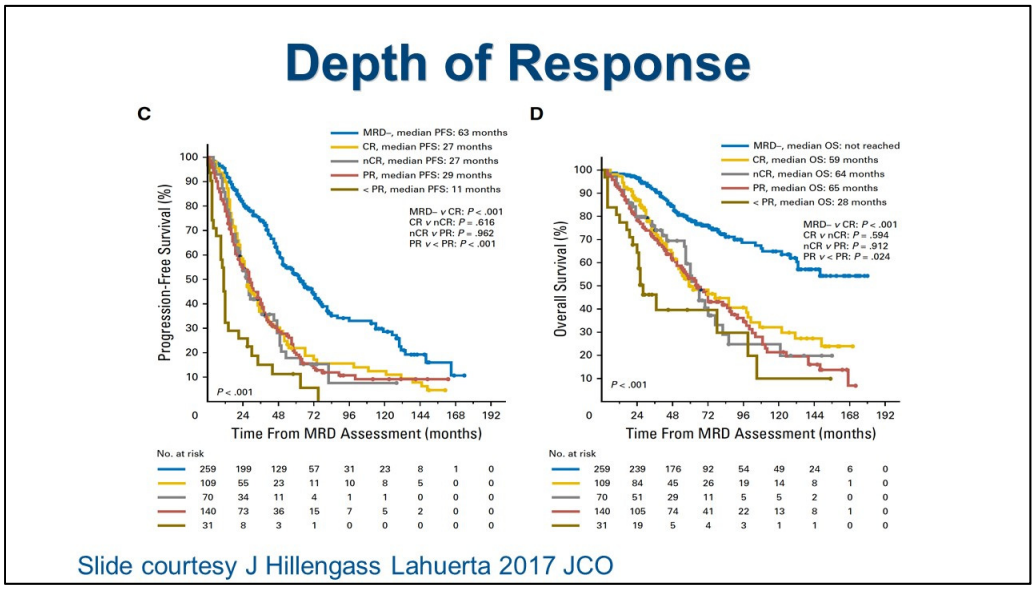



And what they also showed is that, this is relapse, that overall, you'll see on the far left, there was a higher relapse rate in the patients who got chemotherapy only. And then on the far right, it was seen primarily in the patients who had high burden disease. Remember that R-ISS 22 versus 11. This is early data, but at least it suggests that there's still a very strong role for transplant.

## TRANSCRIPT



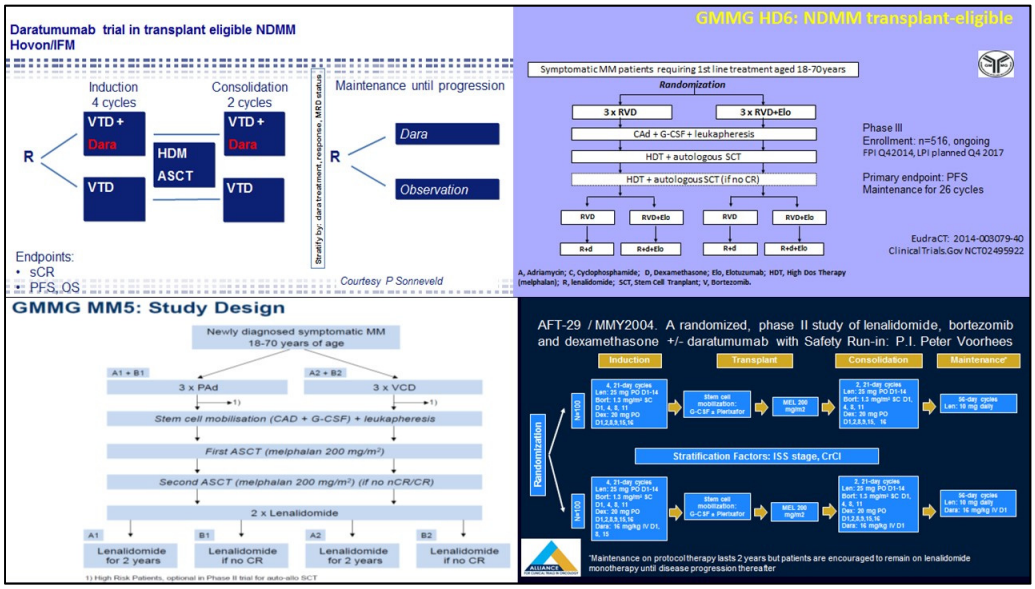

And this is just looking at the risk of relapse. Risk of relapse is higher with higher burden disease. Risk of relapse is higher if you don't get a transplant and if you don't become MRD negative. And so, you can look at this for modeling outcome for patients.




Slide courtesy J Hillengass Lahuerta 2017 JCO

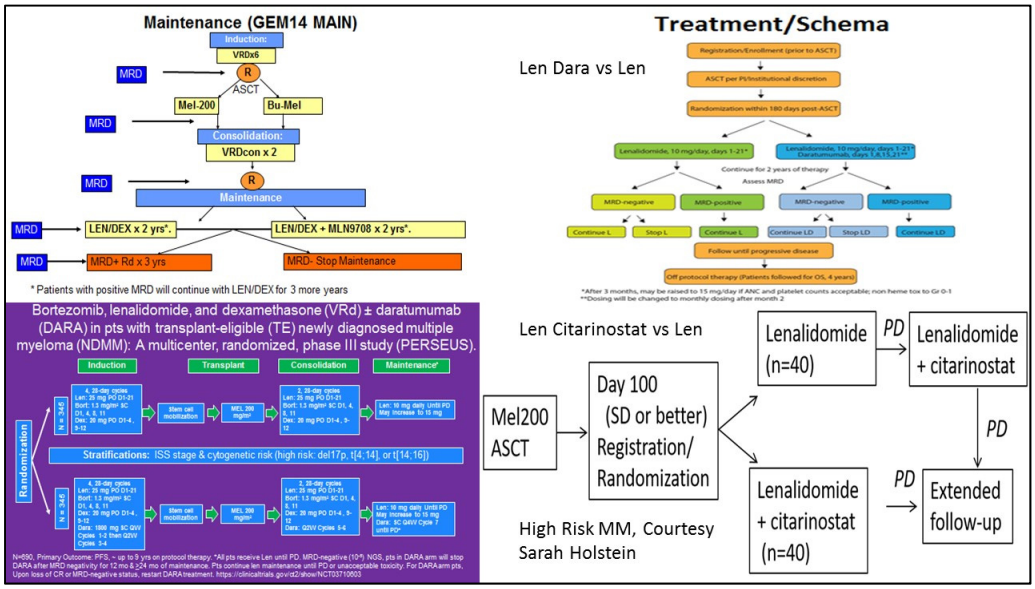
This is also another slide from the Spanish. I won't go over it in great detail but the blue line, you can see, are those patients who are MRD negative and they're treated a variety of different ways. But it points out the fact that MRD negativity in the marrow is an important prognostic feature. We just have to figure out how to incorporate that into long-term prognostication.

## TRANSCRIPT



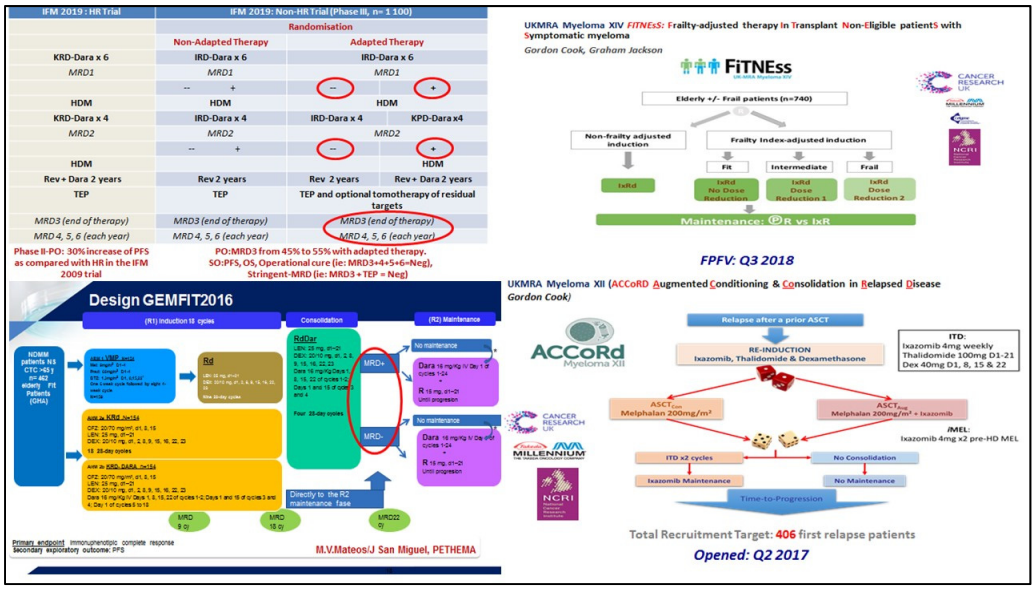

I'm showing you these trials because not to go over them in any detail, but these are trials that have not yet been reported, have just completed or are still enrolling. This trial is still ongoing, the GMMG MM5. The top one, the CASSIOPEIA trial, the D-VTd, that just was reported at ASCO and the paper was just published looking at the induction regimen which is superior for bortezomib-thalidomide-dex and dara versus chemotherapy only.

The upper left one in lavender is, again, another trial from the Germans that's ongoing. And the bottom right is a trial that we completed in the US and only has an early readout. We don't have a long-term one, and this is dara-RVD versus RVD.

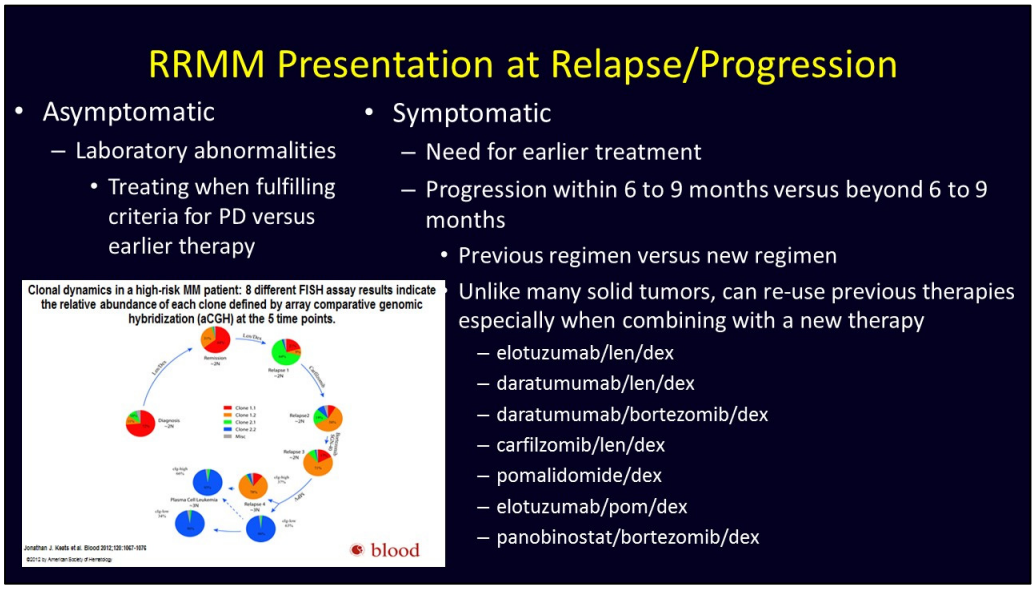



More trials upper left-hand corner is a Spanish trial looking at len-dex versus len-dex-ixa for maintenance. Bottom left is a variation around the US trial. It's just a larger trial. It's dara-RVD versus RVD, and then a consolidation with daratumumab as well as maintenance with daratumumab. This is

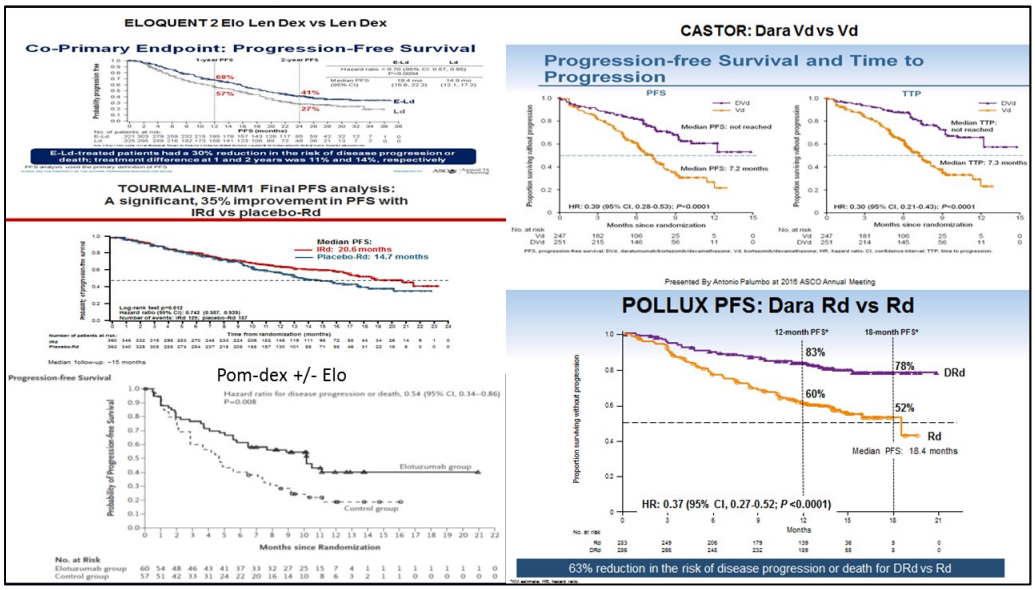
the SWOG trial that'll be done in the US, which is len-dara versus len. And the bottom right-hand side is an HDAC inhibitor we're working on trying to get up and running here in the US.




Lastly, more studies, upper left-hand side is what the French will be doing. It's a rather complicated schema. It may change again. Bottom left is what the Spanish are doing in fit patients who are thought to be nontransplant candidates to provide them with a more aggressive approach. The upper right-hand side is what the British are doing. This is for fit patients and the bottom one is for a transplant patient population. Again, not going to go over details but showing you that there's a lot going on.




Finally, relapse, there's a whole slew of things for relapse. A lot depends on the clinical situation. I won't go over it in great detail but to say there are multiple options.




Finally, these are, again, the various trials, dara-bortezomib-dex versus len-dex: CASTOR, bortezomib-dex, Pomalyst (pomalidomide)-dara-RD versus RD; ELOQUENT, elo-len-dex versus len-dex and then, lastly, pom-dex with or without elo (elotuzumab). All of these trials are showing now potential options for salvage.

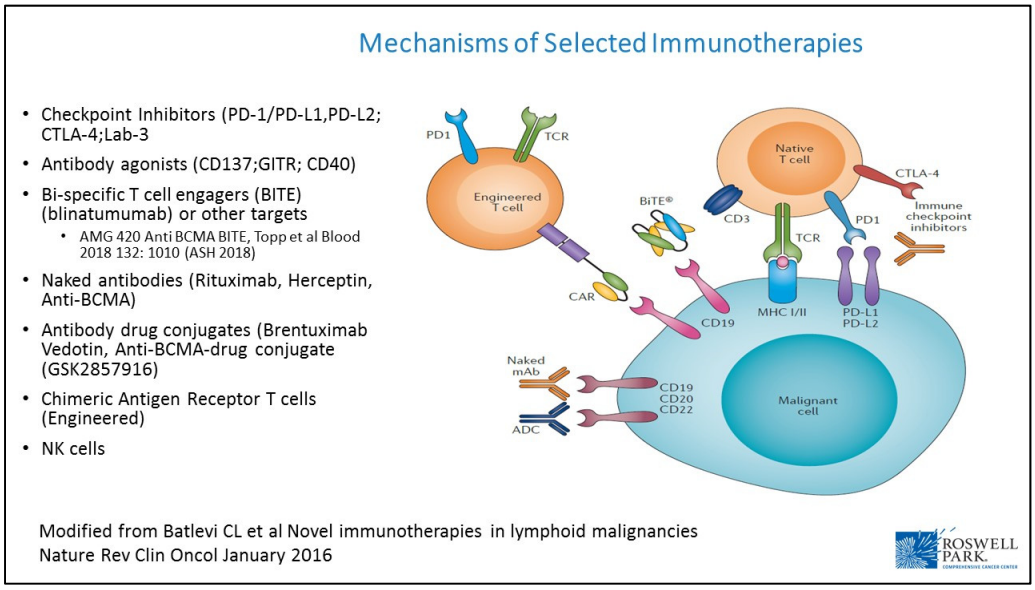
## RRMM Randomized Salvage Therapy Studies

| | Med Rx lines (range) | Exclusion | Study Combination versus Control PFS | OS | Benefit PFS/OS |
|---|---|---|---|---|---|
| Daratumumab Rd vs Rd# Dimopoulos et al NEJM 2016 | 1 (1-8) | Len refractory (refr) or intolerant (intol) | NR vs 18.4 mo; HR 0.37; P<0.001 | 7.4 mo median F/U; 18 mo 4 yr OS 86 vs 76% P=0.0534 | +/+- |
| Elotuzumab Rd vs Rd^ Lonial et al NEJM 2015 | 2 (1-4) | Len refr or intol < 9 mo from last len dose | 19.4 vs 14.9 mo; HR 0.70; P<0.001 | 24.5 mo median F/U; Med OS 48 vs 40 mo; HR 0.78 | +/+- |
| Elotuzumab Pd vs Pd$ Dimopoulos et al NEJM 2018 | 3 (2-8) | Previous P Rx, PCL, Low CrCl | 10.3 mo vs 4.7 mo; HR 0.54; P=0.008 | At 9.1 mo follow up Deaths:22% vs 32% HR 0.62 | +/+- |
| Daratumumab Vd vs Vd* Palumbo et al NEJM 2016 | 2 (1-9) | PI refr or intol | NR vs 7.2 mo; HR 0.39; P<0.001 | 7.4 mo median F/U OS NR vs NR; HR 0.77; P=0.30 | +/+- |
| Ixazomib Rd vs Rd Moreau et al NEJM 2016 | 2 (1-3) | Len or PI refr | 20.6 vs 14.7 mo; HR 0.74; P=0.01 | 23 mo median F/U; OS 77.5 vs 75.2% P=ND | +/+- |
| Carfilzomib Rd vs Rd Stewart et al NEJM 2015@ | 2 (1-3) | Len or PI refr | 26.3 vs 17.6 mo; HR 0.69; P=0.0001 | 67.1 mo median F/U; Med OS 48 vs 40 mo; HR 0.79 P=0.005 | +/+ |
| Carfilzomib 70d vs 27x2d Moreau et al Lancet Onc 2018 | 2-3 | PCL, no PR to any Rx | 11·2vs 7·6 mo HR 0·69; P=0·0029; | 13.2 mo F/U One year OS 77 vs 72% P=ND | +/+- |
| Carfilzomib d (Kd) vs Vd Dimopoulos et al Lancet Oncol 2017 | 2 (1-3) | PI refr or < 6 mo from last PI Rx<PR to all Rx | 18.7 vs 9.4 mo; HR 0.53; P<0.0001 | 37.5 mo median F/U OS 47.6 vs 40 mo HR 0.79; P=0.01 | +/+ |
| Panobinostat Vd vs Vd San Miguel et al Lancet Oncol 2014 | 2 (1-2) | PI or HDAC inhibitor refr | 11.99 vs 8.08 mo HR 0.63 P<0.0001 | 6.5 mo median F/U; Median OS 33.64 vs 30.39 mos HR 0.87 P=0.26 | +/+- |
| Pomalidomide d vs d San Miguel et al Lancet Oncol 2013 | 5 (2-14) | IMid intol or refr to d | 4.0 vs 1.9 mo HR 0.48 P<0.0001 | 4.2 mo median F/U 11.9 vs 7.8 mo HR 0.53 P=0.0002 | +/+ |

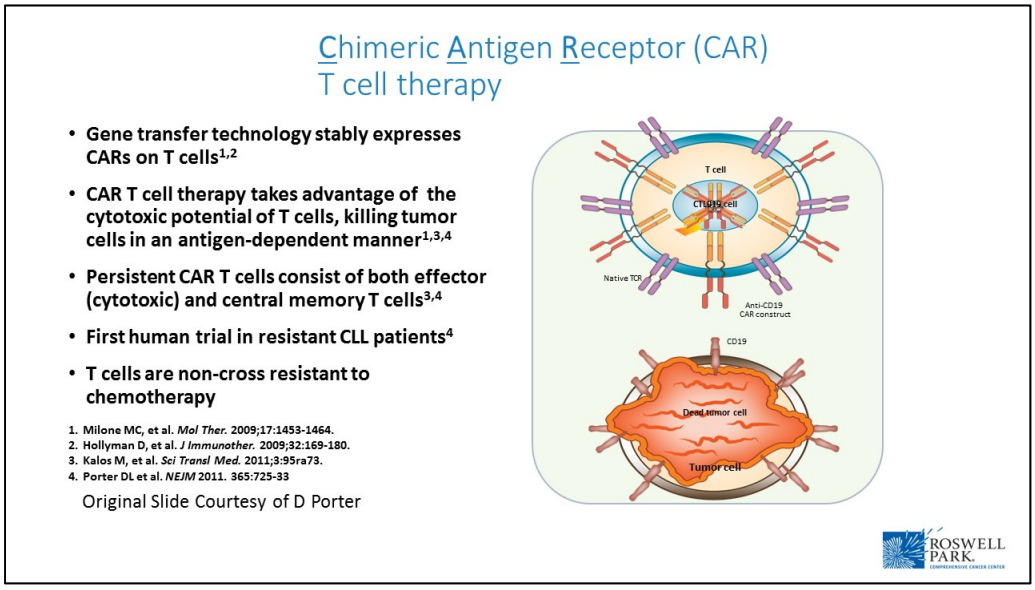
d: Dexamethasone; HR: Hazard Ratio; Len: Lenalidomide; ND: No difference; NR: Not Reached; OS:Overall Survival; PI: Proteasome Inhibitor; PFS: Progression-Free Survival; Rd: Lenalidomide/d; Vd: Bortezomib/d # Update Dimopoulos et al Haematologica 2018, *Update, Spencer et al Haematologica 2018, $Phase II study, ^Update Dimopoulos et al Cancer 2018 @Update Siegel et al JCO 2018

And then this is in aggregate in one place. I'm not going to go over it in great detail, but you can see it's hard to compare these trials, but you have to look at that to see how heavily treated was the patient beforehand, what did they exclude and what's the progression-free and overall survival? And these are just the different options for therapy, which I won't go into detail but, again, gives the clinician and the patient multiple options.

## TRANSCRIPT

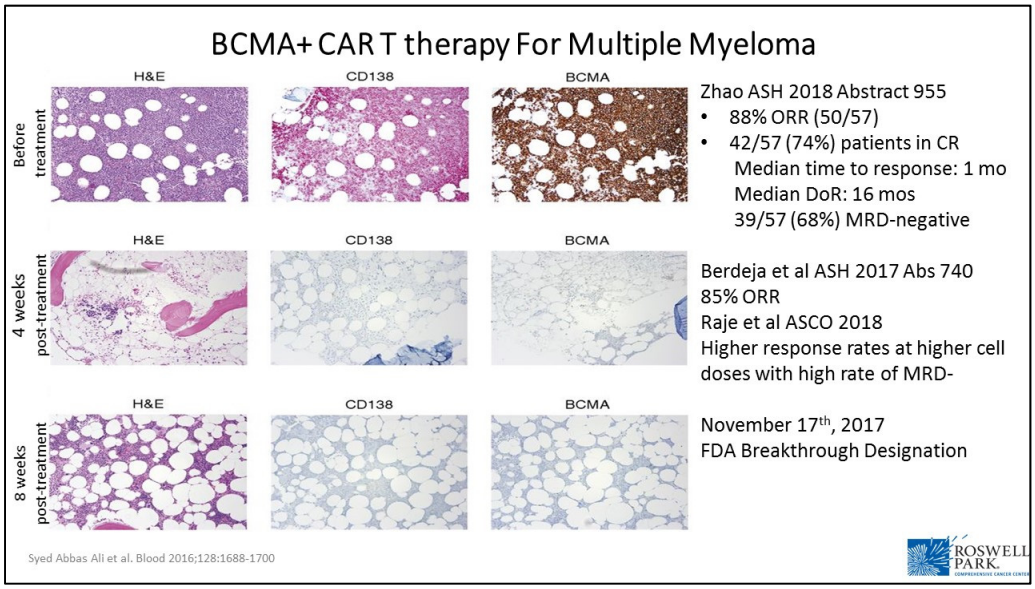



Going to close up with immunotherapy. As you may know, there's a BiTE, which is bispecific T-cell engager. It's an anti-BCMA, which is a molecule on the plasma cell. That's been presented in this clinical trial and now there are CAR T cells which are engineered T cells to kill the myeloma. I'll show you some slides on that. And there's also an anti-BCMA antibody with a poison on it to kill the myeloma cells.

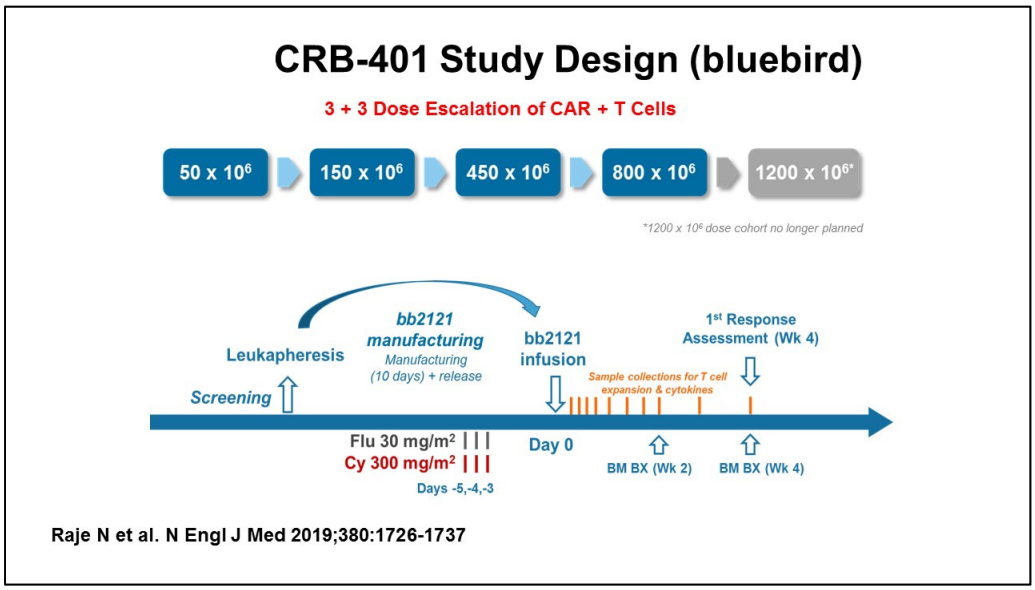



So, this is chimeric antigen receptor therapy (CAR T-cell therapy). Here's our T cell on the upper right. A virus comes in that has a construct in it which actually has, in this case, an anti-CD19 but it can be the target of your choice. And in this case, it comes and is expressed on the T cell, sees the target on the tumor cell and kills it. And this was first approved for both acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL) and is currently being trialed in myeloma.

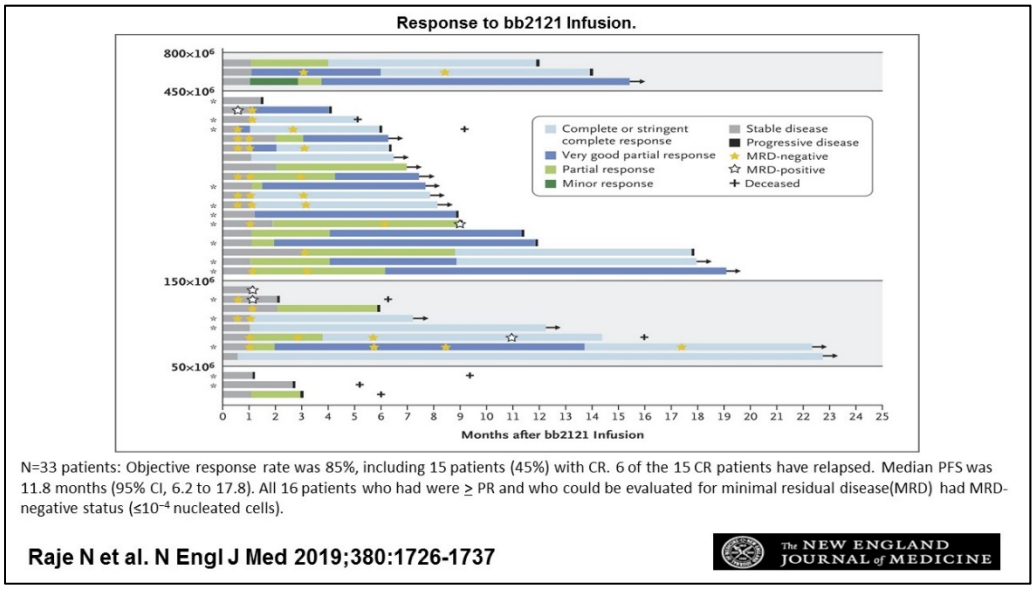
## TRANSCRIPT



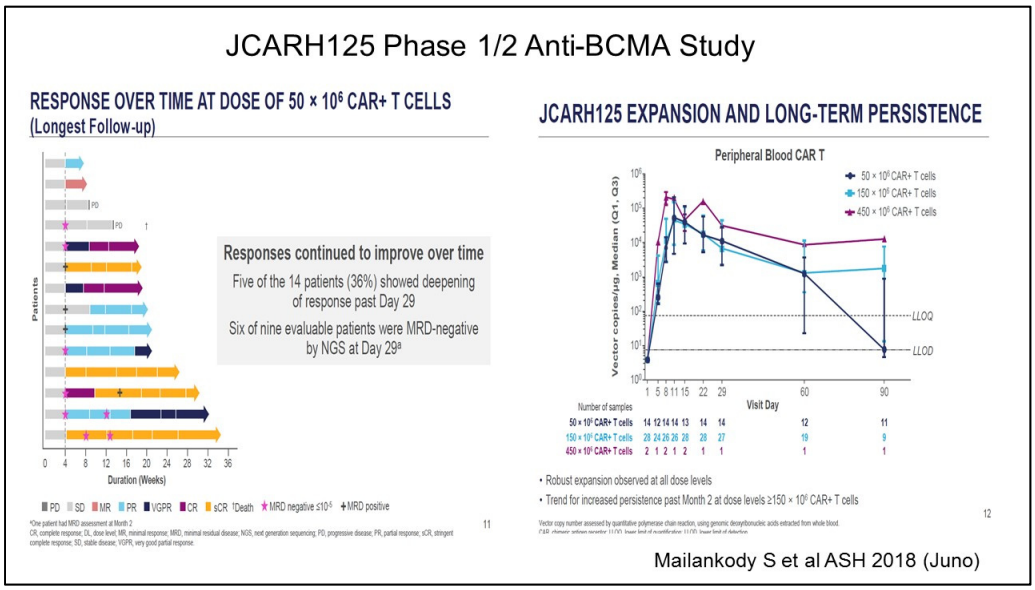

Here is a case that was presented, this is from a couple of years ago. Here you have a patient sample showing that it's full of plasma cells at the top. It's BCMA highly positive. These are all the myeloma cells. Four weeks after the infusion of the CAR T cells, you now have a clean out of the marrow, and eight weeks later the marrow has regrown with normal bone marrow.



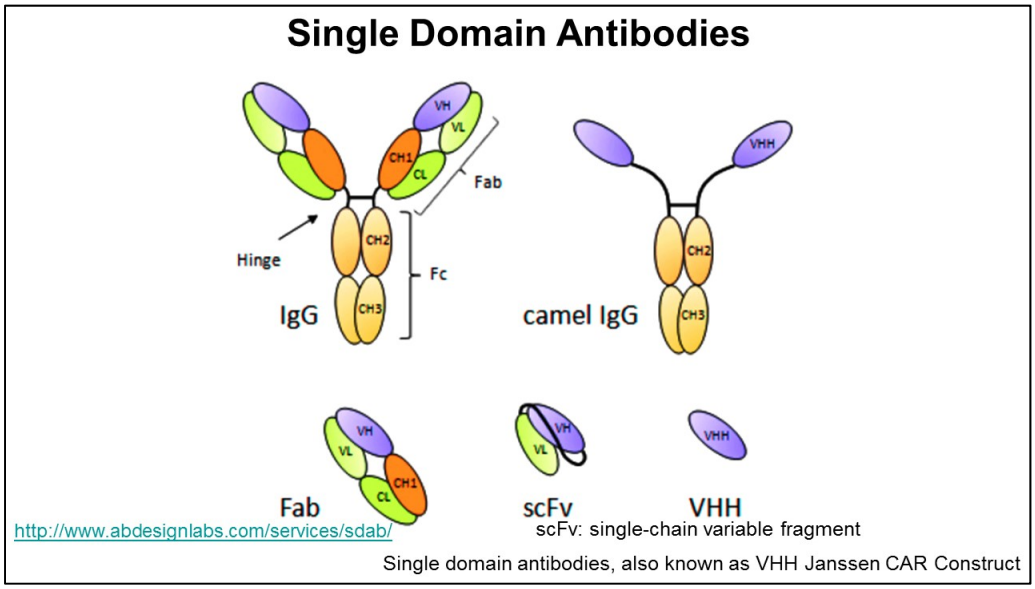

This is the Bluebird trial, which was just published about a month ago. Noopur Raje, MD, is the first author. The patients received a leukapheresis. They get their cells manufactured and then they're infused after a lymphodepleting regimen. And then the cells grow up and, hopefully, kill off the cancer.



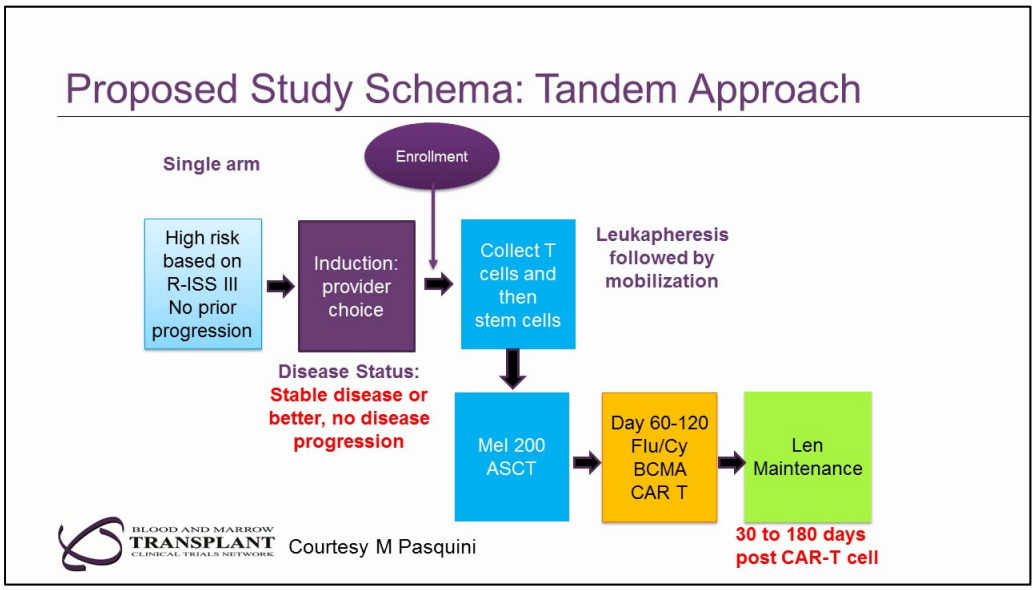

This is called a waterfall plot showing the responses. I won't go into detail, but the overall response rate was 85%; six of 15 complete response patients, however, have relapsed. So, the median progression-free survival was a year. So, that's good, but we need it to be better and so we're going to have to do a lot more research to figure out how to make it better for everyone.



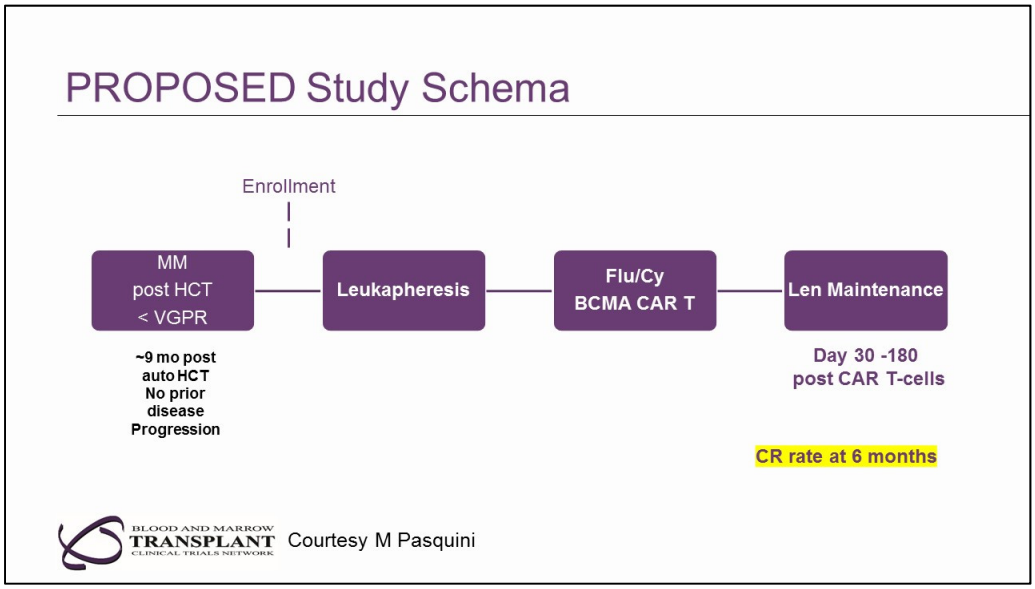

This is another one. This is the Juno one, another company. They're also doing CAR T cells, and this was just presented at the American Society of Hematology (ASH), again, showing some patients with response but it was at higher cell levels as they're trying to escalate the dose to control the disease.



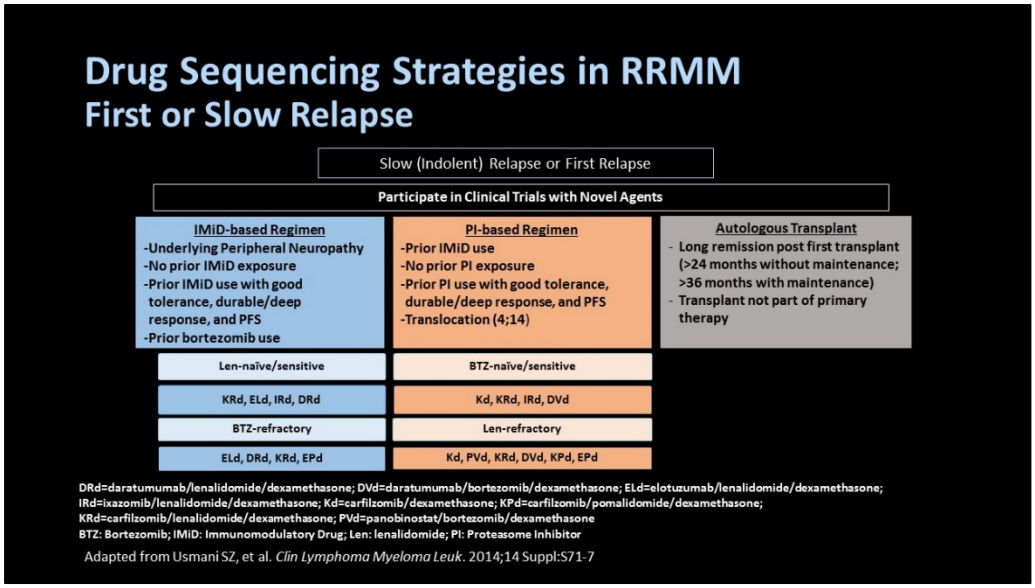

The thing that's kind of interesting, Janssen has one that's using instead of what I showed you before is either a mouse antibody; some cases it's humanized. The Janssen one uses a Llama antibody, which his similar to camel. It's kind of interesting that we're seeing all these different flavors that are going to be available for this type of treatment.



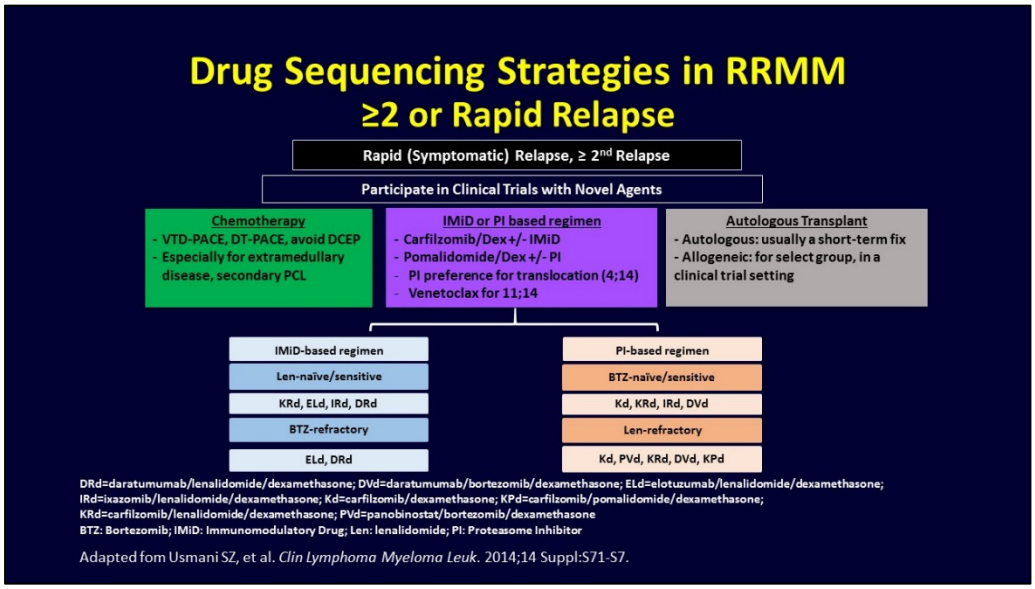

This is something that'll be available for high-risk patients upfront. They have high-risk disease based on the revised ISS. They'll get a stem cell transplant, and then it'll be followed early on after the transplant by a CAR T-cell infusion and then lenalidomide maintenance, again, to see if it can control disease long term.



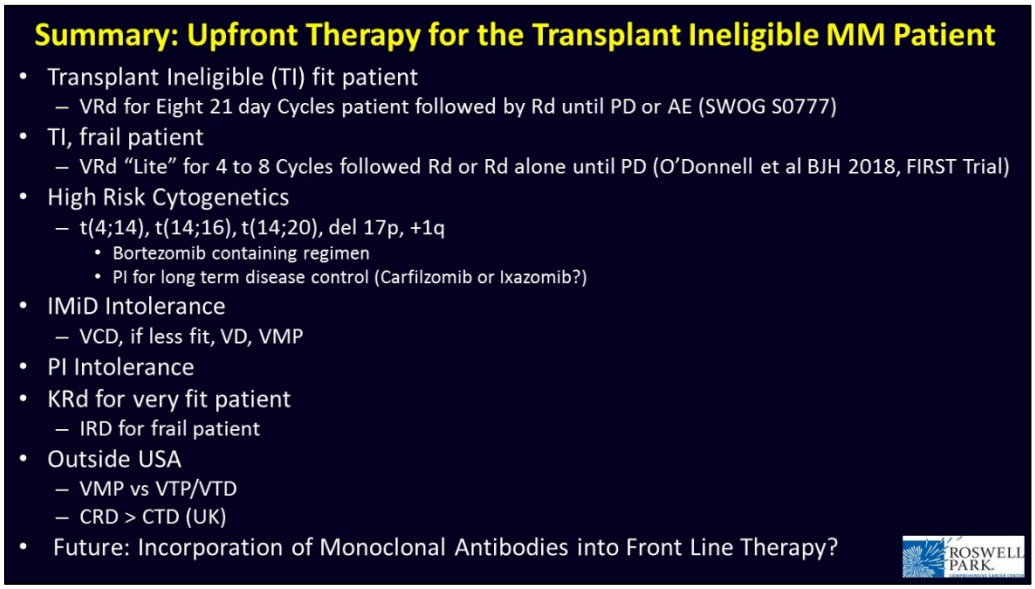

This is one for patients who don't have a good response, lessened VGPR at nine months. They'll get a leukapheresis, a CAR T-cell infusion followed by len maintenance to, again, control disease.



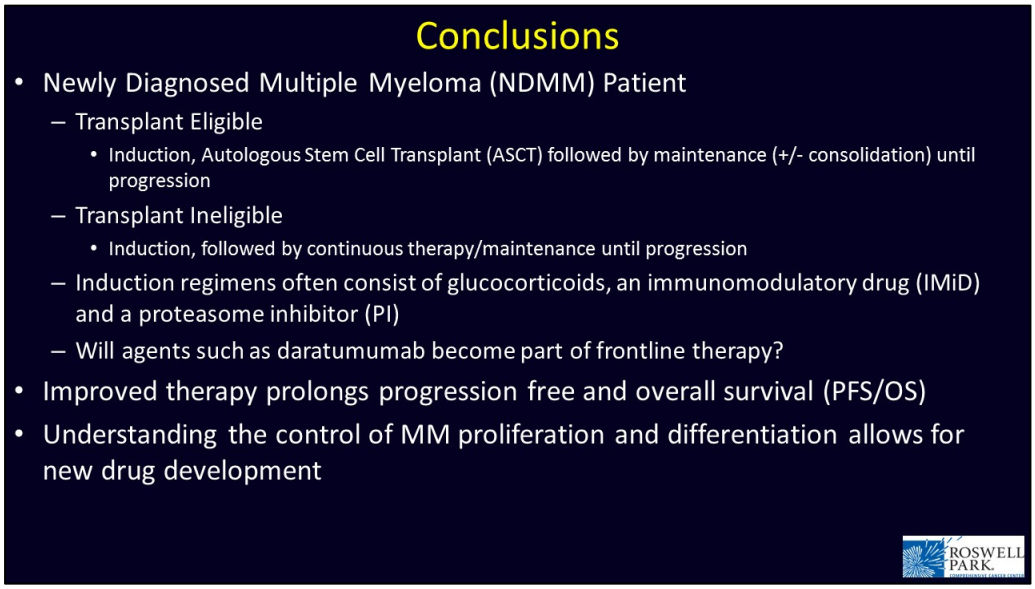

So, I'm not going to go into great detail. This is drug sequencing and relapsed/refractory. Sometimes it depends on the pace of the disease, what the patient was exposed initially, and whether or not it's going to be an IMiD or a proteasome inhibitor-based regimen versus an autotransplant. And there's a variety of different strategies for that.



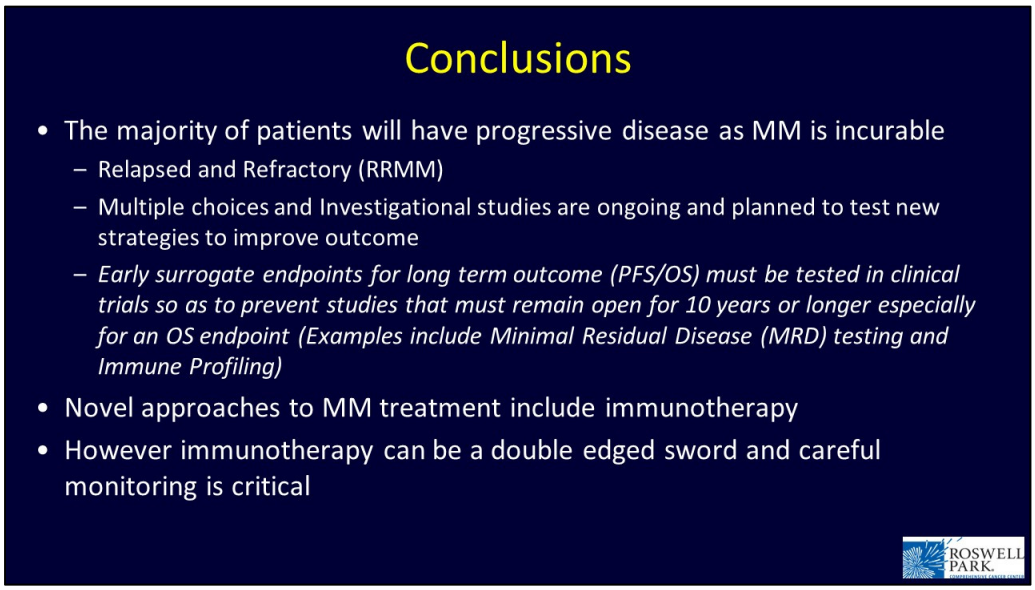

And then, if patients have a more aggressive relapse, we may be using things such as carfilzomib and daratumumab to try and control disease, consider for a transplant, or patients could be considered for study therapy because there are multiple options.




So, in summary, I'll go through this fairly quickly, there's a variety of options. We could argue for an attenuated VRD for the transplant ineligible patient with a very frail doublet. High-risk cytogenetics may need bortezomib exposure. Outside the US, it's very different. We're very lucky to have access to some of these drugs that other places may not have.

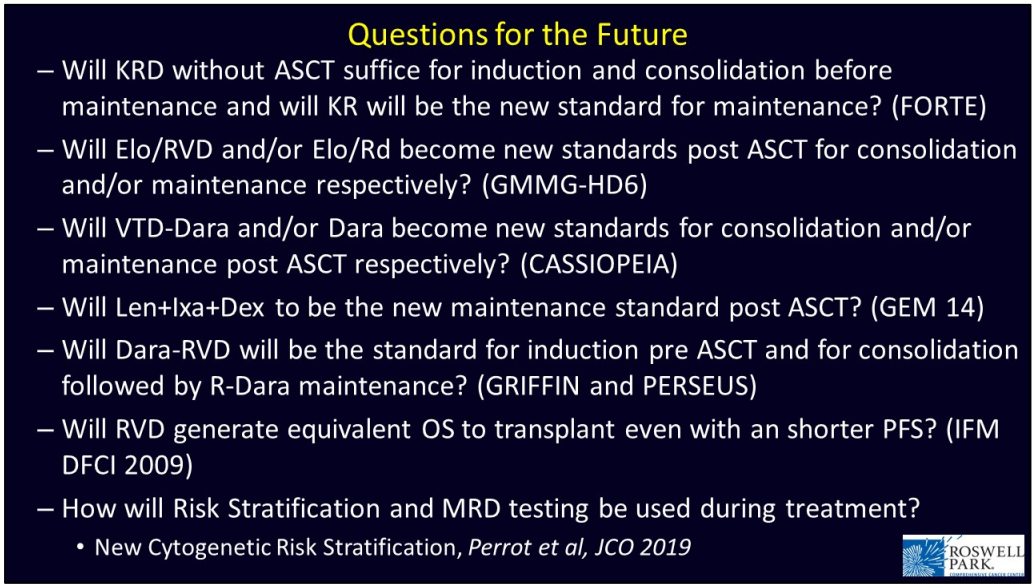



For the newly diagnosed transplant-eligible and -ineligible, continuous therapy. A regimen is usually now a triplet. Will daratumumab become part of upfront therapy? Can we prolong progression-free survival and, in particular, overall survival, and can we understand how to control myeloma through the immune system?




And so, for the majority of patients, progressive disease will occur. Myeloma is currently not considered curable, but we now have multiple choices and we have new trials that will help us because we need to develop early surrogates because some patients are responding so well that median overall survivals are approaching ten years. So, we want to have studies that will give us an early endpoint, so we can move on to the next treatment and figure out the best way to treat our patients.

Immunotherapy I talked about. It can be a double-edge sword. I didn't have time to go through it, but it can be very toxic. And it's something that we need to be aware of, so we can figure out how to control that.




So, these are the questions. Again, will KRD (carfilzomib-lenalidomide-dexamethasone) be the standard over RVD (lenalidomide, bortezomib and dexamethasone)? Will elo-RD (elotuzumab, lenalidomide and dexamethasone) be the standard, VTD-dara (daratumumab + bortezomib, thalidomide, and dexamethasone? So, these are all questions that we're going to have to figure out over the next few years. Again, good problem to have for our patients as we try to figure out the best approach.

## TRANSCRIPT

These are the members of my team who are involved in helping take care of our patients. I know the same thing is everywhere. At all your centers it's a team approach to the treatment of our myeloma patients.

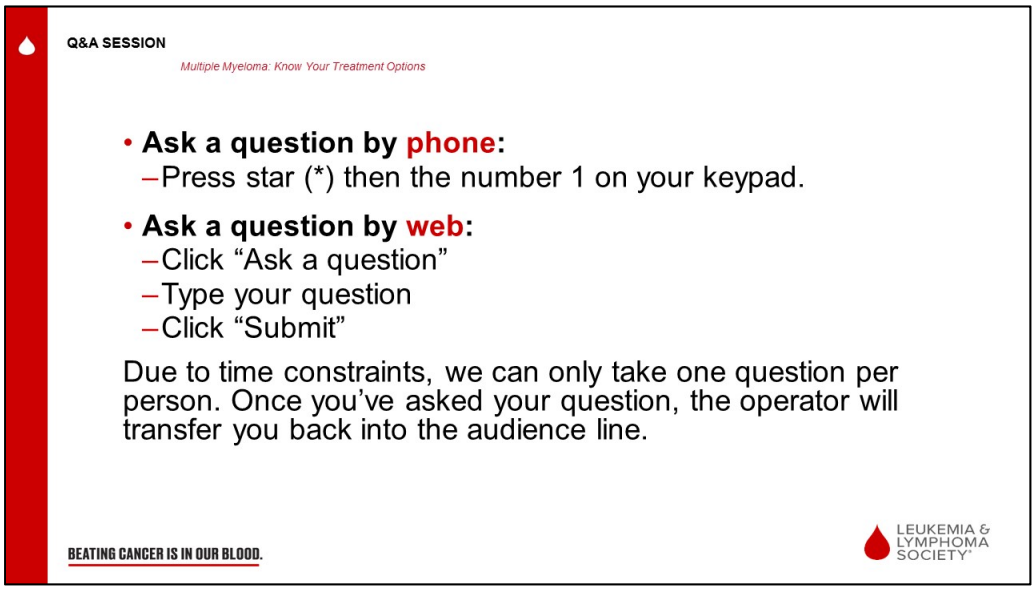

This is something from an ASCO talk I did where all my colleagues who are involved with myeloma around the world have helped me by lending me their presentations for these studies, which I showed you today, as well as my colleagues from the NCI (National Cancer Institute), the FDA (Food and Drug Administration) and, of course, my wife who has to put up with my schedule.


Thank you very much.

## QUESTION-AND-ANSWER SESSION

***Lizette Figueroa-Rivera, MA***

Thank you so much, Dr. McCarthy, for your very informative presentation.




And it's now time for our question and answer portion of our program.

We'll take the first question from our web audience. Doctor, Nancy's asking, what are the benefits and side effects of a second stem cell transplant?

***Philip L. McCarthy, MD***

That's a good question. What we do, potentially, is, if a patient has a long interval from their first transplant, before the disease progresses, we will consider that. And by long, greater than at least two years; some people say 18 months. If we have somebody who's been four or five years since their first transplant and now had progression of disease, we will at least consider a second transplant. I'm not saying to do that but, usually, after a reinduction therapy and control of disease, then, potentially, a second auto (autologous stem cell transplant) might be of great benefit.

Now, a lot depends on if the patient has their stem cells stored upfront. Some places will store enough for more than one transplant, and thus you could do this; you have this option. You can collect stem cells later on, but it can be a little bit more difficult.

So, we at least consider an option. Whether or not that second transplant's going to be replaced by such things as CAR T-cell therapy, I don't know yet. But, if it's an early relapse, in other words, the patient's within a year, I don't recommend a second transplant because we've been able to show that unless you're doing some different thing on a study that is a twist on the standard transplant, the

chances are, unfortunately, the patient will not have that great a benefit from it, and there's a degree of toxicity associated with the autologous stem cell transplant.

***Lizette Figueroa-Rivera, MA***

Thank you, doctor. And our next question is from the telephone audience please.

***Operator***

Your next question comes from the line of Richard of New Jersey. Your line is live.

***Richard, New Jersey***

Doctor, I wanted to thank you for being a crusader for, we, the myeloma patients. I've been fighting it now ten years, and right now I'm on my fourth relapse, and I'm taking Ninlaro® (ixazomib), Pomalyst® (pomalidomide), and dex (dexamethasone). And I was just wondering what's the next step. Is this going to be the CAR T if this doesn't work?

***Philip L. McCarthy, MD***

Well, it depends. It's hard for me to say specifically because a lot depends on what you've seen before. There are patients who benefit from a relook at daratumumab with different partners. A lot depends on, again, the interval so I don't want to give a specific. But, yeah, if your physician is aware of the trials; if you're in New Jersey, there are trials I believe at Hackensack and at Memorial Sloan Kettering, looking at CAR T cells, so that may be an option for you. But I'm not saying that will be the option.

And, again, as you saw, right now the progression-free survival is 12 months, a year, which is good, but we'd like it to be longer. And so, we need to have more studies done to see how can we extend that?

So, that was a lot of hemming and hawing on my part because, again, I'd have to spend probably about a half an hour going through all your records to say specifically, "Oh, yeah, CAR T cell is next in the queue." But there are, hopefully, going to be even more options because I'm hoping, for example, the GlaxoSmithKline Anti-BCMA antibody, which has a poison on it, which finds – it's like a Trojan horse – and it gets into the cancer cell; that may be approved next year. And that may be another option for you.

***Lizette Figueroa-Rivera, MA***

Thank you, doctor. And our next question from the web is from Angie. With multiple myeloma being incurable, as you said in your presentation, she's just asking the percentage of patients that will relapse. But, basically, how long until relapse?

***Philip L. McCarthy, MD***

Oh, I wish I had a crystal ball because I have some patients who I thought for sure were going to relapse within a relatively short period of time. I remember one distinctly. He had a plasmacytoma growing out of the side of his head, and we would give him the chemotherapy and it would shrink. And then, before the next cycle would start, it would grow back again. And I'm thinking, "Oh, this is terrible." So, we took him to an auto transplant, and we had this new drug; this is back in 1999, called thalidomide. And I put him on the thalidomide as part of the induction; that's how we responded. And then we put him on thalidomide maintenance. And then, at three years, he essentially begged me, "I have to stop this drug. It is causing terrible neuropathy. I can't feel my fingers." So, I was so nervous about that. He stopped, and that was back in 2003.

So, he then developed lymphoma in the meantime; he got treated for that. He's still around doing very well. He still has a little trouble feeling his fingers because of the thalidomide. But I thought for sure he was going to progress, and he did not.

So, there's this effort through one of the initiatives from the Myeloma Working Group called the Black Swan Initiative, to figure out who these black swans are. Who are these 10-15% of patients who have long-term control of their disease? And, in fact, they have a little bit; some of them even have a little bit of myeloma, but it's sitting there and it's not growing. And that's why MRD may not always be the answer because there some patients who have long-term control of their disease, probably through their immune system. And these are things that we don't yet understand.

Sorry for the long-winded answer, but there are patients, so it's always reasonable to hope because you may be one of those patients who can have long-term disease control.

***Lizette Figueroa-Rivera, MA***

Thank you. And I know that you just mentioned neuropathy, and I am getting many questions about neuropathy and what can be done for peripheral neuropathy.

***Philip L. McCarthy, MD***

Sure. You can do, well there's drugs such as gabapentin, which is useful for that. There's some other narcotics that can be utilized; sometimes an antidepressant can be used. But the most important thing to do is make sure you let your clinical team know right away if you have any symptoms. They

need to be aware, so they can maybe change the way the bortezomib is being given. It should be given subcutaneously. If it's given with steroids, the dexamethasone on the same day, that helps mitigate the toxicity of the bortezomib. Sometimes, if you start with neuropathy, like you're a diabetic, it may better to consider using carfilzomib instead. So, there's multiple things that can be done because we recognize completely that bortezomib neuropathy can be really problematic.

***Lizette Figueroa-Rivera, MA***

Yes, thank you. And our next question comes from the telephone audience please.

***Operator***

Our next question is from Sue of Colorado. Sue, please state your question, your line is now live.

***Sue, Colorado***

Thank you so much for taking my call. I've had multiple myeloma cancer since 2007. It was not diagnosed until 2008 by a chiropractor I had never met. I won't go into that. As a result, the lower part of my spine exploded; I have eight screws and a titanium-cage holding my spine together. I was in the hospital seven months. While I was there, I got a staph infection in my heart. Apparently, that, and tell me if I'm wrong, that increased my immune system to work to take care of that. And I have been in remission since 2008, I guess. I did have a stem cell in 2011. Could that have caused me to be able to be in remission that long?

***Philip L. McCarthy, MD***

Well, the fact that you had to have a stem cell transplant after the staph infection, would at least imply that the stem cell transplant sure helped likely control the disease. We don't know enough about this, but we do know that there is some issues of how your immune system works. I've had other patients who got terrible infections and it didn't do anything for them. They just continued to get worse.

In fact, I've had one patient who had pneumococcal sepsis in the bloodstream, and it wasn't until – and she had no immunity to pneumococcus afterwards, so we actually had to treat her, and then her immunity to pneumococcus came back as we vaccinated her.

So, there's a lot of questions that we don't know. We do think the immune system is important, and we're going to need to study it over the coming years to help us better understand how the immune system controls disease.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question comes from Jack. Doctor, Jack asks, "Given recent trial results for high-risk smoldering myeloma patients, do you believe these patients should be treated, and if so, with what?

***Philip L. McCarthy, MD***

That's the million-dollar question. I mean, as you know, there are two major studies, one from Spain; I didn't have a chance to show that, from Maria V. Mateos, MD, PhD. Dr. Mateos did a study with lenalidomide versus observation in high-risk smoldering and showed a progression free and overall survival benefit. That was reported in 2012.

The ECOG trial, which was intermediate and high risk, so it was a little different, showed a progression-free survival benefit with the use of lenalidomide.

I think that once we can get closer; remember, I said it was initially around 59%. If we can get close to identifying 100% of patients who are going to progress within two years to multiple myeloma; and we're getting there. Then I think we'll be ready for prime time on this because you don't want to treat somebody who doesn't need treatment. And we may have some patients who are going to have more aggressive disease who we really should be doing more than single agent lenalidomide, or even a doublet. So, we need to identify which patients we should be more aggressive with.

So, we're getting there. We are very close.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from our telephone audience.

***Operator***

Our next call is from Robert of Pennsylvania. Robert, please state your question, your line is now live.

***Robert, Pennsylvania***

Hi, doctor. I have a question about Revlimid. I've been treated with that for the last four or five years off and on as my rates improve on the multiple myeloma, and I was on smoldering myeloma for six years. So, I don't know, I haven't heard the Revlimid medication on your program.

***Philip L. McCarthy, MD***

Oh, I'm sorry. Revlimid is lenalidomide It's like Kleenex and facial tissues. And I try and use the generic as much as possible. Sometimes Revlimid is easier to say than lenalidomide and Velcade is easier to say than bortezomib. But, yeah, Revlimid is lenalidomide.

***Lizette Figueroa-Rivera, MA***

And, doctor, also, participants are asking, and I know that you mentioned maintenance therapy. How long should they be on Revlimid? We have people asking; they've gone on seven years already on maintenance Revlimid.

***Philip L. McCarthy, MD***

Well, the label from the FDA is maintenance until progression. Now some people say, "Oh, you should get it for at least two years and then you can stop," but there's no clear data for that. The ECOG group is doing a trial in nontransplant eligible patients, which is a little different, of two years of len maintenance versus maintenance until progression. So that will help us, but it's a nontransplant study. I'm anticipating it will show a progression-free survival.

The Germans did a study of maintenance until complete remission (CR) versus maintenance for a fixed two years. And they found that the maintenance until CR patients did worse. Why? Because they didn't get lenalidomide as long.

So, I think if the patient is tolerating it and there's no untoward side effects; there is the second cancer risk, but it's relatively small relative to the importance of controlling disease. So, I'm still recommending it until progression if the patient is tolerating the lenalidomide.

***Lizette Figueroa-Rivera, MA***

Thank you. And I know you just mentioned second cancers. Rose has a question that, what are the prevalent type of second cancers from myeloma?

***Philip L. McCarthy, MD***

Yeah. We're all over the place on that. There's a about two to threefold, depending on the cancer risk, of solid tumors. It's not clear if that is just patients are living longer so they get observed more carefully for second cancers. There's definitely a really high risk of skin cancers, in particular, basal cell and squamous cell carcinomas. So, it's really important to have follow-up with the dermatologist if these start occurring. And they often will occur in sun exposed areas because you can't take back the sun that you received when you were 15 years old.

We do know that there is an increase of hematologic malignancies and we are really studying this aggressively so that we can figure out who these patients are. And, again, you go from a 1 or 2% risk to a 3–6% risk. So, it's there, but we need to know who these patients are so that we can, obviously, approach long-term disease control in a different manner.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from our telephone audience please.

***Operator***

Our next call is from Sally of Georgia. Sally, please state your question, your line is now live.

***Sally, Georgia***

Thank you, doctor. My question is you keep mentioning dexamethasone, and I've been told that you shouldn't be on dexamethasone that long, especially with Revlimid, maintenance Revlimid. I was diagnosed in 2017, went into a remission in 2018, had a stem cell transplant, also, in 2018. I think I'm getting my years straight because I was diagnosed 2016, went into remission in 2017, had the stem cell transplant in 2018; that's it. And everything, I've been told, is all right, but don't use dexamethasone.

***Philip L. McCarthy, MD***

Correct. No, no, that's correct. The dex is for; sorry to interrupt. The dex is definitely for part of induction therapy, and it's really good at helping control the disease. The thing is you don't want to use it long term. Now some places do that. The Spanish use len-dex long term. They knock the dose way down so you're getting it once a week at a much lower dose. That's one option, but I prefer not to do that, and I recommend the single agent lenalidomide, or if there are issues with tolerating it, then either bortezomib twice a month. Some people now are using ixazomib. But, definitely, you can't use – the long-term stories aren't good because they're not well tolerated because of hypertension and diabetes. So, we don't normally treat patients' long term with dexamethasone. It's part of the upfront therapy, however.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question, doctor, is from Alan. Alan is asking the status of venetoclax for myeloma treatment.

***Philip L. McCarthy, MD***

It's a BCLN2 inhibitor. BCL2 is the molecule that's involved with how long a cell lives. It really works well in patients with that chromosome 11;14 translocation, especially when combined with bortezomib-dex. It was just presented at the last ASCO (American Society of Clinical Oncology) as well as the European Hematology Association (Annual Meetings) that there's actually in the non-11;14 translocation myeloma patients, there seems to be a higher death rate, and we don't understand this. So, it's really flummoxed a lot of investigators as we try and figure this out.

It definitely has benefit. This trial is called the BELLINI trial, and this is the early readout, the progression-free survival is superior, but there is a concern about the overall survival signal. And I know AbbVie and Genentech, who are partnered on this drug, are working really hard to figure out what is going on here because we know it has benefit. It's just that we're not certain about which patient populations to use it, so, actually, the FDA has put a hold on new studies until we can sort this out.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from the telephone audience please.

***Operator***

Our next call is from Tony of Tennessee. Toni, please state your question, your line is now live.

***Toni, Tennessee***

Yes, ma'am, thank you. I have a question about supplements in the treatment or the controlling, helping with neuropathy and, also, anemia. I'm taking iron, I'm taking turmeric. I could not tolerate gabapentin; it was playing with my thoughts. I had to get off of it. So, I'm just wondering what's your opinion of using supplements with these two issues.

***Philip L. McCarthy, MD***

Sure. I would definitely discuss that, though, with your treating team. The iron may be okay. The only issue is if you've had a lot of blood transfusions, it wouldn't be good to get iron, but I'm assuming that's not the case.

A lot of people are interested in turmeric. I always say, if you like turmeric, go eat Indian food because you'll get plenty of turmeric that way. But it's not clear if that has benefit. If you think it helps, it's fine. Gabapentin, you're right, is psychoactive, it crosses the blood brain barrier, it gets into the brain.

Sometimes I'll just recommend it to people to take a low dose of it, and it may have benefit. But right now, I think, as long as you are discussing it with your team, and they know what you are taking. Please don't take supplements without telling your treating team. And you come to a best practice approach so that you don't have something that might be interfering with some of the therapy.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question comes from Michelle. Is plasma-cell leukemia (PCL) treated with the same protocols as multiple myeloma?

***Philip L. McCarthy, MD***

Plasma-cell leukemia is a more aggressive disease, so, in fact, a lot of them are 11;14, and some people were incorporating venetoclax. It's still an open question. But, often, patients will be treated a little bit more aggressively because it's a more aggressive form of myeloma. But, yeah, it's essentially a variation on a theme for the treatment of what we call PCL.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from our telephone audience please.

***Operator***

Our next call is from Phil of Colorado. Phil, please state your question, your line is now live.

***Phil, Colorado***

Yes. My situation is probably a little bit different than everybody else's. I've had multiple myeloma for six and a half years. I was on Revlimid for five and then I had to go to Pomalyst, and then I started taking that infusion. And every month since that my count has been going up just a little bit every three months. But I take a PET scan and we don't find any damage or any cells in that at all, but my count is still going up a little bit each month. And I'm wondering, is there something I'm not doing to alleviate the problem?

***Philip L. McCarthy, MD***

Are you saying your M protein is rising slowly over time?

***Phil, Colorado***

Yes. It started out at about five, over five years, and then they put me on Pomalyst, and then this infusion drug; I can't pronounce it, but you know which one it is.

***Philip L. McCarthy, MD***

Are you talking about daratumumab or Darzalex®?

***Phil, Colorado***

Yes. I am.

***Philip L. McCarthy, MD***

Now, it may modulate. So, sometimes you may have a negative PET CT, but a bone marrow test may be useful in helping figure out where there might be some occult disease. And as long as the disease remains low; and that's why I do recommend a bone marrow test, potentially, or an MRI to look for an occult lesion. That may tell you where this protein is being secreted from. So, it does mean sort of doing a hunting expedition or some detective work to figure that out.

We do know that daratumumab does have immunomodulatory effects. It just doesn't directly attack the myeloma cell. It actually helps modulate the immune system. So, it could be that the immune system is controlling it, and a lot depends on the pace of how high the M protein is going up. So, is it going up real fast, is it going up really slow? If it's slow, that may be worthwhile. And then, eventually, your doctors will figure out why it is rising and where this protein is coming from, and they may switch therapies, or they may be able to continue as long as you're able to maintain the disease and there's not a high burden of disease. And until then, I would discuss this with your doctors.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question from the web, Furman said that you mentioned an increased risk among African Americans. And if you could please expand on that.

***Philip L. McCarthy, MD***

Oh, that's a really interesting question. We don't know why this is specifically. We do know, for example, 11;14 translocation is higher in African Americans. So there appears to be some issue in the genetics of people of African American descent in terms of developing, having a higher risk of myeloma. We know there's a variety of different issues related to this.

So, for example, my wife has chronic lymphocytic leukemia (CLL), so our children; she's not being treated, but our children have a twofold risk of getting CLL because she's had it. And so, we do know that if you have cancer in the family there will often be a risk, albeit slightly higher. But we just don't understand a lot about the genetics of all of this; we're beginning to understand it more. And so, it does just mean something that to be aware of. We do know there have been studies that have shown that people of African American descent, as long as they have access to the appropriate drugs, the best that's available, their outcomes are very similar to those who are non-African American. Again, if they have access to the best drugs available.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from our telephone audience please.

***Operator***

Our next call is from Linda of California. Linda, please state your question, you line is now live.

***Linda, California***

Yes, I just wanted to lay out a timeline here. My first oncologist was 1973, and I am 73. And due to blood issues, I went to the Mayo Clinic in 1991, and they were happy to inform me that I did not have leukemia but that there was something wrong with me; clearly, I had myeloma. But in 1999 I was diagnosed with breast cancer, had Adriamycin-Cytoxan (AC). And, guess what? Not only did I deal with my breast cancer, but my numbers went down for my myeloma. I was diagnosed in 2007 with the multiple myeloma, and the multiple myeloma I did the EVOLUTION trial, and it knocked my numbers way down. I then went into a transplant; I am now a ten-year transplant survivor. My numbers are starting to hike back up a little. I've never been in complete remission or had a CR; would love that.

But I am currently looking at; Rev-dex helped, but the problem is, as I said, I just had a surgical deal for atrial fibrillation, and I'm concerned about the heart issues and atrial fibrillation with Rev-dex. Can you give me a clue?

***Philip L. McCarthy, MD***

Well, the biology of your disease is such that we know that it behaved in a much more indolent manner. The fact that you probably had MGUS for a period of time and, as you stated, AC for the breast cancer probably controlled the disease.

I think there is a risk, albeit the risk of a-fib is relatively small with lenalidomide. I'd be more concerned about the dex potentiating that. So, I think a cardiac evaluation is going to be very important, cardiac

echo, look at the size of the atria, family history of AFib, and a variety of other things. So, I think that's very important. I think it is a reasonable option to consider because at least your disease is relatively indolent. You potentially can get benefit from say starting at a higher dose of lenalidomide, maybe backing off a bit. Same thing with the dexamethasone, or even starting with a lower dose.

So, I think there are multiple options that could be utilized to help control the disease, knock it back down, and then go on something relatively low dose to control the disease for a longer period of time.

There are other drugs that I'd be much more worried about; most of them are not related to myeloma therapy, that precipitate atrial fibrillation, but with good monitoring and, again, with a low-risk echo cardiogram. If you have some features that would suggest oh, you are at risk for developing a-fib, then, yeah, it may be something where you may have to consider something different.

***Lizette Figueroa-Rivera, MA***

Thank you. And the next question comes from Caroline. Caroline is asking, "If you have participated in previous trials, can you still enter a new one?

***Philip L. McCarthy, MD***

No, good question. Oftentimes it depends. There are things called eligibility criteria, so they may say, "If you've seen this particular drug, you're ineligible for this trial, or have had this particular treatment." But, no, oftentimes, if you're on an investigational drug, and there's usually a time period, if your X days beyond it, and you now are eligible because the disease has come back to be treated on this other trial, oftentimes people will. Some patients will be on three, four, five, six trials because they are eligible. And just because you are on one trial does not mean you can't go on another one.

***Lizette Figueroa-Rivera, MA***

Thank you. And we'll take the next question from our telephone audience please.

***Operator***

Our next call is from Juan of California. Juan, please state your question, your line is now live.

***Juan, California***

Yes, thank you for taking my call. Listen, doctor, I've been in remission state for about two years now. I'm currently taking the Revlimid 10 milligram capsules. I'm on a dosage of 21 days straight and then seven days off.

My main concern is, for how long do I take the Revlimid on long term, or will it have any kind of damage to my other body organs or parts?

***Philip L. McCarthy, MD***

Yeah, no, good question. Three weeks on, one week off is reasonable. It gives the marrow a rest. As I mentioned earlier, there is a second cancer risk. Again, it's outweighed by the benefit of controlling the disease. I've had some patients who have been on this drug now for ten years and who still have their disease under control. I recommend, as long as you're tolerating it and there are no other issues, and if you've gone a longer period of time, I would stay on it. At least the updated label is maintenance until progression, and I do think it's reasonable to consider doing that. You're on a relatively low dose. If you're having side effects from it, that's a different situation, which you could discuss with your doctor about whether or not you should continue or if you're having problems. If you're not having problems, I would recommend staying on it as long as possible.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question is from Roy. Roy is asking for advice for controlling extreme fatigue.

***Philip L. McCarthy, MD***

Oh, it depends on what the fatigue is due to. If it's due to the therapy, that's a discussion with the doc. Sometimes the dexamethasone causes fatigue. Sometimes it's the lenalidomide or the bortezomib, in other words the Revlimid or the Velcade. You really need to discuss that with your team to help work on a strategy; how anemic are you? I'd make sure; sometimes these things can affect your thyroid function, so it means a really strong work-up to make sure you don't have some underlying condition that may predispose you to feeling even more fatigue because most people are usually able to, with good disease control, and especially on a maintenance strategy, able to control their disease and have a reasonable quality of life. Because if you're too tired, you really need to look into why that is.

***Lizette Figueroa-Rivera, MA***

Thank you. And our next question comes from Shyler, is asking about if nutrition could actually assist with the chronic diarrhea, the leg and foot cramps, organ damage, or ankle edema?

***Philip L. McCarthy, MD***

The diarrhea could be due to both bortezomib or lenalidomide; less so dexamethasone. The ankle swelling is often due to the dexamethasone if it's both legs. If it's only one, you need to let your team know because you want to make sure you don't have a clot in that leg.

Nutrition definitely helps, but it's not the be all and end all because you want to stay well-nourished and sometimes you just, it's trial and error to find out what's the best approach. Sometimes working with a dietitian to make sure that you're getting adequate caloric needs. And then, also, working on strategies to control the diarrhea. Sometimes a drug, a bile salt binding agent, cholestyramine, called Questran®, that can help with diarrhea.

So, there are a bunch of strategies that can be done to help mitigate toxicity and decrease the severity of the side effects.

***Lizette Figueroa-Rivera, MA***

Thank you. And, Shyler, we do also have a podcast coming out, *The Bloodline*, with LLS.org is our patient podcast that will be addressing nutrition specifically for myeloma, as well as we have free one-on-one personal nutrition consults with our registered dietitian. And I'll give you the number to our Information Resource Center in a couple of minutes, and they can guide you.

And, Dr. McCarthy, our last question today is from Jessie. Jessie's asking, "How do you address quality of life concerns with your patients? And are support staff integral in goals of care conversations in your clinic?"

***Philip L. McCarthy, MD***

Oh, absolutely. Oh boy, that's like a multi-part answer, but absolutely, because oftentimes it's the nurse administering the therapy, in particular the bortezomib, who you have to let know. "Look, I've been having worsening tingling and numbness in my hands and in my feet." Or, "I am completely wiped out." And it's critically important to let your staff know what's going on.

We are beginning to see the initiation of what are called patient reported outcomes in clinical trials, so the patients are giving immediate feedback as to how the therapy is working for them. There are now quality-of-life instruments that are being utilized so that we can get a better feel for how some of these longer-term therapies are impacting patient's quality of life.

And then, I know you talked about goals of care. I think a lot of that depends. If you have somebody who's 95-years old and they have myeloma, the goals of care are going to be very different than somebody who's 45-years of age. And that needs to be really clear because somebody who's 95, you may not, you're definitely not going to be as aggressive in somebody who is 45-years of age. I know I

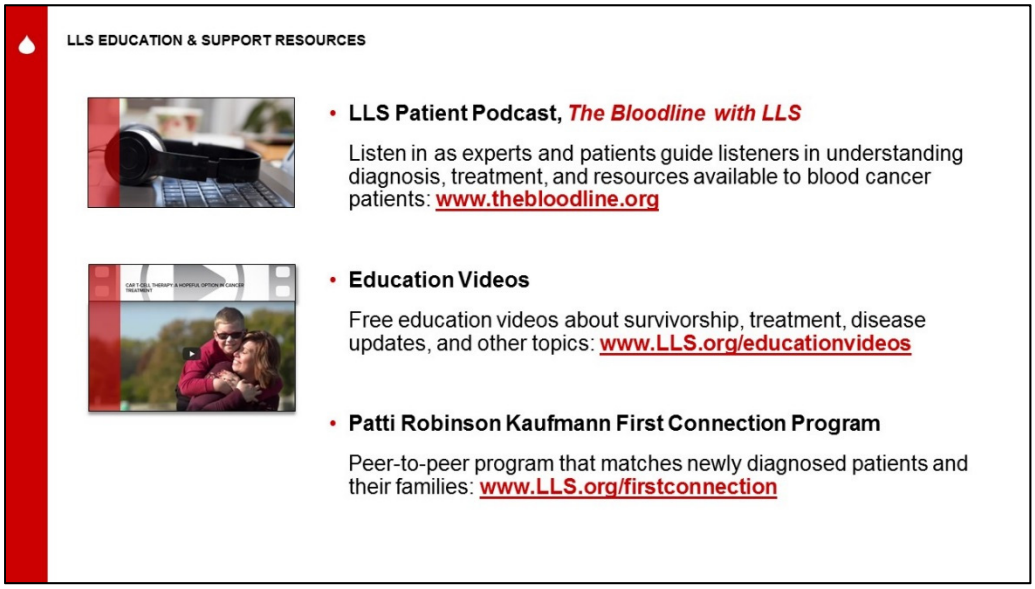
said earlier age doesn't matter as much, but it does when you get to be up there because when you're 95, your performance status just isn't near as good as it was when you were 45.

So, I think it's critically important that goals of care are discussed with the team, you need to discuss that with your physician and the nursing staff, so that everybody's on the same page with regards to symptom management as well as, well, what's the next step if the disease were to come back?

## CLOSING REMARKS

***Lizette Figueroa-Rivera, MA***

Well, thank you for that question, Jessie, and thank you all for your questions. Thank you so much, Dr. McCarthy, for your continued dedication to patients.




If we weren't able to get to your question today, please call a Leukemia & Lymphoma Society Information Specialist at 1-800-955-4572. Information Specialists are available to speak with you from 9:00 AM to 9:00 PM Eastern time, or you can reach us by email at infocenter@LLS.org. We can provide information about treatment, including clinical trials, or answer other questions you may have about support, including questions about financial assistance for treatment and nutrition consults.

Please note that continuing education credit is not being offered for this program.


Again, we would like to acknowledge and thank Amgen, Celgene, and Takeda Oncology for partnering with us to support this program. And thank you, Dr. McCarthy, for sharing your knowledge with us today.


To all the patients, caregivers, and professionals participating in today's program, on behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us.

Goodbye, and we wish you well.