

Update on Hodgkin Lymphoma

Matthew Matasar, MD
April 1, 2016

Slide#1: Update on Hodgkin Lymphoma

Operator:

Greetings, and welcome to The Leukemia & Lymphoma Society Update on Hodgkin Lymphoma Education Program. It is now my pleasure to introduce your moderator, Lizette Figueroa-Rivera.

Slide#2: Welcome and Introductions Update

Ms. Lizette Figueroa-Rivera:

Thank you. Hello, everyone. On behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us. A special thanks to Dr. Matthew Matasar for volunteering his time and expertise with us.

The Leukemia & Lymphoma Society (LLS) exists to find cures and ensure access to treatment for blood cancer patients. Our vision is a world without blood cancer. For more than 60 years, LLS has helped pioneer innovation such as targeted therapies and immunotherapies that have improved survival rates and quality of life for many blood cancer patients. To date, we have invested over one billion dollars in research to advance therapies and save lives. Until there is a cure, LLS will continue to fund promising research from bench to bedside.

In addition, as this program demonstrates, we are the leading source of free blood cancer information, education, and support, and we touch the lives of patients in their communities through our 56 chapters across the United States. LLS also acts as the voice for all blood cancer patients. We advocate for patients, survivors, and their families, helping them navigate their cancer treatments and ensuring that they have access to quality, affordable, and coordinated care.

Slide#3: Disclosures

We're fortunate to have as our presenter, Dr. Matthew Matasar, one of the nation's leading experts in lymphoma. We appreciate his dedication to supporting our mission and his commitment to caring for patients living with blood cancers.

Slide#4: Update on Hodgkin Lymphoma

Dr. Matthew Matasar is a physician at the lymphoma and adult BMT services and Director of the Lymphoma Survivorship Clinic at Memorial Sloan Kettering Cancer Center in New York, New York.

Dr. Matasar, I am now privileged to turn the program over to you.

Update on Hodgkin Lymphoma

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Dr. Matthew Matasar:

Thank you very much. And on behalf of the LLS thank you for this opportunity to present an update on Hodgkin lymphoma.

Slide#5: Roadmap

I have an ambitious plan for this presentation. We're going to try to cover a lot of ground together, starting first with an overview of Hodgkin's disease, talking then about treatment both of newly diagnosed Hodgkin lymphoma, as well as the patients who either are refractory to a relapse after their first treatment, talk next about emerging and novel therapies and therapeutic strategies, and last touch upon the importance of survivorship care.

Slide#6: In The Beginning...

So, let's get started. Obviously, Hodgkin's has a long and storied history. Here, we have a picture of Hodgkin himself. And this is the original journal article from now almost 200 years ago when this was first described. This illness was first described in two children who had abnormalities of their spleen and of their lymph nodes.

Slide#7: Cellular abnormalities

We've come a long way from this first description of seeing these large and abnormal looking lymph nodes to understanding that there are actually cellular abnormalities. It's a cancer inside of these lymph nodes with these characteristic what are called Reed-Sternberg cells, the actual malignant cancerous cells inside these lymph nodes.

For an understanding of the importance of abnormal protein expressions on these cells, here showing the protein CD30, which is both characteristic of and so important in the understanding of Hodgkin lymphoma, to an even greater and more modern understanding both of the actual cellular pathways within these abnormal cells, as well as how these abnormal cancerous cells interact with the surrounding immune system.

Slide#8: Incidence

Let's remember, however, that Hodgkin lymphoma's a pretty rare disease, right? We have about eight to 9,000 cases of this a year in America. Contrast that with non-Hodgkin lymphoma between 60 and 70,000, and then cancers like prostate cancer, breast cancer, lung cancer, which are 200,000 plus a year. It's a rare disease, but it also has this interesting age distribution with what we call a bimodal distribution, where you have a peak of incidence rate of risk in people in their 20s and 30s, and then it goes down somewhat during middle age, and then the second peak for older patients. We're gaining a better understanding that elderly Hodgkin lymphoma and Hodgkin lymphoma in younger people really may represent two somewhat different diseases and really may benefit from two different types of therapeutic approaches sometimes.

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Slide#9: Survivors of Hodgkin lymphoma

Let's not forget, however, that we've come a long way in this disease, and over the last four decades, we've seen tremendous progress with our ability to cure and control this disease, such that now in the modern era, for every 10 patients who are diagnosed with Hodgkin's, we expect that eight of them will be cured through appropriate therapy.

Slide#10: What are the signs of Hodgkin lymphoma?

What are the signs of Hodgkin lymphoma? Most typically it's somebody presenting with swollen lymph nodes in their neck or their armpit, most commonly, although other parts can be as well, or lymph nodes show up on scans done for other reasons, particularly in the middle of the chest, what's called the mediastinum. Common, although not universal, are these so-called B symptoms: recurring fevers, particularly at night, drenching night sweats, unexplained dramatic weight loss. And there are these other symptoms that can happen sometimes as well. Fatigue is very common, a total body itch. "I just can't stop scratching. I have no rash, but I'm itchy all the time." Patients can have a cough, or chest pain, or shortness of breath, particularly if there are large swollen lymph nodes in the middle of the chest. And rarely, although very uniquely to Hodgkin's, patients can have this sensation of an aching, burning pain in an area of swollen lymph nodes right after drinking something alcoholic: beer, wine, or the like.

Slide#11: "Staging" Hodgkin lymphoma

Everyone wants to know what stage of disease and how do we stage Hodgkin lymphoma. And shown here is a cartoon showing everything from Stage 1 on the left, where you have a single area of lymph nodes involved; Stage 2, more than one area of lymph nodes involved. It's on the same half of the body, either the upper half or lower half; Stage 3, where there's lymph nodes in both the upper and lower half; and Stage 4, where it's not just lymph nodes but spread to other organs, such as the liver or bones.

More important than stage, however, is what stage tells us. And staging is about risk and about understanding how dangerous someone's disease is. So, going beyond stage, we really like to classify patients into risk groups. And for early stage disease, Stage 1 and Stage 2, we then split patients into whether they have more favorable or what's called unfavorable early stage disease. And then, for Stages 3 and 4, those are lumped together usually as advanced stage lymphoma.

Slide#12: Roadmap

Let's talk about the treatment of newly diagnosed Hodgkin lymphoma. What's the modern treatment plan?

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Slide#13: Treatment of Hodgkin lymphoma

When we talk about treating Hodgkin lymphoma in the modern era, it's really trying to put together this balancing act of wanting, as we say, the punishment to fit the crime. You want the treatment to be appropriately selected, not too strong and exposing patients to unnecessary risk of toxicity, not too weak and putting patients at unnecessary risk of relapse. We sometimes think about this as Goldilocks' porridge, right? You want it to be neither too hot nor too cold, trying to find this middle ground of balancing the need to cure and the desire to avoid short- and long-term risks.

Slide#14 Early Stage Favorable HL: GHSG: HD10 Study

For early stage favorable disease where do we stand? And this is an important study that was conducted by the German Hodgkin's study group, which took almost 1,200 patients with early risk favorable disease and assigned them randomly to one of four treatment plans. Everything from the treatment on the left shown here, four months of chemotherapy and a slightly higher radiation dose of 30 gray; gray being the unit of measure of radiation treatment, to the right where you only have two months of chemotherapy and only 20 gray of radiation therapy.

Slide#15: Results

So, if you look at those two arms as being the strongest and the weakest treatment, we can then look and say, "How do patients do across all these groups?" And shown here are the results for that most and least treatment group, the left and the right. And we see that there was no appreciable difference with regards to how patients did in terms of relapse risk, shown on the left, freedom from treatment failure, or indeed overall survival.

So, this important study shows us that you can actually work on trying to minimize treatment to try to limit short and long-term risks without compromising cure rates. However, not every patient is appropriate for radiation therapy. Radiation therapy even at a dose of, say, 20 gray does carry risks associated with it, particularly for certain patient groups, as we'll talk about later.

Slide#16: RAPID trial

So, what about trying to use chemotherapy alone in the treatment of early stage disease? Here we have the important results from what is called the RAPID trial, which again took a group of lower risk patients and gave them, in this case three months of ABVD chemotherapy, and performed a PET scan afterwards. And for the patients who had a normalized PET scan here shown as Deauville 1 or 2, and I'll talk about that more in a moment, randomized those patients to either receive radiation therapy or to just

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stop after three months of chemotherapy without radiation treatment or any further chemo; three months of chemo alone.

Slide#17: Deauville criteria for PET scan results

This Deauville criteria for PET scans is a nice aside. Patients will often talk with their doctors, “Is my PET scan positive or negative? Is it good or bad?” And this sort of thumbs up or thumbs down approach loses some of the areas of gray in between, which makes our job sometimes as physicians and certainly radiologists’ jobs harder, is that sometimes it’s not always black and white. And this is the five-point scale that we now use in Hodgkin lymphoma in trying to capture those shades of gray for PET scans. When you have something that’s either a one or a two, this is our really more stringent definition of a normal PET scan, a complete response, a negative scan. And that was what was used in the RAPID trial.

Slide#18: RAPID’s results in the PET-negative patients

How’d we do? What RAPID showed us is in those patients who had a normal PET scan after three rounds of ABVD and were randomized to radiation or no radiation, that there was no statistically significant, no important difference in either progression free survival, risk of relapse or overall survival. Now, you can look at the curves on the left labeled PFS, progression free survival, and say, “Well, maybe the radiation patients did a little better.” When you see that little number in the middle there that says $P=0.16$ that p-value is a description of what we call statistical significance, which is a measure of how confident we are that this difference really matters. And when that number is as high as 0.16 we really think that that is not statistically significant and makes us doubt that the treatments were really different in a meaningful way.

Slide#19: Now and Later

So, where does that leave us? That leaves us with information for now and challenges for later, right? What this teaches us is that PET scanning after three months of ABVD really does identify a group of patients who do extremely well. They have excellent outcomes after just three months of chemo without radiation therapy. But, then we’re left with that little difference in those arms. Maybe that’s important. Maybe it’s not. Maybe the cure rate is a little bit different. We’re not sure.

Either way, we are going to face a challenge as a discipline in the future of what about patients who do have a relapse after this rapid style treatment, such little therapy? Traditionally in the modern era, patients who have a relapse or are refractory to their first treatment go on to get intensified treatment, a stronger chemotherapy program, stem cell transplantation. Is that really going to be necessary for patients who have the disease come back after such minimal treatment as just three months of ABVD, or can

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you get away with a middle ground of more treatment without such definitive and potentially toxic therapy? This is a question we're going to need to answer in the future. Right now, we don't know.

Slide#20: Treatment of advanced stage HL

Enough about early stage disease, what about advanced stage Hodgkin lymphoma, which is how the majority of patients do present? We have data going back all the way to 1992 that established the primacy of the program ABVD over MOPP or the combination of the two largely on the basis of toxicity. ABVD is easier to give and safer to give for most patients than MOPP-like treatments. And we have comparisons of ABVD to a combined modality program where you use chemotherapy and radiation, showing that ABVD is at least as good and maybe in a subset of patients with high-risk disease even better. And then, we have the comparison of ABVD to a truly intensified chemotherapy program called escalated BEACOPP. And here we see the comparison where you see that there is a little bit of a difference in event-free survival, EFS, between ABVD and BEACOPP. Although, again, that p-value is such that we don't call that statistically significant, but the survival difference between the two is truly the same. And what you get with escalated BEACOPP is a program that is extremely toxic and has a lot of important side effects, including a risk of acute leukemia and a high risk of infertility, such that it's hard to justify for the majority of patients the risk and toxicity of escalated BEACOPP over a more standard approach with ABVD.

Slide#21: Treatment of advanced stage HL

Here's sort of an ersatz flow chart that you might think about in terms of use of ABVD in the modern era. You get six months of it for advanced stage disease. Information we have on complete response on the left, or a partial response, but a normalized PET scan, those are both patients that we believe are likely to have been cured, no further treatment or testing is needed. When patients have an abnormal PET scan at the end of treatment, one often considers whether or not a biopsy is relevant in trying to clarify whether or not the patient's disease resisted ABVD or is, as we would say, refractory. Rarely when there is a little bit of leftover PET activity, one might entertain using radiation therapy as a mop-up. This is not a standard treatment approach. Although, this trial HD15, another German study, suggested that there may be a small group of patients that might benefit from such an approach, again, in select cases.

Slide#22: What about "interim PET"?

Well, that's all looking at PET scan at the end of treatment. What about doing a scan along the way to see how you're doing? What we call an interim PET scan. And these are very important and powerful data generated by Dr. Gallamini and colleagues, presented now a couple of years ago, showing that a PET scan done after two months

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of ABVD chemotherapy, patients with advanced stage Hodgkin lymphoma, is very powerfully predictive of what's going to happen. The majority of patients actually do have a normalized PET scan after two months even though they need to go on and complete all six. Patients with that normal PET scan after two months do very well. The overwhelming majority of those patients go on to be cured. Whereas, patients with an abnormal PET scan after two months are really at high risk for having the treatment fail or disease come back afterward. How best to care for those patients with a positive PET scan after two months? Few though they are, it is an area of active and ongoing research and this is a very important question that we're all working hard on trying to answer.

Slide#23: RATHL Trial

But, let's talk about the good news patients, those patients that do have a normalized PET scan after two months. Maybe you can use that as a justification for minimizing or reducing treatment in those lower risk patients, and that's exactly the philosophy and strategy that Dr. Johnson and colleagues have found in the so-called RATHL trial, which took patients with mostly advanced stage Hodgkin lymphoma, gave two months of ABVD and did that PET scan. For patients that had a good PET scan, here defined a little bit more liberally, right, Deauville 1, 2, and 3, so a broader definition of a normalized PET scan, and randomized those patients into either getting four more months of full ABVD chemotherapy or giving AVD without B, without the bleomycin, which is the medicine in ABVD that in many ways is the most toxic. This is the drug that is most associated with lung inflammation or injury and a drug that we're all working very hard on understanding if it really remains necessary in the modern era in the cure of Hodgkin lymphoma.

Slide 24: How'd the PET2 Negative Patients Do?

So, here in patients who had a normal PET scan after two months half of them got the bleomycin removed to try to reduce the risk of lung injury, and they tested to see was that really safe. So, how'd they do? The answer is really well. When you looked at the patients that got all six months in total of ABVD or the four months of AVD, their complete remission rates were the same. Their progression free survival and overall survival were the same. The only difference, as you might have expected, was less lung injury in the patients who didn't get all six months of bleomycin. In my opinion these data really are practice changing, and I'm increasingly comfortable in recommending in patients with a normalized PET scan after two months, of not giving all six months of bleomycin and trying in that way to reduce the risk of lung injury.

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Slide#25: Roadmap

Let's move from the treatment of primary disease to the treatment of those patients who do have relapsed or refractory lymphoma.

Slide#26: Treatment of relapsed/refractory HL

And you can generate complicated flowcharts and schemata of how best to care for these patients, but let's talk about the basic principles. The idea is in patients who do have relapse or refractory disease to give good second treatment, standard of care being platinum-based chemotherapy, programs that are using either cisplatin or carboplatin, for instance, to try to get patients back into remission or into remission for the first time. If that doesn't work, give some other treatment to try to get them into remission. The goal is to try to get the PET scan as normal as you can to get the disease as minimized as you can. And then, take patients once their disease has responded into what is called an autologous stem cell transplant, ASCT. This is a single round of high dose therapy using the patients own stem cells as an antidote to that toxic therapy with the goal of cure. And it's important to remember that the goal here remains cure even though patients have a relapse or never achieve remission in the first place.

Slide#27: Results of pre-transplant regimens in HL

There's a lot of different platinum-based chemotherapy programs that we use and this is simply a way of showing that a lot of them are more or less equivalently active. We often will use ICE, shown about half way down there, simply because there's a long track record of safety and effectiveness with that, but many of these are highly active and useful in this position.

Slide#28: ASCT for relapsed/refractory HL

Well, what do we know? What we know is that patients who achieve a normalized PET scan after their second treatment, whether it's platinum or whatnot, often will be cured by the subsequent transplant. And the top curve shown here, which is patients who have a normal PET scan and had no signs of disease that were outside of lymph nodes, no extra nodule sites, ENS, those patients are overwhelming cured by a stem cell transplant. Even patients who had a normal PET scan but had disease outside of lymph nodes, in the lung or the liver or bones, the majority of those patients will be cured as well, although slightly higher risk. For patients who have an abnormal PET scan going into a transplant, they didn't even achieve remission. Still about a third of those patients will be cured by the transplant. That number is lower than we would like to see, and it's those high risk patients that we'd like to think the most about trying to further advance or develop novel therapies for.

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Slide#29: Brentuximab vedotin: ADC (Antibody-drug conjugate)

So far, we've been talking chemo, chemo, chemo, chemo, chemo. There are other types of medicines that are useful in the treatment of Hodgkin lymphoma. And an important medicine to understand and be aware of is this drug called brentuximab vedotin, which I might occasionally abbreviate either as BV or just as brentuximab. This is not truly a chemotherapy. It is what is called an antibody drug conjugate, ADC, where you have an antibody, a protein that binds to a signal on the surface of a cell. In this case binds to that CD30 protein that is so ubiquitous and Reed-Sternberg cells. But, attached to that protein are these toxins, these molecules of toxin, and their antibody binds to the Hodgkin cell. The Hodgkin cell absorbs the antibody and the toxins attached to it and releases the toxins inside of the cell, leading to cell damage and cell death.

Slide #30: Brentuximab vedotin: ADC (Antibody-drug conjugate)

I try to describe this to my patients sort of either as a Trojan horse, or even better yet as a Trojan piñata, where the cell is willingly bringing this package inside of it and then breaking it open and releasing quite a nasty surprise.

Slide #31: Brentuximab in multiply relapsed HL

Brentuximab, the single drug, is a very potent treatment of Hodgkin lymphoma. And here shown are some of the pivotal data from the early work with this molecule done by my colleague Dr. Younes, showing that even in patients who had multiple relapsed Hodgkin lymphoma, it's come back after multiple chemotherapies, after a stem cell transplant even, giving this medicine all by itself the vast majority of patients have their disease respond. The deeper the bar goes down here the better the response. And everyone who has a blue is achieving the remission just with this drug all by itself.

Slide #32: PET scan

Here's an example of a PET scan from early on in the drug's development. Shown on the left a patient who has a lot of lymphoma in her chest, relatively bulky disease, but after two months with this medicine achieved a complete response with complete disappearance of that bulky lymphoma.

Slide #33: Clinical benefit

An important observation with this medicine is not just that it's active but that there are some patients who receive this medicine that have a very long clinical benefit, duration of remission, after receiving it. And patients can receive the medicine for months and remain in remission afterwards for years. And there's probably about a quarter to a third of patients that can have very prolonged remission after a course of therapy with

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brentuximab even after they've had their disease come back after a treatment with stem cell transplant.

Slide #34: Response adapted salvage therapy

So, given that this drug is so good for patients who've had bad lymphoma coming back after transplants and the like, we're now as a field trying to understand better, well, maybe, we can leverage this activity and take advantage of this medicine earlier on for patients that are earlier in the course of their illness. And here's work done at Memorial by Alison Moskowitz in our group looking at trying to give brentuximab all by itself instead of those platinum chemotherapy programs to try to get people into remission for a transplant, sparing them the toxicity and inconvenience of those chemos. And here we gave medicine a little bit differently. Normally, it's given once every three weeks as an intravenous. Here, we gave it three weeks out of four for two months. And giving it in that way, well tolerated, and about a quarter of patients had a complete response all just with this medicine alone, without any more chemo. For the patients that didn't, they went on to get regular platinum-based chemotherapy programs. And all-in-all with this treatment approach, BV and then followed by platinum chemotherapy, three-quarters of patients were able to have a normalized PET scan, despite having relapsed or refractory Hodgkin and they lived to go on to a transplant. That's a very good number.

Slide #35: Treatment (21-day cycles)

There are other ways that you might be able to take advantage of brentuximab. And here's work done by Ann LaCasce and colleagues up at the Dana-Farber. They used brentuximab in combination with a regular chemotherapy medicine called bendamustine, which is not FDA-approved for Hodgkin's. It is FDA-approved for other forms of non-Hodgkin lymphoma but has been shown to be active in Hodgkin's disease. And this combination was given for up to six cycles, but they could get as little as two cycles of therapy as a way of trying to get disease control prior to a transplant.

Slide #36: Bendamustine + Brentuximab

And they found that this combination is very highly active. Eighty-three percent of patients achieved a complete response by PET, and 96% of patients had disease get at least better, a partial response or a complete response. These numbers in my world definitely get gold stars. It's a dramatic response rate.

Slide #37: {Brentuximab → augICE} vs. {Benda + brentuximab}

The question of which of these approaches is better is a challenging one. Shown here are sort of the survival curves, if you will, time to relapse for patients receiving either the BV followed by ICE if they need it versus the brentuximab bendamustine program. And these data are very early and premature, but perhaps there are differences in terms of

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the longevity of response to these treatments. We really need to follow these patients longer and gain a clearer understanding of how patients do over time.

Slide #38: The AETHERA study

What about patients who go into the transplant but may be at risk for relapse following, either they had a positive PET scan or they had adverse features? Is there a way that brentuximab vedotin could be used as a way to either prolong remission after a transplant or even potentially increase cure rates? And this is the question that was posed by the AETHERA trial, which was an international randomized clinical trial taking patients at transplants and assigning them either to receive brentuximab vedotin or placebo as what is called a maintenance therapy after their transplant. Half of the patients receiving brentuximab up to about a year, and half receiving placebo, and looking to see whether patients who receive brentuximab after their transplant in this ongoing maintenance phase could do better than patients that didn't. And what we see are the following results.

Slide 39: AETHERA: Results

When you look at progression free survival, which is the time to the disease coming back, patients that received brentuximab after their transplant did remarkably better, obviously better in terms of the time to progression. However, we do not yet see any difference in overall survival, meaning that survival is equivalent whether or not patients receive brentuximab maintenance. So, how can we explain this? We're not sure. There are a couple of different ways that you can interpret these data. The first would be to say, "Well, we know we're pretty good at treating Hodgkin's after it comes back after a transplant and sometimes patients can live for many years before they succumb to their illness, which really lacks other clear curative approaches. So, maybe, we'll find this survival difference as we follow patients over time, or maybe brentuximab maintenance is simply delaying the inevitable and when patients relapse they could get their brentuximab at that time and do just as well as getting it in a preventive mode." We don't yet know. This is a very important question.

Slide #40: Who benefits the most?

So, when you look at who gets the benefit in the AETHERA program, clearly, not all patients derive an equivalent benefit, and when you look to see who does the best, the best here being these dot-whisker plots being furthest to the left of the middle line, it's the patients with highest risk disease; patients who had more than two prior treatments that it took to get them into remission or to the transplant; patients who had an abnormal PET scan going into the transplant; patients with higher risk disease at time of relapse either because they had B symptoms, which we know is a worrisome sign, or they had

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disease not just limited to lymph nodes. Those high risk patients seem to derive more benefit from maintenance, which kind of makes sense.

Slide #41: Roadmap

Okay, let's move from what is known to what we're learning, talk about emerging therapies and novel approaches to treatment, not just novel treatments but novel ways of thinking about the disease.

Slide #42: Brentuximab for newly diagnosed HL

So, we've talked a lot so far about how brentuximab is an active drug in this disease. We also mentioned that bleomycin, that B in ABVD, is nobody's favorite medicine. So, maybe there's a way of trying to overcome that challenge and get rid of bleomycin as a treatment of Hodgkin lymphoma and replace it with brentuximab. Early work looking at the combination of brentuximab with either ABVD or subsequently AVD has been very promising.

Slide #43: ABVD or AVD + brentuximab vedotin

And what we see here is that the combination of brentuximab vedotin with either ABVD or AVD is very interesting. First, the numbers on the left, where it's the combination with full ABVD, taught us an important lesson, which is that that combination is not very safe and a 36% major pulmonary toxicity, lung toxicity rate, is very high, much higher than you would have expected from ABVD alone. Adapting to that observation, bleomycin was removed, and AVD without the bleomycin combined with brentuximab vedotin did very well with early work with a complete response rate of over 90% and no lung injury.

Slide #44: FFS/OS

This can be seen differently here when you look at both failure free and overall survival curves where not giving the bleomycin actually improved survival due to less lung injury, of course.

Slide #45: ECHELON-1: ABVD vs. BV-AVD

This has led to a very large nationwide clinical trial called ECHELON-1, which is a randomized trial. Half of the patients got ABVD, half of the patients got brentuximab plus AVD for six cycles. This trial has been completed. It is done. And now we are eagerly awaiting results. They are not yet available. We do not yet know which is the winner. But, what I will say is that if, when we finally see the data, brentuximab plus AVD is better than ABVD, safer and/or more effective, this clearly can be practice changing.

Dr. Matthew Matasar:

Slide #46: Immunotherapy in HL: “Checkpoint inhibitors”

A very hot subject and a very important subject in the ongoing evolution of therapy in Hodgkin lymphoma is the role of immunotherapy, these medicines that are called sometimes in both the medical and other literature checkpoint inhibitors. Shown here is a schematic of what checkpoint inhibitors are all about. One of the ways that Hodgkin cells, these Hodgkin Reed-Sternberg cells, evade detection by the immune system and are allowed to survive is because they put up these signaling shields that tell the T-cells, tell the immune system to leave them alone. And it's this interaction between PD-1 and PD-L1, PD-L2 that tells the T-cell, “Leave me alone.” If you can interrupt that signal, if you can block that signal, then you can expose the Reed-Sternberg cells to the immune system and enable the immune system to attack and kill them. And it's these targets, PD-1, PD-L1, and PD-L2, that are the targets of these checkpoint inhibitors.

Slide #47: Results in Relapsed HL

There are two that have been the best explored so far in the treatment of relapsed Hodgkin lymphoma, pembrolizumab and nivolumab. These medicines are very similar. And what you see is that in patients who are very heavily pretreated, most had had a transplant, most had already had brentuximab vedotin as well, that response rates are excellent; 60, 70, 80% of patients respond, some of them go into complete remission. This isn't even chemotherapy. It's just a medicine meant to potentiate the immune system's ability to kill these cells. It's a very impressive and very important finding.

Slide #48: Nivolumab and Pembrolizumab

Shown here are, again, these waterfall plots that I've been showing throughout this talk, where, again, the deeper down the bar goes the better the response. And you see that almost everybody who receives these checkpoint inhibitor therapies, whether it's nivolumab on the left, pembrolizumab on the right, patients are having excellent responses to these treatments. And, again, as we saw with brentuximab, many of these patients can stay in remission for years after getting or while on these immune potentiating therapies.

Slide #49: Novel agents in relapsed cHL

These are not the only games in town. Including there's a lot of work being done nationwide, worldwide in trying to develop new and potent treatments of relapsed Hodgkin lymphoma. There's a lot of work being done and there's a lot of work that still needs to be done.

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Slide #50: Hodgkin Lymphoma: Future Directions

There are some potential strategies being merged from this, right? So, we have brentuximab; this is an active medicine. What about combining it with some of these other treatment approaches, either the checkpoint inhibitors, biological therapies, or standard chemo? And if we find out that BV and checkpoint inhibitors work well together, then you could build on that even further and say, “Okay, take that and then add another biologic therapy or add chemotherapy,” as we try to build these new multi-agent programs to address disease when standard chemotherapies have failed or even potentially in lieu of chemotherapy in the future.

Slide #51: Roadmap

Okay, enough of all that treatment. What about survivorship? I showed that slide early on showing that the majority of patients, even now in 2016, will be cured of their Hodgkin lymphoma, and as treatments improve and as our care improves the number of people that are surviving Hodgkin lymphoma will only increase.

Slide #52: Goals of survivorship

So, the goals of survivorship care is to try to maximize your survivor’s health and quality of life and in so doing minimizing the preventable health problems that are related either to the cancer itself or to the treatments that were needed to cure the disease.

Slide #53: High quality survivorship care

So, what are the components of high quality survivorship care? I show you sort of my personal list here including things like testing for relapse, focusing on what we call late effects, which is the delayed reaction to therapy, managing those, and then coordinating and overseeing overall preventive healthcare and wellness prevention and promotion.

Slide #54: Late effects of treatment for cancer

So, late effects of treatment, I try to describe this sometimes as imagine throwing a rock into a pond. You know, that rock hits the bottom very quickly, but it takes a long time for the ripples to reach the shore, and that’s late effects of therapy. And it can be disheartening or even frightening to find out that sometimes side effects or problems from treatment can take five, 10, or more years before they’re seen, but this is an important purview of survivorship care, to understand those risks and to mitigate those risks.

Slide #55: Late Effects

There’s obviously a lot of other things other than medical effects like psychosocial effects, such as chemo brain, which is a very real biological process. We know that Hodgkin survivors are at higher risk for anxiety and depression and that they can have

Dr. Matthew Matasar:

major and long lasting impact on work, on their own sexual identify and sexual health, their ability to get healthcare, a wide range of problems.

When you think about this box of late effects, what goes into this puzzle piece, obviously, whatever precancerous conditions can influence the risk of late effects. There may be heredity or genetic factors that are associated, disease characteristics itself, where the disease was, what type of cancer it was, what types of treatments were needed: radiation therapy, which chemotherapies, surgery can have late effects as well; events that happen during treatment, such as lung injury from chemotherapy; host factors, the other parts about your life: socioeconomic status, race and ethnicity, your gender; health behaviors: are you smoking and drinking, what kind of diet and exercise are you engaging in? These have a very powerful interaction with the other risks of late effects. And these are modifiable, right? These are things that we can work on to try to protect and promote our health. And then, there are normal aging and comorbid conditions. All of these together influence the risk and profile of late effects that any one survivor may be exposed to.

Slide #56: Cancer treatments can cause cancer?!

Acknowledging and understanding that our cancer treatments themselves can cause cancer is not my favorite part of my job, but it's important to understand that any treatments that we give can have side effects. These can be off-target, meaning they have nothing to do with the mechanism of action of the medicine. Lung injury from bleomycin is not desired. It's just a bad side effect. Or, you can have what we would consider more like friendly fire, where you're shining radiation therapy onto a tumor in the chest but the heart and the lung is also in that area, so it's getting touched by the radiation. But, fundamentally, any treatment that damages DNA, which is kind of a lot of how chemos work, can lead to this friendly fire oncogenesis because you're damaging DNA not just in the cancerous cells but in other healthy cells.

Slide #57: Breast cancer and radiation therapy

An important potentially increased risk cancer-wise in Hodgkin survivors is the risk of breast cancer. And we know that in younger women who receive radiation therapy to their chest as part of their treatment, that there can be an elevated risk of breast cancer. For very young women or children receiving radiation therapy to the breast tissue, that lifetime risk goes up to about the same as if they had the high risk breast cancer gene BRCA1, one in three. For patients between 20 and 30 receiving radiation therapy to their chest, women have a one in five risk of breast cancer, still much higher than they otherwise would have experienced. Whereas, when radiation is used in more adult patients over the age of 30, particularly over the age of 35, the risk of breast cancer appears to not be drastically different from the general population.

Dr. Matthew Matasar:

This is important because it can help guide selection of therapy. Do you want to use radiation therapy as part of your first treatment? Do you want to give a chemotherapy only approach? Understanding the long-term risks of radiation for an individual patient can help inform the best choice, that Goldilocks bowl, of which treatment we should be giving our patients to cure their disease the first go around.

Slide #58: Breast cancer surveillance guidelines

There are guidelines that now exist both from the National Comprehensive Cancer Network as well as the Children's Oncology Group to help guide oncologists and primary care doctors in monitoring high-risk patients for breast cancer. And the bottom line here is that we believe our best monitoring program for patients who are at highest risk is the combination of MRI imaging of the breast and mammography. That combination has now been shown to be better than either one alone.

We'd like to move beyond screening and maybe think about prevention. And there have been two trials of preventive prophylactic tamoxifen, one at a standard dose, one at lower dose, in these high risk patients to see can we reduce the risk of breast cancer. Can we go beyond screening to actual prevention?

Slide #59: Other cancers after Hodgkin lymphoma

Unfortunately, breast cancer is not the only cancer for which some Hodgkin survivors may be at increased risk. And shown here is a table of other many, thankfully, unusual situations and what the risk factors are and how one might consider screening.

Slide #60: Late effects: Heart health

Another important late effect that we want to incorporate into survivorship care is managing heart health. And we know that Hodgkin survivors can be at increased risk for a variety of cardiovascular diseases depending on their treatments, most notably radiation therapy to the heart or to the neck, and the use of doxorubicin, the A in ABVD. These are both known to be potentially toxic to the cardiovascular system.

Slide #61: Late effects: Heart Health

So, what can you do? Well, we can't take the chemo back. We can't untreat you with radiation therapy. So, we have to focus on controlling that which we can control: low cholesterol, good blood pressure, regular cardiovascular exercise, never smoke. There may be a role for such things as stress testing in a screening mode or taking aspirin for patients who received radiation therapy usually starting five or more years after the radiation was given. We're trying to better understand maybe using more advanced imaging techniques. Maybe that'll be helpful for finding heart disease before it happens,

Dr. Matthew Matasar:

help us guide early intervention programs, things like cardiac CT scans or cardiac MRI scans.

Slide #62: Cardiac CT coronary angiogram

Here's a picture of a modern cardiac CT scan, where instead of doing a traditional cardiac catheterization where the artery in the groin is punctured and dye is injected inside the arteries of the heart to look at the inside of the arteries, we can do the same non-invasively with a CAT scan to look for plaque or hardening of the arteries.

Slide #63: Cardiac MRI

Here is work using MRI as a screening tool for heart disease in Hodgkin survivors, and MRI appears to be a very powerful imaging technique, showing anything from coronary artery disease, hardening of the arteries, to signs of fibrous or scarring of the heart muscle, which can happen after radiation therapy, to damage to the heart muscle itself or to the lining of the heart. The role for MRI as a screening test for Hodgkin lymphoma remains very much an open question but one that colleagues and I are working through support of the LLS to try to answer.

Slide #64: Survivorship care plans

So, survivorship care plans are an important way that we can try to work together: oncologists, primary care providers, and survivors, to try to coordinate and improve the delivery of care to our survivors. Where the oncologist and the survivor together work on creating a document that outlines what the treatment was, what the risks for future late effects might be, what screening test and techniques might be appropriate, and the survivor and the primary care provider and the oncologist work in unison and tandem to try to coordinate in the delivery of best care.

Slide #65: Survivorship Care Plan ingredients

What should the ingredients of this care plan be? It really has to have the overview, an understanding of the what the treatments were, what risks may be associated either to the cancer itself or to the treatments given, what the role for prevention and screening might be for an individual patient given their personal risk profile, and an outlining of what health behaviors and risk behaviors really need to be taken into consideration. But, most importantly, it needs to say who you would go to for which problems and how often. It can be very hard sometimes for our Hodgkin survivors to know, "Do I call my oncologist? Do I call my primary care provider? Who's in charge?" And a care plan can really help make this transparent and clear to everybody and really ensure the patients are getting the care they need.

Dr. Matthew Matasar:

Slide #66: Acknowledgements

I'll end this just with acknowledgements, thanks to my colleagues on the lymphoma service at Memorial Sloan Kettering, including Dr. Younes and Dr. Craig Moskowitz, who were both very kind to share some of their presentation materials with me as I put together this presentation, the physician assistants who work with me in the Lymphoma Survivorship Clinic at Memorial, colleagues and collaborators in the adult long-term follow-up program, our Survivorship Program, and collaborators both at Memorial and at Cornell, and, of course, funding support that I received both through the NIH as well as through The Leukemia & Lymphoma Society, and, of course, to thank last, but certainly not least, the LLS itself.

Slide #67: Acknowledgements

As you heard in the introduction, the LLS has given collectively over a billion dollars over its lifespan to the research of new treatments and techniques to try to eradicate blood cancers. And their support for our patients and our researchers in Hodgkin lymphoma is invaluable and irreplaceable. And I'd like to thank them for their ongoing efforts.

Slide #68: Things are looking up

Remember, guys, things really are looking up. This is a very optimistic time in the treatment of Hodgkin lymphoma. We've come from an era where we give some chemo and hope for the best to we give as much chemo as we can and hope that we don't do the worst to this modern era where we're selecting treatments for individual patients. We're incorporating the need for cure and the need to minimize long-term relapse. Our treatments of relapsed disease are improving with the incorporation of antibody drug conjugates, of immunotherapies. Knowledge is only going to increase. Care is only going to improve. Survivors will be more common, and our care of survivors will get even better.

So, there's nothing but optimism right now in the field of Hodgkin lymphoma, and I look forward to seeing where this field will go over these next years and to be part of that process. Thank you all, I look forward to hearing your questions.

Slide 69: Questions & Answers

Ms. Lizette Figueroa-Rivera:

Thank you, Dr. Matasar, for your very clear and informative presentation. It is time for our question-and-answer portion of our program. We have received some presubmitted questions. And also, Dr. Matasar, I wanted to ask, as you've stated in your presentation escalated BEACOPP seems to have a better overall survival than ABVD but may have more long-term effects. So, how would a patient decide between these two treatments? And what do you, as a doctor, look for when deciding treatment for a patient?

Dr. Matthew Matasar:

Thank you for letting me clarify that point. There really is not an improved overall survival for all-comers if you just look at everybody with advanced stage Hodgkin lymphoma by administering escalated BEACOPP over ABVD. So, it is very uncommon right now for a lymphoma specialist to recommend escalated BEACOPP as initial therapy in America for advanced stage Hodgkin lymphoma.

What is of emerging interest is what we call response adapted therapy, and I didn't present on this because these are still unanswered questions. But, a strategy that is emerging is to start everybody with a more moderate program like ABVD, do that PET scan after two cycles, and then for that percentage of patients, that small group of patients that don't have a great response there, maybe use that as a signal and try then to intensify treatment approaches. And say, "Well, maybe that's the person who should get higher strength therapy like escalated BEACOPP or the like. And can you then response-adapt a treatment plan to tailor to the high-risk, as shown by a poor response to initial therapy."

Ms. Lizette Figueroa-Rivera:

So, this speaks more to a more personalized approach for patients in the future?

Dr. Matthew Matasar:

It's not the future. It's the now. This is really where we stand in Hodgkin lymphoma 2016 is attempts at trying to personalize therapy both on not just how old you are and how big or small you are and where is the disease in your body, but trying to get a sense for how the treatments work in you as an individual patient. And can we then react to those signals that we see for how treatment is going to modify the treatment as we go along. Can we remove bleomycin when it's low-risk like we did in RATHL? Should we escalate therapy for patients who are higher risk? This is where we are and this is where we're going, and it's going to lead to a more personalized and more tailored approach, which is exactly where we need to be as a field.

Ms. Lizette Figueroa-Rivera:

That sounds great. Now, the next question, doctor, we've had many patients with nodular lymphocyte predominant Hodgkin lymphoma, and they seemed very concerned when they heard from their physicians that they may be in a watch and wait protocol for this type of Hodgkin lymphoma. Is that a typical approach to this type?

Dr. Matthew Matasar:

So, truly there has never been a disease that has been worst named than nodular lymphocyte predominant Hodgkin lymphoma, or NLPHL. And it is a unique disease. It

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is uncommon. There are four to 500 cases in America. Compare that to about 3,000 oncologists in America. So, if you spread them all out, somebody might see one every few years. It has a very different biology, a very different clinical behavior. It's a very different disease than what we've been talking about today, which is classical Hodgkin lymphoma. And in many important ways NLPHL is more like a slow growing or indolent non-Hodgkin lymphoma than it is like Hodgkin's disease. It is in other countries sometimes lumped in under the Hodgkin lymphoma umbrella, and that's important when you're reading the research because you want to sort of pull those patients out and look at them separately. But, in America, we do not include NLPHL in our Hodgkin's programs and protocols, and we really think about it largely as more akin to a slow growing non-Hodgkin lymphoma using a watch and wait strategy, using minimal treatment approaches, either giving a little bit of radiation therapy if it's only area, or trying to use more conservative approaches rather than giving treatment with curative intent. This is because we know that even patients who receive curative intent so-called treatment Hodgkin-like therapies, that they can relapse, sometimes years or even decades later, which is more like the behavior of a slow growing non-Hodgkin lymphoma.

So, our treatment has evolved and will likely continue to evolve. But, the goals of treatment with NLPHL are very different, and the therapy approach is very different, and it's very unfortunately named.

Ms. Lizette Figueroa-Rivera:

Thank you, doctor. And the next question, we do have patients that have called our Information Resource Center and have asked if they should be monitored with PET scans or CT scans, and they are concerned about the radiation exposure. Can you speak to that?

Dr. Matthew Matasar:

I can. It's a very interesting question. So, the first thing that I'll say--I'm going to break that question into a couple of different chunks. The first thing is PET scan versus CT scan for surveillance, and I'll say that, overwhelmingly, patients, if they're receiving a scan like this in surveillance mode, should be receiving a CT scan rather than a PET scan. There are very few patients that benefit from PET scan as a surveillance mode, and those are patients in whom, for whatever reason, their disease wasn't ever evaluable by a CT scan. Maybe it only showed up in areas that were invisible to the CT scan for whatever reason, sometimes bone and things like this.

The bigger question is do we even need to be doing CT scan surveillance? And increasingly there is evidence that CT scan surveillance is relatively useless. And

Dr. Matthew Matasar:

patients particularly with early stage Hodgkin lymphoma that achieve a complete remission, there's pretty convincing evidence that scans in those patients aren't all that useful. That you can follow them just clinically, asking your patient how they're feeling, performing routine physical examination and blood tests, and that scans don't really add much to the quality of care.

Then you could ask, "Well, what about the radiation question of scans," and that's a bigger question but an important one. And there's a lot of debate in the medical community about this question of, "Are scans dangerous or safe?" And you could say on one hand, "Well, any radiation"--we talked about friendly fire oncogenesis. "Any radiation has the risk of damaging DNA," but it's not actually quite so easy as that. And the potency, the strength of the radiation beam influences whether or not it actually can damage DNA. And a lot of radiobiologists, people that actually study this for a living, think that the radiation beams and scans are simply not strong enough to damage DNA. And when you read about this in the lay press and the newspapers and magazines, the work that is underlying those discussions is sort of an extrapolation for the atomic bombs dropped in Japan. And they say, "Well, that much radiation was dropped in Japan and caused that many cancers, this much radiation's in a scan so it should cause that many cancers." That's probably not the best way to think about radiation, frankly.

But, if there are concerns about scans, radiation, or the IV contrast, which can place stress on the kidneys, one approach that we're trying to pilot and model at Memorial Sloan Kettering is the use of MRI as a surveillance imaging program and technique in lieu of CAT scans. An MRI has no radiation by definition. It simply sets up a magnetic field that has no risk of damaging DNA, causing cancer. So, for patients that are okay with MRI, they don't have metal in their bodies, they're not claustrophobic, a screening MRI done at a center of excellence has a very nice profile and is an attractive screening technique because of the lack of radiation, because of the lack of contrast.

Ms. Lizette Figueroa-Rivera:

Thank you, doctor, for that very comprehensive explanation. And, doctor, there's a lot of patients also asking about complementary and alternative medicine. They're asking, "What are your thoughts about herbs and supplements during my treatment?"

Dr. Matthew Matasar:

That's a good and tough question. I don't like the whole phrase of complementary alternative medicine. I think it sets up a false dichotomy, right? Well, it's not us versus them. It's us versus the cancer. And anything that you're taking, if it's a supplement, a pill, a vitamin, a chemo, an antibody, whatever it is, you have to be taking it for a reason and it has to be beneficial and it has to work well as a program. I don't give somebody

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four chemos and then add in a fifth chemo sort of willy-nilly. I need to know that they're going to work well together. Same with giving four chemos and adding in some supplements, if it's a potentially beneficial supplement, great, but it needs to sort of make sense and work in concert with the chemotherapy or whatever treatment plan is there.

There's evidence in other cancers that giving antioxidants, for instance, actually reduces the ability of treatments to cure cancer, because the cancer cells absorb the antioxidants just like the rest of you and it can protect them from chemotherapy or radiation therapy. So, sometimes we think we're trying to be healthy by taking supplements, whereas, actually you're working at cross purposes. Now, that's not to say that there's not a role for supplements. And certainly acupuncture I often prescribe to my patients if they're having problems that I think will benefit from acupuncture. What I would say is that these need to be taken as serious treatments not just as health promotion or lifestyle therapies, and you need to talk with your oncologist and your treating physicians about how these other treatment choices interact with the ones that are being prescribed for the cancer.

Ms. Lizette Figueroa-Rivera:

Thank you, doctor. And the next question we have is, "What is the risk of the Hodgkin lymphoma returning? Are there signs and symptoms that people should watch for?"

Dr. Matthew Matasar:

The risk of somebody's Hodgkin lymphoma returning is individualized. It depends a little bit on how bad the Hodgkin was in the first place and what the treatment delivered was, but the majority of patients who are in remission after treatment with Hodgkin lymphoma will never have it come back, and that's important to remember. We talked a lot about screening and surveillance and monitoring, but the truth is that in the majority of patients it will never come back no matter what testing you do because they will end up being cured.

There is a lot of variability amongst practitioners about how they monitor their patients. Do they do scans and blood work or do they just do blood work? And there's room for variability because that's sort of a style. That's an art of medicine, not a science medical question right now.

In terms of the role of patients in monitoring for relapse, I really try to encourage my patients to think about it docilely. I say, "My task for you, my challenge for you is to assume or pretend or whatever, believe that you've been cured and live as if you've been cured, because you'll probably be right. And now -you're not constantly

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interrupting something as a sign or symptom of a return of lymphoma. If you get a cold, sometimes it's just a cold. If you have a sore throat and your glands swell up in your neck, that's okay. That's a normal thing to have happen. That being said, the symptoms of Hodgkin lymphoma initially are also the potential symptoms of Hodgkin lymphoma return. Drenching night sweats that are not going away, unrelated to changes in your period, for instance, unexplained dramatic weight loss, new painless swollen glands that persist over weeks or grow over weeks, these are potentially worrisome signs and certainly would be the types of things that you would want to talk to your physicians about to see whether you need to be checked."

Ms. Lizette Figueroa-Rivera:

Thank you, doctor. And we have a question from a patient. She says, "I'm 60-years-old and diagnosed with Hodgkin lymphoma. I thought it was a disease of young adults. How did I get it?"

Dr. Matthew Matasar:

Right. So, you remember one of the first slides I showed was that bimodal distribution where there's younger person Hodgkin and then there's older person Hodgkin. So, why people get it? I wish we knew for anybody why they get Hodgkin lymphoma. What we know is that this is not your fault, right? This is not because you ate something or drank something or smoked something or didn't eat or drink or smoke something. This is one of a family of cancers that we just call bad luck cancers. The good news is to remember that these are not generally hereditary. This is not something that family members or children need to be screened or tested for in any way.

That being said, Hodgkin lymphoma of the elderly is a real problem. It's not an uncommon disease in the Hodgkin's world, and we are working on trying to get better at treating elderly Hodgkin lymphoma. The key there is remembering that bleomycin drug. We talked a lot about its lung injury risk. That risk is significantly higher in older patients. Sixty and over bleomycin risks of lung injury go up from 5% up to 20% or more depending on which study you look at.

So, we're working very hard as a discipline on trying to advance these non-bleomycin based programs, such as using AB brentuximab vedotin or other treatment approaches to try to reduce our exposure of older patients to bleomycin and its incipient risks.

Ms. Lizette Figueroa-Rivera:

Thank you, doctor. And our last question is what survivorship support services are available to me as a patient or to my family?

Dr. Matthew Matasar:

Great question. There's a lot of stuff out there. And the answer to that question's going to differ a little bit based on where you live. Individual hospitals may have survivorship resources and programs and communities certainly have resources. I'll even point you first to the LLS, which actually has a lot of information and resources for survivors of Hodgkin lymphoma and other blood cancers, including a peer-to-peer program where they can pair you up with somebody facing similar challenges who's managed similar challenges and can help you realize that you're not alone, patient access resources. Communities often will have other resources as well, including social workers, group therapy, where patients will sort of be able to band together and understand that they're not alone in the challenges that they have faced and continue to face.

So, the LLS is a very good starting point, and they can point you towards further resources. And speak to your oncologist and your primary care provider and find out what resources are available to you. But, the answer is they are there and it's just for you to reach out and grab it.

Ms. Lizette Figueroa-Rivera:

And we're hearing more and more about survivorship clinics for people who have ended treatment with medication and are looking for support with their long-term and late effects. Can you speak a little bit about survivorship clinics in general?

Dr. Matthew Matasar:

Certainly. So, we are at a little bit of a crossroads in America of trying to figure out how to take care of our cancer survivors, and there's a lot of different models that exist out there. There are some models where you go to a survivorship clinic and get a one time comprehensive overview of your risk profile and best recommendations for best practices. There are some clinics that will see you on an ongoing basis every six to 12 months and continue to work in concert with your primary care providers, and there are some that try to work in lieu of a primary care provider where they say, "We will assume all of your care" and try to be a one stop shop.

My thinking on survivorship clinics is that I really try to use them, again, on an individualized basis, so try to understand what a patient's risk looks like and then from that derive what their needs are. Our highest risk survivors really need ongoing integrated care within a multidisciplinary survivorship program. Maybe patients at medium risk of problems, intermediate risk of late effects, may benefit from either a one-off consultation or an annual check in to make sure that the field hasn't found something new and important that the patient could benefit from. And many patients are at relatively low risk for long-term side effects, and if they've gone through their treatment well really face very few late effects, and that's the patient that may benefit simply from

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a good survivorship care plan and may not need ongoing access to a survivorship clinic, and it may just be added inconvenience without added benefit.

So, think about individual patient's risk profiles and then try to make access to care match that patient's needs is sort of my philosophy.

Ms. Lizette Figueroa-Rivera:

Thank you, doctor. That concludes the question-and-answer portion of our program. Please help me thank Dr. Matasar for sharing his time and knowledge with us.

Slide 70: The Leukemia & Lymphoma Society (LLS) Offers

The Leukemia & Lymphoma Society offers online chats for young adults and caregivers. The chats provide forums for patients and caregivers to share experiences and support one another. For information on how to participate, please, visit www.LLS.org/chat.

If you have additional questions regarding Hodgkin lymphoma, please, call a Leukemia & Lymphoma Society Information Specialist at 1-800-955-4572. Information specialists are available to speak with you from 9 a.m. to 9 p.m. Eastern time or you can reach us by e-mail at infocenter@LLS.org.

We can provide information about treatments, including clinical trials, or answer other questions you may have about support, including questions about financial assistance for treatment. Information Specialists can also speak to you about the support services that Dr. Matasar mentioned.

On behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us.