

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Mantle Cell Lymphoma (MCL) with Dr. Benjamin Lampson: What Patients Should Know'

Description:

Join Alicia, Lizette and Edith as they speak with Dr. Benjamin Lampson. Dr. Lampson is an instructor in medicine at Dana-Farber Cancer Institute. On this episode, Dr. Lampson explains how mantle cell lymphoma (MCL) is diagnosed and treated. Dr. Lampson gives his advice for MCL patients during the coronavirus (COVID-19) pandemic. He also shares the long-term effects of treatment, the future of treatment for MCL, clinical trials and when they are considered for treatment for lymphoma patients, and the importance of open communication between a patient and their healthcare team.

Transcript:

Alicia: Welcome to *The Bloodline with LLS*. I'm Alicia.

Edith: I'm Edith.

Lizette: And I'm Lizette. Thanks so much for joining us on this episode.

Alicia: Today we will be speaking with Dr. Benjamin Lampson. Dr. Lampson is an instructor in medicine at Dana-Farber Cancer Institute. Welcome, Dr. Lampson.

Alicia: Before we jump into today's topic being mantle cell lymphoma, known as MCL, we always like to get to know our guest speaker and for our audience for them to also get to know you as well. So, what brought you to the field of medicine, specifically hematology and oncology?

Dr. Lampson: Well, thanks for asking. And, and I'll say the answer to this question is going to go back a ways cause I really have two critical experiences that I think would be important to talk about. So, first, way back when I was in high school, I was looking for a summer job, and through a friend of a friend, I eventually got a job in the lab of a researcher named John Byrd at Ohio State University.

Alicia: Wow!

Dr. Lampson: It was just by chance. Yeah.

Alicia: Nice.

Dr. Lampson: Yeah, you guys know that name, yes?

Lizette: Oh, of course.

Alicia: We do, very well.

Dr. Lampson: That's great. So, this was just by chance. You know, if I had looked at a different time or if John Byrd didn't have the money or space in his lab to take on an inexperienced, young high school student, I probably would've had the standard, you know, life guard job. But Dr. Byrd he did take me in and, as you guys know, and as some of your listeners probably know, he's basically a world famous researcher in the field of chronic lymphocytic leukemia (CLL), a disease that's closely related to mantle cell lymphoma. And he also has very close ties to you guys, to The Leukemia & Lymphoma Society. His research has been funded by you guys for decades.

And my experience in his lab was great. I ended up coming back for multiple summers, and it was just a really formative experience that showed me that I loved research. I loved asking big questions about, the most serious issues that pertain to us as humans, our health, our life. So, I'd say first big important experience that brought me to the field of medicine and to research.

And, then the second one actually occurred when I was in medical school. My younger brother, Matt, was, was diagnosed with an advanced blood cancer, stage IV Hodgkin lymphoma, when he was just a freshman in college. And I remember studying for the medical boards as he went through chemo and radiation. And I remember when he got his first set of clean scans showing that the cancer was in remission. And it turns out, you know, with the benefit of time over the years, we haven't heard from the Hodgkin lymphoma again. This young boy my little bro, went on to become a professional goalkeeper in major league soccer.

Lizette: Wow!

Dr. Lampson: He actually, also worked very closely with you guys. He worked with The Leukemia & Lymphoma Society for a while. In like 2013, 2014 thereabouts he was a spokesperson for the Central Ohio Chapter of LLS. And so I think this experience from the other side, from, you know, the patient, the patient's family side, not from the doctor's side, showed me what a wonderful specialty oncology can be

and, and what an impact that the cancer and its treatment can have on the lives of the patient and the patient's family.

That's sort of my, my personal little story and that's a lot of details. And in a week, you know, the, the majority of people listening to this podcast might not remember those details, so what's the big takeaway from those two stories? What do I want the people who are listening to, to remember?

And I guess, I guess what I would say is in both of these stories about the two formative events in my medical career, I mentioned you guys, The Leukemia & Lymphoma Society and that's not a superfluous detail that I just put in there to flatter you. I actually think that it's the bigger point. The bigger point is this. Imagine the people that were donating to the LLS back in the late 1990s. I don't think any of them might've predicted that some of that money might go to John Byrd, might open up a spot in his lab for a young high school student, and that high school student might go onto med school. And I don't know that any of those Central Ohioans who were at a Light The Night Walk that my brother led back in 2013, 2014 would know that there was, you know, a young medical student watching and seeing how many lives were touched and changed by cancer and, and using that experience to decide the specialty that he'd go into. But that's what happened.

And so the big takeaway is that so that's the nature of research, that's the nature of donating to research. It pays dividends. It's just really hard to predict when or how. And, and so I guess that's the takeaway. Not, not really the, you know, the specific details.

Alicia: Thank you for that. Congratulations to your brother on being in remission for so many years. And you had an awesome first job I will say. You were able to see both sides of it because you were with Dr. Byrd and then also saw it affect your brother and go through that with him. And I think it allows for you to speak to both experiences. The power of impact is one in which no one knows when or where the outcome will be, , but there will be an outcome and, and you just hope and pray that it's a positive one and an impactful one. So that's a really awesome story.

Dr. Lampson: Yeah, yeah. Agree.

Alicia: Jumping into mantle cell lymphoma, we know that it is one of several subtypes of B-cell non-Hodgkin lymphoma, but what are the signs and symptoms of mantle cell lymphoma and how is it diagnosed?

Dr. Lampson: Yes, yeah. So, so I think this is a good, this is a good starting question because whenever I meet a patient in clinic for the first time, I take the same approach. My first question is always, "What is the diagnosis? Do I agree with it?" And, as you mentioned, there's a lot of different subtypes of non-Hodgkin lymphoma; there's at least 70 different subtypes. And as a lymphoma doc, I want to know as best as possible exactly which one of those 70 we're dealing with. And this can be a challenging thing to do because the difference between certain types can be very subtle.

So, if a patient shows up in my clinic, even if they already come with the diagnosis of mantle cell, I review their chart make sure I agree.

And so, what does it mean to have a diagnosis of that specific subtype and, how do we arrive at that diagnosis? I would say first we should talk about what mantle cell lymphoma is, so we should probably understand the name first. Okay. We're probably use to hearing the word mantle as the place where we hang our Christmas stockings and it's not a word that we expect to hear in the doctor's office there.

So remember that lymphoma is a cancer of white blood cells, and white blood cells normally circulate in the body back and forth between the blood and the lymph nodes as they hunt for bacteria and other microbes; they protect us from infection. If you take out a normal lymph node and you look at it under the microscope, you can see that there's different regions in the lymph node. There's, one region called the germinal center where the cells are tightly packed together. And then there's a group of cells that encircle that germinal center like a cloak or a mantle, and that's called the mantle zone. And the cells that live in that region around the germinal center are called the mantle cells.

And so it's thought that a mantle cell lymphoma arises when the normal white cells that live in the mantle zone get a mutation in their DNA, an error in the instruction, that tells them instead of going through the normal life cycle of a white blood cell, birth and death, that instead they're going to divide over and over again and they're not going to die. So, one white blood cell becomes two. You know, one abnormal mantle cell becomes two, two become four, four become eight; and then, all of a sudden, you have a large collection of mantle cells tumor cells in the lymph node.

And the lymph node may get so big filled with those mantle cells that the patient notices it or it may get so big that it starts pressing on other organs and can cause the patient pain or other symptoms like weight loss or fevers. And sometimes those mantle cells, those mantle cell lymphoma cells can travel outside the lymph node like

white blood cells naturally do in the blood to other parts of the body and cause problems somewhere else. So, it's usually diagnosed when we biopsy an abnormally enlarged lymph node or an affected organ.

And the pathologists, the doctors who specialize in looking at organs underneath the microscope have a wide variety of tests that they do. They can identify that abnormal white blood cells are present in the biopsy and then they do a variety of special tests that tell them those abnormal white blood cells, those lymphoma cells came from the mantle zone and carry the specific genetic alterations that we see in mantle cell lymphoma. And all that information when you put it together is how you make the diagnosis of mantle cell lymphoma.

Lizette: And like you said, doctor, there is so many types of non-Hodgkin lymphoma. And when we do programs, a lot of times we divide it up by slow-growing types of non-Hodgkin lymphoma and aggressive types of non-Hodgkin lymphoma. And we actually see mantle cell lymphoma patients on both programs. Can you just speak to if it's considered a slow or a more aggressive form of non-Hodgkin lymphoma?

Dr. Lampson: Yeah. So, so you're exactly right. I would say that a broad way to divide up the lymphoma subtypes is in the indolent nonaggressive form or the aggressive fast-growing form. And most lymphomas cleanly fall into either one of those categories, but mantle cell lymphoma does not. Mantle cell lymphoma can stretch between both of those categories and each patient's mantle cell lymphoma is going to be slightly different.

There's a small fraction of patients that have a very indolent form of mantle cell lymphoma that when it's first diagnosed, we don't even need to treat. We can just watch it. And the majority of patients, however, have a faster-growing form that we usually treat right away.

So, so mantle cell lymphoma it's an unusual lymphoma in that it can really span that spectrum of being in a minority of cases indolent and in other cases more fast-growing.

Lizette: Sure. And then depending on if it's indolent or fast-growing, we usually let our patients know the goal of treatment being either a chronic type of lymphoma or a type of lymphoma that can be potentially cured. What is mantle cell lymphoma?

Dr. Lampson: Right. So, mantle cell lymphoma, whether it's the indolent or aggressive form, we generally place into the category of a lymphoma that can respond

very well to treatment so we can get patients into very deep remissions, but the goal is, is not cure. It's, hard to achieve cure in mantle cell lymphoma with anything short of aggressive therapies like an allogeneic stem cell transplant.

So the goal of mantle cell lymphoma is to treat it like a chronic disease, not to minimize it, but to treat it like diabetes or hypertension, you know, diseases that we can't cure but that we treat to minimize the effects that they have on someone's life.

Alicia: Many patients that we talk to will talk about staging and be confused about them having a blood cancer and what that means in regard to their lymphoma staging. How do you answer that question if a patient asks, "How does staging work for an MCL patient?"

Dr. Lampson: Yes. Yeah, so, staging for lymphomas and blood cancers holds a very different meaning and a very different prognosis as compared to staging for cancers of what we call solid organ, like the lung or the intestine or the prostate. So, staging for the lymphomas we basically break it up as, as is one lymph node involved? Is more than one lymph node involved, but they're on the same side of the diaphragm, either above the diaphragm or below the diaphragm? Are multiple lymph nodes involved on either side of the diaphragm? That's stage III. Or stage IV, are organs involved outside of the lymph nodes? And I would say the majority of patients when they're diagnosed generally have stage III or stage IV disease.

And that's a challenging thing for, me to tell patients in the clinic, to tell them that they have stage IV mantle cell lymphoma because people in their minds have carried over information that they've learned from the solid cancers where if you say you have stage IV pancreatic cancer or stage IV lung cancer, that could mean a potentially, you know, very short lifespan and a unfavorable prognosis.

It's not quite the case in mantle cell lymphoma, and that's because stage IV it just holds different meaning. When someone has stage IV pancreatic cancer, that means that the pancreatic cancer cells have learned to travel outside of the organ in which they originated. So, they've learned to travel outside of the pancreas. They've picked up a characteristic that pancreas cells normally don't have.

But blood cancers are designed to travel. It's what they do. So, just saying that a blood cancer is outside of the lymph node does not necessarily mean that the blood cancer has picked up some special ability that a blood cell normally otherwise wouldn't have. So that's why saying stage IV lymphoma does not hold the same prognostic significance as saying stage IV pancreatic cancer.

Alicia: Absolutely. I think it's very important for patients to understand the difference and how it's applied for their specific situation as opposed to what they know of solid tumors.

Earlier we were talking about how there are those who are diagnosed with fast-growing type of B-cell non-Hodgkin lymphoma, aggressive MCL, and those who have slow-growing or indolent mantle cell lymphoma, and then they are then told that they can be on watch or wait or what patients refer to sometimes as wait and worry or watch and worry. How is mantle cell lymphoma treated?

Dr. Lampson: As your question implies, this is a tough question to talk about in generalities because the decision about treatment really hinges on two factors, the individual characteristics of the patient and the individual characteristics of the mantle cell lymphoma. We've already talked about how each mantle cell lymphoma can be different in its own way, and, of course, every patient is unique in their own way. So there's no one universal answer about how mantle cell is treated. But, but I do think, there are some broad generalities we can take away, okay, so I can at least give, a somewhat satisfying answer to, to your question and I won't dodge it completely.

So, the first generality I would say that to take away is that there's two large categories of therapies for mantle cell lymphoma. There's two large buckets that all therapies can be placed into. And in the first bucket is standard therapies. Another related term that I could use would be FDA approved therapies. And what I mean by standard therapies are drugs or treatments that have been previously tested in clinical trials, clearly shown to be effective for the treatment of the disease, in this case, mantle cell lymphoma. And you can walk into any oncologist's office in the country and get these therapies. And there's obviously, an appeal to this approach. It's the tried and the true that we as oncologists have a lot of familiarity with.

But I think there's also a certain appeal to the second category therapies which, which I'm going to all investigational therapies. Another term for this is clinical trials. Okay. These are drugs that we're studying to try and figure out are they better than the options that we routinely offer to patients? So, the appeal to this category is that we're studying treatments because we have some preliminary research data telling us that the investigational treatment might be better in some way than standard of care. Either it's more effective, it's less toxic a combination of those two things. So, it's not a guarantee, that's why we're doing the trial, but it's a real possibility. So that's appealing.

It's important to keep in mind that because, in clinical trials you're studying the drugs and the patients who take them very closely, clinical trials require that a cancer center have people on staff who are specifically trained in the use of these medications. You cannot just walk into any oncologist's office and get an investigational treatment on a clinical trial. Certain clinical trials and certain investigational therapies they're only available at particular research institutions, and even hospitals just down the street might offer a very different set of clinical trials than their next-door neighbors. I'm at Dana-Farber here in Boston, and we have a different set of clinical trials than Beth Israel across the street and then Massachusetts General just a few miles away.

In summary, there's two buckets – standard therapies, investigational therapies – and each and every time before you decide on a path of treatment, it's important for you to ask your oncologist, "What do you recommend for standard of care, and do you have any clinical trials that you would consider for me? And if you don't have any clinical trials, do you have any friends at nearby institutions that might have good clinical trials for me?"

Not every oncologist might have a clinical trial to offer, but they might know somebody who does. Not all patients may ultimately want to do a clinical trial. Not all patients may be able to find a clinical trial that's the right fit for them. But I at least think they should know what's available. So, that's sort of the first generality to take away, the two large buckets that we put treatment for mantle cell lymphoma into.

So, so the second generality now I'm just going to focus on the standard therapy, okay. And I will say that for most patients, initial treatment of mantle cell lymphoma consists of the medication rituximab in combination with chemotherapy.

So first to talk about the chemotherapy, remember that chemotherapy is a very broad term that we use to describe drugs that indiscriminately kill any rapidly dividing cell. And some of the most rapidly dividing cells in the body will be the cancer cells. That's why chemo is so effective. But other rapidly dividing cells in the body are the normal blood cells so chemo can drop the blood counts, cause fatigue, put patients at increased risk for infection. Chemo can affect the rapidly dividing cells in the gastrointestinal tract so patients get nauseous, vomiting, diarrhea. And it can, in some cases, affect the rapidly dividing hair cells, so there's some types of chemo that are going to cause hair loss. So, these are all generalities and the exact chemotherapy your doctor will end up using depends on the patient and the doctor's preference and the doctor's experience. And each chemo has its own side effects, but that's sort of the general picture.

So, I said sort of the combination of rituximab and chemo. I talked some about the chemo. What's this medication rituximab? Well, it's, it's a medication that can be given either intravenously or, or subcutaneously so underneath the skin. I defined chemo previously as a drug that indiscriminately kills rapidly dividing cells. Rituximab is not like that. It specifically binds to the surface of the mantle cell lymphoma cells and causes them to die. So, in general, it's a pretty easy to tolerate medication. It doesn't cause hair loss, doesn't cause nausea.

The side effects that we worry about with rituximab are things like infusion-related reaction. So, the drugs getting infused causes the tumor cells to break apart and patients can feel fevers and chills. Also, allergic reactions. This can range from hives, you know, itchy skin, all the way to shortness of breath, low blood pressure, needing to be admitted to the hospital.

If these side effects to rituximab do happen, it's usually right away when the patients in the infusion chair in the office, so we can usually manage them right away. But that's sort of the, the major short-term side effects of rituximab. Over the long term, it can increase the risk for certain infections. But, in general, it's a very easy to tolerate medication.

Lizette: And we're always excited about new medications or new treatments and clinical trials. We do have a clinical trial support center (CTSC) here where nurse navigators will help patients or caregivers really find a suitable clinical trial or just find out if a clinical trial is the right course of treatment for that patient. Do you talk to your patients about clinical trials as an option when they first come into the office?

Dr. Lampson: So, any time before starting treatment, I talk to them about clinical trials and, as I mentioned, both buckets. So, I talk to them about the standard therapy that I'm considering offering them and if we have any clinical trials available for them, you know, I, I talk about those clinical trials. And if we don't have any clinical trials available for them, I tell them that, you know, we don't have any and if it, but if I know of, you know, one that's good, particularly if it's geographically nearby and I know it's good, I will tell them about that one and, and recommend that they go to that center if I think it's a particularly good fit.

So, at every time there's a change in care. Every time you, start down a particular line of therapy, before starting, it's important to ask, "Okay, what's my standard options and what's my clinical trial options?"

Alicia: What is the patient's reaction to hearing about this possible treatment? I know at LLS, we always encourage patients to ask those questions and clinical trials shouldn't be seen as something where they're giving you a sugar pill or that you're just being a guinea pig, but we really want people to feel comfortable having that conversation with their doctors. So are you seeing that patients and caregivers are opening up more and more to how beneficial a clinical trial may be for them?

Dr. Lampson: You are exactly right in that when I bring up clinical trials with patients, I routinely see two common misconceptions that I address right away. Okay. And the first common misconception is when I bring up a clinical trial, patients say, "Well, I don't want the sugar pill. I don't want placebo." And the simple fact is, in a clinical trial, the vast majority of clinical trials do not have a placebo arm or a sugar pill arm.

Now my career's pretty short, but I can tell you that I have yet to enroll any patient on a clinical trial where there was the chance that they could get a placebo arm. They're just not, typically done, and it's not ethical to do, right. If we have a standard treatment for a patient, it's not ethical to put them on a clinical trial where an option is a sugar pill.

Many clinical trials just have one option where you go on the clinical trial and you know what you're getting and it's very clear. There are some clinical trials that have multiple options that you could be randomized to or randomly get like the flip of a coin. You don't know which one it is, but they're all not placebo, so you know you're going to get some particular treatment, you just don't know which one.

And if there, if you ever were to run across a clinical trial with a placebo arm, it would be very clearly outlined and it would not be a surprise or something hidden from you.

The second common misconception I see with clinical trials is patients think that clinical trials are only for people who have exhausted all other options. So, "Oh, you've, you've used all the standard therapies, you've got nothing left and so now, you know, you're worried about me so you're talking to me about clinical trials since we've ran out of the standard options."

And, again, that's not the case. As, as I mentioned, at every single time that therapy is started, even if it's your first treatment for mantle cell lymphoma, you should be asking, "What do you have as far as clinical trials for front-line treatment of mantle cell lymphoma?" Because often, you know, it could be, for example, if the treatment your doc wants to give you is Y but we also know that treatment X is good for patients who

have relapsed mantle cell lymphoma, sometimes in the frontline we try X plus Y. But if we want to try X plus Y, there has to be a clinical trial. Now, chances are pretty good that X plus Y will work if we know Y does and we know X does in, in patients who have relapsed disease, but we don't know for sure, so it's a clinical trial. And, and, you know, particularly if we're combining drugs for the first time, we've got to watch you closely, but these are the types of, of approaches that we take with clinical trials. So, it's not just for patients who, have no other options. In fact, it's something a patient should ask about at every line of therapy, whether it's their first, whether it's their tenth.

Alicia: Absolutely. Thank you for that breakdown. That was very helpful.

Lizette: Definitely. And what advancements in the field of mantle cell lymphoma, what treatment are you most excited about?

Dr. Lampson: There's a lot going on in mantle cell. I'll focus on two broad categories recent advancements in mantle cell that I think are particularly exciting.

The first is an entire class of drugs called BTK inhibitors that didn't even exist, you know, weren't approved for mantle cell just eight years ago and now we have three of them. So, the drugs in this class, in this BTK inhibitor class, are not chemotherapies, right. They don't indiscriminately kill rapidly dividing cells. Rather they target a specific protein inside the mantle cell lymphoma cell, a specific protein that's important for the life and function of that, of that cancer cell, a protein called BTK. By blocking the function of the BTK protein, these drugs cause the mantle cells to die. And the first drug in this class was a drug called ibrutinib, which, John Byrd, just to bring up another name that we talked about before, John Byrd has studied that drug in CLL. It's also approved for CLL. We also know it's good for mantle cell.

So ibrutinib was FDA approved for mantle cell, for relapsed mantle cell. These are, in patients who have seen other therapies and their disease has come back. Was approved for relapsed mantle cell in 2013. And in general, about 70 to 80% of patients with relapsed mantle cell will have a response to ibrutinib and most of these responses last for at least a year if not longer. Ibrutinib does have some challenging side effects, so one side effect of ibrutinib is atrial fibrillation or an abnormal heart rhythm. And, you know, numbers that I quote to patients, and these numbers are based on, on work done by a lymphoma doctor that I work with, a woman named Jennifer Brown here at Dana-Farber Cancer Institute. She's shown that if you take about 100 patients for a year and a half, 6 to 7 of those patients are going to develop

atrial fibrillation if they're taking ibrutinib. So, it's not zero and it's not 20, but it's a significant fraction of patients will get atrial fibrillation on ibrutinib.

Ibrutinib can also cause severe bleeding, joint pains, rashes. So, the hunts always been for an easier to tolerate BTK inhibitor that doesn't quite have these side effects. And along came acalabrutinib in 2017 and then zanubrutinib, which was just FDA approved last year in 2019. Both of these were approved for the treatment of patients with mantle cell lymphoma that's relapsed after at least one prior therapy.

And, you know, just to give you some numbers. So, on the case of zanubrutinib, this was based on clinical trials. Total of about 100 or so patients who had mantle cell lymphoma that had come back after at least one prior therapy and they gave the patients zanubrutinib and over 80% of the patients had a response. And, again, the response seemed durable in the sense that it lasted a long time, at least a year and a half at the timing of the first publication and the first time the data was presented.

And even better news is that our experience with zanubrutinib in these trials and in other trials tells us that it's probably easier to tolerate than ibrutinib. There seems to be less atrial fibrillation, less major bleeding. So now in mantle cell, we have three different BTK inhibitors to choose from, and two of them seem to have a better side effect profile than the first generation ibrutinib. So, this is really fantastic. So, that's the first category of treatments that I'm excited about, BTK inhibitors.

The second category that's even newer is an exciting treatment called CAR T-cells. And I'm sure you guys have chatted about CAR T-cells before, but just to give a brief background. So, CAR T-cells are basically a form of immunotherapy, using the patient's own immune system to fight off the cancer. And how it works is you take the white blood cells out of the patient's body using a special machine. You send the white blood cells off to the lab. And there in the lab they're educated to recognize mantle cell lymphoma cells. And then after a few weeks at school the white blood cells come back, they get infused into the patient, and we cross our fingers. And because these cells are a living therapy, they, they grow and multiply inside the patient and, hopefully, they recognize, attack, and kill the mantle cell lymphoma cells.

And just this month, just this month, in early April, the results of a clinical trial of CAR T-cells used for the treatment of mantle cell lymphoma was published in a prestigious journal called *The New England Journal of Medicine*. We've already used CAR T-cells, and we know they're effective and they're FDA approved for a type of lymphoma called diffuse large B-cell lymphoma, but this was the first report of using them in mantle cell lymphoma.

This study was led by a physician named Dr. Michael Wong at MD Anderson Cancer Center in Texas, but it included research centers and patients all over the country including, including at my institution here at Dana-Farber. And in this trial of about 70% of patients, 85% of the patients had their tumors shrink when the CAR T-cells were infused and about 60% of the patients had a complete response and still hadn't heard from their disease a year out.

Dr. Lampson: So, you know, these are very impressive numbers.

Lizette: That's great! We always hear, patients and caregivers are always asking about CAR T-cell therapy, and we try to provide as much information as possible. And I know that mantle cell lymphoma patients have always been asking, since they heard the term CAR T-cell therapy, whether it would be an appropriate treatment for them. So I'm really glad to hear this news.

Dr. Lampson: Yes. This trial demonstrates that CAR T-cells, particularly this CAR T-cell product is effective for mantle cell lymphoma. Now it's not yet FDA approved for the treatment of relapsed mantle cell lymphoma, meaning that CAR T-cells are still technically considered investigational therapy and you can only get them for mantle cell lymphoma through clinical trials, but we expect based on these results, that the FDA is going to eventually approve, perhaps very soon, CAR T-cells for the treatment of mantle cell lymphoma.

Alicia: When we create, podcast episodes like this, we want to share information about the diagnosis, but patients and caregivers want to hear what is new, what's happening, what can they look forward to, especially for those who need further treatment or have not responded to standard treatment. So it's really exciting to hear what you're excited about and then what's actually working for many, many patients.

Dr. Lampson: Yeah, agreed. And what does the future hold? Well, you know, we have a lot of great medications. You can think about combining them. You can think about combining the BTK inhibitors and CAR T-cells. You can think about using the CAR T-cells even earlier for the treatment of the disease. Not waiting until patients have relapsed but perhaps trying it, as initial therapy. These are all things that are being investigated, you know, clinical trials. So, it's a very exciting time in mantle cell lymphoma.

Alicia: We might have to have you back on and do a follow-up.

Lizette: Um-hmm. Exactly. Exactly. And so, what should patients and caregivers be looking at when it comes to long term and late effects of treatment? I know that you did mention some of the side effects of the medications that are being utilized right now. But what are some of the long-term effects?

Dr. Lampson: Yeah. So, I talked about how the initial therapy for mantle cell lymphoma is commonly rituximab plus some chemotherapy. So, let's talk about first though the long-term effects of rituximab and then we can talk about the long-term effects of chemo.

So long-term effects of rituximab, as I mentioned, rituximab binds to the surface of the mantle cell lymphoma cells and causes them to die. But it also binds to the surface of normal B-cells. So normal white blood cells, the particular subset of normal white blood cells in the body, it causes those normal white blood cells to die. And those normal B-cells are useful for making antibodies that protect us from infection.

So, some patients that have been treated with rituximab can be more susceptible to infection. And these effects on the immune system can last for months to years after the last dose of rituximab. So, this means you need to be in regular contact with your oncologist so that if recurrent infections do become a problem, we can think about ways to treat this. For example, it's possible to do things like administer supplemental antibodies. If the body isn't making, we can give supplemental antibodies also called immunoglobulins or IVIG to help prevent recurrent infection.

And, I guess, you know, just to be timely, these are the patients that I worry about with COVID exposure, right. If patients are at increased risk for infection, I'm particularly worried if they happen to be exposed to, to COVID or coronavirus. So, so those patients should right now be practicing very strict social distancing and doing their best to limit contact with other people.

As far as the long-term effects of chemo, so we talked about rituximab and then the chemo part, the long-term effects of chemo. I would say it's important to remember that chemotherapy can rarely cause second cancers. Now, obviously, the benefit of adequately treating the mantle cell lymphoma outweighs any small risk of a second cancer at some distant timepoint in the future, but that risk is still there. So, patients need to make sure to stay up to date with all their other cancer screening tests. Things like mammograms, colonoscopy, having the PSA checked if necessary. They need to reduce any other lifestyle habits that may increase their risk for other cancers, so smoking. And they need to continue to have regular visits with their oncologist to

be monitored for both recurrence of the mantle cell lymphoma or for the appearance of any other blood cancers.

You know, other long-term effects of chemo can include symptoms like fatigue, also effects on fertility. These long-term effects I would say differ a bit on exactly what type of chemo is used. So, it's important once, you know, a particular chemotherapy is recommended for, for you to ask your doctor, you know, specifically what are the long-term effects of these.

Lizette: Sure. And I know one question that's being asked from our patients and caregivers at this time with the COVID nineteen-19 pandemic they're asking if their immune system is always going to be compromised. So even after and, and being in remission, are they still compromised?

Dr. Lampson: Yeah. I do consider them at slightly increased risk than the general overall population for infectious diseases. So, how does this manifest? So it's not a big enough increased risk that I recommend taking an antibiotic every day or taking your temperature every day or anything like that, but it is an increased risk to the point where I recommend staying up to date on your vaccinations. So, every year get that flu vaccine. And, you know, God willing when the coronavirus comes out, I want my lymphoma patients to be first in line.

So, pneumonia vaccines as well are important. There's two different pneumonia vaccines, the 13-valent pneumonia vaccine, the 23-valent pneumonia vaccine. I like to have my patients up to date on all their vaccines. The vaccines do need to be appropriate spaced out from the rituximab. As I mentioned, rituximab can have effects on the immune system and may blunt the response to vaccines, so usually I like to give some time, at least six months to a year, in the patient who's had rituximab before administering the vaccines. But, otherwise, I would say that's the most important thing that patients can do to keep their immune system functioning at a level to, to keep those infections away.

Lizette: You mentioned vaccines. Do these have to be killed vaccines for our patients?

Dr. Lampson: Yes. So, you're right that there's two general types of vaccines. One type of vaccine is called live virus vaccines, where they actually administer a very weakened form of the, of the bacteria or the virus to the patient, and that weakened form can be recognized and killed by the immune system before it causes any

problems. And then there's a completely separate type of vaccines that are the inactivated or dead form of the virus or bacteria.

The first category I do not administer to my patients with lymphoma. So live virus vaccines I, believe are contraindicated in lymphoma patients. What falls under this category? Well, the most common one is there's an old shingles vaccine called Zostavax, which is a live virus shingles vaccine, and I don't recommend that for lymphoma patients.

But there is a new shingles vaccine called Shingrix which is an inactivated form of the shingles virus, and I do strongly recommend that one for my lymphoma patients. And if you've ever known anybody with shingles, you'll know why I strongly recommend it. It can be a very painful disease when it happens.

So, you're correct, the live virus vaccines we do not recommend for patients with lymphoma, but all of the inactivated dead vaccines and this includes things like the flu, the two pneumonia vaccines, Shingrix, those we all recommend for our patients with lymphoma.

Edith: LLS always encourages patients and caregivers to speak openly with their healthcare team as that has shown to have positive effects on the patient's overall outcome. How important is it for a person to share all their concerns with their healthcare team?

Dr. Lampson: Yes. So, I completely agree on the importance of open communication with a person's healthcare team. And, in fact, when I'm about to start patients on chemo, I give them, really when I meet them, I give them four rules. And, I could talk about one of the rules cause I think it's particularly relevant to your question, and if we have time, we could talk about the other three.

But the rule that's relevant to your question is, is, one of the rules for my patients on chemo is don't be a tough guy. So, and I've said that to 80-year-old women, and I've said that to 20-year-old men.

What do I mean by that? I mean aggressively treat your symptoms and be very communicative with your treatment team if your symptoms are not being adequately managed. If you're having pain, let your doctor know. We've got great pain medications. We can find one for you.

If you're having a fever while you're on chemo, don't say, "I'll just tough it out and call the doc in the morning. It's 11 PM at night. He doesn't want to hear from-". You call

the doctor now because a fever could be a sign of a serious infection, and we want to get on top of it right away.

If you're having nausea and can't keep down food or water, let the doctor know. We probably have an anti-nausea medication that's going to work for you that we just haven't tried yet. And because the worst thing that could happen would be we don't treat the nausea. You come into the office for cycle two, and because you're dehydrated, we have to delay chemotherapy so that we can give you fluids and fix the dehydration and the nausea. So, treat your symptoms aggressively. Speak up for yourself if symptoms persist.

Edith: What are common questions you hear from your MCL patients?

Dr. Lampson: Yeah. So, I'd say a, a very common question is, is a question about diet, what's the right diet for me while I'm on chemotherapy. And, it's so common that that's actually one of my rules that I talk to about patients as well. So, the first rule was don't be a tough guy. The second rule is don't lose weight while you're on therapy.

So, what does this mean? How does a patient put this into practice? Well, we don't have any evidence that one diet is better than any other for making sure that mantle cell lymphoma is effectively treated by chemo. So as a researcher, I can't sit here and recommend a low carb diet or a vegan diet or a paleo diet as better than another other. But I can tell you that when a patient is on chemo, I don't like to see them lose weight. It makes me worry that either the disease is progressing or the treatment's causing bad side effects. I want to see my patients maintain their weight or, even better, gain weight while on chemo. And I want them eating whatever diet it is that's going to help them gain weight.

And while you're on chemo, if that's ice cream for dinner, then you have ice cream for dinner. If that's frequent small snacks throughout the day, then that's what you do. When we get on the other side of chemo, you know, when we're able to put the mantle cell lymphoma on the back burner, then, obviously, my recommendations change and I want patients to have a life that includes a healthy diet, lots of exercise. But when my patients are on chemo, I want them to have ten extra pounds for a rainy day. Ten extra pounds to lose in case we have a hospital admission for fevers while on chemo. Everybody loses weight in the hospital. But that's sort of my simple advice about diet.

Another common question that I get is, “Why did I get mantle cell lymphoma? Why did this happen to me?” And, and the challenging thing about that question is, is I don’t have a satisfying answer. As we talked about when we talked about, you know, how mantle cell lymphoma is diagnosed, it starts with one of those white blood cells in the mantle zone of a lymph node picked up a mutation in its DNA.

And why did that mutation happen? You know, why, why did that cell go awry? The answer is we don’t know. And that’s an area of active research, and, obviously, we’d love to figure out why that’s happening because if we can understand why that’s happening, we could prevent it from happening. But unfortunately, the answer to why did this happen to me right now is an unsatisfying, we don’t know.

Alicia: And for our listeners who also may have questions about nutrition, LLS offers free one-on-one phone and email consultations with a registered dietician with expertise in oncology nutrition, and the service is offered to patients and caregivers of all cancer types not just blood cancer patients. And for those who would like more information about this service, you can visit www.lls.org/nutrition or call 1-877-467-1936.

Dr. Lampson: That sounds about 5,000 times better than my ice cream recommendation so because everybody should.

Lizette: Yeah, I don’t think we’re, we’re opposed to that.

Alicia: We’re not opposed. Doctor, what is one last thing you’d like to leave with our listeners today?

Dr. Lampson: I guess the final thing I’ll talk about is one of my final rules for life on chemo and, and life with cancer that, I’ll be honest, has actually been sent into retirement because of the coronavirus epidemic, but I hope to bring it out of retirement soon because I think it’s the most important thing to remember. And the rule is it’s okay to live your life.

So, a lot of patients ask me, “Is it okay to go out to dinner while I’m on chemo? Is it okay to see my grandkids? Is it okay to go bike riding?” And there’s certainly some exceptions around the, around the edges, but for the most part, the answer is, “Yes, yes, yes. It’s okay to live your life.” There’s some days when you’re on chemo that you’re not going to feel well. You’re just going to want to lay in bed. And on those days, you should just lay in bed. But on the days when you’re feeling better, it’s okay to be up and, and about and live your life, including going to work if you can. And, in



fact, I want you doing these things because, in the end, that's why we treat the cancer to get you more days with the grandkids, to get you more days at the beach, get you more time enjoying life.

Now, of course, in the coronavirus era, this rule has been retired. I strongly encourage all my lymphoma patients to limit contact with others as much as possible. And, certainly, patients on active therapy are at high risk for infection, if they got infected, it would require us to delay therapy if they had coronavirus. So for now, practice, you know, strict social distancing and limit your exposure to others outside the house as much as possible.

But in the future, I think we, you know I think it's important to remember to bring this rule out of retirement and to remember that it's okay to live your life and that's the whole reason we treat it.

Alicia: Well said. We definitely agree. Dr. Lampson, thank you so much for joining us today and for all that you do for patients. You've shared such important information with us. And we're thrilled to actually share today's conversation with our patients and caregivers, so thank you so much. And stay well during this crazy time and beyond.

Dr. Lampson: All right, will do. Thanks for inviting me.

Alicia: Of course.