



CLL SOCIETY

Webinar Transcript

Understanding Immunity and CLL

October 8, 2026

In science and medicine, information is constantly changing and may become out-of-date as new data emerge. All articles and interviews are informational only, should never be considered medical advice, and should never be acted on without review with your health care team.

This text is based off a computer-generated transcript and has been compiled and edited. However, it will not accurately capture everything that was said on the webinar. The time stamp is approximately 10-minutes off due to editing. The complete recording of this webinar is available on-demand.

00:10:00.000 --> 00:10:07.000

Hello and welcome to today's webinar. I am Liza Avruch, Program Director with CLL Society.

00:10:07.000 --> 00:10:17.000

We are dedicated to bringing credible and up-to-date information to the CLL and SLL community, because we believe smart patients get smart care.

00:10:17.000 --> 00:10:27.000

As a reminder, you can rewatch all of our educational programs by going to the section of our website called Education on Demand.

00:10:27.000 --> 00:10:32.000

Prior to beginning, we'd like to mention a few pre-event items.

00:10:32.000 --> 00:10:39.000

All attendees in this webinar are muted, and the only people on camera are the speakers.

00:10:39.000 --> 00:10:45.000

We ask you to please direct all questions to the Q&A section displayed on your screen.

00:10:45.000 --> 00:10:52.000

Questions will be sent directly to our moderator, speakers, and staff, and are not visible to the audience.

00:10:52.000 --> 00:11:02.000

After today's event, you will receive a very brief survey that will help us plan for future events. We greatly appreciate your feedback.

00:11:02.000 --> 00:11:08.000



This session will be recorded and made available to everyone on our website

00:11:08.000 --> 00:11:19.000

Closed captions are available if you want to turn them on or off, go to Captions and select Show Captions or hide captions.

00:11:19.000 --> 00:11:26.000

This program was made possible through donor support and grant support from our industry partners.

00:11:26.000 --> 00:11:31.000

At this time, I'd like to welcome our moderator. Thank you.

00:11:31.000 --> 00:11:46.000

Thank you, Liza. My name is Ed Ratner. I'm a CALL patient advocate, a member of the CLL Society Patient Advisory Board, and a co-facilitator of the CL Society's Physicians with CL support group.

00:11:46.000 --> 00:11:50.000

As well as the Twin Cities and veterans CLL support groups

00:11:50.000 --> 00:11:54.000

I'd like to welcome you all to today's event.

00:11:54.000 --> 00:12:09.000

We are joined by our speaker, Dr. William Wierda, Clinical Medical Director and Professor in the Department of Leukemia and Executive Medical Director of Inpatient Medical Services at the University of Texas MD Anderson Cancer Center.

00:12:09.000 --> 00:12:20.000

We will be answering audience questions at the end of this event, so please take advantage of this opportunity and type your questions in the Q&A box.

00:12:20.000 --> 00:12:25.000

Before we begin, I'd like to share a few important disclaimers.

00:12:25.000 --> 00:12:33.000

The information provided today is for educational purposes only and should not be considered medical advice.

00:12:33.000 --> 00:12:38.000

For any personal health or treatment questions, please consult with your healthcare team.



00:12:38.000 --> 00:12:51.000

Please note that while CLL Society may have its own opinions and policies, our speakers may offer differing viewpoints, especially regarding management of CLL and its complications.

00:12:51.000 --> 00:13:00.000

Now it is my pleasure to welcome Dr. William Wierda.

00:13:00.000 --> 00:13:14.000

Good morning. My name is Bill Wierda. I lead the CLL program at MD Anderson, and this morning I'm going to be talking about understanding immunology and CLL.

00:13:14.000 --> 00:13:20.000

So a little bit of background to sort of set the stage for the discussion.

00:13:20.000 --> 00:13:34.000

As you... I'm sure you know, immunology is a very important topic in CLL. It's a very important topic for me and in our research that we're working on at MD Anderson, because this is really

00:13:34.000 --> 00:13:48.000

remaining area that we need dedicated attention to and work to improve outcomes for our patients with CLL, as you'll hear through my talk.

00:13:48.000 --> 00:13:56.000

Background slides to start with on immunology. Immunology is a very complicated topic.

00:13:56.000 --> 00:14:15.000

If you don't have a medical background, it is very complicated. And so what I'm going to try to do is walk through a few slides to set the stage and to give you some perspective, and then if there are things that need to be clarified during the discussion, we can talk about them.

00:14:15.000 --> 00:14:33.000

So the immune system basically functions to keep bad things away or out of the body and to maintain a state where individuals are healthy and well, and so it's the body's way of eliminating

00:14:33.000 --> 00:14:41.000

invading agents and it also is the body's natural way of protecting against development of



CLL SOCIETY

00:14:41.000 --> 00:14:57.000

bad things like cancerous cells that are developing. There are function and functional components to the immune system, and those are summarized here. An important aspect or function to the immune system is recognition. Recognition of things

00:14:57.000 --> 00:15:10.000

that are foreign, like bacteria and viruses that the immune system wants to get rid of, or recognition of things that should be in the body but are abnormal or altered

00:15:10.000 --> 00:15:17.000

And, that the body should want to eliminate, like cancerous cells.

00:15:17.000 --> 00:15:26.000

It's a very complicated process that involves multiple different cell types, coordination of interaction between cell types, activation

00:15:26.000 --> 00:15:33.000

production of various proteins and mechanisms to eliminate

00:15:33.000 --> 00:15:48.000

bad cells or toxic features. So, the immune system has a very highly regulated component to it, and coordination for these functions. The effector functions shown here are

00:15:48.000 --> 00:16:00.000

examples of ways that the immune system will eliminate foreign material. So killing of viruses, killing of bacteria

00:16:00.000 --> 00:16:13.000

killing and eliminating abnormal cancerous cells. And then the fourth component here, function is memory, and that is the immune system has the capacity to

00:16:13.000 --> 00:16:16.000

remember and

00:16:16.000 --> 00:16:24.000

work to more rapidly eliminate something that is trying to invade the body again, like a virus, etc.

00:16:24.000 --> 00:16:41.000

And we'll talk a little bit about that as we go through. So a few terms to talk about. So antibodies are proteins. They bind to specific proteins on bacteria or viruses or



00:16:41.000 --> 00:16:55.000

And that's one of the mechanisms to eliminate or mediate this effect or function of the immune system. Antigens refer to proteins that are recognized by the immune system

00:16:55.000 --> 00:17:11.000

Cytokines are proteins that immune cells release and other cells of the body release in this process of a coordinated communication and regulation of the immune function.

00:17:11.000 --> 00:17:25.000

Cytotoxicity and cytotoxic refers to a killing mechanism, and then lymphocytes, which we'll talk a little bit more, are a very prominent cell type that is involved in immune function

00:17:25.000 --> 00:17:40.000

is a very important cell. Also for CLL, because the cells that become abnormal and are the resultant patient developing CLL are lymphocytes that have become abnormal.

00:17:43.000 --> 00:17:59.000

So there's two arms to the immune system, the innate immune system and the adaptive immune system. We're going to focus on the adaptive immune system, but both are extremely important. The innate immune system is

00:17:59.000 --> 00:18:16.000

Really, the first line of defense against infections and in the immune response. It does not have this feature of necessarily specificity or memory.

00:18:16.000 --> 00:18:34.000

And again, it's really the first line of defense for eliminating infections. What we talk about and have studied quite a bit more extensively is the adaptive immune system. This is what I was referring to in terms of this highly regulated and coordinated

00:18:34.000 --> 00:18:46.000

response against specific invading agents or cells that have become abnormal. And the components to the adaptive immune system are shown there on the right.

00:18:46.000 --> 00:19:02.000

Some of the cells that are involved in the immune function and the immune system are illustrated through the next three slides. And you've probably heard of these cells. They all have their own specific function

00:19:02.000 --> 00:19:14.000

in the immune response and or in regulating the immune system. To start here, on the first left column are natural killer cells. Those are cells that are



00:19:14.000 --> 00:19:31.000

Important in innate immunity. They're very important in eliminating viral infections, and they have been a cell that's been described as a, in immune surveillance or tumor surveillance in eliminating

00:19:31.000 --> 00:19:44.000

Tumor cells if they arise. Cytotoxic T cells, or CD8 positive T cells are effector cells of the immune system. These are cells that are very effective at

00:19:44.000 --> 00:19:59.000

killing things, killing cells, killing tumor cells, or killing cells that have become infected with a virus... with viruses. Helper T cells are important in this regulating function or regulatory function

00:19:59.000 --> 00:20:14.000

And particularly in terms of activating and stimulating other cells. For example, cytotoxic T cells can be stimulated by helper T cells. And then regulatory T cells are important to regulate the immune system

00:20:14.000 --> 00:20:20.000

An immune response and really function to suppress

00:20:20.000 --> 00:20:25.000

Because you wouldn't want to have an overactive immune response. They can suppress the immune

00:20:25.000 --> 00:20:29.000

response to help keep things under control.

00:20:29.000 --> 00:20:45.000

Macrophages and dendritic cells are important to recognize foreign proteins and to present them to other cells of the immune system, like the T cells and to B cells in order to activate those cells.

00:20:45.000 --> 00:21:00.000

Plasma cells are cells that produce the antibody. Those originally are normal B cells that become activated and are triggered to produce antibody, and again, antibody is the specific protein that binds

00:21:00.000 --> 00:21:15.000

to foreign proteins or antigens or they can, the antibodies can bind to normal cellular proteins again to activate the immune system to eliminate



00:21:15.000 --> 00:21:30.000

whatever they bind to. And then B cells, naive B cells are very important memory B cells are also important. These are cells that ultimately produce the antibody and become plasma cells and they recognize the foreign antigen

00:21:30.000 --> 00:21:35.000

Or whatever antigen is that's intended to be eliminated.

00:21:35.000 --> 00:21:51.000

These are some other what are referred to as granulocytic cells. They're predominantly important in the innate immune system and function, and I won't go through in detail the function of these, only to say that neutrophils are very important

00:21:51.000 --> 00:22:07.000

for protecting against infections, and that's really the cell that we follow closely in patients who are on treatment, because we don't want the neutrophil count to be too low, because that significantly will increase risk for infections

00:22:07.000 --> 00:22:16.000

So talking about immune dysfunction and an immune system that doesn't function normally or well in patients with CLL.

00:22:16.000 --> 00:22:27.000

This slide summarizes the manifestations of that immune dysregulation. It does result in an increased risk for infection

00:22:27.000 --> 00:22:42.000

These are predominantly bacterial infections, respiratory tract infections, skin infections, and also there is the concern for a low response to vaccination

00:22:42.000 --> 00:22:54.000

the immune dysfunction in CLL is characterized, as you'll hear in a bit, characterized by low antibody levels, IgG levels, so the immune system

00:22:54.000 --> 00:23:06.000

is dysregulated so that the natural amount of antibody in an individual's body is lower for those patients who have CLL, and that's even when they're not

00:23:06.000 --> 00:23:08.000

getting any treatment.

00:23:08.000 --> 00:23:16.000



And unfortunately, even when patients get treatment and are in a good deep remission, their antibody levels

00:23:16.000 --> 00:23:18.000
tend to remain low.

00:23:18.000 --> 00:23:32.000
And there is something we can do for that, and we'll talk about that in a minute. So risk for infection, risk for developing other cancers, and there's a lot of data and we've done a lot of work demonstrating an increased risk for skin cancer

00:23:32.000 --> 00:23:41.000
and other cancers listed there, breast cancer, prostate cancer, GI malignancies associated with the diagnosis of CLL.

00:23:41.000 --> 00:23:57.000
I'm not going to talk a lot about it, but there is autoimmunity that we see in patients with CLL. The autoimmunity is usually directed at other cells, hematologic cells, red blood cells, platelets.

00:23:57.000 --> 00:24:10.000
And that autoimmune process triggers an elimination of those cells, so patients can acquire severe anemia if their immune system is recognizing it

00:24:10.000 --> 00:24:25.000
fighting and eliminating red blood cells, ITP, or immune thrombocytopenia, is where the immune system is eliminating the patient's own platelet, and will result in a very low platelet count.

00:24:25.000 --> 00:24:38.000
And one of the concerns and areas that we focused on significantly lately is this immune dysregulation, which results in a lower effectiveness of some of the immune system.

00:24:38.000 --> 00:24:53.000
Treatments that we use, like CAR T-cell, and I'll talk a little bit about that in a minute. Things that we can do currently are vaccinations for infection prevention and screening for other cancers so that early detection is very important.

00:24:53.000 --> 00:25:10.000
Because you can eliminate those cancers without having advanced second malignancies that can cause death in individuals if they are advanced and progressive

00:25:10.000 --> 00:25:26.000



CLL SOCIETY

Okay, so we're going to talk about vaccines first, and then we'll talk about other cancers and then we'll talk about some of the things that we're doing at MD Anderson. So I have a slide here that has a few questions on it sort of to set the stage for vaccination.

00:25:26.000 --> 00:25:33.000

I'll go through some of the details. So the first question here is, people with CLL should not receive any vaccinations ever.

00:25:33.000 --> 00:25:40.000

That is absolutely a myth and not true, and we'll talk about the vaccinations that are currently recommended.

00:25:40.000 --> 00:25:44.000

People with CLL don't respond as well to vaccinations.

00:25:44.000 --> 00:25:59.000

That is actually true. And we saw that through COVID. We've seen that with some of the other vaccinations that we give in terms of a lower response rate.

00:25:59.000 --> 00:26:05.000

People with CLL shouldn't receive vaccinations while in the middle of chemotherapy or chemo immunotherapy.

00:26:05.000 --> 00:26:07.000

That is true.

00:26:07.000 --> 00:26:22.000

And that's true, particularly for the chemotherapy that we used to use, we don't use anymore, drugs like fludarabine and bendamustine. But it's also true with the CD20 antibody, obinutuzumab or rituximab.

00:26:22.000 --> 00:26:39.000

We know when patients are receiving the CD20 antibodies, the B cell, normal B cells are depleted, and those are the cells that we want to stimulate and to respond against the vaccination. So if you're giving a drug that will eliminate those

00:26:39.000 --> 00:26:52.000

it's a good idea not to do the vaccination while patients are receiving those drugs. And then vaccinations can give you infection, you're trying to prevent, for example, flu and COVID-19.

00:26:52.000 --> 00:27:07.000



CLL SOCIETY

That is actually untrue [false]. You can get activation of the immune system with a vaccination, and you may have symptoms from that, but you won't actually get the infection from the vaccination. So you can have

00:27:07.000 --> 00:27:19.000

flu-like symptoms with a flu vaccination, and that's the result of the immune system getting stimulated by the vaccine, but the vaccine's not actually causing an infection.

00:27:19.000 --> 00:27:37.000

So because the immune system is not normally functioning in patients with CLL we do not recommend live vaccinations for our patients with CLL. And some of those live vaccinations to stay away from are listed on this slide

00:27:37.000 --> 00:27:52.000

Things like yellow fever, live virus vaccines, there's a flu vaccine called FluMist that's a nasal flu vaccine that is a live virus vaccine that patients with CLL should not receive.

00:27:52.000 --> 00:27:58.000

This is a list of vaccinations that patients with CLL should not receive

00:27:58.000 --> 00:28:10.000

In terms of vaccinations that patients should receive, one of the vaccinations that we recommend regularly is for influenza. Influenza is a seasonal flu

00:28:10.000 --> 00:28:27.000

And we recommend annual flu vaccine. The annual flu vaccine is a vaccine that changes each year. It's generated each year, a new vaccine is generated because they add strains that were active strains

00:28:27.000 --> 00:28:42.000

in parts of the world in the previous flu season that they want to avoid patients getting in the subsequent flu season. So, it is something that we revaccinate for each year. It's a new, different vaccine

00:28:42.000 --> 00:28:49.000

Each year. It's a protein-based vaccination. The immunity from it lasts for several months, but is not

00:28:49.000 --> 00:29:05.000

years of protection, and that's why we revaccinate each year for that reason, and for the reason that the influenza will mutate and modify each season, so there are new strains that



00:29:05.000 --> 00:29:10.000
emerge with the season.

00:29:10.000 --> 00:29:21.000
We'll talk a little bit about the specific types. The high-dose flu shot is recommended for patients over 65 years of age.

00:29:21.000 --> 00:29:39.000
The standard dose for patients under 65, those are listed there at the bottom, and there's a subsequent slide. We don't revaccinate in the middle of the flu season. Sometimes I will recommend, if it's a bad season, especially vaccination, towards the end of the season, just to cover patients into

00:29:39.000 --> 00:29:49.000
the spring months as a strategy, but that's... I don't... I don't recommend a second vaccination routinely for patients.

00:29:49.000 --> 00:30:00.000
So these are the different types of flu vaccinations. Again, I mentioned there's a high dose, and there's a standard dose. The high dose especially is recommended for patients over 65.

00:30:00.000 --> 00:30:09.000
And then the standard doses for patients under 65, all patients with CLL should receive the flu shot annually.

00:30:09.000 --> 00:30:12.000
Regardless of age

00:30:12.000 --> 00:30:24.000
The next vaccination is zoster, so this is shingles. This is a reactivation of the virus that causes

00:30:24.000 --> 00:30:36.000
chickenpox, and we vaccinated. In fact, everybody over 50 should be vaccinated for shingles

00:30:36.000 --> 00:30:46.000
Because our immunity wanes as we age, particularly for this virus. And this virus lays dormant in our nerve roots

00:30:46.000 --> 00:30:50.000
And our immune system keeps it suppressed



00:30:50.000 --> 00:30:59.000

And then, if the immune system is dysregulated or suppressed, then the virus can become reactivated, and that's what results

00:31:01.000 --> 00:31:18.000

In the development of shingles, and I'll show you a couple pictures of examples of this. Again, our patients with CLL are at increased risk for reactivation of the chickenpox virus and development of shingles.

00:31:18.000 --> 00:31:34.000

We have drugs that can treat those outbreaks, but one of the things that we really need to avoid is what's called post-herpetic neuralgia, which is pain... nerve pain that can occur after the outbreak of the virus.

00:31:34.000 --> 00:31:48.000

Because the nerve endings in the skin have become stimulated and the patient experiences that as pain that can last long after the outbreak has resolved

00:31:48.000 --> 00:31:54.000

This is an example of shingles. It usually happens on one side of the body

00:31:54.000 --> 00:32:07.000

And it starts out as a rash, but you can have these small vesicles, and it usually follows what's called a dermatome distribution, which is one nerve

00:32:07.000 --> 00:32:09.000

One nerve route

00:32:09.000 --> 00:32:25.000

That, again, is on one side of the body. It can also occur on the head, and what we have to really be careful of is outbreaks that occur on the head that can involve the eye.

00:32:25.000 --> 00:32:34.000

If it's not treated and it becomes extensive, patients can lose vision from this. So, if you have something that

00:32:34.000 --> 00:32:47.000

rash that could potentially be a shingles outbreak, particularly on the face and or around the eye, you need to see your oncologist and ophthalmologist as soon as possible.

00:32:47.000 --> 00:32:52.000



Shingrix is the vaccination that we use for shingles.

00:32:52.000 --> 00:33:11.000

As I said, the general population should be vaccinated over 50 for patients with CLL, it's everybody, all patients with CLL should receive the shingles vaccination with Shingrix. Shingrix is not a live vaccination. It requires two doses separated by two to six months

00:33:11.000 --> 00:33:19.000

And that's all you need to do. Sometimes I have patients who have a shingles outbreak, even though they've had

00:33:19.000 --> 00:33:25.000

Shingrix. And for those patients, I will usually give them extended

00:33:25.000 --> 00:33:42.000

prophylaxis with acyclovir or valacyclovir, because their immune system has demonstrated that it's not adequate protecting against reactivation of the

00:33:42.000 --> 00:33:48.000

of the virus, despite the fact that they've had a vaccination. So I believe they need

00:33:48.000 --> 00:33:53.000

prophylaxis or suppression with antiviral treatment.

00:33:53.000 --> 00:34:04.000

Pneumococcal pneumonia is an important bacteria that can cause bad pneumonia, and we recommend vaccination against pneumococcal pneumonia.

00:34:04.000 --> 00:34:21.000

These are the vaccinations. Pneumococcal pneumonia is caused by streptococcus pneumonia, and there have been several vaccines available over the years. And so, we're sort of in this situation where some patients have received

00:34:21.000 --> 00:34:30.000

an older vaccine, and typically we have boosted after those vaccinations with a newer

00:34:30.000 --> 00:34:47.000

product. And so you'll hear this PCV13, PCV15, PCV23 The current strategy for patients who've not had a pneumococcal pneumonia vaccination, they should get either PCV20 or PCV2

00:34:47.000 --> 00:35:02.000



CLL SOCIETY

PCV20 is generally the one that's most readily available. For patients who've been previously vaccinated with an older version, PCV13, PCV15, should be boosted

00:35:02.000 --> 00:35:12.000

And historically, we've recommended a booster every 5 years. Now, with the PCV20 and PCV21, that may not be necessary

00:35:12.000 --> 00:35:25.000

And this just goes over the strategy for vaccinations and boosting for patients who've had the older version of the PCV, pneumococcal pneumonia vaccine

00:35:25.000 --> 00:35:40.000

So, what about COVID-19? We have exited the era of the pandemic and are now into an endemic situation with COVID-19, meaning that it is with us

00:35:40.000 --> 00:35:46.000

cases are arising somewhat in a seasonal fashion

00:35:46.000 --> 00:35:57.000

We are still recommending vaccinations for COVID-19. The CDC's current recommendation for vaccination for COVID-19

00:35:57.000 --> 00:36:12.000

is two vaccines for this 26-27 season. There are options for vaccinations, as you can see on this slide. There are the mRNA-based vaccines, Moderna, Pfizer

00:36:12.000 --> 00:36:28.000

And Janssen, and then there is a protein alternative, the Nuvoxavid or Nuvax, which is an alternative for those who have any concerns about the mRNA-based vaccine. So we are still vaccinating for COVID-19 and

00:36:31.000 --> 00:36:41.000

This probably will continue at least for the foreseeable future. Evusheld is no longer commercially available.

00:36:41.000 --> 00:36:58.000

So this is a summary slide for vaccinations. I talked about most of these, and you can use this slide for reference. The one that I didn't touch on is RSV. We do recommend RSV vaccination. That is yet another

00:36:58.000 --> 00:37:14.000



CLL SOCIETY

virus that can cause a typical respiratory tract infection like influenza can, and like some of the other ones that we... that we see. Rhinovirus is another example, but we don't have a vaccination for rhinovirus. At the bottom there, you see the tetanus vaccine that

00:37:14.000 --> 00:37:27.000

Should be current every 10 years. And then we also do recommend for patients at risk, healthcare workers, etc., hepatitis vaccination.

00:37:27.000 --> 00:37:29.000

That's the summary for

00:37:29.000 --> 00:37:43.000

the vaccination component. The low antibody issue is an issue again that we see in CLL we see it in untreated patients. It usually gets worse

00:37:43.000 --> 00:37:52.000

As time goes on, even in the absence of treatment. There are things that we can do to

00:37:52.000 --> 00:38:00.000

to help with that, predominantly that is replacement of the antibody, particularly IgG.

00:38:00.000 --> 00:38:08.000

And we do that for patients who have had significant infections and have an IgG level that's less than 500.

00:38:08.000 --> 00:38:24.000

And so the two criteria are infection or recurrent infections and an IgG less than 500. The IVIG or subcutaneous immunoglobulin is given as a way to restore that level back up over

00:38:24.000 --> 00:38:30.000

500 and then that way reduce the risk for infections.

00:38:30.000 --> 00:38:34.000

It does not replace IgA or IgM.

00:38:34.000 --> 00:38:42.000

And the goal with that treatment is, again, to maintain over 500. I find that it's most helpful during the winter months

00:38:42.000 --> 00:38:52.000

when patients are at greatest risk for infections. And in the summer and spring, it's usually less essential because



00:38:52.000 --> 00:39:09.000

Again, it's usually past the flu season, the number of respiratory tract infections is going down or has gone down. People are not indoors and exposed as intensely as they are during the winter months.

00:39:09.000 --> 00:39:19.000

Okay. Other cancers. And again, the increased risk for other cancers is important in CLL and

00:39:19.000 --> 00:39:26.000

There are things that we do, particularly screening, that's recommended

00:39:26.000 --> 00:39:37.000

Not as a way to prevent, but as early detection so that it can be efficiently, effectively treated before it is a problem. Early detection is extremely important in cancer

00:39:37.000 --> 00:39:42.000

And in this, in this area

00:39:42.000 --> 00:39:55.000

And the cancers that we recommend screening for are the standard cancers that pretty much everybody should be screened for. We don't have an intensive recommendation for more intensive

00:39:55.000 --> 00:40:01.000

screening, but we do recommend that patients remain

00:40:01.000 --> 00:40:19.000

Very vigilant and adhere to the standard recommendations that are provided. Those recommendations can be escalated if there's an increased risk. So, for example, individuals who have a family history of colon cancer or

00:40:19.000 --> 00:40:28.000

Some other malignancy, their breast cancer, is another example for patients who have

00:40:28.000 --> 00:40:44.000

A gene mutation associated with increased risk for breast cancer. The screening for those individuals will be escalated and is more intense than standard recommendation, but for patients with CLL in general, unless they have an increased

00:40:44.000 --> 00:40:56.000



An additional increased risk feature, we recommend vigilant screening as the standard is recommended, and I'll talk a little bit about that in just a second.

00:40:56.000 --> 00:41:12.000

One topic is that last bullet there on multi-cancer early detection testing. There are several platforms. There isn't one that's yet approved. These are blood tests that can potentially detect cancers that

00:41:12.000 --> 00:41:26.000

If patients aren't having any symptoms from, and this is a way for an additional way potentially for early detection. And some of those tests are listed there. Again, this is not a standard recommendation. This is an area that I would

00:41:26.000 --> 00:41:34.000

keep attention to because it may emerge as a recommendation moving forward. This is

00:41:34.000 --> 00:41:45.000

List of recommended screening patients should have an annual skin exam by their dermatologist. I recommend seeing a dermatologist because dermatologists can see things that

00:41:45.000 --> 00:42:01.000

Other people, regular doctors, oncologists can't see. And sometimes they'll want to see patients more frequently within just once a year. And so the recommendation in that case is to follow the recommendation of the dermatologist. Standard mammography is shown there

00:42:01.000 --> 00:42:12.000

annually up to 54 years of age, and then every other year, 55 and older. Colorectal screening

00:42:12.000 --> 00:42:29.000

colonoscopy every 5 years if there are polyps, 10 years if there are no polyps seen. Prostate cancer, PSA is the prostate specific antigen blood test and a routine exam

00:42:29.000 --> 00:42:40.000

With your primary care provider. And then there is also recommendation for lung cancer screening for patients or individuals who have a smoking history with low dose CAT scans.

00:42:40.000 --> 00:42:58.000

So these are the general recommendations. They're general recommendations that are consistent with what's recommended for the general population. And then again, these



CLL SOCIETY

might be modified if individuals have additional increased risk features like genetic abnormalities or family history.

00:42:58.000 --> 00:43:05.000

I just have a couple more slides and those are to sort of touch on some of the immune

00:43:05.000 --> 00:43:21.000

Therapeutic strategies that we're interested in for patients with CLL. As I mentioned, the effectiveness of these immune-based strategies is lower in patients with CLL, and we're working now intensely to try to figure out why that is

00:43:21.000 --> 00:43:31.000

And try to figure out how to restore the immune system back to a more normal state

00:43:31.000 --> 00:43:48.000

These are three examples and then in the next slide are several more examples of immune-based treatment for cancer. For CLL, we've tested most of these. The ones that have moved forward and are effective are the CD20 antibody

00:43:48.000 --> 00:44:03.000

monoclonal antibody-based therapy. The bispecifics, there's activity, but there isn't yet a drug that's approved as a bispecific for patients with CLL, but we're very interested in that strategy. CAR T-cell therapy is approved

00:44:03.000 --> 00:44:07.000

And we have that strategy, although there are

00:44:07.000 --> 00:44:16.000

complications associated with that that make it a bit more challenging, and we would like the effectiveness to be higher.

00:44:16.000 --> 00:44:32.000

And then we've also used drugs like lenalidomide, immune-modulating drugs in the past. We don't use those routinely, these days because we have much more effective therapies with our oral targeted agents

00:44:32.000 --> 00:44:42.000

This is, I believe, my final slide, and this is sort of what we're doing and our strategy that we're taking currently at MD Anderson.

00:44:42.000 --> 00:44:46.000

We've done a lot of work with combined targeted therapies.



00:44:46.000 --> 00:44:55.000

BTK inhibitors plus BCL2 inhibitors with and without a CD20 antibody. We have extremely effective

00:44:55.000 --> 00:44:59.000

Targeted therapies to get patients in a very deep remission.

00:44:59.000 --> 00:45:05.000

The challenge is to keep the disease from coming back after a period in remission. And so

00:45:07.000 --> 00:45:24.000

Again, I mentioned that the immune system does not norm restore to a normal immune system even when patients are in this deep remission. So we're looking to understand why that is, and if patients, in fact, may have immune restoration, how long does that take.

00:45:24.000 --> 00:45:39.000

Once they're in remission. So we're doing more extended follow-up and looking at patients who remain in remission to see if they have immune restoration, and we're looking for drugs that potentially can accelerate immune restoration.

00:45:39.000 --> 00:45:55.000

Because we can achieve this very deep remission, we know that vaccinations are very effective, but they're not effective in patients who have active disease. And so my opinion is that the best time to vaccinate and stimulate and train the immune system.

00:45:55.000 --> 00:46:03.000

To keep the cancer away is after they've had this very effective treatment and they're in remission.

00:46:03.000 --> 00:46:17.000

And so we're looking at new vaccines and we're interested in developing a strategy where we can vaccinate patients once they're in a very deep remission as a way to prevent the disease from coming back.

00:46:17.000 --> 00:46:19.000

And that's where

00:46:19.000 --> 00:46:31.000

I have a large group that we're working with at Anderson, and that's where we're focusing most of our attention these days and are working on developing clinical trials



00:46:31.000 --> 00:46:37.000

So that we can demonstrate the rationale and this strategy.

00:46:37.000 --> 00:46:47.000

And ultimately with immune restoration, we'll fix the problems that I talked about a lot earlier, which are the increased risk for infection and increased risk for other cancers.

00:46:47.000 --> 00:46:55.000

So with that, I'll thank you for your attention, and I look forward to our discussion.

00:46:55.000 --> 00:47:17.000

Well, thank you, Dr. Weir. The importance of this topic is obvious. We have over 900 people who are attending and your presentation covered many of the questions that people sent in advance and posted currently, but I have a few that we can follow up on.

00:47:17.000 --> 00:47:35.000

And we're not going to be able to get to every question, because there were... there's, I think, well over 100. So I combined some of them. If we don't get to your question, that it... we may be able to answer it if you email the trusted care exchange email, which will be provided in the closing slide, people can send in questions and they're getting answered.

00:47:42.000 --> 00:47:58.000

So, you know, you mentioned that the immune system declines with aging in general, and I think that explains some of the much increased rate of death from COVID during the pandemic in older people

00:47:58.000 --> 00:48:00.000

But how much

00:48:00.000 --> 00:48:15.000

Does the CLL or SLL add to that age-related decline and particularly over the course of the illness? People, you know, are diagnosed, even the MBL before they even have 5,000 lymphocytes, and then

00:48:15.000 --> 00:48:28.000

through treatment, and then after treatment, is this just progressive getting worse, or does it go up and down, or at what point, is... is this a serious concern?

00:48:28.000 --> 00:48:44.000

So this is a complicated... that's a very complicated question, and it's difficult to put, sort of, numbers and detail to an answer to give to you, so my answer is going to be a bit general, and that's because we just don't have



00:48:44.000 --> 00:48:59.000

I have the detailed understanding of the immune system that we would like to quantitate the deficiencies and to be able to more clearly describe what's happening in our patients with CLL.

00:48:59.000 --> 00:49:14.000

I became interested in CLL early on when I was working with Tom Kipps, because I had an immunology background, my PhD was in immunology, and CLL is a unique immunologic disease.

00:49:14.000 --> 00:49:32.000

Different than other B cell malignancies that are similar in the sense that they're B-cell diseases, but very different in terms of the effects of the disease on the normal immune system. And so, I became very interested in CLL early on because

00:49:32.000 --> 00:49:48.000

of my background in immunology and understanding that things are not normal in patients with CLL and it's brought about by the presence of the leukemic cells, so the abnormal immune system starts early on.

00:49:48.000 --> 00:50:02.000

When there's a very low level of CLL present, there's been animal models where they have had animals that have developed a CLL-like disease, and they can demonstrate in that model that

00:50:02.000 --> 00:50:19.000

Very early on, when there's, barely any detectable disease, there are abnormalities in the immune system that can be seen in these animals. And those get worse as patients get more disease present.

00:50:19.000 --> 00:50:35.000

The abnormalities, I would describe them as somewhat global, meaning I mentioned that there are various aspects to the immune system. There's innate immunity, there's adaptive immunity, there's

00:50:35.000 --> 00:50:50.000

various cells involved in immune function and an immune response, and we can see abnormalities across these different cell actors of the immune system and the chemical messengers

00:50:50.000 --> 00:51:09.000



of the immune system are not normal. So those... there are quantitative, meaning numbers of cells that are abnormal, and the function of those otherwise normal cells is not normal because of the presence of the CLL. Now.

00:51:09.000 --> 00:51:28.000

The other aspect I mentioned was the low antibody levels, and we see where patients have a progressive lowering of their immunoglobulin levels, which increases their risk for infection as time goes on, even in the absence of treatment. In patients who are in very deep remissions, those don't correct and restore

00:51:28.000 --> 00:51:44.000

Right away. And one of the things that we're working on now is looking at because we have had many patients treated on our clinical trials recently who are achieving very deep remissions, MRD undetectable by the most sensitive method that we have

00:51:44.000 --> 00:52:03.000

We're looking at, well, what happens to the immune system, the numbers of normal T cells, B cells, this exhaustion phenotype that we describe in T cells where they just can't do what they're supposed to do, do those reverse in patients who don't have any detectable disease

00:52:03.000 --> 00:52:18.000

And how long does it take for that to occur? So that's ongoing work that we're doing. If you ask me to come back in a year, I'll probably have more detailed understanding of that and can provide information around that. And those are

00:52:18.000 --> 00:52:33.000

Abnormalities and derangements that we see in CLL, we don't see that necessarily in the aging population. The aging population, we tend to see tired T cells, tired B cells, some holes in the immune repertoire

00:52:33.000 --> 00:52:48.000

But it's not this global effect that we see in CLL. So they are different, and you, as you say, they're patients who... individuals who, as they age, their immune system, they lose effectiveness of their immune system, but

00:52:48.000 --> 00:53:02.000

It's not as profound an effect as we see in patients with CLL.

00:53:03.000 --> 00:53:21.000

Great. So let me just follow up and kind of confirm that how you described is that there's a problem, even at the time of diagnosis, or probably some months or years before that. So the things that you've described in terms of, let's say, vaccination, that



00:53:21.000 --> 00:53:22.000

Yeah.

00:53:22.000 --> 00:53:24.000

that should start right away, rather than saying, it's not... your immune system's not going to get better later. So if you're going to do something about catching up on getting vaccinations, that's right away. Is that correct?

00:53:24.000 --> 00:53:40.000

Absolutely. So I do recommend vaccination. That is the first discussion I have when I see new patients in the clinic. These are the vaccinations that we recommend. You don't need treatment. You're on observation. The best thing that you can do right now is to

00:53:40.000 --> 00:53:47.000

Work on your vaccination menu and make sure you have all the vaccinations that we recommend.

00:53:47.000 --> 00:54:06.000

That also occurs, that discussion of patients haven't had them, that also occurs, it's a loud message that I'll give patients who are about to go on treatment. I'll say, okay, you're about to go on treatment. Things may not be normal for a while in terms of your immune function.

00:54:06.000 --> 00:54:17.000

Now's the time to vaccinate to get you through that period where, if you get a CD20 antibody, for example, you're a bit better protected than you would be if you didn't have the vaccinations.

00:54:17.000 --> 00:54:33.000

Okay, on the back end, the post-treatment, you talked about if things don't recover, other than CAR-T, which... or transplant, where you wipe out the immune system, do people lose the benefits of prior vaccines, if they have treatment?

00:54:33.000 --> 00:54:38.000

Do they need to say, oh, I need to get revaccinated other than the annual type of vaccines

00:54:38.000 --> 00:54:49.000

Yeah. As you indicate, the two situations that we recommend revaccination are post CAR T-cell therapy



00:54:49.000 --> 00:54:58.000

And we recommend that patients wait at least six months after CAR T-cell therapy to start working on their revaccination and stem cell transplant.

00:54:59.000 --> 00:55:06.000

We're not recommending revaccination after patients receive a course of obinutuzumab with venetoclax as a standard first-line therapy.

00:55:08.000 --> 00:55:25.000

Okay, so the question has come up quite often in the Q&A is about how do we measure this? And you mentioned measuring IgG and the level of 500, but in general, how can

00:55:25.000 --> 00:55:40.000

immune function being measured, and how often should this... should measuring IgG start, like, right away and be routine, or wait until you have an infection? Are there other things that should be measured, like response to vaccines to see how things are going.

00:55:45.000 --> 00:55:59.000

There isn't a single test that we have available that is a measure of immune function. It's not like you can order a blood count and know what the blood counts are. There isn't an analogy that we have for immune function.

00:55:59.000 --> 00:56:15.000

There are various things that we can measure, but it's very we're sort of in a that's one of the reasons that we're intensively studying various aspects of the immune system to say, okay, what are the important parameters

00:56:15.000 --> 00:56:34.000

that we can measure that are deranged or abnormal in patients with CLL that might improve when they're in remission as a way to have a tool to study ways that we can intervene and restore immune function, identifying medications, et cetera, that can accelerate or enhance

00:56:34.000 --> 00:56:46.000

correcting the abnormality that we identify as an important measure of immune function. So we're working on looking for those types of tests. We don't have anything clinically available now.

00:56:46.000 --> 00:57:04.000

You can do flow cytometry panel and do testing for what the T cell counts are, what the normal B cell and NK cell counts. That tells us the number of those cells, but it doesn't tell us about the function of those cells. So



CLL SOCIETY

00:57:04.000 --> 00:57:19.000

We're not routinely doing any laboratory testing that are immune parameters for the cells or the function of the cells. We do, as you indicate, measure antibody levels

00:57:19.000 --> 00:57:34.000

That's very important in patients who have infections, severe infections, or recurrent infections, because if the IgG level is low, we can restore that by giving IVIG. So that's the one test that

00:57:34.000 --> 00:57:41.000

I use very frequently that is useful in managing and intervening

00:57:41.000 --> 00:58:00.000

to help patients who've had recurrent or significant infections. It's probably not necessary to monitor at every time a patient comes into the clinic who is otherwise doing well and not having frequent infections, because you're not going to do anything different in that situation

00:58:00.000 --> 00:58:06.000

But it is very helpful for individuals who have recurrent infections or severe infections.

00:58:06.000 --> 00:58:21.000

So, people with CLL, particularly in watch and wait, are like, I want to do something. And I think the immune problems fall into the same, what can I do? You know, the doctor can give me vaccines, but what can I do? Do you have

00:58:21.000 --> 00:58:40.000

recommendations of how people can boost their immunity or their immune system, ranging exercise, supplements, vitamins, foods, and recognizing that most oncologists don't have your level of training in immunology. Where can people get

00:58:40.000 --> 00:58:46.000

good advice on self-care outside of their oncology clinics.

00:58:46.000 --> 00:58:58.000

Yeah, so self-care is very important. I typically have a conversation with patients about moderation, things in moderation are very good. I'm not a proponent of

00:58:58.000 --> 00:59:17.000

sort of excessive use of dietary supplements, because those are things that can cause problems if you're overdoing it with supplements. So I don't have recommendations specifically for that type of strategy. The things that I recommend are adhering to the recommendations



00:59:17.000 --> 00:59:32.000

for vaccination, I think that's extremely important. I think it's important to have a good diet and to not... to stay away from processed foods, simple carbohydrates, eating clean, so to speak, fresh fruits and vegetables.

00:59:32.000 --> 00:59:40.000

Something that we have known about for a long time, it's harder to do that because

00:59:40.000 --> 00:59:56.000

We do get some pleasure from the things that we eat, but it's very important to have a clean diet, to eat sensibly, to get plenty of rest. Stress reduction is very important. As you indicate, exercise is very important. I have had a lot of discussions lately about

00:59:56.000 --> 00:59:58.000

about that

00:59:58.000 --> 01:00:14.000

topic with patients who will come and say, I've got some fatigue, it's probably not enough to start me on treatment. What can I do? And it's... I mean, there isn't a simple and easy answer to that. You have to get out and exercise.

01:00:14.000 --> 01:00:34.000

And you wouldn't, you would recommend that to an athlete who wants to stay in shape and to be healthy. I think it's equally important or more important for our patients to understand that, you know, getting out, getting some regular exercise, eating sensibly are extremely important in maintaining their health.

01:00:34.000 --> 01:00:40.000

And then, as I mentioned, the second cancer screening is very important, and nothing excessive

01:00:40.000 --> 01:00:46.000

stick to the standard screenings for other cancers that we recommend.

01:00:46.000 --> 01:00:53.000

Great, thank you. So the COVID pandemic led people to

01:00:53.000 --> 01:01:09.000

Literally fear being around other people. And so, kind of at this point, at what points in the CLL journey for people, you know, diagnosis, treatment, kind of remission, ongoing treatment, should people be



CLL SOCIETY

01:01:09.000 --> 01:01:25.000

hesitant to be around just generally other people, and I'm not talking about, you know, the... going to visit the person with measles in the hospital, which you certainly wouldn't want to do, but... or, you know, being around sick grandchildren, if you

01:01:25.000 --> 01:01:32.000

don't have to otherwise take care of them. So when should people be avoiding other people or wearing a mask at this point?

01:01:32.000 --> 01:01:45.000

Yeah, I mean, it's common sense. I think you should patients should stay away from individuals who are sick. If they have family members, steer clear. Going around crowds in

01:01:45.000 --> 01:02:00.000

constrained, tight places where there's a lot of people. If you're doing that, or you need to do that, you probably should wear a mask. I would wear a mask if I were in that situation. But I think, you know, COVID was traumatizing for everybody

01:02:00.000 --> 01:02:16.000

Particularly patients with CLL because of their immune function, and we had problems with losing patients during that time when before we had vaccinations and before we had the antiviral agents that we use. So to some extent, I think there's

01:02:16.000 --> 01:02:31.000

Some post-traumatic effects from the pandemic. That said, we do have drugs that we can use to treat if patients get a COVID infection and it's significant enough

01:02:31.000 --> 01:02:38.000

The CDC is recommending continued vaccination for COVID-19.

01:02:38.000 --> 01:02:44.000

As I mentioned on the slide, there are options for vaccination. I still recommend

01:02:44.000 --> 01:02:50.000

vaccinations for COVID and the flu for my patients.

01:02:50.000 --> 01:02:56.000

And again, back to the question, which was, when should I wear a mask?

01:02:56.000 --> 01:03:14.000

And who should I stay away from? You should stay away from sick patients or sick individuals. You should stay away from anybody who could potentially be infected with



CLL SOCIETY

the measles. That would be a situation where if I were in an area where there were measles outbreaks.

01:03:14.000 --> 01:03:32.000

I would be wearing a mask in that situation, because we don't have a vaccination that's a dead vaccination for measles, and we're not recommending vaccination for measles for our patients now because we only have a live

01:03:32.000 --> 01:03:35.000

vaccination, so...

01:03:35.000 --> 01:03:40.000

Those are the... those... those are the instances that I would recommend mask wearing.

01:03:40.000 --> 01:03:56.000

Okay, there are a number of questions about IgG treatment and can you kind of elaborate a little more on the route and frequency and duration? It's like once you start it and kind of do you have to anticipate this is kind of a lifelong

01:03:56.000 --> 01:03:57.000

kind of commitment

01:03:57.000 --> 01:03:58.000

Yeah.

01:03:58.000 --> 01:04:07.000

So there's a few guidelines around this topic that we adhere to. There are other things that

01:04:07.000 --> 01:04:20.000

physicians do as part of their practice, and you might hear variations in what is done in that regard. So the areas that are... there are clearer recommendations are

01:04:20.000 --> 01:04:35.000

We recommend IVIG for patients who have either recurrent infections, and they're usually sinopulmonary infections or respiratory tract infections. Sometimes skin infections, but predominantly in the respiratory tract.

01:04:35.000 --> 01:04:50.000

Patients have recurrent infections, or they have a severe infection, they get hospitalized for a pneumonia, and they need IV antibiotics. That would be another situation. And their IgG level is less than 500.



01:04:50.000 --> 01:04:56.000

That's when we recommend IVIG. For IgG replacement. Now, you can get

01:04:56.000 --> 01:05:15.000

Ig or immunoglobulin and it's given either intravenously, and that's what we refer to as IVIG, or it can be given subcutaneously. There's not a preference between those two, so that's one area where you might see different practice patterns

01:05:15.000 --> 01:05:28.000

across physicians, whether a physician will prescribe IVIG or subcutaneous. There isn't any data that says one is better than the other. I use IVIG

01:05:28.000 --> 01:05:35.000

Because I have easy access to it at our institution, it's harder for us to get subcutaneous

01:05:35.000 --> 01:05:42.000

The frequency of administration for IVIG, it's monthly

01:05:42.000 --> 01:06:00.000

For the subcutaneous formulation, it is usually more frequently, once every week or every other week administered because the volume is smaller for... so the dose is smaller for the subcutaneous administration. We can't give as large a volume as we can

01:06:00.000 --> 01:06:03.000

When we're given it... giving it intravenously

01:06:03.000 --> 01:06:13.000

I've found that it's most useful for patients during the winter months when we have all these infections and viruses circulating around

01:06:13.000 --> 01:06:28.000

And so I will be diligent about giving IVIG for IgG replacement through the winter months in patients who've had infections, and their IgG is less than 500. I give it so that

01:06:28.000 --> 01:06:44.000

The goal is to keep the IgG level at the time the next dose is due at or around 500. So I don't like it if I give a dose, for example, today, and in a month the level is

01:06:44.000 --> 01:06:50.000

Before their next dose is due, I like to dose it frequently enough that

01:06:50.000 --> 01:07:03.000



CLL SOCIETY

the dose level, what we call the trough level, is at 500 when we give the next dose. I will give it monthly through the winter months, and then after that, if I want to continue it

01:07:03.000 --> 01:07:17.000

You can space the dosing out so that you're achieving that 500 level, but may not need to be giving it every 4 weeks. It could space it out to 6 weeks, or 8 weeks if I continue it

01:07:17.000 --> 01:07:21.000

So have you had people who have

01:07:29.000 --> 01:07:31.000

graduated off it, where they kind of... so that they... particularly after treatment, if their immune system would recover enough that they... so they don't... starting it doesn't mean you have to do this forever.

01:07:31.000 --> 01:07:47.000

Correct. Yeah. And it's again, I find that I'm more aggressive about it during the winter. In the summer, spring, summer, when people are outdoors and we've passed through

01:07:47.000 --> 01:07:56.000

The cold and flu season, that's when I'll say, okay, how do you feel? How do you feel about taking a break? And it'll be a discussion and a mutual decision about

01:07:56.000 --> 01:08:02.000

Going off of it until the winter comes again, and then

01:08:03.000 --> 01:08:04.000

Oftentimes they'll go back on it through the winter, the following winter

01:08:04.000 --> 01:08:13.000

And so my impression, it's pretty well tolerated, but expensive. Can you comment on those two topics?

01:08:13.000 --> 01:08:28.000

It's pretty well tolerated. I have seen patients who have had infusion reactions. It's uncommon. I have had an uncommon experience, very uncommon experience, where the kidney function can

01:08:28.000 --> 01:08:34.000

The creatinine can rise in patients who are on IVIG. That's very uncommon

01:08:34.000 --> 01:08:42.000

In general, I would say that it's very well tolerated



01:08:42.000 --> 01:08:44.000

And the other question was

01:08:45.000 --> 01:08:57.000

The cost. Yeah, I don't know exactly how much it is, but it's expensive.

01:08:58.000 --> 01:09:10.000

Okay, so I just, I give you any perspective because I don't know how much different insurers pay, but my wife is on it for not CLL, but something else, but the commercial insurance we have

01:09:13.000 --> 01:09:20.000

At the... each treatment is over \$1,300 out of pocket. So you can see how they cost and what they've done the total cost is, I think, \$10,000, \$12,000 kind of thing.

01:09:20.000 --> 01:09:34.000

Yes, that's my understanding, but I... and I also understand that some insurance companies will pay for subcutaneously administered because of the cost benefit in that situation over

01:09:34.000 --> 01:09:38.000

IVIG, so we do see some

01:09:38.000 --> 01:09:51.000

influence, in terms of which is used occasionally based on patients' insurance and their constraints that maybe applied by their insurance

01:09:51.000 --> 01:10:09.000

So it is worth it, since we're at open enrollment season, if you're not on Medicare because it's probably pretty standard across all the Medicare plans in terms of co-pays, but if you're on other plans too and you're on IG or anticipating that to look at

01:10:09.000 --> 01:10:16.000

Your plan for the coming year, because it doesn't have to be the same as last year, and so you don't want to run into a problem with that.

01:10:16.000 --> 01:10:32.000

Okay, you know, you mentioned a little bit about autoimmune problems and anemia, but a couple that have come up in the comments and are fairly common are hives and bug bites

01:10:32.000 --> 01:10:40.000



CLL SOCIETY

And can you comment on how those are immune-related?

01:10:41.000 --> 01:10:42.000

I think the excess response to bug bites that people with CLL routinely get

01:10:42.000 --> 01:11:02.000

That is a unique feature of CLL. We don't see that with other B cell malignancies. It doesn't happen in all patients. And it's an immediate reaction. So it happens. We don't understand the actual immune mechanism of

01:11:02.000 --> 01:11:14.000

what's happening when patients get this reaction? It's probably the chemicals that are delivered when you get the insect bite into the skin

01:11:14.000 --> 01:11:31.000

subcutaneous area triggers some reaction from the cells in that surrounding area, whether it's mast cells that are making and releasing histamines and other things, but it's an inflammatory reaction that

01:11:31.000 --> 01:11:40.000

occurs and can cause a larger bumps, redness, irritation, lots of itching

01:11:40.000 --> 01:11:56.000

And the big problem that it has caused, in my experience, isn't that initial reaction, but the fact that you can get an infection in that area where there's been this reaction, and so patients can get nasty cellulitis

01:11:56.000 --> 01:12:11.000

following the bug bite. We don't have any medicines to prevent that initial reaction, other than mosquito repellents and insect things to prevent insect bites

01:12:11.000 --> 01:12:26.000

Okay, and then another example, kind of a bug bite that has come up recently is, and we have one person, one of my groups who had a West Nile virus and had a terrible response to that. And can you comment on

01:12:26.000 --> 01:12:40.000

Kind of any of those kinds of infections that we need to be more diligent, not just, you know, a bigger bite, but to use bug repellent if we're going out in the evening or things like that.

01:12:40.000 --> 01:12:51.000



CLL SOCIETY

I am not aware of any specific insect bites or other than the reaction that you're talking about.

01:12:51.000 --> 01:13:07.000

that are... that activate the immune system in a way that the insect bites do. It's not unique to mosquito bites, though. You can see a hyperreaction and response from other insects other than, like, spider bites

01:13:07.000 --> 01:13:09.000

Other than the mosquitoes.

01:13:09.000 --> 01:13:24.000

Okay. In addition to all the people with CLL who worry about infections, family members kind of worry about it on behalf and kind of what they contribute. Can you comment

01:13:24.000 --> 01:13:39.000

how families should deal with trying to prevent exposure to the person with CLL and how a whole family can be diligent. And kind of referring to, you know, in

01:13:39.000 --> 01:13:47.000

some parts of the world, they don't worry about vaccinating older people for flu as much as children, because they're the ones who spread it

01:13:47.000 --> 01:14:03.000

Yeah, so I think it's important for family members, close family contacts to be also vaccinated to support their family members with CLL. You know, most patients with CLL are over 65 years of age

01:14:03.000 --> 01:14:29.000

That's the age group where we recommend, you know, flu shots, pneumococcal pneumonia vaccination, shingles vaccination, even in individuals who don't have CLL. So it is important for family members to also maintain their

01:14:30.000 --> 01:14:31.000

Vaccinations schedule to support their family members who have CLL.

01:14:31.000 --> 01:14:43.000

Yeah, so it's another kind of question about the intersection of vaccines and IVIG. So you get other people's antibodies. Does that affect

01:14:43.000 --> 01:14:57.000

Your response to getting a vaccine, for example, like the flu shot or COVID shot, should the timing of when you get those shots be affected by when you last got your IVIG?



01:14:57.000 --> 01:14:58.000
I think that makes a difference?

01:14:58.000 --> 01:15:08.000
Not that I'm aware of. So your question would be if I get a dose of IVIG this week, can I get a vaccination this week or next week

01:15:08.000 --> 01:15:18.000
And there isn't any data that would suggest, and that I'm aware of that would suggest that the timing or the sequencing of those needs to be

01:15:18.000 --> 01:15:38.000
managed or changed, I think their individual and separate activities. Theoretically, you could propose that when you get a vaccine, you get an immune response that's a B cell immune response and a T cell immune response.

01:15:38.000 --> 01:15:50.000
So it's a cell-mediated response. The antibody that's present in the IVIG that you get may help with that, actually, if it's binding to the antigen.

01:15:50.000 --> 01:16:05.000
Shepherding the antigen into an area where there is antigen presentation and activation of an immune system. So I'm not aware of any data that would suggest, and maybe you are, I would be interested.

01:16:06.000 --> 01:16:21.000
No, I've just heard the recommendation, I'll wait for a week or two after. The kind of concept is like, does your body not develop response if it already has some

01:16:21.000 --> 01:16:28.000
kind of antibodies floating around, and that would imply that you should, you know, that a prior vaccine, that you have any residual effect might affect the new one, and I am not aware of any concerns about that.

01:16:36.000 --> 01:16:52.000
Okay. And the other kind of thing is, you know, children, get a bunch of vaccines at one time, and it... some of that is convenience, because you go to the pediatrician, you can't go every week, but now that we, adults get their vaccines at the pharmacy.

01:16:52.000 --> 01:17:02.000
Should we space our vaccines or just get them all at once? If we don't mind going back twice



01:17:02.000 --> 01:17:10.000

The CDC says you can get your COVID booster and a flu shot at the same time.

01:17:10.000 --> 01:17:25.000

I will oftentimes, you know, patients have can have reactions to these vaccinations, inflammation, pain, they can feel like they have the flu when they get a flu shot

01:17:25.000 --> 01:17:30.000

So, my opinion is that, okay, if you want... if you want to minimize that

01:17:30.000 --> 01:17:37.000

or the potential severity, you could space them out by a couple weeks.

01:17:37.000 --> 01:17:45.000

But otherwise, there isn't a recommendation that you can't get a flu shot and a COVID booster, for example, at the same time.

01:17:45.000 --> 01:18:04.000

I don't like the concept of giving multiple vaccines at one time, so if I have a patient who comes in the clinic and they haven't had their pneumococcal pneumonia vaccination, they haven't had their shingles vaccination, they haven't had a flu shot, etc., I won't tell them to go and get all of them at the same time. I will give them some instruction about

01:18:04.000 --> 01:18:13.000

spacing those out and sort of prioritizing which ones you want to do first, etc.

01:18:24.000 --> 01:18:26.000

Okay, makes sense. And if you do have some sort of reaction, they know which one because that's always the concern. Antiviral therapy is sometimes used during targeted therapy and some people seem

01:18:26.000 --> 01:18:34.000

stay on it. And I was wondering if you could comment, particularly on acyclovir and its use and when that's appropriate.

01:18:34.000 --> 01:18:49.000

Sure. So acyclovir, valacyclovir are medications that are used for herpes viruses. We use them in CLL predominantly to minimize the risk for a shingles outbreak

01:18:49.000 --> 01:19:02.000



CLL SOCIETY

If a patient has had a shingles vaccine, they might ask, well, what do I need that for? If I've been vaccinated, my preference is to have patients on those drugs while they're getting treatment.

01:19:02.000 --> 01:19:20.000

Because their immune system does get disrupted by the treatment, and they can have... I have... we have seen shingles outbreak in patients who are on treatment. So I usually recommend antiviral prophylaxis during treatment, even if patients have had

01:19:20.000 --> 01:19:23.000

their vaccine previously

01:19:23.000 --> 01:19:29.000

And then I'll continue it for 3 to 6 months after they finish treatment, and then they can stop it.

01:19:29.000 --> 01:19:40.000

The exception to that might be in an individual who's been vaccinated. If they have a shingles outbreak despite having had

01:19:40.000 --> 01:19:56.000

The vaccination, either after they've had treatment or before they've had treatment. If they've had it during the treatment and they're on an antiviral, then for sure that those situations would be situations where I would extend the coverage with

01:19:56.000 --> 01:20:02.000

The antiviral beyond completion of their treatment.

01:20:02.000 --> 01:20:08.000

For perhaps it's not very common, but for perhaps an indefinite period of time

01:20:08.000 --> 01:20:21.000

And that is, again, shingles that occurs after vaccination, recurrent shingles after vaccination, or shingles while patients are on the prophylactic medication.

01:20:21.000 --> 01:20:38.000

Okay, going back to Covid for a minute, so somebody with CLL kind of, I guess of kind of where they're at in their journey, they get COVID and then the question of Paxlovid or

01:20:38.000 --> 01:20:53.000

Remdesivir. Is it... are you kind of pushing it hard, pushing it lightly? Is rebound more or less of a problem in people with CLL because they're not clearing it within the



01:20:53.000 --> 01:20:57.000
the 5 days of being on Paxlovid

01:20:57.000 --> 01:21:07.000
So, at this point, most patients have had vaccination, or they've had an infection that they've cleared. It's very, very unusual to see

01:21:07.000 --> 01:21:18.000
A patient who's never had a vaccine and has never had COVID infection. So, my opinion is that there is some level of immunity that patients have as a baseline

01:21:18.000 --> 01:21:23.000
Because of the... those... that... that aspect.

01:21:23.000 --> 01:21:37.000
We are still using Paxlovid. That's an oral medication, as you say, it's given for 5 days. It's usually an outpatient treatment. And I usually reserve it for patients who are

01:21:37.000 --> 01:21:43.000
don't have mild flu or cold-like symptoms with COVID, but have fever and are sick

01:21:43.000 --> 01:22:00.000
And or who have not cleared an infection previously. So we do still use Paxlovid, and again, if it's for patients who... it's usually for patients who have symptoms or symptomatic, and if we catch... if we catch the infection early

01:22:00.000 --> 01:22:17.000
The remdesivir is an IV medication that's given in the hospital if patients are admitted with COVID, then they are usually more symptomatic and so we would be more likely to use remdesivir if patient needs to be hospitalized for

01:22:17.000 --> 01:22:23.000
COVID infection. So I have not seen recently

01:22:23.000 --> 01:22:40.000
this flare post discontinuation of Paxlovid flare like we were seeing before. And I think that, again, reflects back to the fact that most patients have some level of immunity and their immune system kicks in, and they're able to clear the infection

01:22:40.000 --> 01:22:44.000
With the help of the five-day course of the antiviral.

01:22:44.000 --> 01:23:00.000



CLL SOCIETY

Okay, good. Going back to the alphabet soup of antibodies, people have asked about, gee now I got my IgG levels normal with infusions, but my other antibodies are still low

01:23:00.000 --> 01:23:06.000

IgM, IgA, how big a concern is that, and is there anything that can be done about that?

01:23:06.000 --> 01:23:26.000

Yeah, so there isn't anything that can be done about it. IVIG only replaces IgG, as you know. The IgA is an important antibody. It's in the blood, but it's also on the mucosal surfaces. So it's a very important functional

01:23:26.000 --> 01:23:37.000

antibody in terms of sort of a first level of defense against infection, particularly of the respiratory tract. Unfortunately, we don't have any way to

01:23:37.000 --> 01:23:45.000

fix that to fix a low IgA level and to help with mucosal immunity

01:23:45.000 --> 01:23:51.000

by restoring or enhancing the IgA levels in that area. Perhaps someday we will, but currently we don't.

01:23:51.000 --> 01:24:11.000

IgM is an antibody that's found predominantly in the blood. Also, we don't have ways to restore that as well. It is an important antibody, but in general, what we have seen with patients who do have recurrent infections, replacement with IVIG has been very helpful

01:24:11.000 --> 01:24:15.000

Minimizing the risk for subsequent infections.

01:24:15.000 --> 01:24:30.000

So, a number of questions came in about cancer screening, and the most easily detected and most common increase in

01:24:30.000 --> 01:24:36.000

And second cancers or additional cancers, is skin.

01:24:36.000 --> 01:24:52.000

And your slide suggested that other than kind of adding routine annual skin exams, just follow the age-related recommendations. And as you and I spoke, I'm doing some review of the literature on

01:24:52.000 --> 01:25:06.000



CLL SOCIETY

the frequency of other cancers. Do you have a sense that the risks are, for some of the cancers besides skin are high enough that people should be screened more often or more intensively?

01:25:06.000 --> 01:25:17.000

Well, we do see that. Like, for example, the skin, the skin issue. The standard recommendation is an annual dermatology visit for skin cancer screening

01:25:17.000 --> 01:25:29.000

The dermatologist may want to see you more frequently than once a year, and that is based on their expertise, your history, and what they feel is your risk for having a subsequent

01:25:29.000 --> 01:25:44.000

A subsequent cancer diagnosis, so it's common, actually, to see patients being seen more than once a year for skin cancer screening. One thing that I probably should mention is that sometimes I'll have patients

01:25:44.000 --> 01:25:54.000

who say, well, my primary care provider looks at my skin, and that I feel that, like, that might be enough. And my response is that

01:25:54.000 --> 01:26:06.000

Probably not, it's probably best to have a dermatologist looking at your skin, because in my experience, they can see things and see suspicious things that need to come off

01:26:06.000 --> 01:26:15.000

Because of their trained eye, that your primary care provider might not pick up on. And so I advocate for

01:26:15.000 --> 01:26:29.000

a dermatology visit and following the recommendation from them about the frequency of visits, and seeing them at least once a year, and if they recommend more frequent visits, that would be what you should do.

01:26:29.000 --> 01:26:44.000

So, each of these webinars talks about things that can go wrong, and you spoke some about the effectiveness of our current treatment. Can you comment on, kind of, where we're at in terms of

01:26:44.000 --> 01:26:59.000

How long people with CLL are going to live compared to people who don't have CLL and the kind of relationship of infection versus disease versus other cancers



01:26:59.000 --> 01:27:08.000

As to what's what is going to go wrong, and how much do people need to kind of worry about this relative to all the other things you can worry about in life?

01:27:10.000 --> 01:27:25.000

So I would start out by saying today, these days, when I see patients in the clinic, I spend a lot more time talking about infection prevention, vaccinations, screening for second cancers, because it's now more important than ever

01:27:25.000 --> 01:27:39.000

As you indicate, we've made tremendous progress in terms of treatments for patients with CLL. If you look at the data, more recent data that's been reported for ibrutinib

01:27:39.000 --> 01:27:56.000

If an analysis was reported where the life expectancy for patients who went on ibrutinib on the trials, at least, who received ibrutinib as their first treatment, their life expectancy was similar to the age-matched

01:27:56.000 --> 01:28:01.000

unaffected general population.

01:28:01.000 --> 01:28:06.000

That's true for individuals probably over 60, if you have

01:28:06.000 --> 01:28:21.000

20-year-old or a 30-year-old with CLL my opinion is that their lifespan they may not have a normal life expectancy if they're diagnosed very young with CLL

01:28:21.000 --> 01:28:29.000

Even if they need treatment and we have very effective treatments today. We are working on

01:28:29.000 --> 01:28:38.000

Therapies and strategies for curative treatment for patients with CLL. So I think for those individuals will definitely have cure

01:28:38.000 --> 01:28:48.000

And cure to me means elimination or extinction of those leukemia cells from the body, never to return again.

01:28:48.000 --> 01:28:56.000



CLL SOCIETY

But we're working on that. So, for most patients with CLL, and we know the vast majority of patients with CLL are over 60

01:28:56.000 --> 01:29:12.000

years old, their life expectancy is not shortened by their diagnosis of CLL, even if they need treatment. We do not recommend chemotherapy for patients. I don't recommend it. I haven't given chemotherapy to any patients for

01:29:12.000 --> 01:29:14.000

For many years now.

01:29:14.000 --> 01:29:27.000

And I think chemotherapy is something that was contributing. The fact that it's not as effective as effective a treatment, and I think it does bad things to the cells that

01:29:27.000 --> 01:29:38.000

sort of stresses them into being more aggressive. We're seeing much better outcomes these days. We're seeing less Richter transformation

01:29:38.000 --> 01:29:40.000

When we don't use chemotherapy for patients.

01:29:40.000 --> 01:29:57.000

Okay, just to clarify the chemotherapy, the most common kind of strategy was called FCR. And so that was the last kind of iteration, I think of. And it was very successful for most people if they survived it

01:29:57.000 --> 01:30:09.000

But the complications, as you described, other cancers and Richter's transformation were a problem, so survival long-term wasn't necessarily

01:30:09.000 --> 01:30:30.000

Enough better. So, well, good. You mentioned, not

01:30:31.000 --> 01:30:32.000

getting vaccinated while you're on certain treatments. Does that apply to, for example, the BTK inhibitors, or kind of how should people, like, stop their BTK inhibitors to get vaccinated, things like that?

01:30:32.000 --> 01:30:47.000

I don't usually recommend stopping treatment in order to get vaccinated, whether we're talking about any of the targeted therapies we use. I don't like giving concurrent vaccination with a CD20 antibodies, like obinutuzumab and rituximab



01:30:49.000 --> 01:30:59.000

Because those drugs specifically will deplete the CLL cells, but they also deplete normal B cells, which are the cells you're trying to stimulate with the vaccination.

01:30:59.000 --> 01:31:17.000

So I don't give concurrent vaccinations with a CD20-based therapy. I will give vaccinations when patients are on a BTK inhibitor or on venetoclax or combined BTK plus venetoclax without holding the treatment.

01:31:24.000 --> 01:31:28.000

It's predominantly the CD20 antibody that I'll say, you know, they need to vaccinate before they start on treatment.

01:31:28.000 --> 01:31:33.000

Okay, here's a question that I haven't

01:31:33.000 --> 01:31:45.000

heard even raised before, a GLP-1 drugs at any intersection with CLL that you can imagine.

01:31:45.000 --> 01:31:53.000

Not to my knowledge, we have patients who are on GLP-1 inhibitors

01:31:53.000 --> 01:31:59.000

There isn't really any concern in terms of interactions with our current treatments that we use, that I'm aware of

01:31:59.000 --> 01:32:14.000

Are there beneficial effects? We don't know. I don't... that's not been studied. I don't know of any detrimental effects by taking a GLP-1 in terms of the disease or in terms of patients who are on treatment.

01:32:14.000 --> 01:32:30.000

Okay, and kind of talking about during treatment, how can people judge their immunity during treatment in relation to their comfort traveling or kind of being around other people?

01:32:32.000 --> 01:32:47.000

So again, going back to sort of the drugs, the drug drugs, two drugs that we use now that are known to be suppressive, more suppressive of the immune system are the CD20 antibodies, obinutuzumab, rituximab.



CLL SOCIETY

01:32:47.000 --> 01:33:03.000

So if I have a patient who... and those are usually given for six months of treatment. So if I have a patient on those drugs, I will make a recommendation that, okay, maybe you should think about twice about your trip to Africa.

01:33:03.000 --> 01:33:09.000

Or some exotic place where you can get infections that you don't want.

01:33:09.000 --> 01:33:14.000

So travel and getting out

01:33:14.000 --> 01:33:24.000

For patients who are on a BTK inhibitor or a BTK plus a BCL2 is not as much of a concern as it would be for individuals on the CD20 antibody.

01:33:24.000 --> 01:33:42.000

Okay, and I think we're getting really close to the end, but a question coming back to autoimmune. You mentioned the things that are kind of most closely linked to CLL, like the autoimmune anemia, but are lupus and RA and derma myositis. Are there overlaps or kind of effects of having CLL that would make any of those either more common or more severe?

01:33:54.000 --> 01:34:11.000

My impression and my understanding is that they're not more common among patients with CLL. I have had patients with those diagnoses, but I mean, I have a lot of patients and it's not like you can't get anything else if you have CLL. But I don't get the

01:34:11.000 --> 01:34:26.000

impression, or I don't have the understanding that those other autoimmune phenomena are at increase occurrence among patients with CLL. I've had patients with rheumatoid arthritis, with lupus, etc.

01:34:26.000 --> 01:34:32.000

With Wegeners, it's the autoimmune phenomena that

01:34:32.000 --> 01:34:49.000

occur against the blood-forming cells that is a problem and is a high association with CLL, the autoimmune hemolytic anemia, the ITP, the pure red cell aplasia that I mentioned that are the culprits that cause

01:34:49.000 --> 01:34:52.000

Autoimmune problems in patients with CLL more frequently.



CLL SOCIETY

01:34:52.000 --> 01:35:09.000

Okay, we'll wrap it up with one last question that is very general, but some people don't like to share that they have leukemia with other people. They're concerned about the reactions, whether in the workplace or people

01:35:09.000 --> 01:35:24.000

kind of having pity for them, even though, as you said, it's not a particularly lethal disease. Would it be fair in relation to this whole talk for people who have CLL and might have to make some lifestyle changes and want to tell people that they have a change in their life

01:35:24.000 --> 01:35:38.000

to say, you know, I got a blood disorder, it's mostly an immune problem, without getting into labeling it and having to explain, kind of more about the disease itself.

01:35:38.000 --> 01:35:55.000

You know, that from my perspective, is a very personal choice that patients should make. I don't know that I would even make a recommendation in that situation. I have had patients

01:35:55.000 --> 01:36:10.000

Many patients say, well, I haven't told my family members about my diagnosis of CLL because they struggle with what to tell their family members and how their family members might react. And so even in that situation.

01:36:10.000 --> 01:36:17.000

So I don't know that I have a recommendation in that regard.

01:36:17.000 --> 01:36:30.000

CLL is a chronic disease, like I said, the life expectancy is similar to the age-matched population who don't have CLL in patients 60s and over.

01:36:32.000 --> 01:36:36.000

Other than avoiding people who are obviously

01:36:36.000 --> 01:36:44.000

Sick with infection, there aren't really any lifestyle recommendations, et cetera, that we make, and it's really patients

01:36:44.000 --> 01:36:46.000

choice about what they tell social contacts or even family members. So I don't have a good recommendation. And, you know, everybody's different. Patients are very



CLL SOCIETY

different. Some are more private than others, etc. So that's the type of thing that I should probably

01:37:08.000 --> 01:37:09.000

keep to myself in terms of... because what I would do is not necessarily the same as what somebody else would do.

01:37:09.000 --> 01:37:25.000

Well, thank you for all your presentation, which was kind of really excellent. I couldn't imagine how you can get through all those slides when I saw the slide set. And answered all these questions. Do you have any closing thoughts?

01:37:25.000 --> 01:37:41.000

Sure, as you can tell, the immune system is very important for patients with CLL. As I mentioned, it's more important now than ever. We have some immune-based treatments that we know are very effective that don't work quite as well in patients with CLL.

01:37:41.000 --> 01:37:56.000

I am aggressively studying the immune system in... particularly for patients with CLL to identify ways that we can measure immune function, and looking for drugs that we can use to restore immune function.

01:37:56.000 --> 01:38:08.000

And also looking for vaccines, as I mentioned on my last slide, as strategies to cure the disease and to eliminate the disease. And, you know,

01:38:08.000 --> 01:38:21.000

I have been extremely fortunate in the 25 years that I've been working in CLL. I started working with Michael Keating 25 years ago, when we had FCR, which was a difficult treatment

01:38:21.000 --> 01:38:32.000

for patients to take, it was devastating to the immune system and have experienced and had the great pleasure to work with a lot of the new targeted agents

01:38:32.000 --> 01:38:45.000

and to be through that progression to the point where we're at now with extremely effective treatments, and it's a great pleasure to get to talk about

01:38:45.000 --> 01:38:55.000

vaccinations and screening for other cancers as opposed to spending most of my time talking about Richter transformation and refractory disease.



01:38:55.000 --> 01:38:57.000

So I'm very grateful.

01:38:57.000 --> 01:39:06.000

Great, okay, well, so thank you very much and there are a couple slides that are coming up.

01:39:06.000 --> 01:39:20.000

So we appreciate in the CLL Society also appreciates individual donations and so please be supportive of the society.

01:39:20.000 --> 01:39:35.000

And as I mentioned earlier, if your question — we had a number of questions, but my disease is at this stage, and what should I do, and I think in general, you need to talk to your oncologist about things, and there's a second opinion

01:39:35.000 --> 01:39:50.000

program you can look on the CLL Society about if you're not feeling comfortable with the advice you're getting, but please do send in, and we can organize responses if you send it in to trustedcare@CLLSociety.org.

01:39:50.000 --> 01:40:07.000

The next event is in about a month, and it's one of these Ask Me Anything, so, we covered a lot of stuff around immunity, but, if you have other kind of questions, you can bring those, to the meeting on the 16th.