Treating Uncommon Lymphomas: Dialogue With an Expert on T-Cell, MALT and Waldenström Macroglobulinemia

Richard R. Furman, MD
October 14, 2009 ● 12:00pm ET

OPERATOR: Good afternoon and welcome to "Treating Uncommon Lymphomas: Dialogue With an Expert." All lines have been placed on mute to prevent any background noise. After the speaker's remarks, there will be a Question and Answer Session. If you would like to ask a question during this time, simply press star, then the number 1 on your telephone keypad. If you would like to withdraw the question, press the pound key.

At this time, it is my pleasure to introduce your moderator, Carson Jacobi.

CARSON JACOBI: Thank you Operator. Hello everyone. On behalf of the Leukemia & Lymphoma Society, thank you for choosing to spend this hour with us today. We welcome you to the program "Treating Uncommon Lymphomas: Dialogue With an Expert on T-Cell, MALT, and Waldenström Macroglobulinemia."

Today we have our guest expert, Dr. Richard Furman. We thank him so much for sharing his time and expertise with us today, and for his dedication to serving families touched by cancer. We would also like to acknowledge and thank Allos Therapeutics and Eisai for their support of today's program.

You should have received information today regarding the program, including an agenda, a biography of Dr. Furman, and an order form for the Leukemia & Lymphoma Society's materials. We encourage you to look through those materials at your leisure if you have not already done so. You will also find an evaluation form for you to fill out for today's program, and for nurses and social workers, you can receive one hour of continuing education credit. All participants may visit our online evaluation center to complete your evaluation, or you can mail it in the enclosed self-addressed envelope. I'll provide more information for nurses and social workers at the end of our program today.

After Dr. Furman's presentation, we will open up the lines for you all to ask questions from our telephone audience. We have over 800 individuals registered for our program today, from across the United States, and several international participants from Austria, Canada, and Israel; a special welcome to all of you.

If we are not able to get to your questions today, you can call the Leukemia & Lymphoma Society's Information Resource Center. That toll-free number, included in your packet, is 1-800-955-4572. This will connect you with an oncology professional who can answer your questions, help you obtain information, or order free material specific to your needs. The Information Resource Center's hours are 9 a.m. to 6 p.m. Eastern time, Monday through Friday.

We are audio taping and transcribing today's program for posting on the Leukemia & Lymphoma Society's website in several weeks. This provides an opportunity for you to read or listen again to today's presentation again, especially to follow up on any terminology or therapies that you may have missed.

I now have the pleasure of introducing our speaker, Dr. Furman. Dr. Furman is a member of the Center for Lymphoma and Myeloma in the Division of Hematology/Oncology at New York Presbyterian Hospital and Weill Cornell

CARSON JACOBI: Medical College. He is the head of the CLL and Waldenström Macroglobulinemia program at Weill Medical College and focuses on identifying new and promising therapies for patients with CLL and Waldenström's macroglobulinemia.

Along with collaborators at the Mayo Clinic, Roswell Park Cancer Institute, and Ohio State University, Dr. Furman has initiated the Waldenström's Research Consortium to enhance the treatment and understanding of Waldenström's macroglobulinemia.

We're so happy that Dr. Furman has joined us again, and Dr. Furman, I'll now turn the program over to you.

DR. FURMAN: Thank you Carson. I would like to once again thank the Leukemia & Lymphoma Society for organizing the teleconference. I think this is a great opportunity to help so many people who have such a myriad of different diseases, and those diseases that not are diseases most oncologists have a great deal of experience taking care of. Additionally, given the low numbers for most of these lymphomas, there is often a limit to the amount of information that is out there for the patients.

The one thing I do want to emphasize at this time is a word of caution in the dangers in talking on a topic of uncommon lymphomas. I am discussing a very heterogeneous group of diseases, and all these lymphomas are very different in terms of their presentation, treatments, and the clinical course that they likely follow. I'm certainly going to try to talk in general terms to everybody, and I will also try to talk in specific terms to specific conditions. But it is important for everyone to remember that everything I say or that you hear may not be pertinent to you and your condition. Hopefully there will be enough for everyone to come away from the teleconference with a better understanding about what's going on.

The first question that is always important to address is: Why are we all here together on this teleconference? What is it about these very heterogeneous diseases that bring them all together? The answer is that all lymphomas are all defined by being a cancer of the lymphocytes. The lymphocytes are one of the white blood cells that help protect us from infections.

Lymphocytes come in three different types: B-cells, T-cells, and NK-cells. B-cells are the cells that make antibodies. Antibodies are proteins that are made to attack bacteria and viruses. The T-cells are sort of the quarterbacks of the immune system and are responsible for directing the immune response and shepherding the rest of the immune cells to where they need to be. The NK-cells, which stand for "natural killer" cells, are the cells that are responsible for killing virally infected cells, as well as some cancer cells.

These lymphocytes typically make up approximately 2,000-4,000 white blood cells in a normal person, out of a normal white blood count of 4,000-10,000. Normally, T-cells make up about 60 percent of the lymphocytes, the B-cells about 25 percent, and NK-cells, 15 percent.

Any one of these lymphocytes can become a cancer, and that is what lymphoma is. Lymphocytes like to live in the blood, the bone marrow, the lymph nodes, and the spleen; and these are the typical sites where we find lymphomas. There are

DR. FURMAN: two other areas of the body that do sometimes harbor lymphocytes and these lymphocytes can give rise to lymphomas that are characterized as uncommon lymphomas. One is the skin, which is often a site for T-cells, and the GI tract, which is often a site for B-cells.

Lymphomas are typically divided into being either from the cell they are derived from, either a T-cell, B-cell, or NK-cell, or that aggressiveness that they manifest, indolent (or low-grade) or aggressive (intermediate or high grade).

Aggressive are the type of lymphomas that are sometimes curable, but they're also the ones that behave more aggressively, meaning that they grow quickly and require immediate treatment to control their symptoms. The indolent lymphomas grow slowly and often do not need immediate therapy. In the indolent lymphomas, we often utilize a strategy of watch and wait.

Lymphomas themselves are all caused by different things. With B-cell and T-cell lymphomas, we believe that a lot of what occurs is the result of the rearranging of the DNA that happens when every B-cell goes to make its antibody. It is important to remember that this is the DNA in that one B-cell. This is not the DNA in the liver cells, lung cells, or heart cells, and it is not the DNA that you share with your sisters and brothers or your children. This is the DNA that's in one B-cell. What happens is that when the B-cell rearranges its DNA in an attempt to make a good antibody, mistakes often happen during that time that cause two genes to be put next to each other that shouldn't be. This mistake results in a gene being turned on or off that affects the function of a lymphocyte.

Normally, a lymphocyte might be born and live anywhere from two weeks to twenty years and then die. In a lymphoma cell, the genes are altered so the lymphocyte just doesn't die; in fact, it often grows quicker than it should as well.

It's important to remember that you have clones of lymphocytes that were created many years ago. When you were vaccinated as a child against the measles, you created clones of lymphocytes that were responsive to the measles virus that will remain in you for the rest of your life. They're all derived from those same parenteral cells that were present when you were vaccinated. These are not the original cells, but daughter cells of those original cells. Those original cells should have died off.

With T-cell, we think it's sort of a similar process, where the DNA of the genes of the T-cells is also rearranged in an attempt to make the T-cells better able to target individual infections. During the rearrangement of the T-cell genes, similar types of mistakes happen.

An additional cause of lymphomas, especially for T-cell and NK-cell lymphomas are viruses. These viruses are always in us, but they sometimes cause changes in the cells that can lead to lymphomas.

Overall, we talk about a lymphoma being a cancer of lymphocytes and there being two major types of lymphomas: Hodgkin's Disease, which represents about 7,500 per year in the United States, and non-Hodgkin's lymphoma, which represents 67,500 cases per year. So out of the 75,000 lymphomas a year in the

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DR. FURMAN: United States, which makes lymphomas the fifth most common malignancy in the United States, the vast majority are going to be non-Hodgkin's lymphomas.

Just for comparison, we talk about prostate, breast cancer, and lung cancer being close to 200,000 a year each. Within the non-Hodgkin's lymphomas there are approximately 45 different types. Non-Hodgkin's lymphomas are derived from either a B-cell, typically 85% of the total, or a T-cell or NK-cell.

The number of different types of lymphomas does increase every couple of years when the classification systems are revised. As of now, there are probably about 15 different T-cell and NK-cell lymphomas, but that number itself will continue to change as we learn more.

What I'd like to do is just talk about symptoms in general and then I'll talk about specific lymphomas. With the lymphomas, most of the symptoms are derived from the lymphocytes taking up space. The symptoms depend mostly upon where the lymphocyte happens to be. If the lymphocyte is in a lymph node and that lymphocyte makes many copies of itself, the lymph node becomes enlarged and that's what we call lymphadenopathy.

Lymphadenopathy causes symptoms relating to its size. It might be uncomfortable or painful, be pushing on an organ like a kidney or the bladder, or be located in the neck and keep you from being able to button your shirt collar.

Similarly, when the lymphocytes accumulate in the spleen, it becomes big, which we call splenomegaly, and can cause pain and discomfort. But the spleen, when it gets enlarged, can also cause a low white blood count, low platelet count, or anemia, and the spleen sort of soaks up blood cells.

With regard to the bone marrow, which is where normal blood cells are made, the lymphoma cells take up space and could interfere with the production of normal blood cells, resulting in a decrease in red cell production or anemia, a reduction in the amount of platelets, or thrombocytopenia, or a reduction in the numbers of normal white blood cells, or leukopenia.

Those are most of the symptoms related to taking up space.

The second means that lymphomas can produce symptoms is by causing what are called B-symptoms, which are fevers, chills, night sweats, and weight loss. B-symptoms are thought to be due to cytokines, or chemicals made by the lymphomas, that affect areas of the body that are far removed from the actual lymphoma itself.

A third means that lymphomas can cause symptoms is by the production of antibodies, which is specific to the B-cell lymphomas. B-cells are responsible for making antibodies to protect us from bacteria and viruses. B-cells lymphomas can make antibodies and sometimes this could result in very high levels that make the blood extra thick or viscous. This hyperviscosity can result in the blood not flowing as well as it should and could lead to problems such as a stroke.

The antibodies can also react with other parts of the body instead of a bacteria or

DR. FURMAN: virus. The more common self-reacting antibodies react with and damage the nerves, red blood cells, or platelets. When the antibody reacts with the nerves, it can result in neuropathy, which is numbness, tingling or pain involving the peripheral nerves, primarily the fingers and toes. When the antibodies react against the red blood cells or platelets, they result in destruction of the red blood cells or platelets.

Finally, the antibodies can also precipitate in the blood, causing a vasculitis, which is an inflammation of the blood vessels that can be painful or lead to other problems.

It is also important to remember that many symptoms are the result of our treatments. It is important to determine whether the symptoms are caused by the lymphoma or treatment, because the solution would be different.

Moving on to discussing different types of treatment, we define treatments as either radiation, chemotherapy, monoclonal antibodies, or a group of new treatments that I am going to call biologically targeted therapies.

Chemotherapies are medications that are administered by vein or mouth that target, in a relatively nonspecific manner, dividing cells. The cells often injured from the chemotherapy are the lymphoma cells because they are dividing more rapidly and cannot repair themselves and die. The normal cells, which are dividing more slowly, are damaged; but the hope is either that they will repair themselves or that others will grow back and replace the ones that were killed.

Chemotherapy treatments are typically named for the different drugs in the regimen. Most of the time, with lymphomas, we use several drugs together.

One of the more classic treatment regimens for aggressive lymphomas is CHOP, C-H-O-P. The C stands for cyclophosphamide; the H stands for Adriamycin® or doxorubicin, as its name used to be hydroxydaunomycin; the O stands for vincristine because it is also known as Oncovin®; and the P stands for prednisone. Other treatment regimens include: ESHAP, ICE, DICE, or MACOP-B and it can really be an alphabet city.

For low-grade lymphomas, sometimes CHOP is used, but often single agents are used by themselves: pentostatin, fludarabine, or cyclophosphamide. These agents can also be combined together.

The second type of treatment is radiation. Radiation is very effective at killing lymphoma cells. The problem with radiation is that it is very effective. So it kills whatever cells it is directed at, but it doesn't work anywhere else and it often kills mostly everything in the path where it is. So radiation is a helpful therapy when you have a very small area to treat and you can actually just focus the treatment in an area that won't damage other parts of the body.

The other type of treatment that most people are familiar with are monoclonal antibodies. An antibody is a protein made by B-cells to target bacteria and viruses. Someone in the laboratory made antibodies against different proteins on cells and chemicals the cells need to survive. By targeting these cells with an antibody or binding to the chemicals that cells need to survive, you can make the

DR. FURMAN: cells undergo apoptosis or cell death.

The most commonly used antibody is an antibody called rituximab or Rituxan®, which is directed against a protein called CD-20 on the surface of B-cells and almost all B-cell lymphomas. When the rituximab binds to the B-cell, it targets the immune system to that B-cell. The immune system then kills the target cell by activating complement, which is a protein that can punch holes in the cells as well as bacteria, or by activating a T-cell or NK-cell to kill the cell.

Rituximab is a very nice treatment because it will only target B-cells; it won't hurt NK-cells, T-cells, liver and spleen cells, or red blood cells. Rituximab cannot differentiate a normal B-cell from a lymphoma B-cell, but the normal B-cells will grow back. Rituximab is really an important additive to almost all treatment regimens used for B-cell lymphomas.

A second antibody is called alemtuzumab or Campath®. Campath binds to a protein that is present on all lymphocytes: T-cells, B-cells and NK-cells called CD-52. Since CD-52 is found on almost all lymphomas, T-cell, NK-cell and B-cell, it can be used for almost any type of lymphoma. The problem with alemtuzumab is that it is very immunosuppressive because it kills all lymphocytes, putting patients at risk of serious infections.

Two other antibodies that are approved for the treatment of lymphomas use radiation instead of the immune system to kill lymphoma cells. These antibodies, Bexxar® and Zevalin® both target CD-20 and have a radioactive molecule bound to them. The antibody serves to carry the radiation to its target. Standard radiation treatments have the problem of the radiation destroying the cells in the path of the radiation on its way to the target; these antibodies carry the radioactive molecule straight to the cells where they need to be.

Another antibody worth mentioning, just because it is likely to be approved shortly, is called ofatumumab or Arzerra™. This antibody used to be called HuMax-CD20. Ofatumumab targets CD-20 and works a little bit differently than rituximab. We don't know if ofatumumab is better than rituximab, just that it will be a nice addition to our treatment options for patients.

Many new therapies are being developed for the treatment of lymphomas. One group of these therapies is termed small molecule inhibitors, which inhibit individual enzymes inside cells, like Syk, or PI 3-kinase. These enzymes are not necessarily the cause of the lymphoma, but are important for lymphocyte survival. By targeting these enzymes, we will hopefully be able to kill off the lymphoma cells without damaging other cells as well.

Another group of new agents are the IMiDs®, which stands for Immunomodulatory Drugs. Two IMiDs® are already approved: thalidomide, or Thalomid®, and lenalidomide or Revlimid®, both of which are pills. Thalidomide was initially approved in the 1950s for morning sickness associated with pregnancy. It was taken off the market because its use in pregnant women resulted in all sorts of limb defects in the children born to mothers that were taking it.

DR. FURMAN: What we have found is that the way thalidomide causes those birth defects is the same way that it can effectively treat cancer. Thalidomide's use is limited by its side effects: neuropathy, sedation, and constipation. Revlimid is a derivative of thalidomide, with just one atom changed. As a result, lenalidomide is far more active, and has a different side effect profile, causing usually neutropenia, thrombocytopenia, and anemia instead of constipation, neuropathy, and sedation.

A third class of drugs is the HDAC inhibitors. HDAC stands for histone deacetylase, which is an enzyme that is responsible for helping wind and unwind the DNA. The DNA needs to be unwound in order for the genes to be read. If you interfere with the ability of the cells to read the genes, you can in essence turn them off, hopefully causing the lymphoma cell to die. There is one HDAC inhibitor currently approved called vorinostat, or SAHA, for the treatment of cutaneous T-cell lymphomas which is also being tested in many different lymphomas.

I'd just like to touch on some specific characteristics of these different types of lymphomas. T-cell lymphomas occur in about 5,000-10,000 people a year in the United States. The most common type of T-cell lymphoma is what is commonly called a cutaneous T-cell lymphoma, but is really much more appropriately called mycosis fungoides. Any T-cell can involve the skin, but the vast majority of them are going to be mycosis fungoides.

In mycosis fungoides the lymphoma goes through several stages, called patch, plaque, or tumor, depending upon the thickness of the skin area that is involved, and disseminated, where it involves other areas of the body.

The thing that's important to remember with all lymphomas, but in particular with cutaneous T-cell lymphomas, is that no matter where the lymphoma cell is it is still part of the same lymphoma. So when mycosis fungoides involves a lymph node, it is still mycosis fungoides.

With mycosis fungoides, which is a type of low-grade lymphoma and therefore slow growing, the treatments are often directed towards the skin, including superficial radiation, ultraviolet light or topical creams.

The other big category of T-cell lymphomas are peripheral T-cell lymphomas. These are more aggressive and typically reside in lymph nodes. They can also be in the bone marrow, the spleen, and as well, the skin. Peripheral T-cell lymphomas are often associated with a lot of cytokine production, which are chemicals cells use to communicate with one another, that result in a great deal of symptoms, like fevers, chills.

The other types of lymphomas I want to discuss today are some less common B-cell lymphomas, marginal zone or MALT lymphomas, lymphoplasmacytic lymphoma and Waldenström macroglobulinemia.

Marginal Zone or MALT lymphomas make up about 6 to 7 percent of all B-cell lymphomas and are low-grade lymphomas that are usually responsive to some antigen or target. MALT stands for mucosal-associated lymphatic tissue. MALTs typically involve the mucous membranes. Most commonly they are in the

DR. FURMAN: stomach, which would be called a gastric MALT, but it can be in the small bowel, the lung, the parotid gland or the tear glands in the eye.

In all these locations, these B-cells are often thought to be responding to some target. For gastric MALTs, it is a bacteria called Helicobacter pylori. For other MALT lymphomas, we're not sure what that target or bacteria is.

MALT lymphomas occur with a higher frequency in patients with rheumatologic conditions like Sjögren's syndrome. In these conditions, the lymphoma cells are thought to be responding to a part of the person themselves and not a bacteria, sort of a form of autoimmunity.

Another type of lymphoma is called lymphoplasmacytic lymphoma. Lymphoplasmacytic lymphoma and MALT lymphomas both tend to make IgM antibodies. When the level of IgM antibodies becomes high, the antibody itself causes problems, and this is technically what is called Waldenström's macroglobulinemia. Almost all cases of Waldenström's macroglobulinemia will be due to a lymphoplasmacytic lymphoma. Therefore, most physicians use the terms interchangeably.

With these lymphomas, similar to other low-grade lymphomas, treatment is indicated when symptoms arise. With a cutaneous T-cell lymphoma or a mycosis fungoides, the symptoms might be skin-related changes, either pain, itching, or cosmetically disfiguring. With lymphoplasmacytic lymphomas or the Waldenström and the MALT lymphomas, it might once again be the cells taking up space or a high level of IgM. These types of lymphomas are treated with therapies that are typically used for low-grade lymphomas, including the nucleoside analogs (fludarabine, pentostatin, cladribine) or rituximab (if a B-cell). With gastric MALT lymphomas, there are even circumstances where early disease can be treated with antibiotics.

With all that being said, let me turn things back over to Carson Jacobi, and we can open up the telephone lines for questions.

CARSON JACOBI: Thank you so much Dr. Furman. What a great explanation of all the different types of orphan lymphomas. As Dr. Furman said, it's now time for the interactive part of our program, the Question & Answer session. Before the operator gives you instructions for you to enter the Question & Answer queue, I would like to remind you that because we have so many participants on the line, for everyone to benefit, if you could please keep your questions general in nature and Dr. Furman will provide an answer general in nature.

Your phone line will be muted after you ask your question so Dr. Furman can respond. Operator, if you can please give instructions so our audience can queue themselves to ask a question.

OPERATOR: To participate in the call by asking a question, please press star then the number 1 on your telephone keypad. If you would like to withdraw your question, press the pound key. We will take questions in the order they are received. Be aware that due to time constraints, we can only take one question per person. Once your initial question has been voiced, the operator will transfer you back into the

OPERATOR: audience line. Again to participate in the call by asking a question, please dial star 1 on your telephone keypad now.

CARSON JACOBI: When you're ready Operator, we'll take our first question please.

OPERATOR: Thank you, the first question will come from Kelly.

QUESTION: Hi Dr. Furman, thank you for your time. My husband was diagnosed in April of 2008 with angioimmunoblastic T-cell lymphoma. His disease has never shown up in any blood work, CT scan, PET scan, or bone marrow biopsy. The places where it shows up is that he suffers from severe congestion, and they've done biopsies out of his nasal area and that's the main place that they seem to find it and where it causes him the most problems.

Currently, they're declaring it kind of an indolent pattern. His doctors are a bit confused. We're doctoring at Mayo Clinic in Rochester, Minnesota. My question is have you ever seen this disease in any patients that have suffered with this severe congestion, and is it common for this disease to be indolent?

DR. FURMAN: Angioimmunoblastic T-cell lymphoma is a type of lymphoma that is very rare and it typically doesn't follow an indolent course. Angioimmunoblastic lymphomas are one of those classic T-cell lymphomas that have systemic effects, being able to impact on the body areas that are far-flung from where the actual lymphoma is found.

Of course with any of the lymphomas, it's always important to confirm the diagnosis as the diagnosis helps to determine (1) what could be expected in terms of symptoms, (2) what time course that we expect the disease to play itself out over, and (3) how best to treat it. Because T-cell lymphomas are harder to characterize than the B-cell lymphomas, you'll find many differences in the pathology reported.

I always encourage patients to get second opinions and be prepared for differing opinions. Ultimately, the most important decision is going to be deciding whether or not the treatment should be geared towards the symptoms, which is what you'd want to do for an indolent lymphoma, or more geared towards eradicating the lymphoma, which is what you'd want to do for an aggressive lymphoma.

CARSON JACOBI: Thank you very much for your question. Let's take our next question please.

OPERATOR: Our next question will come from Douglas.

QUESTION: Hello Dr. Furman. Thank you for taking my call. I have a 24-year-old daughter who is 27 months in remission from large T-cell anaplastic lymphoma. Since going into remission, she's had regular checkups, but no CT or PET scans. Should she be considering a PET or CT scan to ensure that she's still in remission?

DR. FURMAN: For everyone's information, CT scans or CAT scans use radiation to take pictures of the inside of the body. They are good at identifying the structures and the presence and size of any lymph nodes. A PET scan, or positron emission tomography, is like a CT scan, but uses radioactive sugar to measure the metabolic activity of the cells. PET scans are often done in conjunction with CT

DR. FURMAN: scans, and are therefore called PET/CT scans.

PET scanning is much more sensitive for aggressive lymphomas than CT scans. But many low-grade lymphomas will not be detectable on PET scans because they are not active enough. There are always going to be subtle differences between cases that might explain why a CT or PET scan is being done, but my belief is that for most aggressive lymphomas PET scanning is more advantageous than CT scans. For an aggressive lymphoma like an anaplastic large cell lymphoma, the appropriate follow-up would be with CT scanning or PET scanning, typically every three to six months for at least a couple of years.

The thing to remember of course is that CT scans are associated with radiation. I do believe that the risk posed by the radiation is low when you're talking about using it to follow someone for a couple of years to make sure their lymphoma is in remission. It's also low when you're talking about using it in someone who is in their seventies and has a low-grade lymphoma. So there really is very little risk to following up the lymphoma, but there might be something specific about your daughter's condition that might have indicated to the physician that scanning was not necessary.

CARSON JACOBI: Thanks Douglas for your question. Let's take our next question please.

OPERATOR: The next question will come from Charlene.

QUESTION: Thank you doctor, for taking my question. I have Waldenström's, which then became aggressive large B-cell. I was treated with CHOP-R and finished two years ago, and was on a Rituxan maintenance every three months, and then every four months, and am now on every six months. What I'd like to know is your opinion of Rituxan maintenance for lifetime when Waldenström's was essentially the culprit leading to my lymphoma.

DR. FURMAN: I'll try to generalize the question a little bit. I think that one thing I didn't talk about, which is just worth mentioning here, is that a lot of lymphomas can change into other lymphomas. What typically happens is, a low-grade lymphoma will become more aggressive and that is what we call a transformation.

In a transformation, one of the cells develops a second change the causes it to grow rapidly. This one cell grows very very rapidly and takes over. The low grade cells are still there, it's just that you have to change your strategy to treat the aggressive lymphoma now. That might be a situation where you would use CHOP in a patient with Waldenström's because you need to treat the transformed lymphoma.

For large cell lymphoma and Waldenström's macroglobulinemia we don't typically use maintenance therapy. The risk of Rituxan as the maintenance therapy is low. But the only data we have really showing that maintenance therapy is helpful is with a type of lymphoma that's called follicular lymphoma.

For follicular lymphomas, which really represent the most common type of non-Hodgkin's lymphomas, we typically do two years of maintenance therapy. But there really are no data suggesting that maintenance therapy has a role to play in Waldenström's or diffuse large B-cell lymphoma. There is some theoretical

DR. FURMAN: rationale though, that certainly knocking down the Waldenström's will keep perhaps another transformation from occurring. That, once again, is theoretical.

CARSON JACOBI: Charlene, thank you for the question. Let's take another question please.

OPERATOR: The next question is from Deborah.

QUESTION: I had a lobectomy in 2002 and was diagnosed with a MALT lymphoma. In 2006 I was diagnosed with a 2.5 lymphoma in another lobe of my lung. Since that time I've been on watch and wait, CT every six months, normal blood work, no change in size, has become a little less dense with a course of antibiotic regimen, low activity on PET scan and SUV uptake of 4.2. What would be a trigger to watch for starting to treat it and how would you treat it?

DR. FURMAN: It sounds like you had a MALT lymphoma of the lung. We call MALTs of the lung BALTs, for bronchial-associated lymphatic tissue. But the name aside, it really is just a MALT lymphoma.

The thing about these lymphomas is really just to treat symptoms. These lymphomas tend to be very indolent and slow growing, and the only real common type of symptom that I would see with this type of lymphoma might be if the lymphoma were to get big enough that it might interfere with your breathing. So if it were to grow big enough to close off one of the airways to part of your lung, that part of the lung might collapse.

Typically what you might see is just a little bit more shortness of breath or a little bit more difficulty exercising. But that's something that might come on very gradually and may not come on at all. You would want to start treatment before the symptoms develop. Usually I just use rituximab because it's very well tolerated and effective. What we often see is patients will go five, six, seven years before they need treatment, get treated, and then go another five, six, seven years until they need treatment again. And this is something that will hopefully play out over a very, very, long time.

CARSON JACOBI: Deborah thank you for the question. Operator, we'll take another question please.

OPERATOR: The next question will come from Diane.

QUESTION: Hi Dr. Furman, thank you for being with us today. I wanted to ask you: You mentioned about MALT lymphoma also going to the carotid area, and I just recently had an MRI for cervical vein and they said…

CARSON JACOBI: Diane, your line is still open?

DR. FURMAN: Hello? I think we lost that question.

CARSON JACOBI: Are you there Diane? Maybe we can get her back. Operator let's take another question please.

OPERATOR: Yes, ma'am, the next question will come from Barbara.

QUESTION: I have Waldenström's. I have a question about treatment. Do you recommend treatment only for symptoms or for a certain IgM level, and if that is correct, what

QUESTION: level do you look at for treatment?

DR. FURMAN: We use the phrase, "you treat for symptoms", but what I think is most important is the idea that you want to treat before the symptoms happen. For a high IgM the symptoms could be very quick and dramatic, like a stroke. Fortunately, you can follow the IgM level easily and be able to intervene long before that becomes an issue. What is the more important measure is the serum viscosity, which is a measure of how the antibodies interact with one another to make the blood a little bit more viscous.

Every antibody has a little bit different impact on the serum viscosity. So there could be a patient with an IgM of 5,000 and a serum viscosity of 2.4, while another patient with an IgM of 5,000 has a serum viscosity of 6.0. So it is important for each physician to determine how a patient's IgM corresponds with their serum viscosity.

As a general rule, we do not see problems with hyperviscosity until it reaches above 3.5-4.0. Likewise, an IgM of 5,000 or less is unlikely to cause problems related to a high serum viscosity. But there will always be some variation between patients. The IgM of 5,000 is the cut-off that I often use. One caveat is that choosing a cut-off lower than necessary affords the opportunity to try a gentler therapy, like rituximab. Should rituximab not work, or there is an associated tumor flare, you have time to try an alternative therapy before the IgM becomes too high.

CARSON JACOBI: Thank you Barbara for your question. Operator, I don't know if you were able to get Diane's line back?

OPERATOR: No ma'am, I'm not showing her line back in the queue.

CARSON JACOBI: Okay, let's take our next question please.

OPERATOR: The next question will come from Shirley.

QUESTION: Thank you for taking my question; it's been very informative, Dr. Furman.

I just wanted to know what we should do about the swine flu shot. I have been in remission. I have non-Hodgkin's lymphoma and so does my husband, but he has the Waldenström's case. We have been in remission for almost two years, and we have taken the flu shot but we don't know what to do about the swine flu shot.

DR. FURMAN: I think this is a very good question and I'm glad that you asked it, because I think it's one that's on everyone's mind. The thing that I want to point out to everyone is that the seasonal flu vaccine, which is directed against the "regular" flu that happens each year, is made up of different antigens or proteins that the body can mount an immune response against. The scientists at the Centers for Disease Control decide early in the year what the flu that will strike in the coming winter will look like. They then direct the vaccines to be made against these viruses.

The vaccines come in two types. They come in either an attenuated, or weakened, live vaccine or a killed vaccine. For the flu, and this is just for the flu, the nasal spray is the live vaccine and the injectable form is the killed vaccine.

DR. FURMAN: It is very important to remember the difference because patients who are immunosuppressed and their household contacts should not get live vaccines. The concern, of course, is that, if you don't have a functioning immune system, the live virus could really take hold and cause a lot of problems.

Along those lines, if a household contact were to be vaccinated with the live vaccine, they might run the risk of spreading the vaccine to the patient. That's why I always recommend the killed vaccines.

I recommend both the seasonal flu and the swine flu, or H1N1, vaccines for all my patients, assuming the H1N1 vaccine will be available. The reason that the swine flu has generated such concern is that there has not been a flu virus similar to it for quite some time. What happens normally with the flu, which is highly contagious, is that it spreads from person to person until it finds a person who has some immunity against it, and that breaks the chain of the spread.

No one has any immunity against the swine flu because it is so different from the other flu viruses that we have been vaccinated with previously. It therefore has the ability to spread unimpeded throughout the population. Fortunately, the swine flu is much less dangerous than the seasonal flu. The seasonal flu might kill 1 percent of the people that it infects, but for swine flu the number is one one-hundredth of that.

Given that both of them are associated with a lot of illness and potential morbidity, I do recommend both vaccines for all my patients. And I just want to emphasize that it should be killed vaccines for the patients and their household contacts.

It is also important to remember that the flu vaccines, both the seasonal and H1N1, are made in chicken eggs. People who are allergic to eggs should not receive any of these vaccines. I would also like to emphasize that because a lot of the lymphoma patients won't be able to mount an immune response because of either the lymphoma or the chemotherapy affecting the immune system, vaccinating household contacts is an important means for keeping lymphoma patients from getting sick.

CARSON JACOBI: Shirley, thank you for the question. Let's take another question please, Operator.

OPERATOR: The next question will come from Penny.

QUESTION: Hello, Dr. Furman I'd like to ask you a question. I have anaplastic large cell lymphoma and I went through CHOP. After two treatments I had an MRI. It showed nothing. So I went through the six treatments and then it showed nothing. And then it was about a month-and-a-half and I got a tumor on my leg, so I went for the MRI and I had the anaplastic large cell lymphoma several places in my body. Now I'm on oxaliplatin and gemcitabine. Is that a better medicine than CHOP?

DR. FURMAN: When oxaliplatin and gemcitabine are used together, we typically call the regimen gem/ox. It's not really a question as to whether it's better or not. CHOP is the tried-and-true standard that's been tested again and again for many, many, years. Oxaliplatin and gemcitabine are both new drugs that we've just started

DR. FURMAN: using in lymphomas. We don't know whether or not gem/ox is better than CHOP or vice versa. It's just that for many reasons we use CHOP first because it's tried and true.

When someone relapses after CHOP, then we search for agents that are different, and hopefully the tumor will still be sensitive to these different agents.

CARSON JACOBI: Penny, thanks for the question. Let's take our next question please.

OPERATOR: The next question is from Marilyn.

QUESTION: I'm a little off. I have central nervous system lymphoma and I'm considered stable, but I have fluid around my brain and I wonder if that's the usual thing for any lymphoma.

DR. FURMAN: It's sort of hard to know. Everyone always has fluid around the brain called the cerebral spinal fluid. A primary CNS lymphoma is really a B-cell lymphoma, most commonly, that just happens to be found in the brain only and not in a lymph nodes. It requires a different treatment strategy because a lot of our chemotherapy agents don't penetrate into the brain. That's why it's an important distinction. So the treatments are usually directed just to the brain and not to the rest of the body.

Regarding the fluid, I'm not exactly sure what you're referring to because there should always be cerebral spinal fluid acting as a cushion of the brain. And there are perhaps lymphoma cells in the cerebral spinal fluid that are making up the lymphoma.

QUESTION: The mass that I have is solid; it's next to the brain, actually on the brain.

DR. FURMAN: Did you say MALT or primary CNS lymphoma?

QUESTION: CNS. I had it in my eye and my back.

DR. FURMAN: You are probably referring to an orbital MALT lymphoma and not primary central nervous system lymphoma.

QUESTION: Right.

DR. FURMAN: I'm having a little bit of trouble hearing you. A MALT lymphoma of the eye most commonly involves the conjuctiva, which is the lining outside of the eye. Like MALT lymphomas of the stomach or the lung, the lymphoma is found in the mucosa around the eye.

We typically once again just watch until people develop symptoms. Even though it's near the brain, it usually doesn't go into the brain because a MALT lymphoma tends to go only where lymphocytes should go. And so since normally there shouldn't be lymphocytes in the brain, the MALT lymphomas of the conjunctiva typically just spread to other parts of the eye, other lymph nodes, or other areas of mucosa, like the stomach, the mouth, or the lungs.

CARSON JACOBI: Marilyn, thank you for the question. Actually thank you all very much for your questions. Our program has come to an end. If you can, please help me thank Dr. Furman. We are so very grateful that he has donated his time to us today,

CARSON JACOBI: and again we thank him for all the work that he does every day in supporting families touched by cancer.

We would also like to again thank Allos Therapeutics and Eisai Incorporated for their support. And we hope that many of your questions were answered and that the information will assist you in your next steps.

A reminder to all: Please fill out your evaluation forms. Our Information Resource Center is open. The number is 1-800-955-4572, and our specialists are ready and available to speak with you or to answer any further questions that you may have.

On behalf of the Leukemia & Lymphoma Society, Dr. Furman and I would like to thank you all for sharing this time with us. Goodbye and we wish you well.

OPERATOR: Ladies and gentlemen, thank you for participating in today's conference call. You may now disconnect.

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