Episode: 'How is Acute Lymphoblastic Leukemia (ALL) Diagnosed and Treated?'

Description:
Join Alicia and Lizette as they speak with Dr. Shella Saint Fleur-Lominy, MD, PhD, a hematologist and physician scientist from NYU Langone Health in New York, New York. Dr. Saint Fleur-Lominy is triple board certified in internal medicine, hematology and medical oncology. On this episode, Dr. Saint Fleur-Lominy explains the signs and symptoms of acute lymphoblastic leukemia (ALL), tests and examinations that are used to detect and diagnose ALL, how ALL is treated and the potential side effects of treatment. Dr. Saint Fleur-Lominy describes when transplant as well as chimeric antigen receptor (CAR) T-cell therapy may be considered as a treatment option and her excitement for promising new treatments. Dr. Saint Fleur-Lominy shares in great detail about the chromosomal changes for those with in ALL and emphasizes that there is nothing that a patient did to get their ALL diagnosis. She encourages patients to seek support and clarity about their disease so that they are not left feeling like their diagnosis is their fault.

Transcript:

Alicia: Welcome to The Bloodline with LLS. I’m Alicia.

Lizette: And I’m Lizette. Thank you so much for joining us on this episode.

Alicia: Today we will be speaking with hematologist Dr. Shella Saint Fleur-Lominy, from NYU Langone Health in New York, New York. Dr. Saint Fleur-Lominy is a physician scientist. Her medical school training was a combined MD and PhD training program. Her postgraduate training included a research track residency and fellowship; and she is now triple board certified in internal medicine, hematology and medical oncology.

She is currently studying the biology of leukemia with a goal of finding pathways important for better treatment outcomes. Welcome Dr. Saint Fleur-Lominy.

Shella Saint Fleur-Lominy, MD, PhD: Thank you. It’s a pleasure to be with you today.
Alicia: Now before we jump into the topic of this episode, which is acute lymphoblastic leukemia known as ALL, we always like to get an idea of who the speaker is. So, what brought you to the field of medicine?

Dr. Saint Fleur-Lominy: Okay. So, I can say I grew up with the idea of going into medicine. I am an immigrant. I came from Haiti. And when I was growing up, I used to see the dire situation of people who are sick, and we don’t have enough human resources; and I wanted to be part of the solution. I wanted to become a doctor. So, from very early on in my childhood, that’s what was my idea.

Then my family immigrated to the United States; and I came right after I finished my high school, so I still had the very strong desire to go into medicine, and I went to college with the idea of being a premed. And when I started, I also kind of fell in love with research because I felt like, oh, when you are a medical doctor, you are taking care of patients. Your impact is limited to the patient that you have in front of you. But when you are doing research, you can actually impact medicine in a more impactful way.

So, I started doing research, and that’s how I decided instead of just going into medical school to be an MD, I want to do an MD/PhD. So that’s what kind of brought me into the field I am right now.

Alicia: That is awesome, and that’s such a great, I guess, outlook on research versus MD.

Lizette: That was a great way to put both together.

Alicia: So, doctor, jumping into ALL, how does leukemia develop, specifically acute lymphoblastic leukemia?

Dr. Saint Fleur-Lominy: Acute lymphoblastic leukemia, it’s a disease that come from the lymphoid cells. So, in our immune system, we have different subtypes of white blood cells. And those white blood cells, they’re what we call lymphocyte and then those we call the myeloid cells.

And from the lymphoid, we have two subtypes. We have the B and the T, and they go through different stages of development before they become mature cell that are capable of doing the work of protecting us against infection because both B and T cells are important to fight infection, and they are part of what’s called adaptive immune system.
So during development, if there is something faulty in the genetic makeup of the cells during how they are dividing or differentiating, then the differentiation of the cells kind of become arrested, it doesn't proceed to go to the next step, then those immature cells that are not able to proceed further, they accumulate and they start multiplying and making more of themselves. That's what become what we call a acute lymphoblastic leukemia.

And because we have in the lymphoid, the normal cells are B or T, the same way for the acute lymphoblastic leukemia we can have a B-cell acute lymphoblastic leukemia, and we can also have a T type as well.

**Lizette:** And in the United States the B-cell type is more prevalent.

**Dr. Saint Fleur-Lominy:** Yeah. It's more common. The B-cell is more common, so it's about 70% of them are the B type and then the rest are of the T type. The distribution between kids and adults, it's slightly different; but the B is more common in both groups for sure.

**Lizette:** And do we know why these cells become abnormal?

**Dr. Saint Fleur-Lominy:** When cells are being made, the B-cell, the T-cells, they have a lot of genetic changes that happen in order for them to have acquired diversity and to be able to respond to a lot of antigens, to be able to respond to a lot of parts of microbes. So, because of that professionally they are cells that divide a lot, and they are also cell that changes a lot in the genetic makeup. And errors happen during those changes. And if an error happen and then there is part of chromosomes that are exchanged and then you have a gene that normally should be under very strict control and now it goes next to another gene where like the control of that gene is that it should be expressed all the time, and then the gene that was supposed to be under strict control and expressed at a very specific time, now it’s not being expressed all the time because it kind of changed pace and location. And by that change, it becomes under control of some, another thing that we call promoter, so it has a different promoter that’s controlling it. And it starts producing all the time, and then it can change the behavior of the cell. So, either the cell proliferates more or either the cell doesn’t continue with this differentiation or the cell doesn’t die when it’s supposed to die. So, a lot of these changes that happen in the signal of the cell that make it not behave the way it’s supposed to behave, and the accumulation of those cells become cancer.
Alicia: Okay, now jumping into tests and examinations, what are a few of those that would be used to detect and diagnose, adult ALL?

Dr. Saint Fleur-Lominy: So in terms of tests, when people present with ALL, sometime they can, they present with abnormalities in the blood count; and they may present with symptoms of fever that or other symptoms like night sweats and things like that. And when they present with those symptoms, some of the tests may include blood count and also when you do the blood count and you find either the white blood cell count is too high and you’re seeing cell that you’re not supposed to see, that we call blasts because blasts are immature form of cells; and they’re supposed to be in the bone marrow, and you see them in the blood that prompted more testing.

And some of those testing include doing something called flow cytometry. And the flow cytometry is when you take those cells and you extend them with specific antibodies to see what exactly they express and also what type of cells that they are.

So, the flow cytometry will tell you whether it is a leukemia, if it’s an acute leukemia versus in a chronic leukemia. And if it’s an acute leukemia, whether it’s AML, whether it’s ALL. And if it’s ALL, whether it’s B or a T because there are certain specific markers that those cells are stained for. So that’s, the diagnostic part.

And then we also do some genetic testing looking at chromosomal abnormalities to see if there is any exchange of chromosome piece between two different chromosomes. some of those exchanges put the patient in a classification as a very high risk versus others will put the patient in a, in a lower risk. Sometimes you see also mutation of genes like you do some PCR [Polymerase chain reaction] like to look for changes in genes. And those help you subclassify the patients.

For T ALL because a good subset of them present as a lymphoma instead of a leukemia, so imaging, I mean CT [computed tomography] scan or PET [positron emission tomography] scan, is also part of the diagnostic testing. And then in male, you also do a testicular exam because ALL also can involve the testes, so that’s part of the diagnostic test. And then for all patients you’re also going to be doing what’s called a lumbar puncture, again, to, not only to analyze the cerebral spinal fluid for involvement by the leukemia but also to administer chemotherapy in that space to prevent the leukemic cell from going there.

Alicia: Now you mentioned fever being one of the most common symptoms. What are other signs and symptoms of ALL?
Dr. Saint Fleur-Lominy: So other symptoms have to do with abnormalities in the blood because when you have leukemia, when the leukemic cells accumulate in the bone marrow, they prevent normal hematopoiesis, normal forming of blood. Some of the thing that could be manifested in the patient is that patient may develop anemia and usually will have symptoms of anemia like fatigue, feeling kind of very like, you know, headache and sometimes shortness of breath because they don’t have a very good capacity to carry oxygen because of the anemia.

Other symptoms that may happen is you can see bruising. You can see bleeding because of platelet count drop because they lose the capacity to make platelet because of the accumulation of the blasts in the bone marrow occupying the space.

Another symptom include infection because also when you are occupying the bone marrow space and you’re not making neutrophils like the good white blood cell that you need to fight infection, so you’re more susceptible to having bacterial infection. But you also have a fever for noninfectious reason because cytokines like, as production by the leukemia cells as they are developing and releasing cytokines, so those also will cause you to have fever, you can have night sweats. Patients can present with big spleen, big liver because of accumulation of the lymphoblasts in those organs. And they also can have lymphadenopathy, like lymph nodes that are growing in different places in the body. You can feel them in the neck, under the arm, in the groin area.

Alicia: So how is ALL treated?

Dr. Saint Fleur-Lominy: We have a very complex regimen where we use chemotherapy that target different part of a cell. Some involve with like inhibiting DNA synthesis. Some involve inhibiting like protein synthesis. And we have others that have to do with cytoplasmic process that are involved in cell division like vincristine.

So, we have a combination of chemotherapy that we use, and then also we use steroid. In the different phases, the first phase of treatment is called induction. And the induction treatment is for about four weeks. And at the end of induction, the majority of patients are in remission. Then after induction, then you have multiple different phases of consolidation or intensification treatment that also takes several months; and they are very intense, a combination of different type of chemotherapy and different dosage. And that also involve in doing chemo not only IV, some chemo by mouth, and also some chemo in CSF directly by what we call intrathecal chemotherapy.
And then after we complete those phases, we go into something called maintenance phase. And the maintenance phase is a combination of three different chemotherapy that, again, target different aspect of similar processes. And with the maintenance therapy, the patient, he is on, it could be for about a year and a half or to two years from the time they finish consolidation basically.

And with that regiment, the majority of pediatric patients are cured. But for adult, the cure rate is much lower; and the older you are, the lower is the cure rate. So, if you take someone who is in their 30s versus someone who’s in their 60s, the cure rate is much different.

**Alicia:** In addition to age, what other factors affect prognosis and treatment options?

**Dr. Saint Fleur-Lominy:** Looking at the genetic background of the disease, the gross chromosomal changes as well as the small gene changes.

For example, I think one gene that most people who know about leukemia have heard about is something called Philadelphia, or BCR-ABL, which is an ABL gene, and it’s one of the Philadelphia chromosomes.

So the BCR-ABL gene, which is something that derive from two piece of, that come from two different chromosome coming together, and that brought the BCR part and the ABL part together; and it’s supposed to exist at different places, but they brought together. One is from chromosome 9 and one is from chromosome 22. And these actually are considered to be high-risk ALL. If you have that change, it’s considered high risk, and beside the chemotherapy, those patients are also treated with a targeted treatment which is a tyrosine kinase inhibitor. Before we had imatinib. Now we dasatinib; we have nilotinib. We have ponatinib. So, we have different generation of tyrosine kinase inhibitor that is incorporated into the backbone of the chemotherapy for those patients. So that affect prognosis.

And whereas for pediatric patients with the pH-positive who are treated with the TKI together with the chemotherapy, then they would still consider a lower, like lower prognostic group or a higher risk group than people who don’t have it. You typically do not go straight into transplant if they get into remission on time and they stay into remission.

For adult patient, currently, most patients who have these changes because the prognosis are lower to begin with, they go into transplant, so they have an allogeneic transplant at the end of once they get into remission.
Lizette: When is it appropriate and who is it appropriate for ’cause not all patients get transplants, correct?

Dr. Saint Fleur-Lominy: Yeah, not all patients. For adult patient, it’s the higher-risk group, and that’s determined at the time of diagnosis when you do those genetic studies and also at the end of induction for those people who don’t go into remission. So those are what we call refractory disease. And so, they go with second-line treatment; those patients also will go into transplant. And in patient who relapse after treatment. So those patients are those who go to transplant.

Lizette: And I know that there’s a lot of newer treatments that are emerging now, especially with immunotherapies and targeted therapy for patients. Is that something that in the future will take over for transplant, or are people still going to go for transplants?

Dr. Saint Fleur-Lominy: People will still go into transplant because with immunotherapy, we are able to put a lot of relapse or refractory patients into remission; but for the most part, the studies we have so far, what we are seeing is that those patients do not stay in, remission for long. So that’s why those patients after they get into remission after the immunotherapy, they typically go to transplant because they’re not staying in remission for long.

Lizette: There’s a lot of side effects for transplant. Do patients usually do well after transplant?

Dr. Saint Fleur-Lominy: So, yes, there are side effect, but it’s a risk-benefit balance. The benefit is that those patients we send to transplant are those we know that that’s their best chance of staying in remission. And in terms of side effects of transplant, I’m not a transplanter. I should say that up front. But I know we are doing better and better with transplant. There always used to be a lot of peritransplant mortality because of complication patient develop during the transplant or immediately after the transplant. But now we have better supportive care, and we can get people through the transplant more successfully.

Now things that can happen even much later is what we call graft-versus-host disease (GVHD) because when you do the transplant, you’re using somebody else’s immune system to fight the leukemia and keep the leukemia in remission. But a side effect on that is that that other person immune system can also attack other organs in that host, in that patient. And those organs typically are the skin, the gastrointestinal system, the liver, and some of those side effects can be very morbid. They can cause a lot of
symptoms and even death sometimes. But, again, with better treatment now and with more research, so there is like better ability to kind of control the immune system and prevent the, what we call GVHD, or graft-versus-host disease.

And it’s a balance because you want to make sure that while you are suppressing that immune system so that it doesn’t cause side effects for the patient, we don’t suppress it too low that you actually lose the graft-versus-leukemia effect. You want to keep the important graft-versus-leukemia effect without having too much graft-versus-host disease.

**Alicia:** There’s a term or a therapy that everyone pretty much has heard this in the last few years, and that is CAR T-cell therapy, chimeric antigen receptor T-cell therapy. What is that and how is it proving to be successful for ALL patients?

**Dr. Saint Fleur-Lominy:** It’s been very successful in putting relapse and refractory patients into remission. So, what it is it’s, actually for B ALL because we are nesting the T-cells of the patient, the normal T-cell of the patient to attack the B lymphoblasts. And so basically, those patients who relapse, they collect their T-cells, and those T-cells are engineered, to have a new receptor to recognize a marker on the lymphoblast. And that marker, the one we’re using right now, is CD19 because all those B lymphoblasts express CD19. And we also are able to use the same CAR T-cell to attack B-cell lymphoma because they also express CD19. And so those T-cells are engineered to be able to recognize those, markers on the B lymphoblast, and they can go and kind of kill those lymphoblasts and put the patient into remission.

**Alicia:** It’s so exciting hearing about something like that. I’m sure as a researcher you are thrilled and super excited because so many people are benefiting from it. Like you said, remission rates, unprecedented remission rates for adults and pediatric patients with relapsed/refractory B-cell ALL. It’s a hopeful option for so many; and I can only imagine how excited that is for researchers to see

**Dr. Saint Fleur-Lominy:** Oh yeah, definitely. Yeah. And beside the CAR T-cell, with this very similar idea, we have an antibody called blinatumomab, which is a bispecific antibody. And because the CAR T-cell, you have to engineer it for the specific patient, collect it from the patient, and then give the patient back the T-cell. Whereas for the blinatumomab is something that’s off the shelf, you can take and then treat the patient.

And the blinatumomab still harness the patient T-cell, but it’s the antibody that you give. The antibody have two things on it like it binds to the T-cell via an anti-CD3
because the T-cell express CD3, and it also have the anti-CD19 part so it’s kind of take the patient T-cell and bring them into contact with the lymphoblast. But it’s not that you engineer the T-cell outside. It’s just putting the antibody in that allow the two to come into contact inside the patient body.

**Alicia:** And with CAR T-cells there are, of course, toxicities. I mean it’s a great thing, but it also comes with its risks. And those can include cytokine release syndrome, B-cell aplasia, cerebral edema. What toxicities may occur for someone who may undergo this type of therapy?

**Dr. Saint Fleur-Lominy:** So the cytokine release syndrome is actually the biggest one that we have seen; and it’s actually a lot of those patients end up going to the ICU to be closely monitored because this is a very, terrible side effect, especially if it’s high grade. Usually, when it’s starting, depending on where, the patient is with the treatment, so there are things that you can do to kind of taper it a little bit, to bring it down. But not all patient will respond to those approaches, so you can see that it can progress to very high grade.

And you mentioned the cerebral edema, and also there are people who don’t even develop cerebral edema, but for what, some reason that we see that they develop altered mental status. So, they have this CNS toxicity, but you can’t really find a specific thing that’s causing it. It could be part of the cytokine also; but this is something we see even in patients who don’t have CNS involvement, CNS involvement of disease.

**Lizette:** So, doctor, for CAR T therapy, the pediatric ALL CAR T therapy right now is approved. Do you know when and if there would be an adult CAR T therapy approved by the FDA?

**Dr. Saint Fleur-Lominy:** I know it’s approved for people less than 25, so young adult can actually get it. And I suspect that is one of the reasons we don’t have it adults yet is because of the side effects as well. And adult patient have a harder time tolerating certain treatment because of other comorbidities. I don’t know when we may have one.

**Lizette:** And what treatments are you most excited about at this point in time?

**Dr. Saint Fleur-Lominy:** So at this point, the immunotherapy I’m very excited about, not only the blinatumomab or the CAR T, but also we have inotuzumab which is another targeted therapy, because it’s an antibody targeting therapy that have a
chemotherapy drug attached to it, and it’s for those BLL that express CD22. And, again, for all those things that I mentioned, either blinatumomab, CAR T, or inotuzumab, for those patients who are, who have been heavily pretreated, we see a higher proportion of patients going into remission compared to chemotherapy.

The one thing about the inotuzumab is that we tend not to do it if the patient is set to straight into transplant because there is also some toxicity associated with it, and that can get worse during transplant.

Alicia: Thank you for explaining that. The target audience for this podcast are patients and caregivers and, you know, many friends and family of those who they know diagnosed with a blood cancer. Are there any common questions that you get from patients that our listeners would benefit from hearing your answer to?

Dr. Saint Fleur-Lominy: Actually, one of the most common question I get is, “Is this something that I did that cause the disease?” And it’s not just for leukemia but for other cancers ’cause a lot of time patients are trying to find answers why I have this disease. Is it something that I ate? Is it something, you know, some kind of behavior thing that contribute to it?

I just want to make sure, you know, patients are really reassured that it’s not something they did.

For the most part, we don’t know. Those are errors of nature, and how I explain with those chromosomal changes or change in some genes that happen and that kind of make the cells behave abnormally and they accumulate and then cause the cancer. So, it’s not something that they have done.

Other things that I have heard is like, “Is there something I can eat that can help me through disease better?” And patients typically ask about if there is any specific multivitamin that they can take that can help them while they’re doing the, the chemotherapy. Again, we do not have evidence that those help, and I usually discourage patient to take multivitamins while they’re doing treatment and chemotherapy because we don’t have evidence that they help and in, in some cancers, we actually do have evidence that they can hurt, especially in breast cancer like because some of those vitamins are antioxidants. So, it seems that they interact with the way the chemotherapy affects the cancer cells. And there have been studies showing that people who are taking certain vitamins during chemotherapy do worse than those who are not taking, so I usually discourage patient. Unless you are really
treating a deficiency, I encourage patient not to take those during treatment and chemotherapy.

**Alicia:** When a patient is sitting with you and they are newly diagnosed and, unfortunately, they’re given the news that they have this diagnosis, and they say, “Doctor, where can I find more resources?” Where do you guide people to for resources about their disease that they can then later read about once they leave your office?

**Dr. Saint Fleur-Lominy:** I usually send them to the websites of either LLS or American Cancer Society. Sometimes we have some brochures also in our exam room that we share with patients. We also refer them, to a support group.

**Alicia:** Dr. is there any additional info that you’d like to share with our listeners?

**Dr. Saint Fleur-Lominy:** I think we, covered the major part. I mean there are a lot of research being done. The T-cell, most of what we talk about today covered the B-cell part. The T-cell is still kind of lagging behind because, especially for the immunotherapy, we do not have much for the T-cell right now. We have had trials looking at some targeted therapy for specific genes that are commonly mutated in T-ALL, but so far nothing had gone far enough to be approved and kind of help with the relapsed/refractory T-LL because there is one gene that’s called Notch1, which is commonly mutated in the T-LL and there have been a lot of effort trying to target that, but so far we haven’t been that successful clinically. And research has looked promising but then clinically haven’t been that successful.

So, I think there is a lot of room for improvement, and that’s why a lot of us is devoting a lot of time in the lab trying to study more the biology of the disease. And currently what I do in the lab is looking at epigenetic markers that can explain some certain genes in the gene expression in those leukemic blasts and to see whether we can target those to help them render the cells more sensitive to chemotherapy.

**Alicia:** Awesome. Thank you so much for joining us on today’s episode, doctor, and for everything that you continue to do for cancer patients. It’s been a pleasure speaking with you, and we’re thrilled to share this episode with our listeners.

**Dr. Saint Fleur-Lominy:** Thank you. It was a pleasure.