**Transcript Details**
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Asparaginase Therapy in Patients with ALL/LBL

**ReachMD Announcer:**
You're listening to *Project Oncology* on ReachMD. This medical industry feature, titled "Asparaginase Therapy in Patients With ALL/LBL," is sponsored by Jazz Pharmaceuticals. Here's your host, Dr Jennifer Caudle.

**Dr Caudle:**
This is *Project Oncology* on ReachMD, and I'm your host, Dr Jennifer Caudle. Joining me to discuss the use of asparaginase therapy in adolescents and young adults, or AYA, patients with acute lymphoblastic leukemia and lymphoblastic lymphoma is Dr Leidy Isenalumhe, who's the Director of Clinical Operations and Co-Director of Inpatient Outpatient Service in the Department of Hematologic Malignancies at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida.

Dr Isenalumhe is a paid consultant for Jazz Pharmaceuticals.

Dr Isenalumhe, welcome to the program.

**Dr Isenalumhe:**
Thank you so much for having me. It's a pleasure to be here.

**Dr Caudle:**
Well, thank you for being here. So, I'd really love to jump right in and ask about the role of asparaginase therapy in your AYA patients with acute lymphoblastic leukemia and lymphoblastic lymphoma, which we'll be referring to as ALL/LBL throughout the program. Can you tell us a bit about that?

**Dr Isenalumhe:**
Absolutely. For some background, asparaginase has been a backbone of pediatric-based regimens for quite a long time now.[1] This is because the data tell us regimens that include asparaginase typically result in better outcomes.[1,2] So, for my AYA patients, we typically use regimens that include asparaginase, because we really believe that it makes a difference. There are enough data out there to show us the importance of asparaginase and the impact of not using it in our AYA patients.[3]

**Dr Caudle:**
So then let's talk a little bit about that data you're referring to. How has the use of asparaginase therapy impacted clinical outcomes in AYA patients?

**Dr Isenalumhe:**
Right, so as far as the data goes, it's been shown that using asparaginase increases disease-free survival.[4] This is why it's been used in protocols for quite some time.[1,2] In order to better understand the survival rates of AYA patients being treated for ALL/LBL, a prospective US cooperative group trial, known as CALGB 10403, was performed to determine if AYA patients with ALL could tolerate intensive pediatric regimens while also achieving improved survival rates.[3] Now, the CALGB 10403 data showed us that the AYA patients aged 16 to 29 have lower overall survival when adult regimens are utilized, as opposed to pediatric, asparaginase-containing regimens.[3] We also know how important it is to complete the full asparaginase protocol, as the data have shown that missing asparaginase doses has a negative impact on disease-free survival outcomes.[4]

And so, since the data are clear, our approach is to use asparaginase-based protocol in our AYA patients with ALL and LBL to help them achieve better overall survival and event-free survival rates. The NCCN Clinical Practice Guidelines in Oncology (NCCN

Guidelines®) do a great job showing the data as well, recommending that AYA patients should be treated with an asparaginase-based regimen as a preferred treatment.[5] So there would have to be a contraindication or a serious toxicity for us to not proceed with using asparaginase in the AYA population.

**Dr Caudle:**
That's an interesting point you bring up regarding contraindications. And so if we shift to safety events associated with asparaginase use in AYA patients, can you tell us a bit about your experience with that?

**Dr Isenalumhe:**
Yes, we do have to monitor our patients that are receiving asparaginase for toxicities. That way, if they do experience those toxicities, we can manage them. In my patients, we specifically look out for transaminitis, clotting, bleeding, pancreatitis, and hypersensitivity reactions. And sometimes, hepatotoxicities and hyperbilirubinemia may occur as well.[4,6] These are events we would typically look for when using asparaginase. Now, I will say that it takes a lot of patient education and nursing support to identify and manage these events, but it is very doable.

Additionally, there is a perception that if you are outside of the pediatric age group, you may be at higher risk of experiencing toxicity. However, prospective and retrospective studies report that protocols containing asparaginase are feasible and tolerable in the AYA patients.[3,7,8] Now, when looking at these studies, pediatric-inspired, asparaginase-containing regimens led to lower rates of some adverse events compared with adult regimens in the AYA patients with ALL.[3] Now, if we can manage asparaginase-associated toxicities, we can certainly do this in our AYA patients as well. Fortunately, we have a lot of experience with knowing what to look out for, and how to intervene and manage any safety event that may be associated with asparaginase. And by addressing the fear that it isn't safe for the AYA patients, we can continue to push for asparaginase regimens to be used in this patient population, which is consistent with the NCCN Guidelines®.[5]

**Dr Caudle:**
So, Dr Isenalumhe, if we continue examining the toxicities and safety events that are associated with asparaginase therapy, could you tell us a bit more about hypersensitivity reactions and how that impacts the overall regimen for your patients?

**Dr Isenalumhe:**
Of course. So, when hypersensitivity from asparaginase occurs, it impacts the regimen to the point that we're not going to introduce that drug again in that patient.

Luckily, we know what to look out for because our treatment protocols will include anything we might need in order to mitigate a hypersensitivity reaction.[6]

So, we also test for silent inactivation because patients can develop antibodies against the drug.[9,10] And if they have these antibodies and the drug is no longer working, then we would be increasing the risk for toxicity without any added efficacy, so it would not make sense to continue with the same product.

At that point, we would switch to an immunologically distinct asparaginase as soon as clinically possible, ideally within 48 to 72 hours, in order to continue the regimen.[9]

It's really important to weigh the risks and benefits for each patient in terms of continuing asparaginase. In my practice, I haven't had an instance where hypersensitivity was severe enough to result in us discontinuing asparaginase altogether. We're not generally in favor of removing asparaginase unless it's a severe toxicity. Overall, I think it's very important to try to continue the regimen.

**Dr Caudle:**
As a quick follow-up, Dr Isenalumhe, how does switching to an alternative asparaginase work if a patient previously experienced a hypersensitivity reaction?

**Dr Isenalumhe:**
If a patient is having a hypersensitivity reaction to an *E. coli*-derived asparaginase, you do want to find an alternative asparaginase.

This is because patients who have experienced a hypersensitivity reaction are at an increased risk of another reaction when treated with asparaginase from the same source.[10] We would switch based on their protocol as soon as clinically possible, and ideally within 48-to-72-hour timeframe to avoid interrupting therapy and to keep them on track.[9] In this case, we would switch to something like RYLAZE® (asparaginase erwinia chrysanthemi [recombinant]-rywn) in order to continue the regimen.[6]

**ReachMD Announcer:**
And now let's review the Indication and select Important Safety Information for Rylaze.

**Indication**
RYLAZE (asparaginase erwinia chrysanthemi (recombinant)-rywn) is indicated as a component of a multi-agent chemotherapeutic regimen given by intramuscular injection for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

**Important Safety Information**

**Contraindications**
RYLAZE is contraindicated in patients with:

- History of serious hypersensitivity reactions to *Erwinia* asparaginase, including anaphylaxis
- History of serious pancreatitis during previous asparaginase therapy
- History of serious thrombosis during previous asparaginase therapy
- History of serious hemorrhagic events during previous asparaginase therapy
- Severe hepatic impairment

**Please see additional Important Safety Information throughout this video.**

Now back to Dr Isenalumhe for more information on RYLAZE.

**Dr Isenalumhe:**
RYLAZE is different from other asparaginases because it is not *E. coli* based.[6,10] It has minimal immunologic cross-reactivity to *E. coli* asparaginase, so if a patient experiences hypersensitivity, switching to RYLAZE can help them try and continue their regimen.[6,13] Now, we will monitor them closely, especially when switching, to ensure we can intervene if a hypersensitivity reaction does occur again. However, there is enough data to show that switching in order to continue and to complete the regimen is better than stopping asparaginase altogether.[4] We're also fortunate to have great pharmacists who understand how to make that switch, so we're able to utilize their support to make the switching the therapy as smooth as possible. And so, the bottom line is, when patients are receiving treatment with *E. coli*-derived asparaginase, and they experience a hypersensitivity, we do switch to RYLAZE.

**Dr Caudle:**
Thank you so much for sharing your approach to asparaginase therapy in your AYA patients with ALL/LBL, Dr Isenalumhe. So as we wrap up this discussion, you know, what final piece of advice would you have for your colleagues who may be hesitant to use asparaginase regimens in the AYA population?

**Dr Isenalumhe:**
Well, I'm a big champion for letting the data do the talking. Whenever I'm speaking with other physicians, I show them the data that using asparaginase—and even in the number of asparaginase doses—makes a difference in survival outcomes.[3,4] Specifically, I show data from the CALGB 10403 study, which showed median event-free survival was more than doubled in AYA patients using asparaginase-based regimens versus historical controls.[3]

In addition to that, educating patients on the importance of not missing doses based on the available data is key. In patients with NCI high-risk B-ALL, missing asparaginase doses increased the risk of events such as relapse, second malignant neoplasm, or death by 50 percent. Among NCI high-risk patients who failed to receive all prescribed asparaginase doses, 21.3 percent of patients experienced relapse, underscoring the importance of patient education.[4]

Lastly, in places where asparaginase regimens are less likely to be used in AYA patients, having a good partnership with community hospitals can help with education and co-management of patients so we can help ensure patients are on the preferred protocols. And while there still needs to be more education, I've definitely seen a shift where educating on the importance of using asparaginase regimens makes a difference.

**Dr Caudle:**
And as we come to the end of today's program, let's take a moment to review some Important Safety Information for RYLAZE.

**ReachMD Announcer:**
**Important Safety Information**

**Warnings and Precautions**

Monitor for signs or symptoms of hypersensitivity reactions, including life-threatening anaphylaxis. Administer RYLAZE in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis. Discontinue RYLAZE for serious hypersensitivity reactions.

Monitor for symptoms of pancreatitis, which, if left untreated, could be fatal. Discontinue RYLAZE if severe or hemorrhagic pancreatitis occurs.

Discontinue RYLAZE for severe or life-threatening thrombosis. Provide anticoagulation therapy as indicated.

Discontinue RYLAZE for severe or life-threatening hemorrhage.

Discontinue RYLAZE and provide supportive care for grade 4 increases of bilirubin and for hepatic veno-occlusive disease.

**Adverse Reactions**

The most common adverse reactions (incidence >20%) with RYLAZE are abnormal liver test, nausea, musculoskeletal pain, infection, fatigue, headache, febrile neutropenia, pyrexia, hemorrhage, stomatitis, abdominal pain, decreased appetite, drug hypersensitivity, hyperglycemia, diarrhea, pancreatitis, and hypokalemia.

**Pregnancy and Lactation**

RYLAZE can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective non-hormonal contraceptive methods during treatment with RYLAZE and for 3 months after the last dose. Advise women not to breastfeed during treatment with RYLAZE and for 1 week after the last dose.

Before administering RYLAZE, please read the Prescribing Information and additional Important Safety Information, which can be accessed on RYLAZEPro.com.

**Dr Caudle:**
I'd like to thank my guest, Dr Leidy Isenalumhe, for helping us better understand the importance of using asparaginase in the AYA population with ALL/LBL.

Dr Isenalumhe, it was great speaking with you today.

**Dr Isenalumhe:**
Thank you so much for having me. It was a pleasure.

**Dr Caudle:**
And, for ReachMD, I'm your host Dr Jennifer Caudle.

**ReachMD Announcer:**
This program was sponsored by Jazz Pharmaceuticals. If you missed any part of this discussion or to find others in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge.

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