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Reviewing sAML Standards of Care

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode 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. And joining me today for a review of secondary acute myeloid leukemia, otherwise referred to as secondary AML and the current guidelines for its diagnosis and treatment is Dr. Eunice Wang. Not only is she a hematologic oncologist but she's also the Chief of the Leukemia Service at Roswell Park Comprehensive Cancer Center. Dr. Wang, thank you so much for being here today.

Dr. Wang
I'm delighted to be here.

Dr. Caudle
Well, we're very happy to have you. And before we dive into the standards of care around secondary AML, Dr. Wang, could you discuss some key considerations for differentiating secondary AML and AML?

Dr. Wang
So AML, or acute myeloid leukemia, is the most common aggressive blood cancer that we see. It's diagnosed primarily in older individuals, with the median age of 70. So these are people that are retired and in their later life. Secondary AML actually makes up to 25 or 30 percent of patients that have acute myeloid leukemia and is defined as acute myeloid leukemia that comes out of a prior hematologic disorder or prior chemotherapy or radiation from something else. And you can see that as our general population ages, this phenomenon of secondary AML coming out from something else is increasingly more commonly diagnosed. And this is something that we have to recognize as separate from de novo AML, which occurs in younger individuals and is like a spontaneous clonal genetic event. These secondary AMLs are coming out of conditions that our older individuals have had for many, many years or even decades and is a consequence of those other problems.

Dr. Caudle
Thank you for that. And what is the unique severity of secondary AML, and why does it warrant the strongest treatments available?

Dr. Wang
Well, secondary AML that can arise from bone marrow cells or blood cells that are already damaged and dysfunctional is actually very difficult to treat because unlike de novo AML where the cells are freshly mutated and something goes on, and these are otherwise very healthy, robust bone marrows. And individuals these secondary AMLs occur in, as you know, in older individuals that have other medical problems, and their disease is characterized by a lot of genetic abnormalities and DNA damage, these patients might have had myelodysplastic syndrome, which is a bone marrow failure syndrome, or they might have had polycythemia vera or essential thrombocytosis or aplastic anemia. And those are primary hematologic disorders that can persist for a long time. And those mutations and damage in those bone marrow cells accumulate to the point where they become an aggressive malignancy. So these are difficult to treat. And therapy-related, secondary AMLs, which arise from potentially breast cancer patients that have had prior chemotherapy or lymphoma patients that might have had an autologous stem cell transplant, those are really difficult to treat because disease that's arriving out of something that's already been damaged by chemotherapy or radiation may not be responsive to additional chemotherapy.

Dr. Caudle

Okay. Thank you for that. And with that background in mind, let's turn to the guidelines. Dr. Wang, what are some key guidelines from the latest updates for the diagnosis and treatment of secondary AML?

Dr. Wang
Well, we've actually had a lot of research that's been done in the etiology or pathogenesis of these secondary AMLs. A few years ago it was identified that we make these diagnoses based on clinical history, older individuals that had the relevant clinical problems, but now we can actually make the diagnosis secondary AML based on the presence of specific mutations that we are found at the time of diagnosis. Those involve mutations that can be found on next-gen sequencing. And these are really, really difficult to treat, both as I mentioned because of the individuals that have them in most cases and because they don't respond. So standard chemotherapy with our standard in what we call seven plus three or cytarabine anthracycline-based regimens don't do really well in many of these patients because they just are very resistant because of all of those mutational events and a complex karyotype, complex cytogenetic abnormalities. So it's a combination of the patient, as well as the disease just not being that responsive to standard therapy.

Dr. Caudle
For those of you who are just tuning in, you are listening to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Eunice Wang about secondary acute myeloid leukemia.

So now that we have a better understanding of the diagnosis and treatment guidelines for secondary AML, Dr. Wang, let's zero in on intensive chemotherapy. Why is this a consistent recommendation for these patients, and is there any data to support this?

Dr. Wang
So intensive chemotherapy is potentially the most aggressive chemotherapy that we really give across all of cancer therapy. It typically involves giving seven days of continuous infusion cytarabine plus three days of an anthracycline drug. Patients are in the hospital for a month or more, they lose their hair. We eradicate all their normal blood cells, as well as their cancer blood cells because acute myeloid can be a very clinically aggressive disease. This is patients coming in with white counts of like 50, a hundred thousand, platelet counts of nothing. So this is really pretty intensive, and this has been the standard of care for treatment of more fit patients with acute myeloid leukemia because the treatment has to match the disease aggressiveness. Since this is such an aggressive cancer, we have to be aggressive as well. And this remains the standard of care even for our patients that, as I mentioned, have the secondary because this is the fastest, quickest way to just eradicate and eliminate the cells from the bone marrow.

And it is the safest way because we often have these people in our hospital under our surveillance and close guidance for the entire first month of their therapy when they don't have any blood counts. It's also the most effective therapy because not only does it get rid of the disease quickly, but it allows these patients to go on to potentially curative therapy. And as we know, a lot of these patients can't be cured, and the only way to cure them is to get them to a bone marrow or allogeneic stem cell transplantation and wiping out the bone marrow this way is often the best way to move forward with a transplant. So instead of using the standard intensive therapy, we've been using a liposomal version where the chemo is like wrapped in these fat globulins, and then the chemo can get into the bone marrow a little bit easier. These liposomal formulation CPX has become the standard of care, particularly for our older patients with secondary AML because of the fact that we can get rid of the disease quickly and because we know that we can get them to that transplant, they'll do better and potentially be cured with that subsequent step in their treatment process.

Dr. Caudle
That's very helpful, thank you. And before we close our discussion today, what tips would you like to leave with our audience for incorporating the most recent standards of care into practice?

Dr. Wang
So we'd like to remind you that most of these older patients with secondary AML should be referred to comprehensive or dedicated medical centers to have this intensive chemotherapy, particularly that liposomal formulation incorporated early into that treatment plan and for them to potentially be referred to that bone marrow stem cell or t-cell therapy unit for potentially curative management. These are centers that specialize in looking at whether that intensive approach would be reasonable. There are national and international guidelines now from the American Society of Hematology, the European Society of Medical Oncology, the National Comprehensive Cancer Network that all endorse that these patients with secondary AMLs really should get intensive regimens, ideally with a liposomal formulation. We also have regimens that can be given to older less fit individuals that can get them through that initial stage of therapy.

And those lower dose regimens have also potentially in some cases been shown to lead to some patients going to transplant. But these patients typically involve specialized treatment with these cares we're not giving intensive chemotherapy in the community. I'm obviously, not bone marrow transplant. So getting those diagnoses made, getting potentially a comprehensive workup that includes that genetic and mutational information to make the diagnosis of secondary AML and then being aggressive about the treatment course, I

think is going to lead to the best outcomes in those patients that can get it as well as in those patients that can't.

Dr. Caudle
And with those strategies in mind, I'd like to thank my guest, Dr. Eunice Wang, for joining me to discuss the most recent diagnosis and treatment guidelines for secondary acute myeloid leukemia. Dr. Wang, it was great having you on the program today.

Dr. Wang
Thank you. It's been a pleasure, and I hope this information is helpful for you and your viewers.

Announcer:
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