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Factoring Unique Patient Profiles into CLL Treatment Considerations

Announcer:
Welcome to *Project Oncology* on ReachMD. This episode is sponsored by Abbvie and Genentech. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to discuss unique patient profiles for those with chronic lymphocytic leukemia, or CLL for short, and how we can tailor our treatment approaches to each population is Dr. Jennifer A. Woyach, a professor in the Division of Hematology at Ohio State University. Dr. Woyach, welcome to the program.

Dr. Woyach:
Thanks for having me.

Dr. Caudle:
Well, we're excited that you're here. So let's start off with some background Dr. Woyach, you know, which patient population is at highest risk of CLL?

Dr. Woyach:
Yeah, so CLL is actually the most common leukemia in adults and it's seen most commonly in people who are older, about three-quarters of CLL patients are diagnosed after the age of 65. And the average age of diagnosis is between 70 and 72. So we think about those older patients as ones who are at higher risk of the disease. There also is a slight male predominance in CLL and that's more common in the younger patients and actually goes away when you reach people who are 75 or 80 years old.

Dr. Caudle:
Okay, and can you give us an overview of some of the unique patient populations impacted by CLL?

Dr. Woyach:
Yeah, so you know, CLL is a really heterogeneous disease. And there's a lot of unique characteristics to any individual patient. So certainly, with any patient, there are unique features of the patient and of the disease that need to be taken into consideration when thinking about therapy. However, for the purposes of this discussion, I think, you know, thinking about the very young patients with CLL, very old patients, and those with high-risk genomic features are ones that I always think about a little bit separately than other patients.

Dr. Caudle:
So Dr. Woyach, now that we have a better understanding of these unique patient profiles, I'd like to go through each one, one-by-one, and discuss how they impact our treatment approach. Starting with young patients, what considerations do we need to keep in mind?

Dr. Woyach:
Yeah, I think for those patients who are very young, and you know, with CLL, it's predominant demographic, I really consider those people very young if they're under the age of 60. And so, you know, we have to think about both how we can sequence and strategize our therapies to maximize lifespan. And also, I think this patient population is one that you especially want to think about risks of secondary cancers. So, in terms of sequencing of therapies, we actually are really lucky in CLL right now that we have a number of very excellent targeted therapy approaches, and especially when used in the frontline setting, these therapies can produce remission durations on excess of five years, and for some patients, even 10 years or longer.

And so, you know, when we do have multiple treatment approaches we can think about. So, for many patients, we can say, you know,

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with our currently available therapies, we're likely to produce remissions with sequential treatments in excess of 20 years. So, for most patients, this is great, but when you think of somebody in their 40s, that still really isn't ideal. So, for these patients, I like to be sure that we're looking into options of clinical trials that might combine therapies, add new treatment options or treatment modalities that could maximize therapeutic potentials maximize remission durations, and hopefully give people time off therapy. So, treatment approaches that are fixed durations that can give people potentially many year remissions where they don't have to be on treatment.

Also, one important thing to think about is that our therapy for CLL is also rapidly evolving. So even though right now we may say that we can offer people sequential treatments that may last 15 or 20 years, 15 or 20 years from now, our therapies are likely to be completely different. And we're very likely to have more and more things to offer as time goes along.

So, the other thing that I think is a really important consideration in all CLL patients, but especially relevant to those very young patients are the risk of secondary cancers. So, anybody with CLL, no matter the stage of disease, or where they are in their treatment course is at higher risk for cancer than patients without CLL. And this is due to the immune dysfunction associated with the disease. So you know, especially for those young patients who just have many more years to be at risk of other cancers I'd like to make sure that we're discussing and really thinking about strategies for early detection of cancers, and as well minimizing risk wherever we can.

So, in terms of looking for early detection, really right now, what's recommended is basically standard cancer monitoring. So making sure people are up to date on mammograms, prostate cancer screening, colonoscopies, and for CLL patients specifically, we recommend annual skin exams because of the risk of non-melanoma skin cancers, as well as melanoma skin cancers. And as well for people who have been or are current smokers, making sure that we're doing screening for lung cancer as well. And in terms of minimizing risk it's always important to talk to patients about smoking cessation, other tobacco use cessation and you know, maintaining healthy weight, exercising but just minimizing risk of things that may contribute to long term cancer risk.

Dr. Caudle:
For those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle and I'm speaking with Dr. Jennifer Woyach, about unique patient profiles and chronic lymphocytic leukemia, and how we can tailor our treatment approach to each population.

So now continuing on with our discussion, Dr. Woyach, let's zero in on our next patient population, which is older adults. What factors are unique to this population? And how can we address them in our treatment approach?

Dr. Woyach:
Yeah, so again, for CLL, I think about older patients really as those who are over the age of 80. This encompasses actually a lot of our CLL patients, and for this patient population, especially, we need to really be thinking about our therapies and finding a balance between efficacy and tolerability. So, you know, like I mentioned, we have a lot of very effective targeted therapies, they also tend to be very well tolerated. Because we have this abundance of therapies we can choose from, it's really important for these older patients that we're being sure that we are giving therapies that are improving people's quality of life, and not doing anything to reduce their baseline functional capacity. So, you know, for this reason, I think, you know, it's always important in every patient to be talking about toxicities that people are experiencing with their therapies but certainly in this older patient group, I'm a little bit more proactive at doing dose reductions, holding, or even switching therapies if it seems like we're not getting the desired quality of life.

I also think it's really important in these patients to consider multi-specialty approaches. So, in addition to the oncologist who's taking care of the patients, you know, having physical and occupational therapy helping in order to maximize functional potential is really helpful. Nutrition can be extremely helpful both in patients who are symptomatic from the disease as well as symptomatic potentially with any therapies we're giving. Also pharmacy is, you know, a really important part of the team, especially for these older patients. I try to minimize polypharmacy, wherever we can both to minimize drug-drug interactions, minimize toxicities, and also improve compliance.

Dr. Caudle:
And for the final patient population we're going to discuss today let's take a look at those patients with deletion 17p. What do we need to consider here?

Dr. Woyach:
Yeah, and so this is a special group of patients that really have the highest genomic risk of all of our patients with CLL. And we consider this both patients who have a deletion of part of chromosome 17 to 17p deletion, or those patients who have mutations in the TP53 gene, which is located within that 17p region. So both of these abnormalities disrupt the TP53 gene, which is a very important tumor suppressor protein and lead to just much higher risk of needing therapy early and not having great responses with our standard treatments.

So currently, with our frontline therapies, there's accumulating data that BTK inhibitors of Bruton's tyrosine kinase inhibitors potentially

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ibrutinib specifically, though, this may be a class effect appear to be very effective in those patients with these TP53 abnormalities or the 17p deletion. And actually, patients with or without this abnormality have the same therapeutic benefit with BTK inhibitors. So thinking about BTK inhibitors as the first line treatment for these patients, I think is really important. As well, though I, you know, just for these patients in general looking into clinical trials so novel therapies, new combinations I think these patients especially benefit from some of these newer approaches and novel things that we're doing on clinical trials because we know that just the standard therapies overall are not going to produce as long term remissions as other patients.

Dr. Caudle:
Understood. You know, now, unfortunately, we're almost out of time for today and you've really given us a lot of great insights, Dr. Woyach. But before we close do you have any other thoughts or advice on how we can select treatments that better address considerations for each patient profile?

Dr. Woyach:
Yeah, so you know, again, we're so lucky in CLL right now that we have a number of therapies we can use in the frontline setting that are tolerable and extremely effective. And in fact, you know, the studies that don't have such long term follow up that we can really differentiate much among our different treatment paradigms. There's being, for most patients, either BTK inhibitors or BCL2 inhibitors, like venetoclax.

The data we have so far suggests that in the frontline setting, these treatment paradigms are fairly equivalent in terms of efficacy. So with that in mind, I think it's just really important for the treatment decisions to involve a pretty in-depth discussion between the oncologist and the patient of pros and cons of each type of treatment. So this is both looking at, you know, things like efficacy, but also side effects that can be experienced with these different regimens you know fixed duration therapies versus indefinite therapies. And then as therapies are starting, you know, how time intensive is that going to be in coming back and forth to that infusion clinic or the doctor's office? You know, I think all of these are important considerations for patients and for caregivers and for oncologists. But it just really, I think, this is one of the places in oncology right now that I believe just has the most opportunity for shared decision making between the patients and the providers.

Dr. Caudle:
Wonderful. Well, with those pieces of advice in mind, I'd like to thank my guest Dr. Jennifer Woyach, for joining me to discuss chronic lymphocytic leukemia treatment considerations for different patient populations. Dr. Woyach, it was great having you on the program.

Dr. Woyach:
Thanks so much. It was great to be here today.

Announcer:
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