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Evolutions of the CLL Treatment Paradigm: A Look at Long-Term Data

Announcer:
You're listening to *Project Oncology* on ReachMD. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss the evolution of treatment paradigms for chronic lymphocytic leukemia, or CLL for short, is Dr. Ehab Atallah. Dr. Atallah is a Professor of Medicine and the Section Head of hematological malignancies at the Medical College of Wisconsin Division of Hematology and Oncology. Dr. Atallah, welcome to the program.

Dr. Atallah:
Thank you very much. Thanks for having me.

Dr. Turck:
Let's get started, Dr. Atallah. What are the current frontline treatments available for CLL?

Dr. Atallah:
So currently for frontline treatment for CLL, we have several groups of drugs. First, is chemotherapy and combination chemotherapy such as FCR or BR. And in all honesty, we rarely use chemotherapy up front currently with the excellent results we have with the newer drugs. The second group of drugs are the BTK inhibitors, and as for what's currently FDA-approved for frontline, we have both ibrutinib and acalabrutinib. The third regimen commonly used is a combination of obinutuzumab with a BCL2 inhibitor, which is venetoclax, and that also has yielded great results. And because of the great results we have with the BTK inhibitors or with a combination of the BCL2 inhibitors, chemotherapy is rarely used frontline currently.

Dr. Turck:
As a quick follow-up to that, would you tell us a little bit more about how some of these combinations are being used to address CLL?

Dr. Atallah:
In the frontline setting and in the relapse setting, combination therapy is frequently used. Currently FDA-approved is a combination of an antibody – either obinutuzumab or rituximab – with venetoclax, and both in the frontline setting and in the relapse setting this has yielded excellent results. BTK inhibitors as single agents have also yielded great results in both the frontline and relapsed settings, and what's most interesting currently is the combination of a BTK inhibitor and venetoclax, which is currently in clinical trials. It's not FDA-approved yet, but in my opinion, will get FDA-approved very soon because of the great results we have with this combination, both in the frontline setting and in the relapse setting.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Ehab Atallah about evolving treatment paradigms for chronic lymphocytic leukemia, or CLL. Switching gears a bit here, Dr. Atallah, let's take a look at some of the emerging, longer-term outcome data that are available. Starting with the MURANO trial, what were the key findings?

Dr. Atallah:
So just as a quick reminder of what the MURANO trial was, the MURANO trial was a randomized study looking at bendamustine and rituximab, which was the standard of care at that point, and comparing it to venetoclax and rituximab in the relapse setting. And the results were really quite impressive for the rituximab and venetoclax combination. With that combination, more than 75 percent of patients were able to achieve MRD negativity, and recently, there was a long-term follow-up paper published showing that more than 50

percent of patients continued to respond and not need treatment, which is very, very impressive in the relapse setting. Obviously, the results were better than using bendamustine/rituximab with significantly less toxicity with rituximab and venetoclax. So really, really great results with the MURANO trial.

Dr. Turck:
And how about the CLL14 trial? Would you tell us about those results?

Dr. Atallah:
As a quick reminder again on the CLL14 trial, that trial was in the frontline setting and compared obinutuzumab with chlorambucil versus obinutuzumab with venetoclax. Again, more than 70 percent of patients achieved MRD negativity, which was great. And in the last European Hematology Association meeting, the five-year results were published, and at five years, 60 percent of patients remained in remission.

And think of how these results are great given that the venetoclax and obinutuzumab were given for only a time-limited period, so treatments were only one year. Think of it: a patient with newly diagnosed CLL gets treatment for one year, no chemotherapy, and 60 percent of those patients have remained in remission five years out. Not only that, but also 20 percent of patients remained in MRD negative state, and in patients with 17p deletion or P53 mutation, which is a high-risk group of patients, 40 percent of patients remained without disease progression. So quite impressive results for a time-limited therapy that also overall has toxicity – there's nothing for free, there are no drugs that don't have toxicity – but compared to chemotherapy, definitely less.

Dr. Turck:
So with all that in mind, how else might the findings from those and other trials change the outlook on treatment approaches for CLL?

Dr. Atallah:
I think they definitely change a lot. We have more long-term data now for this combination. We've always had questions whether these excellent responses will hold up for our patients, and having a five-year follow-up on both MURANO and on CLL14 shows that these results are good. We can tell our patients that five years out, 60 percent of patients will not need treatment, which is very, very encouraging. In terms of a patient who would like to have a time-limited therapy, definitely an antibody, whether rituximab or obinutuzumab, in combination with venetoclax is really the best choice for them.

Dr. Turck:
And as we come to a close, Dr. Atallah, would you like to leave our audience with any final thoughts?

Dr. Atallah:
I think we're in a great time for CLL treatment. Obviously, no one wants to have leukemia and no one wants to have treatment at all, but in terms of the options we have now and their toxicity, they're much, much better than before. And not only less toxicity, but better efficacy compared to standard chemotherapy. I'm really looking forward to the results of the trials with a combination of a BTK inhibitor and a BCL2 inhibitor when we can have a readout of those results and possibly FDA approval because in that case, our patients would be getting two pills, no infusions, and it just opens up the door more for different options for our patients and they can have excellent results.

Dr. Turck:
It's a great way to round out our discussion on present treatment approaches for CLL, and I wanna thank my guest, Dr. Ehab Atallah, for joining me to share how CLL treatment paradigms are changing. Dr. Atallah, it was great having you on the program.

Dr. Atallah:
Thank you very much.

Announcer:
This was an episode of *Project Oncology*. To access other episodes in this series, visit ReachMD.com/ProjectOncology, where you can Be Part of the Knowledge. Thanks for listening!