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Poster Pearl: Combined IT Chemotherapy and Systemic Treatment Show Efficacy in BPDCN Patients

Announcer Introduction

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Dr. Turck:

This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Here with me today to share findings from a poster that was presented at the 2022 European Hematology Association Annual Congress that focused on the treatment of blastic plasmacytoid dendritic cell neoplasm, or BPDCN for short, is Dr. Justin Taylor. He's an Assistant Professor of Hematology at the Sylvester Cancer Center of the University of Miami Miller School of Medicine. Dr. Taylor, thanks for being here today.

Dr. Taylor:

Great to be with you.

Dr. Turck:

Now before we dive into this research, Dr. Taylor, could you tell us a little bit about BPDCN and the treatment challenges we often encounter?

Dr. Taylor:

Yeah, so BPDCN is a rare cancer. It stands for blastic plasmacytoid dendritic cell neoplasm, which is a mouthful and why we refer to it as BPDCN. But it does come from the plasmacytoid dendritic cells. And because of its rarity, I think sometimes the challenge is in the diagnosis and also in getting treated at a center that has enough expertise of treating BPDCN, which, as you can imagine, since it's very rare, not a lot of centers have that expertise. So I think the major challenges of today are getting the patients to the right treatment as soon as possible.

Dr. Turck:

Now with that background in mind, let's turn our attention to the poster that was presented. What was the overall goal?

Dr. Taylor:

Yeah, so this poster, which was presented by an Italian group at the EHA Conference as you said, focused on looking at patients with BPDCN who had received a drug called tagraxofusp, which is a targeted drug approved for BPDCN in the U.S. in 2018. And then it later got approved in Europe in 2021. However, during the studies that led to the approval of tagraxofusp, they did not use any intrathecal or CNS-directed therapies in combination with the agents. So I think the main point of this poster was to try to address what is the safety of combining intrathecal chemotherapy with tagraxofusp, again, during this period when it was approved in the U.S. but not yet approved in Europe, and they were treating the patients there under an expanded access program.

Dr. Turck:

And as a follow-up to that, what could you tell us about the patient sample?

Dr. Taylor:

Yeah, so in this study, there were five patients included, which doesn't sound like a lot, but for BPDCN being a rare disease, that's pretty typical to see at a single center during a 2- or 3-year period. So all these patients were treated at the single center, and they were on this expanded access program. So they were monitored pretty closely for any adverse effects. And they were treated in a standardized method. And the population is pretty typical of what is seen for BPDCN. This is a disease that is diagnosed in older patients with a median age at diagnosis of 65 and a male predominance. So with the exception of one 16-year-old female, this was mostly an older male-dominant patient population. And I'll just say with a caveat that BPDCN can be diagnosed in infants and younger people. But that's not typically what we see of the adult population.

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. Justin Taylor about a poster featured at the 2022 European Hematology Association Annual Congress.

So, Dr. Taylor, if we zero in on the results, what do we need to know about the safety of tagraxofusp alone or in combination with intrathecal chemotherapy?

Dr. Taylor:

So, this poster that we're discussing that was presented at EHA last year looks at five patients that got tagraxofusp plus IT chemotherapy, or intrathecal chemotherapy, cytarabine plus or minus methotrexate, and dexamethasone in some cases, which is a pretty standard intrathecal chemo. And from these five patients, they saw that there was no adverse-related effects due to the intrathecal chemotherapy. There were some toxicities seen from the tagraxofusp, but it was not any different than what was seen from the drug alone. So this capillary leak syndrome is on the label in a warning to monitor for this and treat accordingly. So four out of the five patients did experience capillary leak; most of them were low grade, although there was a grade 4. They did all resolve. And that's, again, pretty typical of the tagraxofusp label. And so they did not see an increase in that by adding the intrathecal chemotherapy, and notably, they didn't see any side effects related to the intrathecal chemotherapy, such as neuropathy or any of those kinds of expected side effects you might rarely see from intrathecal chemotherapy, so there didn't seem to be an interaction there.

Dr. Turck:

And what could you tell us about the efficacy results?

Dr. Taylor:

So again, with five patients, it may be hard to judge the efficacy, but they did see that all patients were able to clear the CNS. So out of the five patients, three of them had CNS involvement diagnosed at the beginning, and two of them did not. Once the patients that had CNS involvement cleared, they stayed clear. And the ones without CNS involvement never developed CNS involvement. And so the outcomes, for those patients who were still being treated, some of them went to stem cell transplant, and some of them only had the tagraxofusp treatment and were in remission or had been relapsed and treated with subsequent lines of therapy, which is pretty common for BPDCN. So I think it's difficult from the small study to judge the efficacy, but it seems safe. And it did effectively clear the CNS involvement in those three patients.

Dr. Turck:

Now understanding that this was a smaller study, Dr. Taylor, is there any way it could help shape your approach to treating patients with BPDCN?

Dr. Taylor:

Yes, so again, with this study, and there were others from different groups that also looked at the involvement of CNS at diagnosis, and in this study, again, three out of five is around 60 percent, and that's in line with other studies that anywhere between 30 to 60 percent of patients will have CNS involvement at diagnosis. So based on those high levels of CNS involvement, as we do with other acute leukemias such as ALL or AML, if CNS involvement is detected, then we treat with intrathecal chemotherapy; so that certainly has become the practice in the U.S. It's in some of the North American BPDCN guidelines, and it's now spreading around the world to look for CNS involvement at diagnosis of BPDCN and treat with intrathecal chemotherapy or perhaps systemic methotrexate, although most people are favoring the intrathecal chemotherapy. And this study shows that that's safe and can clear out the CNS disease. So I think that is my practice, and for most of the BPDCN experts I've talked to, that's their practice. So I think now we're trying to spread the word to more people that might see BPDCN occasionally, it may not be their main focus of their practice, to make sure they check for CNS involvement through a lumbar puncture at diagnosis, and then treat if CNS involvement is detected.

Dr. Turck:

Now because we've covered a lot of ground today, to bring this all together before we close, what key takeaways might we draw from this research?

Dr. Taylor:

We discussed many things, and the key I want people to remember is that the frontline treatment may still betagraxofusp. We should be checking for CNS involvement, though. And keep in mind that tagraxofusp is not thought to get into the central nervous system, so this is a kind of larger immunotoxin type drug that may not necessarily penetrate the CNS. So we should be monitoring for CNS involvement at diagnosis and treating with intrathecal chemotherapy or systemic chemotherapy that does get to the CNS if it's detected.

Dr. Turck:

Well with those final thoughts in mind, I want to thank my guest, Dr. Justin Taylor, for joining me to discuss a poster presented at the 2022 European Hematology Association Annual Congress and how it might impact our approach to treating patients with blastic plasmacytoid dendritic cell neoplasm. Dr. Taylor, it was great having you on the program.

Dr. Taylor:

Thank you. It was great to talk with you.

Announcer Close

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