Transcript Details
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Managing BPDCN as a Targeted Treatment Option

ReachMD Announcer:
You're listening to *Project Oncology* on ReachMD. This medical industry feature, titled "Managing BPDCN as a Targeted Treatment Option," is sponsored by Stemline Therapeutics, Inc., a Menarini Group Company. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Joining me to discuss the preliminary results from a real-world study focusing on a treatment option for blastic plasmacytoid dendritic cell neoplasm, or BPDCN, is Dr. James Foran. Dr. Foran is a Professor of Medicine at the Mayo Clinic College of Medicine and Science and is a paid consultant for Stemline Therapeutics. Dr. Foran, thanks for being here today.

Dr. Foran:
Thank you, I'm excited to be here.

Dr. Turck:
Before we take a deep dive into the data, can you tell us about the hallmark characteristics of BPDCN?

Dr. Foran:
Sure! So for some background, BPDCN is a rare, aggressive myeloid malignancy, and unfortunately, many patients receive a poor prognosis as it has a median overall survival of about a year.[1]

Now in terms of clinical presentation, a good majority of patients present with visibly identifiable skin lesions.[2] And if we look at this on a molecular level, it's caused by an overexpression of CD123, which is the interleukin-3 receptor alpha of plasmacytoid dendritic cells. In fact, this overexpression occurs in all instances of BPDCN.[1] And so this hallmark aids in its diagnosis, which is confirmed using a combination of clinical, histologic, and immunophenotypic tests. Specifically, the presence of CD4+, CD56+, and CD123+ cells in the peripheral blood or bone marrow makes it distinctly different from other forms of leukemia and lymphoma.[3]

Dr. Turck:
And once a patient is diagnosed with BPDCN, are there any treatment options available to us?

Dr. Foran:
Yes, there are treatments like chemotherapy, stem cell transplantation, and targeted therapies, but most are used off-label. But the treatment option TAGRAXOFUSP, also known as ELZONRIS, is a CD123-directed cytotoxin. It's indicated for the treatment of BPDCN in adults and in pediatric patients two years and older. And it's the first and only FDA-approved therapy for BPDCN. TAGRAXOFUSP is a unique fusion protein composed of recombinant human IL-3 and a truncated diphtheria toxin payload.[1,4] So when IL-3 binds to its receptor and enters the cell by endocytosis, the diphtheria toxin is taken into the cell and inhibits protein synthesis, which is then followed by cell lysis.[4] It's important to note that this mechanism is distinguishable from antibody-drug conjugates that are used to deliver other chemotherapies.[4]

ReachMD Announcer:
For more information on TAGRAXOFUSP, please see full Prescribing Information, including the Boxed WARNING, at ELZONRIS.com/hcp.

Boxed WARNING: CAPILLARY LEAK SYNDROME

- **Capillary Leak Syndrome (CLS), which may be life-threatening or fatal , can occur in patients receiving ELZONRIS. Monitor for signs and symptoms of CLS and take actions as recommended.**

Dr. Turck:
So with all that in mind, Dr. Foran, let's turn our attention to the data. What can you tell us about the design of the trial?

Dr. Foran:
The goal for this real-world study was to confirm the findings from the pivotal trial, which consisted of 40 patients with BPDCN that were treated with TAGRAXOFUSP. Of those patients, 22 were treated in the first-line setting while 18 were treated in the relapsed or refractory treatment arm. And results showed that treatment with TAGRAXOFUSP at 12 micrograms per kilogram demonstrated a well-characterized safety profile and resulted in an overall response rate of 75% in first-line patients, and 58% in relapsed or refractory patients.[1]

So, using data from an expanded access program in Europe, 40 patients were enrolled in this real-world, non-interventional, retrospective, observational, multicenter, single-arm study.[1] Patients were eligible if they had a diagnosis of BPDCN, confirmed by hematopathology and immunophenotyping analysis for CD123, CD4, and CD56.[1] Patients received a total of five doses on days one through five of a 21-day cycle. Note that the five doses could be administered over up to 10 days of TAGRAXOFUSP, at 12 micrograms per kilogram, by IV infusion once daily.[1] The primary objectives of the study were to assess the complete response after two to three cycles of TAGRAXOFUSP treatment for frontline and relapsed or refractory BPDCN and to evaluate the incidence and severity of capillary leak syndrome, or CLS.[1]

Based on this criteria, 22 patients were treated for frontline BPDCN and 18 for relapsed or refractory BPDCN. More than 85% of these patients were male, and more than 77% involved skin lesions.[1] Lastly, no significant differences between the two groups at baseline were reported.[1]

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. James Foran about the data from the European expanded access program on the treatment option TAGRAXOFUSP for BPDCN.

So Dr. Foran, now that we have an understanding of how the trial was designed, let's zero in on its preliminary results. Starting with the safety profile of TAGRAXOFUSP, can you share those findings with us?

Dr. Foran:
Of course! So for patients who were treated in the first-line setting, a median of three TAGRAXOFUSP cycles were administered, and two cycles were administered to the patients with relapsed or refractory BPDCN. The majority of grade 3 or 4 reported adverse events were thrombocytopenia, anemia, and neutropenia being the most frequent at 23%, 18%, and 13%, respectively. All grade 3 or 4 adverse events occurred during the first cycle throughout the required hospitalization phase.[1] Additionally, each investigator reported that all CLS events—mostly grade 1 and grade 2. In the first-line setting, nine out of 22 patients experienced a total of 12 CLS events, with eight of those 12 events occurring in cycle one. And in the relapsed or refractory setting, 11 out of 18 patients had a total of 13 CLS events, with 11 of those 13 occurring in cycle one. But CLS events were managed and then resolved by TAGRAXOFUSP dose interruption and IV albumin supplementation.[1] And this underscores the importance of adhering to the CLS monitoring and management guidelines.[1]

Dr. Turck:
And how about its efficacy? What were those results?

Dr. Foran:
Well first, I'd like to note that of the 22 treatment-naïve patients, 88% saw an overall response rate. Likewise of the 18 relapsed or refractory BPDCN patients, 67% saw an overall response rate as well. And these results are consistent with the original pivotal trial. Specifically for treatment-naïve patients, a complete response, plus complete response with residual skin abnormality not indicative of active disease, was observed in 71% of those with frontline BPDCN.[1] Investigators also observed partial responses and disease stability in these patients, but to a lesser extent.[1] Disease progression was reported in one of the frontline patients, and median response duration of 8.8 months was reported.[1] Finally, median overall survival in these treatment-naïve BPDCN patients was 16.7 months when treated with TAGRAXOFUSP.[1]

On the other hand, for patients with relapsed or refractory BPDCN, 40% experienced a complete response with TAGRAXOFUSP.[1] Partial responses and disease stability were also observed in these patients as well, but again to a lesser extent.[1]

Investigators reported disease progression in three patients, and median response duration was 5.6 months for these relapsed or refractory patients.[1] Lastly, median survival in these patients was 10.5 months.[1]

Now if we shift our focus a bit to those who received TAGRAXOFUSP and then bridged to allogenic hematopoietic stem cell transplantation, 10 frontline patients, or 45%, and seven relapsed or refractory patients, or 39%, were identified.[1] The median overall survival time for frontline-treated patients was 16.7 months compared to 9.5 months for patients who did not receive a transplant.[1] And for patients with relapsed or refractory BPDCN, the median overall survival was not reached, and it was 6.2 months in those who did not receive a transplant.[1]

Dr. Turck:
Thanks for breaking down all of that data for us, Dr. Foran. And as we come to the end of our conversation, do you have any final thoughts for our listeners?

Dr. Foran:
Yes, so overall in my opinion, preliminary analysis of this study confirms a positive benefit-to-risk ratio in adult patients with BPDCN.[1] And this study supports the clinical efficacy found in the pivotal BPDCN study with consistent response rates.[5] In addition, TAGRAXOFUSP provided an effective bridge to allogenic hematopoietic stem cell transplantation for both first-line and relapsed or refractory patients.[1] Adverse events can occur during treatment with TAGRAXOFUSP, the most frequent being thrombocytopenia, anemia, and neutropenia. And again, 12 of the treatment-naïve and 13 of the relapsed or refractory patients had CLS events. So what we found is that the adverse reactions are consistent with what was reported in the pivotal trial, and there is a well-defined mitigation strategy that can help manage side effects with a multidisciplinary care team.[5]

Dr. Turck:
Well, as those final thoughts bring us to the end of today's program, I'd like to thank my guest, Dr. James Foran, for speaking with us about the key safety and efficacy data on TAGRAXOFUSP from the European extended access program. Dr. Foran, it was great having you on the program!

Dr. Foran:
It was great to be here. Thank you.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Please listen to the following Important Safety Information, including the Boxed WARNING.

ReachMD Announcer:

INDICATION

- ELZONRIS is a CD123-directed cytotoxin indicated for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

IMPORTANT SAFETY INFORMATION

Boxed WARNING: CAPILLARY LEAK SYNDROME

- **Capillary Leak Syndrome (CLS) which may be life-threatening or fatal, can occur in patients receiving ELZONRIS. Monitor for signs and symptoms of CLS and take actions as recommended.**

WARNINGS AND PRECAUTIONS

Capillary Leak Syndrome

- Capillary leak syndrome (CLS), including life-threatening and fatal cases, has been reported among patients treated with ELZONRIS. In patients receiving ELZONRIS in clinical trials, the overall incidence of CLS was 53% (65/122) patients, including Grade 1 or 2 in 43% (52/122) patients, Grade 3 in 7% (8/122) patients, Grade 4 in 1% (1/122) patients, and four fatalities (3%). The median time to onset was 4 days (range - 1 to 46 days), and all but 5 patients experienced an event in Cycle 1.
- Before initiating therapy with ELZONRIS, ensure that the patient has adequate cardiac function and serum albumin is greater than or equal to 3.2 g/dL. During treatment with ELZONRIS, monitor serum albumin levels prior to the initiation of each dose of ELZONRIS and as indicated clinically thereafter, and assess patients for other signs or symptoms of CLS, including weight gain,

new onset or worsening edema, including pulmonary edema, hypotension or hemodynamic instability.

Hypersensitivity Reactions

- ELZONRIS can cause severe hypersensitivity reactions. In patients receiving ELZONRIS in clinical trials, hypersensitivity reactions were reported in 43% (53/122) patients treated with ELZONRIS and were Grade ≥ 3 in 7% (9/122) patients. Manifestations of hypersensitivity reported in ≥ 5% of patients include rash, pruritus, and stomatitis. Monitor patients for hypersensitivity reactions during treatment with ELZONRIS. Interrupt ELZONRIS infusion and provide supportive care as needed if a hypersensitivity reaction should occur.

Hepatotoxicity

- Treatment with ELZONRIS was associated with elevations in liver enzymes. In patients receiving ELZONRIS in clinical trials, elevations in ALT occurred in 79% (96/122) patients and elevations in AST occurred in 76% (93/122) patients. Grade 3 ALT elevations were reported in 26% (32/122) patients. Grade 3 AST elevations were reported in 30% (36/122) patients and Grade 4 AST elevations were reported in 3% (4/122) patients. Elevated liver enzymes occurred in the majority of patients in Cycle 1 and were reversible following dose interruption.
- Monitor alanine aminotransferase (ALT) and aspartate aminotransferase (AST) prior to each infusion with ELZONRIS. Withhold ELZONRIS temporarily if the transaminases rise to greater than 5 times the upper limit of normal and resume treatment upon normalization or when resolved.

ADVERSE REACTIONS:
Most common adverse reactions (incidence ≥ 30%) are capillary leak syndrome, nausea, fatigue, pyrexia, peripheral edema, and weight increase. Most common laboratory abnormalities (incidence ≥ 50%) are decreases in albumin, platelets, hemoglobin, calcium, and sodium, and increases in glucose, ALT and AST.

Please see full Prescribing Information, including the Boxed WARNING.

To report SUSPECTED ADVERSE REACTIONS, contact Stemline Therapeutics, Inc. at 1-877-332-7961 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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This program is brought to you by Stemline, a Menarini Group company. If you missed any part of this program, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge.

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