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Progress in Small Cell Lung Cancer Therapy: A Fresh Perspective

ReachMD Announcer:
Welcome to *Project Oncology* on ReachMD. This medical industry feature, titled "*Progress in Small Cell Lung Cancer Therapy: A Fresh Perspective*" is sponsored by Jazz Pharmaceuticals. This program is intended for healthcare providers.

Here's your host, Dr. Charles Turck.

Dr. Turck:
This is *Project Oncology* on ReachMD. I'm Dr. Charles Turck and joining me to help us recognize treatment challenges in small cell lung cancer and share insights on an alternate treatment option is Dr. Jason Porter. Dr. Porter is a Medical Oncologist/Hematologist with West Cancer Center and Research Institute in Memphis, Tennessee. He also serves as Director of the Lung Cancer Disease Research Group and his specialties are molecularly altered lung cancers and lung cancers with no actionable driver mutation. Dr. Porter, thanks for joining us.

Dr. Porter:
Thanks for having me.

Dr. Turck:
To start us off Dr. Porter, can you tell us about small cell lung cancer and the therapeutic challenges it poses?

Dr. Porter:
Of course. Small cell lung cancer, or SCLC, is difficult to detect early because it typically doesn't cause any symptoms until it's at an advanced stage. So most patients are diagnosed with extensive-stage disease.[1] Now, the therapeutic challenge goes beyond the lack of early detection, as small cell lung cancer is a very aggressive disease.[1,2] Even though it represents about 15% of all lung cancer patients, it has an exceptionally high proliferative rate and only a 7% five-year survival rate.[1,3,4] This is further complicated because there are no targeted therapies currently available, meaning that treatment options are limited.[1-3] And despite first-line treatment options having a strong response for most patients, they may be difficult for many patients to tolerate, and there is a high relapse rate with ultimately poor prognoses.[3,5]

Dr. Turck:
And based on your experience, how many of your patients relapse and require second-line therapy?

Dr. Porter:
Nearly all patients will relapse, and at least 75% of my patients relapse at or after 6 months.[3,5] To add even more challenge to this disease state, there are only a few FDA approved second-line therapies for adults with small cell lung cancer, with one of them being ZEPZELCA.[6,7]

Before we continue, I'd like to review the indication and some important safety information for this treatment option. ZEPZELCA, or lurbinectedin, is indicated for the treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy.[6]

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial or trials.[6]

There are no contraindications.[6]

ZEPZELCA can cause myelosuppression.[6]

In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, grade 3 or 4 neutropenia occurred in 41% of patients, and median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients.[6]

Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than small cell lung cancer). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days, and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.[6]

For full prescribing information, please visit ZEPZELCAPro.com.

Dr. Turck:
Thank you for that, Dr. Porter. And with that important safety information in mind, can you expand on the limited therapeutic options and what treatment options mean for this space?

Dr. Porter:
Yes. So topotecan was first approved in 1998 for second-line small cell lung cancer. And it wasn't until June of 2020, over 20 years later, when ZEPZELCA was granted accelerated approval that we had another second-line therapy.[6,8] In fact, there have been more than 40 failed phase 3 clinical trials since the 1970s, and the list of failed drug trials for small cell lung cancer continues to grow.[2] And because research into second-line small cell lung cancer has been so difficult, it's critical for us to consider all approved alternate treatment options for our patients.[2,3]

Dr. Turck:
Given the challenges and limitations in SCLC, can you speak briefly about therapeutic goals that are meaningful to both clinicians and patients?

Dr. Porter:
Clinical endpoints are essential for assessing safety and efficacy of new cancer therapies.[9] While overall survival has frequently been regarded as an established standard clinical endpoint, it is becoming evident that other endpoints add valuable information.[9] Overall response rate, or ORR, and disease control rate, or DCR, are both meaningful endpoints for oncology patients, particularly in a challenging disease state, such as a small cell lung cancer.[9] While many are familiar with ORR, which is the proportion of patients who achieved a complete response and partial response to therapy, DCR describes the percentage of patients whose therapeutic intervention has led to a complete response, partial response, or stable disease.[9]

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to look at ZEPZELCA as a second-line treatment option for adults with small cell lung cancer is Dr. Jason Porter.

So Dr. Porter, let's dive further into ZEPZELCA. What can you tell us about the clinical trial findings that led to its approval?

Dr. Porter:
ZEPZELCA, based on a compound found in a particular species of marine sea squirts, was granted accelerated approval based on the results from a phase 2 open-label, multicenter, single-arm basket trial.[6,10-12] The overall study population consisted of 105 patients with both small cell lung cancer and an ECOG performance status of 2 or lower, who progressed on or after platinum-based therapy.[6,11] The primary endpoint was the overall response rate in the total population, which was 35% by investigator assessment and 30% by an independent review committee. All responses were partial responses.[6] Secondary endpoints in the study were duration of response, overall survival, and progression-free survival.[11] ZEPZELCA demonstrated clinically meaningful duration of response with a medium for the patients to respond to therapy of 5.3 months by investigator assessment, and 5.1 months by an independent review committee.[6] The median overall survival was 9.3 months by investigator assessment in the overall population, while the median progression free survival was 3.5 months by both investigator assessment and an independent review committee.[11,13] Notably, ZEPZELCA demonstrated efficacy in both platinum-resistant and platinum-sensitive patient subgroups.[6] Now, in terms of safety, ZEPZELCA demonstrated a tolerable safety profile with a low discontinuation rate of 1.9% due to adverse reactions. Adverse reactions resulting in permanent discontinuation in greater than or equal to 1% of patients included peripheral neuropathy and myelosuppression.[6] For additional efficacy data and full safety results, please see the clinical data section of ZEPZELCAPro.com.

Dr. Turck:
Dr. Porter, you mentioned other meaningful outcomes in SCLC earlier, can you tell us about these in the clinical trial?

Dr. Porter:
Disease control rate was an exploratory endpoint in the phase 2 trial.[11] As such, results are descriptive only. And no conclusions about efficacy can be drawn since exploratory endpoint analyses were not powered to determine statistical significance. That said, the disease control rate in the overall population was 69% by investigator assessment, with 35% of patients achieving a partial response, and 33% achieving stable disease. Disease control rate was 62% by an independent review committee, and partial and stable disease rates were both 31%.[13]

Dr. Turck:
Thanks for breaking down those data for us, Dr. Porter. Now, in your experience, how does ZEPZELCA address the unmet needs for an effective and tolerable second-line option?

Dr. Porter:
Responses in my patients are in line with the clinical data for the phase 2 trial. The most common adverse events I have observed are cytopenia and fatigue, which are expected. In my experience cytopenia, particularly neutropenia and febrile, generally, is manageable. And I use GCSF for patients if they've experienced neutropenia during previous therapy. My need to use antiemetics is usually low.

In addition, ZEPZELCA demonstrated a tolerable safety profile with a low discontinuation rate of 1.9% due to adverse reactions. Adverse reactions resulting in permanent discontinuation in greater than or equal to 1% of patients included peripheral neuropathy and myelosuppression.[6] Dosage interruptions due to an adverse reaction occurred in 30.5% of patients. Adverse reactions requiring dosage interruption in greater than or equal to 3% of patients included neutropenia and hypoalbuminemia.[6] Dose reductions due to an adverse reaction occurred in 25% of patients. Adverse reactions requiring dosage reductions in greater than or equal to 3% of patients included neutropenia, febrile neutropenia, and fatigue.[6]

Dr. Turck:
And what are your thoughts on ZEPZELCA's dosing and administration schedule?

Dr. Porter:
In addition to considering its efficacy and safety, I reach for ZEPZELCA as a second-line option due to its dosing and administration schedule. It's administered at 3.2 milligrams per meter squared (mg/m2) as 60-minute intravenous infusion every 21 days, and I found this to be convenient dosing schedule for my patients.[6] Another benefit is that dosing adjustments are manageable, which helps us address treatment modifications and keep patients on therapy.[6]

Dr. Turck:
To wrap up our discussion, Dr. Porter, can you share your opinion on how ZEPZELCA fits into the overall SCLC landscape?

Dr. Porter:
Yes. I consider ZEPZELCA a preferred second-line option for my patients with metastatic small cell lung cancer who relapse after platinum-based chemotherapy. I would recommend ZEPZELCA for patients with disease progression within 6 months or even right at the 12-month mark, as I have found it effective in either scenario. As of May 2023, more than 17,000 adult patients have been treated with ZEPZELCA in the United States, demonstrating its impact on the small cell lung cancer landscape.[13] That said, it remains important to closely monitor for disease progression even during treatment. Ultimately, our goals revolve around what matters most to the patients, because considering their wishes and values can help us improve the care experience.

Dr. Turck:
It's a great comment for us to think on as we come to the end of today's podcast. And I'd like to thank my guest, Dr. Jason Porter, for joining me to talk about ZEPZELCA in the treatment of small cell lung cancer. Dr. Porter, it was great speaking with you today.

Dr. Porter:
It was great to be here.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Before we close, let's review some additional Important Safety Information for ZEPZELCA.

ReachMD Announcer:
Important Safety Information

ZEPZELCA, lurbinectedin, for injection is indicated for the treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy.

Accelerated approval is based on overall response rate and duration of response. Continued approval may be contingent on clinical benefit in a confirmatory trial or trials.

ZEPZELCA can cause myelosuppression. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients. Febrile neutropenia occurred in 7% of patients.

Sepsis occurred in 2% of patients and was fatal in 1%. All cases occurred in patients with solid tumors other than SCLC. Grade 3 or 4 thrombocytopenia and anemia occurred in 10% and 17% of patients, respectively.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 and platelet count of at least 100,000.

Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 or less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce, or permanently discontinue ZEPZELCA based on severity.

ZEPZELCA can cause hepatotoxicity. Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations were observed in 0.4% and 0.5%, respectively. Monitor liver function tests, prior to initiating ZEPZELCA, periodically during treatment, and as clinically indicated. Withhold, reduce, or permanently discontinue ZEPZELCA based on severity.

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. Consider use of a central venous catheter, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during infusion. Immediately discontinue the infusion if extravasation occurs. Administer supportive care as needed. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis has been reported.

Monitor creatine phosphokinase prior to initiating and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose.

There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 2 weeks after the last dose.

The most common adverse reactions occurring in 20% or more of patients, including laboratory abnormalities, are leukopenia, lymphopenia, fatigue, anemia, neutropenia, increased creatinine, increased alanine aminotransferase, increased glucose, thrombocytopenia, nausea, decreased appetite, musculoskeletal pain, decreased albumin, constipation, dyspnea, decreased sodium, increased aspartate aminotransferase, vomiting, decreased magnesium, cough, and diarrhea.

ZEPZELCA interacts with strong and moderate CYP3A inhibitors; consider appropriate dose reduction of ZEPZELCA if clinically indicated. ZEPZELCA also interacts with strong CYP3A inducers; avoid coadministration. Drug interactions can affect safety and/or efficacy. Please see full Prescribing Information for more details.

Although no overall difference in effectiveness was observed, there was a higher incidence of serious adverse reactions in patients 65 and older than in patients less than 65 years, 49% and 26%, respectively. The serious adverse reactions most frequently reported in patients 65 and older were related to myelosuppression and consisted of febrile neutropenia in 11%, neutropenia in 11%, thrombocytopenia in 8%, and anemia in 8%.

Please see full Prescribing Information for ZEPZELCA at www.ZEPZELCApro.com for further information.

This program was brought to you by Jazz Pharmaceuticals. If you missed any part of the podcast, visit ReachMD.com/Project-Oncology. This is ReachMD. Be Part of the Knowledge.

References:

1. Huber RM, Tufman A. Update on small cell lung cancer management. *Breathe*. 2012;8(4):314-330.
2. Byers LA, Rudin CM. Small cell lung cancer: where do we go from here? *Cancer*. 2015;121(5):664-672.

3. Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. *Nat Rev Dis Primers*. 2021;7(1):3. doi:10.1038/s41572-020-00235-0
4. American Cancer Society. Lung cancer survival rates. https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/survival-rates.html. Accessed June 13, 2023.
5. Povsic M, Enstone A, Wyn R, Kornalska K, Penrod JR, Yuan Y. Real-world effectiveness and tolerability of small-cell lung cancer (SCLC) treatments: a systematic literature review (SLR). *PLoS One*. 2019;14(7):e0219622. doi:10.1371/journal.pone.0219622
6. ZEPZELCA (lurbinectedin). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.
7. Topotecan [package insert]. Research Triangle Park, NC: GlaxoSmithKline: 2014.
8. US Department of Health and Human Services. Drug approval package. Hycamtin (topotecan hydrochloride) Injection. Approval letter. Approval date: November 30, 1998. https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/20671s004.cfm. Accessed June 13, 2023.
9. Delgado A, Guddati AK. Clinical endpoints in oncology - a primer. *Am J Cancer Res*. 2021;11(4):1121-1131.
10. PharmaMar. Company about us. https://pharmamar.com/en/company/about-us/. Updated 2022. Accessed June 16, 2022.
11. Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol*. 2020;21(5):645-654.
12. American Association for Cancer Research. Secrets of the sea to treat lung cancer. https://www.aacr.org/patients-caregivers/progress-against-cancer/secrets-of-the-sea-to-treat-lung-cancer/. Accessed June 15, 2023.
13. Data on File. Palo Alto, CA: Jazz Pharmaceuticals, Inc.