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An Expert Interview for 2L SCLC: A Look Into the Patient Journey

Announcer:
Welcome to ReachMD. This medical industry feature, titled "*An Expert Interview for 2L SCLC: A Look Into the Patient Journey*," is sponsored by Jazz Pharmaceuticals. This program is intended for healthcare providers.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD. I'm your host, Dr. Jennifer Caudle. In this episode, we are joined by Dr. Mark Socinski, who is the executive medical director at AdventHealth Cancer Institute in Orlando, Florida, to discuss a patient profile in the treatment of small cell lung cancer to help us better understand the burden of this disease and how to approach treating patients who've relapsed after their initial therapy. Dr. Socinski, thanks so much for joining us.

Dr. Socinski:
It's a pleasure to be here.

Dr. Caudle:
Before we begin, let's take a moment to review ZEPZELCA's indication and some important safety information.

Dr. Socinski:

- ZEPZELCA is indicated for the treatment of adult patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy[1]
- 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(s)[1]
- ZEPZELCA can cause myelosuppression[1]
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients[1]
  - 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[1]
- For more information regarding ZEPZELCA or for the Full Prescribing Information, please visit ZEPZELCApro.com

Dr. Caudle:
Dr. Socinski, to start us off, can you tell us about Irene, the patient profile we will be discussing today?

Dr. Socinski:
Absolutely. Irene is a 73-year-old current smoker with about 40 pack-years. Nine months ago, she was diagnosed with extensive-stage small cell lung cancer. A contrast chest CT revealed encasing of the right upper lobe bronchus, pleural effusion, and bilateral nodules. Irene also has hypertension, which is controlled with 10 mg of lisinopril daily. After being diagnosed, she was promptly treated with triplet therapy of carboplatin+etoposide+durvalumab followed by durvalumab maintenance. Irene achieved a partial response. She maintained an ECOG performance status of 1, but experienced myelosuppression and alopecia. Six months after completing her first-

line platinum therapy course, she began to experience fatigue, shortness of breath, and mild chest pain that had worsened over the past month. At her follow-up visit, a contrast CT of her chest, abdomen, and pelvis was ordered, which unfortunately revealed progressive disease in the liver—indicating that the cancer had progressed while on treatment.

Dr. Caudle:
Wow, relapse by six months? Is that typical in patients with small cell lung cancer?

Dr. Socinski:
Yes. Unfortunately, Irene's case is a situation we're very familiar with. Although small cell lung cancer is usually sensitive to first-line agents,[2] relapse is highly likely after platinum-based therapies, with a median progression free survival time of less than 6 months.[3]

In my clinic, I would estimate that approximately half of my small cell lung cancer patients relapse at six months or greater

Dr. Caudle:
Since relapse is expected, how do you discuss treatment with your patients upon diagnosis?

Dr. Socinski:
When I give patients news of their diagnosis, it's extremely emotional. Small cell lung cancer can be devastating for patients and their families, since it's an aggressive disease with a low survival rate.[5,6]

At initial diagnosis, I share with patients that small cell lung cancer is treatable but not curable,[8] so our goal revolves around what matters most to the patient. My goal is to induce as good of a response as I possibly can, and maintain that response for as long as possible. While my immediate priority is to get them started on a first-line treatment, it's crucial to discuss our overall treatment approach, and to take the time to understand each patient's personal goals and expectations.

You know, I never want patients to feel like relapse is inevitable, but since it's so common in this disease,[7] it's important to keep a close eye on disease progression. I do reassure my patients that there are other options available beyond first-line,[8] and if and when relapse happens, we can have a conversation about additional treatment options.

Dr. Caudle:
Can you tell us more about how you communicate with your small cell patients about their disease progression over time?

Dr. Socinski:
You know, when it comes to talking to patients, I tend to be old school and address options with the patient and their family first. I take the time to walk them through the disease biology and educate them on their available options. By this point in the patient care process, they've had CT scans before and know what they are looking at, so I find it's best to be direct. If the scan looks good, I'll tell them right away to help the patient get rid of their anxiety. If the scan looks worse or the cancer has progressed, I'll often show the patient the scan because they want to know how and where the cancer progressed.

Dr. Caudle:
So let's talk about side effects for a moment. What concerns do you most often hear from patients about the side effects of their treatment?

Dr. Socinski:
In my experience, patients typically worry about myelosuppression, nausea and vomiting, hair loss, particularly for women, and fatigue. To help with the nausea and vomiting, we tell patients that we have a regimen that works very well[9]. Preventing it from occurring in the first place works better than alleviating it. It's important for patients to understand that they receive a dose of cytotoxic chemotherapy tailored to them-keeping in mind their cardiac and liver function, along with bone marrow counts. [10,11]

It's often finding a balance between the toxicity and side effects of the treatment regimen and the patients' ability to tolerate that over time.[7] That choice is very personal, we have to take into account what the patient wants. Some patients may decide to move to palliative care or hospice after first-line treatment since they can't tolerate the side effects of first-line treatment any longer. [12]

Dr. Caudle:
And how do patients typically react to the news of their relapse?

Dr. Socinski:
Relapse brings back many of the same emotions felt when first diagnosed with cancer. Patients often experience uncertainty regarding the future, and they're left wondering "what's next?". They're dealing with several medical appointments, first-line maintenance infusion

visits, the inability to work, and the challenges of being sick. It's important to let them know that there are still treatment options available even when the first therapy does not work or is no longer working. [8]

Patients understand that CT scans may help in identifying relapse. I typically restage patients after the first 4 cycles of treatment, before giving the patient maintenance therapy. If a positive treatment response is seen, then I scan patients every 3 months unless they present in my office with a pressing symptom. Scanning earlier only happens with visible symptoms of disease progression.

You know, when relapse occurs, patients may or may not be feeling symptomatically different. If symptoms get progressively worse, we want to try a different approach in the second-line setting to try to control the disease

Dr. Caudle:
And what are some goals a patient has after relapsing?

Dr. Socinski:
For some of my patients, they have a specific event, such as a vacation or graduation, that they want to be able to attend and be mentally present for. Patients want to get back to doing things that are meaningful to them, whether it's a wedding or birth of a grandchild.

This may involve a delay in making care decisions, as long as the end result is what is right for the patient. My relationship with the patient is a partnership-we're in this together-and we accomplish our goals by focusing on what's important.

Dr. Caudle:
For those of you who are just joining us, this is ReachMD. I'm your host Dr. Jennifer Caudle, and I'm here discussing small cell lung cancer And now that we've taken a look at our patient, Irene, let's review some second-line treatment options, including ZEPZELCA.

So Dr. Socinski, can you review some of the new therapeutic options for patients with small cell lung cancer who relapse after platinum-based therapy?

Dr. Socinski:
There are few FDA-approved second-line therapies. Intravenous topotecan was approved in 1998,[13] and oral topotecan was approved in 2007. [14]

ZEPZELCA, granted accelerated approval in June 2020, was the first FDA-approved therapy in second-line small cell in over 20 years.[1,15,13,16] Remember, there are no category 1 options available for small cell lung cancer; all therapy recommendations are category 2A or 2B. [8]

According to NCCN Guidelines, the chance of responding to subsequent therapy depends on the time from initial therapy to relapse.[8]

For patients who relapse in up to six months, preferred regimens include ZEPZELCA, topotecan, and enrollment in a clinical trial.[8] For patients who relapse after six months, ZEPZELCA and the original regimen are both recommended. [8]

Dr. Caudle:
And when considering a second-line treatment option, what patient characteristics and medical information do we need to keep in mind?

Dr. Socinski:
The most important consideration in my mind is time to relapse after a first-line treatment. If you have patients that go 12-14 months before relapsing, by this point in time, I consider them to be truly treatment sensitive, and would likely consider going back to the original treatment regimen. [8] For patients with disease progression within 12 months, I would consider choosing ZEPZELCA. While NCCN has several available options, this would be my primary choice. [8,17] I also see relapse right at the 6 month mark. In these patients, I've found it effective to try a different option, such as ZEPZELCA. [8] There are also a few additional things to consider: I think about patient-specific characteristics such as performance status. Performance status scores correlate with quality of life, overall survival, response to treatment, and comorbidity[18]

Finally, I consider previous treatment(s).[8]

Dr. Caudle:
Given Irene's treatment history, what is your preferred approach for her?

Dr. Socinski:
For Irene, I feel ZEPZELCA is the best treatment option for a few different reasons. It was seen to have substantial efficacy in both

platinum-resistant and platinum-sensitive patients. [19,20] In the overall population, the investigator-assessed overall response rate was 35 percent and 30 percent by independent review committee. [1] There was also a clinically meaningful duration of response of 5.3 months as seen by investigators and 5.1 months by independent review committee. [1] Lastly, the disease control rate as seen by investigators was 69 percent and 62 percent by independent review committee.[21] However, no conclusions about efficacy can be drawn from this as it is an exploratory endpoint in a phase 2, single-arm study. [19] ZEPZELCA is dosed at 3.2 mg/m^2 as a 60-minute intravenous infusion every 3 weeks,[1] which may be convenient for Irene. 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.[1] 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.[1] 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. [1] In the phase 2 study, 22% of patients received G-CSF treatment as secondary prophylaxis or therapy for neutropenia. [1,19] Lastly, alopecia occurred in 1% of patients[21]

Dr. Caudle:
And before we come to a close, Dr. Socinski can you offer some advice for oncologists treating small cell lung cancer, specifically in regard to second-line treatment?

Dr. Socinski:
As I said earlier, small cell lung cancer is an aggressive disease[6] that takes both a physical and emotional toll, so it's important for treating physicians to consider all available options. [8]

In relation to what's available for small cell lung cancer, the introduction of ZEPZELCA monotherapy into the treatment paradigm is an attractive option because of its efficacy, tolerable safety profile, and convenient dosing of a 1-hour infusion every 3 weeks. [1]

In order to gain additional insight on the types of patients who would benefit from treatment with ZEPZELCA, I would suggest reaching out to local oncologists who have experience using it in a range of patients.

Dr. Caudle:
That's a great comment for us to think on as we come to the end of today's podcast.

And before we close, let's have Dr. Socinski review some important safety information.

Dr. Socinksi:

- 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, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients[1]
- 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[1]
- Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 and platelet count of at least 100,000[1]
- Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity[1]
- ZEPZELCA can cause hepatotoxicity. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively. The median time to onset of Grade 3 or greater elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days[1]
- Monitor liver function tests, prior to initiating ZEPZELCA, periodically during treatment, and as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity[1]
- Based on animal data and its mechanism of action, 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 with ZEPZELCA and for 6 months after the final dose. Advise male patients with female partners of

reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the final dose[1]

- There are no data on the presence of ZEPZELCA in human milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the final dose[1]
- The most common adverse reactions, including laboratory abnormalities, (≥20%) are leukopenia (79%), lymphopenia (79%), fatigue (77%), anemia (74%), neutropenia (71%), increased creatinine (69%), increased alanine aminotransferase (66%), increased glucose (52%), thrombocytopenia (37%), nausea (37%), decreased appetite (33%), musculoskeletal pain (33%), decreased albumin (32%), constipation (31%), dyspnea (31%), decreased sodium (31%), increased aspartate aminotransferase (26%), vomiting (22%), decreased magnesium (22%), cough (20%), and diarrhea (20%)[1]
- Avoid coadministration with a strong or a moderate CYP3A inhibitor as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration of ZEPZELCA with a moderate CYP3A inhibitor cannot be avoided, consider dose reduction of ZEPZELCA, if clinically indicated[1]
- Avoid coadministration with a strong or moderate CYP3A inducer. Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy
- Of the 105 patients with small cell lung cancer administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. No overall difference in effectiveness was observed between patients aged 65 and older and younger patients
- There was a higher incidence of serious adverse reactions in patients ≥65 years of age than in patients <65 years of age (49% vs. 26%, respectively). The serious adverse reactions most frequently reported in patients ≥65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%)

Announcer:
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