MEET THE EXPERT

ISSUE 1

SMALL CELL LUNG CANCER

INSIDE THIS ISSUE:

- Patient considerations and treatment strategies in second-line small cell lung cancer
- Efficacy and safety considerations in treatment selection
- Exploring data for an alkylating agent

FEATURING

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"Nearly all patients with small cell lung cancer will relapse. You have to have a plan."
— David Waterhouse, MD, MPH

THE IMPORTANCE OF SECOND-LINE TREATMENT OPTIONS IN SMALL CELL LUNG CANCER

*Dr Waterhouse is a paid consultant of Jazz Pharmaceuticals. This content is intended for informational purposes only and is not a substitute for your clinical knowledge or professional judgment. The views and opinions expressed in this article are those of the author and Jazz Pharmaceuticals and do not necessarily reflect the opinions of OHC.

A LOOK AT **SECOND-LINE** SCLC PATIENT CONSIDERATIONS AND TREATMENT STRATEGIES

with **Dr David Waterhouse**

Q. What are the biggest challenges when it comes to treating small cell lung cancer (SCLC)?

A. One of the biggest challenges from the beginning is that many of our patients present with advanced disease and comorbidities. Approximately 70% of patients with SCLC are going to have extensive-stage disease.[1-3] And initially you can tell them, "Your chance of responding to treatment is very high." Up to 80% of patients will respond to initial treatment, and some of them may even go into a complete remission.[2] However, the majority of patients will relapse—nearly all of them within 12 months after initial treatment.[4] It's hard to tell patients this, but you have to be honest.

Q. What are some of the important points practitioners should keep in mind regarding relapse after first-line therapy in SCLC?

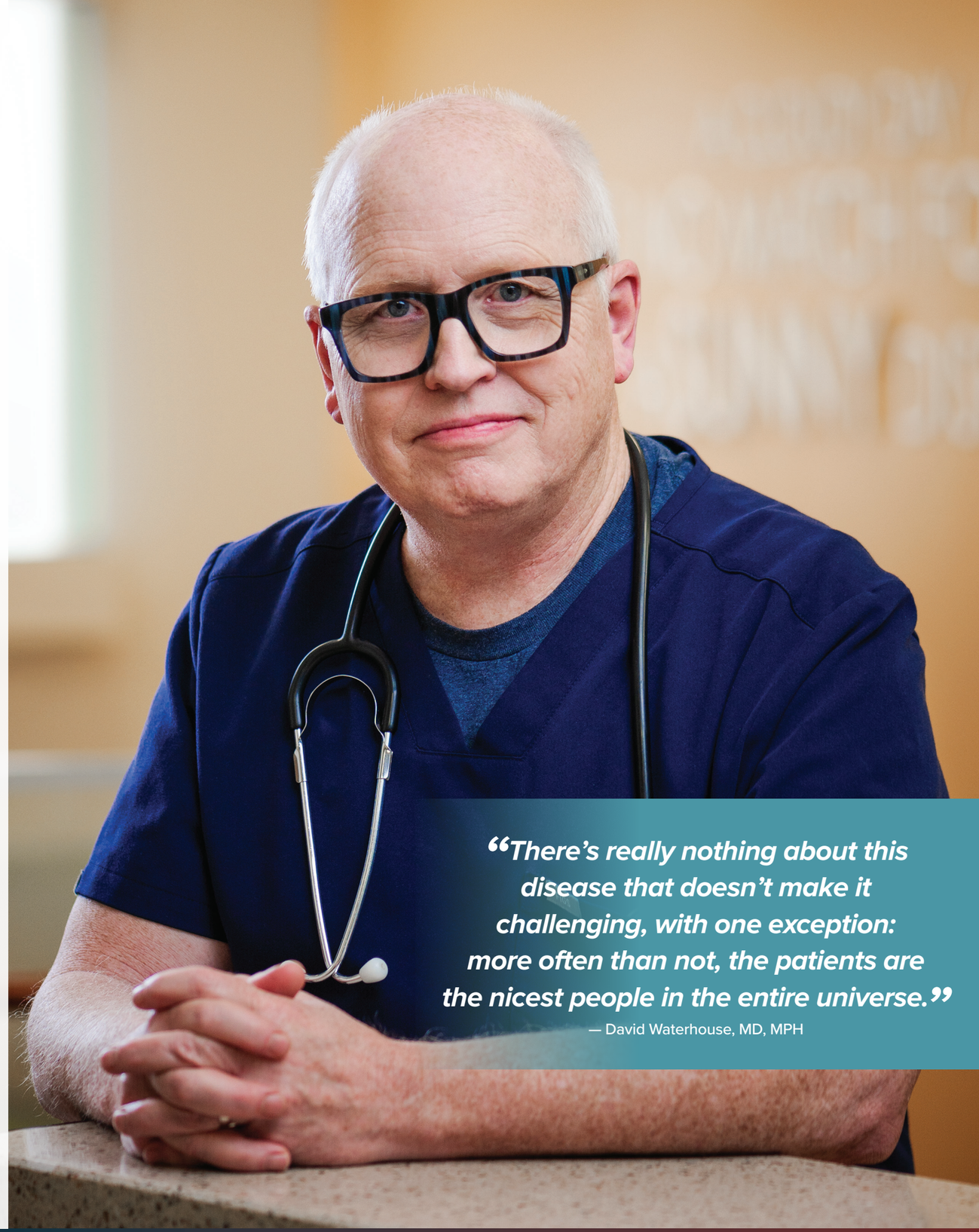
A. The first thing is that you have to be vigilant about looking for disease progression and making sure your patients will come to you or call you about their symptoms. Listening to the patient is probably one of the most important things. The second is that when the cancer comes back, it's going to come back ferociously.[3] And third, you have to have a plan. I always tell my patients, "There's only going to be 3 possibilities: your disease is going to get better, worse, or stay the same, and I have a plan for all of those scenarios." I think saying that addresses the seriousness of the disease and having to be vigilant in monitoring and planning for what to do next.

Q. How many of your patients with SCLC require a second-line treatment option?

A. They will all likely need second-line therapy, but unfortunately, not all of them will receive it. In fact, only about one-third of patients receive further treatment after platinum-based therapy.[4,5] The question used to be, "Do I treat them or do I not treat them if I'm only able to give them platinum?" But that conversation has begun to change.

Q. What patient characteristics or medical criteria do you keep in mind when you're considering a second-line option?

A. The first is performance status; is the patient capable of being treated in second line? The second is how they responded to first-line therapy and how well they tolerated that treatment—what I consider to be the depth and cost of response. Additionally, it's important to consider what the patient wants. Some of my patients have told me the treatment can be worse than the disease and they are looking for something with a more manageable tolerability profile.



"There's really nothing about this disease that doesn't make it challenging, with one exception: more often than not, the patients are the nicest people in the entire universe."

— David Waterhouse, MD, MPH

CLINICAL EXPERIENCE: SECOND-LINE TREATMENT FOR SCLC WITH ZEPZELCA® (lurbinectedin)

Q. Why do you consider prescribing ZEPZELCA for your patients with SCLC who have relapsed?

A. I've been fortunate enough to treat several patients with ZEPZELCA, and for me, the decision is data-driven. When choosing a second-line treatment, I think that it's a balance of efficacy and safety. Does it work, and what is the impact to the patient? The safety and efficacy data from the ZEPZELCA pivotal phase 2 trial closely align with the experience I have had with my patients. In the phase 2 trial in adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy, ZEPZELCA provided an ORR of 35% by IA and 30% by IRC. The median DoR was 5.3 months by IA and 5.1 months by IRC.[6,7]

As I mentioned earlier, there are 3 outcomes from a scan: better, worse, or stayed the same. If it's better, that's fantastic. For the patient, what's the first thing they're going to do as soon as you walk out the door? They text someone they love, "My scans were okay. Nothing's growing, nothing new."

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STUDY DESIGN[6,7]

The phase 2 trial was a multicenter, open-label, multi-cohort trial evaluating ZEPZELCA as a single agent in 105 adult patients with advanced or metastatic SCLC with disease progression on or after platinum-based chemotherapy. Patients received ZEPZELCA 3.2 mg/m^2 by intravenous infusion every 21 days (one cycle) for a median of 4 cycles (range: 1 to 24 cycles). The median age was 60 years (range: 40 to 83 years). Baseline ECOG PS was 0–1 in 92% of patients. The primary efficacy outcome was confirmed ORR by IA. Additional efficacy outcome measures included DoR and an IRC-assessed ORR using RECIST version 1.1.

DoR=duration of response; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IA=investigator assessment; IRC=independent review committee; ORR=overall response rate; RECIST=Response Evaluation Criteria in Solid Tumors.

INDICATION

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

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).

"A response is a win . . . for the patient, what's the first thing they're going to do as soon as you walk out the door? They text someone they love, 'My scans were okay. Nothing's growing, nothing new.'"

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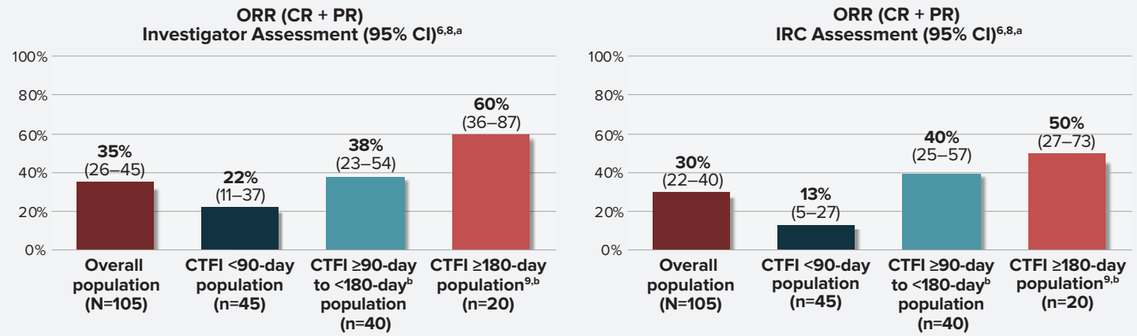
For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy, **ZEPZELCA PROVIDED SUBSTANTIAL EFFICACY IN BOTH PLATINUM-RESISTANT AND PLATINUM-SENSITIVE PATIENTS[6]**



[a]According to RECIST v1.1. CR: Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.[10]

[b]These subgroup exploratory analyses were not powered to determine statistical significance. Results are descriptive only.[8,9]

CI=confidence interval; CR=complete response; CTFI=chemotherapy-free interval; PR=partial response.

IMPORTANT SAFETY INFORMATION

Myelosuppression

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.

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 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.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm^3 and platelet count of at least 100,000/mm^3.

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.

Please see page 7 for Important Safety Information and CLICK HERE for full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

CLINICAL EXPERIENCE: SECOND-LINE TREATMENT FOR SCLC WITH ZEPZELCA® (lurbinectedin)

"Weighing in toxicity is really important. The toxicity gets overlooked if there's efficacy. But the patient isn't overlooking it; they're living it."

— David Waterhouse, MD, MPH

Q. What do the safety results from the clinical trial tell you about ZEPZELCA as a monotherapy?

A. To me, they speak to the tolerability of ZEPZELCA. For example, the permanent discontinuation rate in the trial due an adverse reaction was 1.9%; 29% of patients were on ZEPZELCA for 6 months and 6% were on it for 1 year. There were 11 patients (10.5%) who had a serious adverse reaction (SAE), and in 9 of these cases it was related to hematological events; all SAEs resolved.[6,8]

Q. How do you feel ZEPZELCA fits into the treatment landscape?

A. Looking at the clinical trial data, ZEPZELCA provided efficacy in both platinum-resistant and platinum-sensitive patients. I've used ZEPZELCA successfully in both of these patient types. Historically, physicians have considered platinum rechallenge in these patients, and I can recommend an interesting retrospective analysis (Subbiah et al. 2020) that examines efficacy and safety outcomes amongst ZEPZELCA and platinum rechallenge.[9] Small cell lung cancer is an aggressive disease that takes both a physical and emotional toll.[2,11,12] The introduction of ZEPZELCA monotherapy into the treatment paradigm is an attractive option because of its balanced efficacy and safety profile, and 1-hour infusion every 3 weeks for minimal infusion visits.[6]

Please see Important Safety Information below and on the opposite page.

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity

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 elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days.

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.

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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.

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion.

If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

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

Embryo-Fetal Toxicity

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 last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.

Lactation

There are no data on the presence of ZEPZELCA in human milk, however, 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 last dose.

MOST COMMON ADVERSE REACTIONS

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%).

DRUG INTERACTIONS

Effect of CYP3A Inhibitors and Inducers

Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.

Avoid coadministration with a strong CYP3A inducer as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

GERIATRIC USE

Of the 105 patients with SCLC 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%)

Please CLICK HERE for full Prescribing Information.

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"My decision to use ZEPZELCA® (lurbinectedin) is data-driven. I look at the balance between safety and efficacy."

— David Waterhouse, MD, MPH

LEARN MORE ABOUT A SECOND-LINE OPTION
FOR YOUR PATIENTS WITH RELAPSED SCLC AT
ZEPZELCAPRO.COM

Dr Waterhouse has more than 25 years of experience treating patients with small cell lung cancer as a physician and researcher.

David M. Waterhouse, MD, MPH, is a medical oncologist/hematologist with Oncology Hematology Care, Inc (OHC) and serves as Co-Director of OHC Research. His specialties are lung cancer and urologic cancer, while his passion is for cancer clinical research. Dr Waterhouse has been an active member of American Society of Clinical Oncology® (ASCO) committees, including the Cancer Research Committee (2013-2016), the Research Community Forum Council (2017-2021, chair 2020), the Research Site Qualifications Task Force, and the Dose Optimization Task Force. Dr Waterhouse also serves as a National Network Principal Investigator for The US Oncology Network and US Oncology Research. He is a member of the Network's Research Executive Committee. He is Associate Chair of their Thoracic Committee and an active member of their Health Economics and Outcomes Research (HEOR) group. Dr Waterhouse is a well-published scientific author and highly sought-after national speaker.

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