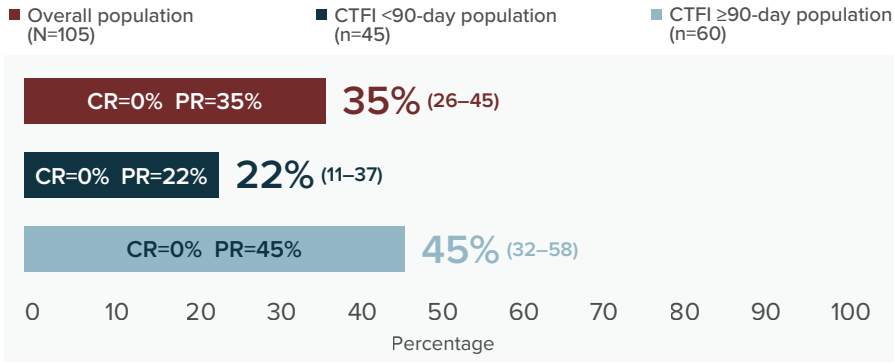
For adults with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy,

PURSUE A RESPONSE WITH *ZEPZELCA*® (lurbinectedin)

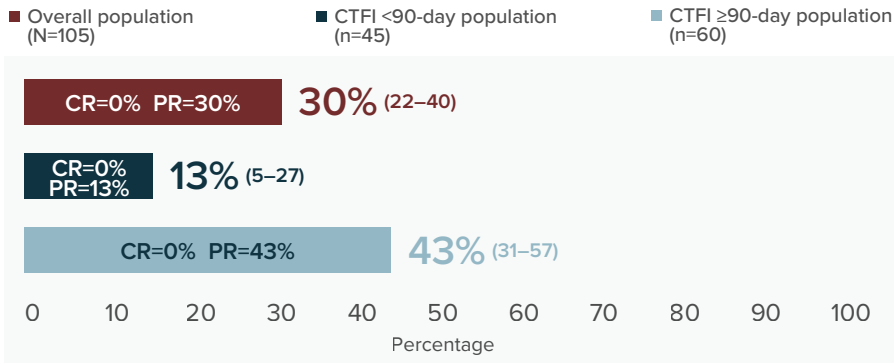
Energizing healthcare providers to change their approach to metastatic *SCLC*

ZEPZELCA PROVIDED SUBSTANTIAL EFFICACY IN BOTH PLATINUM-RESISTANT AND PLATINUM-SENSITIVE PATIENTS

ORR (CR + PR) by Investigator Assessment (95% CI)[1]



ORR (CR + PR) by Independent Review Committee (IRC) Assessment (95% CI)[1]



In the overall population, **>1 in 3 patients** achieved ORR by the investigator assessment[1]

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CR=complete response; CTFI=chemotherapy-free interval; ORR=overall response rate; PR=partial response.
CTFI refers to the time from the last dose of platinum-containing chemotherapy until recurrence or progression.

INDICATION

ZEPZELCA is indicated for the treatment of adult patients with metastatic 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).

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.

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ZEPZELCA® (lurbinectedin) for injection 4 mg

In a phase 2, single-arm study of 105 adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,

Exploratory Analysis of Disease Control Rate (DCR)

- **69%** (95% CI: 58.8–77.3) of patients achieved **DCR** according to investigator assessment[2*]
  – CR=0%; PR=35%; SD=33%[†]
- **62%** (95% CI: 51.9–71.2) of patients achieved **DCR** according to IRC assessment[3*]
  – CR=0%; PR=31%; SD=31%[†]

ZEPZELCA® (lurbinectedin) Demonstrated Clinically Meaningful Duration of Response[1]

- **5.3 months**[‡] (95% CI: 4.1–6.4) by investigator assessment
- **5.1 months**[‡] (95% CI: 4.9–6.4) by IRC assessment

Limitations of DCR data
No conclusions about efficacy can be drawn from these descriptive data because they are results from exploratory end points in a phase 2, single-arm study.

Study Design[1,2]

The phase 2 study 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 Performance Status was 0–1 in 92% of patients. The major efficacy outcome measure was confirmed investigator-assessed ORR. Additional efficacy outcome measures included duration of response and an IRC-assessed ORR using Response Evaluation Criteria In Solid Tumors version 1.1.

ORR IN THE OVERALL POPULATION

- 35% (95% CI: 26–45) ORR by investigator assessment (CR=0%; PR=35%)[1]
- 30% (95% CI: 22–40) ORR by IRC assessment (CR=0%; PR=30%)[1]

LOW DISCONTINUATION RATE

- Adverse reactions resulting in permanent discontinuation in ≥1% of patients included peripheral neuropathy and myelosuppression[1]

MINIMAL INFUSION VISITS

The recommended dosage of ZEPZELCA is 3.2 mg/m^2 by intravenous infusion over 60 minutes, repeated every 21 days until disease progression or unacceptable toxicity.[1]

Initiate treatment with ZEPZELCA only if absolute neutrophil count (ANC) is ≥1,500 cells/mm^3 and platelet count is ≥100,000/mm^3.[1]

ECOG=Eastern Cooperative Oncology Group; SD=stable disease.
*According to Response Evaluation Criteria In Solid Tumors 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. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameters while on study.[4]
†Includes 5 patients with partial response not confirmed.[2,3]
‡Median in months.

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IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Myelosuppression (*continued*)

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® (lurbinectedin) 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.

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.

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 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.

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IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Lactation

There are no data on the presence of ZEPZELCA® (lurbinectedin) 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 final 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

Strong and Moderate CYP3A Inhibitors

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.

Strong and Moderate CYP3A Inducers

Avoid coadministration with a strong or moderate CYP3A inducer. Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy.

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 see additional Important Safety Information throughout and accompanying full Prescribing Information.

References: 1. ZEPZELCA (lurbinectedin). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** 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. **3.** Data on file. LUR-2020-003. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **4.** Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009;45(2):228-247.

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