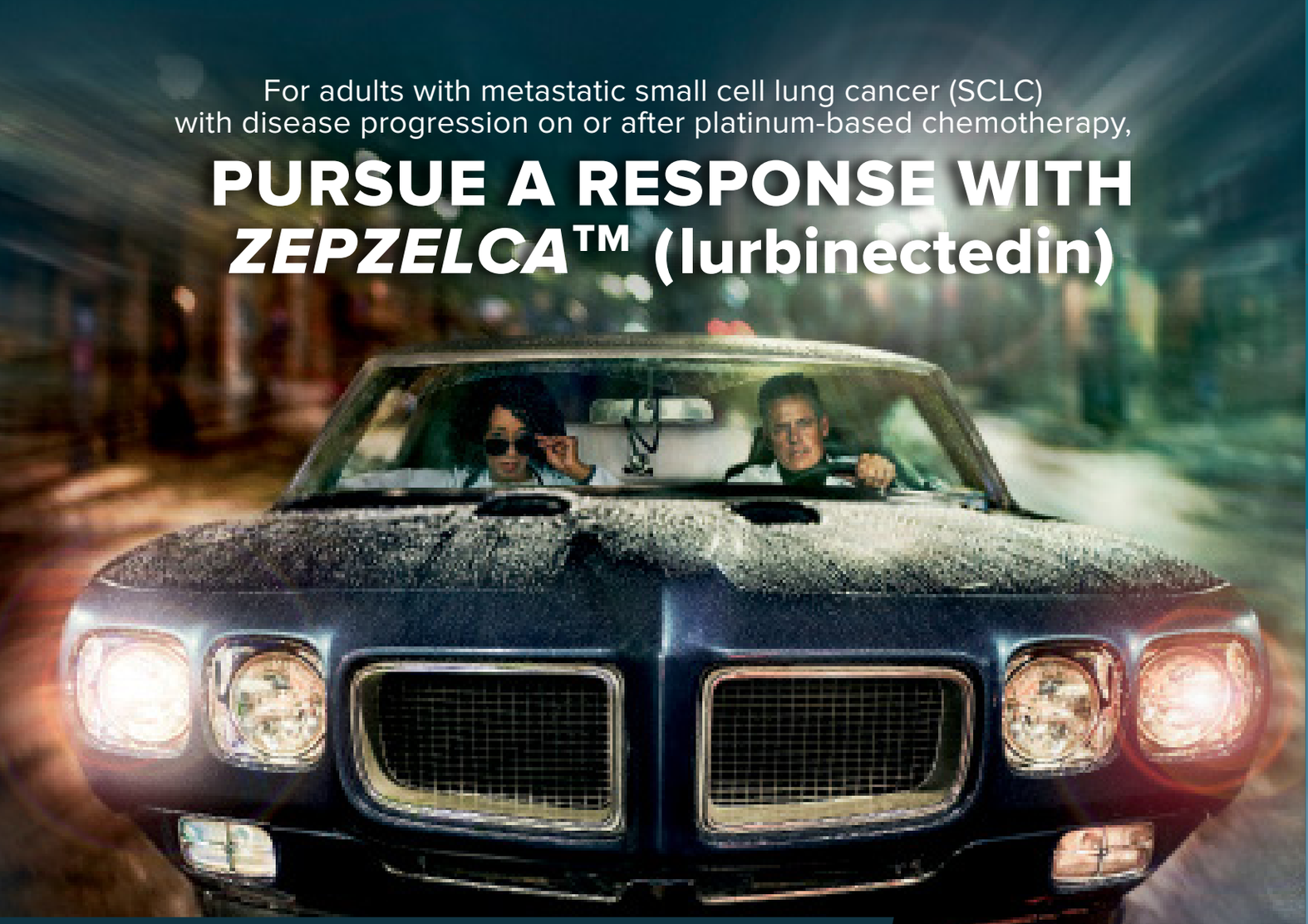
For adults with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy,

PURSUE A RESPONSE WITH *ZEPZELCA*™ (lurbinectedin)



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

INDICATION

ZEPZELCA™ (lurbinectedin) 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.

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.

Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

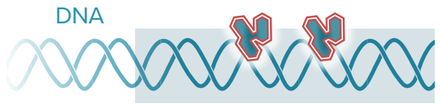
ZEPZELCA™ (lurbinectedin) for injection 4 mg

Contact me for further discussion.

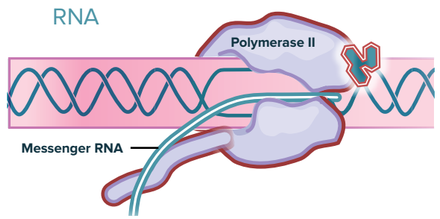
For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,

ZEPZELCA™ (lurbinectedin) INHIBITS TRANSCRIPTION, A KEY PROCESS IN SCLC PATHOLOGY[1-3]

Effects on the tumor



- Binds to guanine residues in the minor groove of DNA[1]
- Affects activity of transcription factors[1]



- Stalls RNA polymerase II[4]
- Affects DNA repair pathways[1]
- Results in eventual cell death[1]

Effects on the tumor microenvironment[1,5]

Based on a preclinical study, ZEPZELCA may:

- Induce apoptosis in tumor-associated macrophages
- Reduce macrophage infiltration
- Reduce inflammatory chemokines (CCL2 and CXCL8) and VEGF

VEGF=vascular endothelial growth factor.

IMPORTANT SAFETY INFORMATION

Myelosuppression (*continued*)

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.

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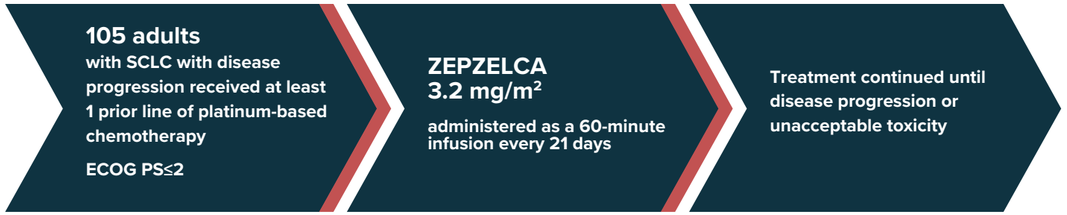
ZEPZELCA™ (lurbinectedin) for injection 4 mg

ZEPZELCA™ (lurbinectedin) WAS STUDIED IN A PHASE 2, OPEN-LABEL, MULTICENTER, SINGLE-ARM STUDY[1,6]



Primary end point: overall response rate (ORR) as assessed by study investigators.[6]

Secondary end point[6]:

- Duration of response

Exploratory outcome measure[6,7]:

- Proportion of patients with disease control (complete response [CR] + partial response [PR] + stable disease [SD])

The primary end point and secondary end points were analyzed by an **independent review committee (IRC)** to confirm investigator assessments and minimize data interpretation bias.[1,6]

The safety profile of ZEPZELCA includes[1]:

- A pool of 554 patients with advanced solid tumors (includes the 105 patients with metastatic SCLC in the phase 2 study) exposed to ZEPZELCA as a single agent at a dose of 3.2 mg/m² given intravenously every 21 days

ECOG PS=Eastern Cooperative Oncology Group Performance Status.

IMPORTANT SAFETY INFORMATION

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.

ZEPZELCA WAS STUDIED ACROSS THE PLATINUM-RESISTANT AND PLATINUM-SENSITIVE SCLC SPECTRUM

Platinum sensitive was defined as recurrence or progression **≥90 days** after the last dose of platinum-containing chemotherapy (chemotherapy-free interval [CTFI] ≥90 days).[1]

Platinum resistant was defined as recurrence or progression **<90 days** after the last dose of platinum-containing chemotherapy (CTFI <90 days).[1]

Patient Population According to CTFI[1,6,7]

N=105	CTFI	n
Platinum resistant (n=45)	<30 days	21
	30 to <90 days	24
Platinum sensitive (n=60)	90 to <180 days	40
	≥180 days	20

Baseline Characteristics[1]

	N=105
Median age (years)	60
Age range (years)	40–83
≥65 years	35%
Male	60%
White	75%[a]
ECOG PS 0–1	92%
Former/current smokers	92%

[a]1% was Asian, 1% was Black, and 23% were not reported.

IMPORTANT SAFETY INFORMATION

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.

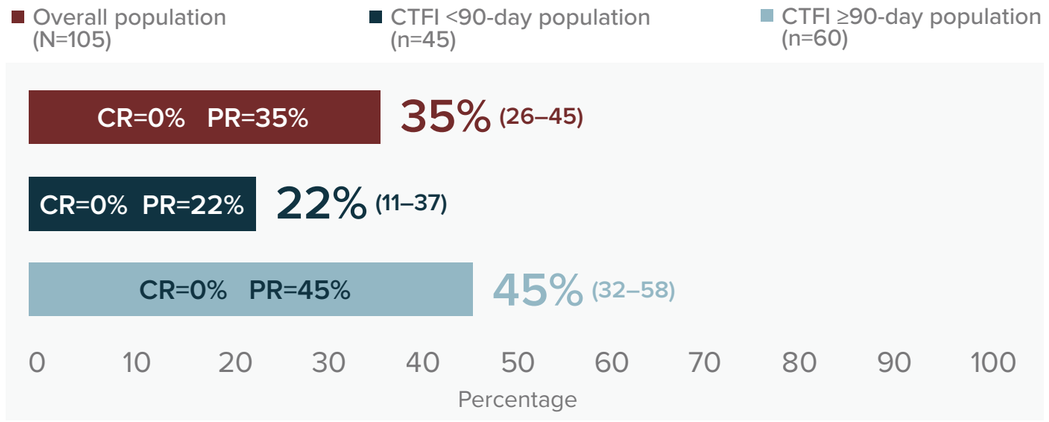
Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

ZEPZELCA™ (lurbinectedin) for injection 4 mg

For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,

ZEPZELCA™ (lurbinectedin) PROVIDED SUBSTANTIAL EFFICACY IN BOTH...

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



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

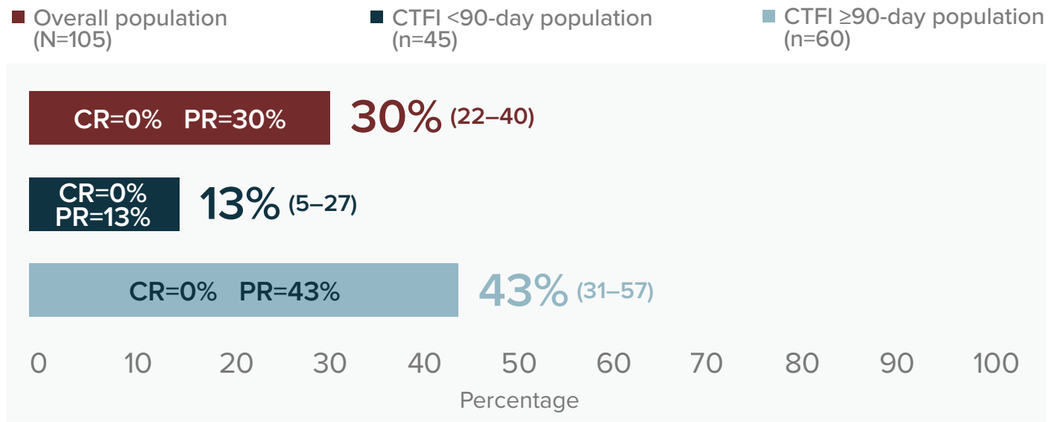
IMPORTANT SAFETY INFORMATION

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 final dose.

...PLATINUM-RESISTANT AND PLATINUM-SENSITIVE PATIENTS

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



In a post hoc analysis of 20 patients with CTFI ≥180 days, ORR was[7]:

- 60% (95% CI: 36.1–80.9) by investigator assessment
- 50% (95% CI: 27.2–72.8) by IRC assessment

This subgroup exploratory analysis was post hoc and not powered to determine statistical significance. Results are descriptive only.

IMPORTANT SAFETY INFORMATION

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%).

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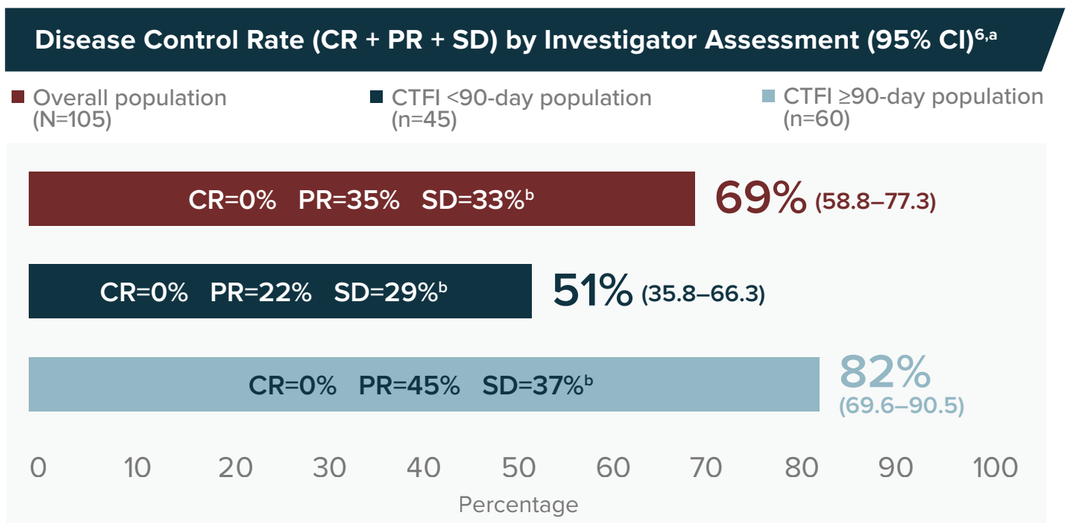
ZEPZELCA™ (lurbinectedin) for injection 4 mg

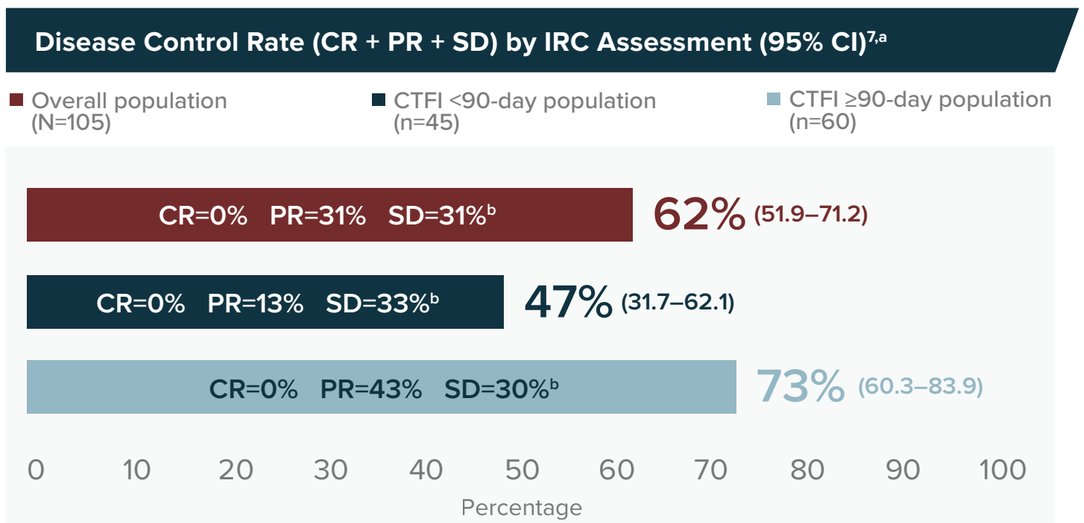
For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,

EXPLORATORY ANALYSIS OF DISEASE CONTROL WITH *ZEPZELCA*™ (lurbinectedin)

Disease Control Rate (CR + PR + SD) by Investigator Assessment (95% CI)[6,a]



Disease Control Rate (CR + PR + SD) by IRC Assessment (95% CI)[7,a]



[a]According to Response Evaluation Criteria in Solid Tumors version 1.1. 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.[8]
[b]Includes 5 patients with partial response not confirmed.[6,7]

Limitations of 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.

IMPORTANT SAFETY INFORMATION

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.

IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (*CONTINUED*)

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.

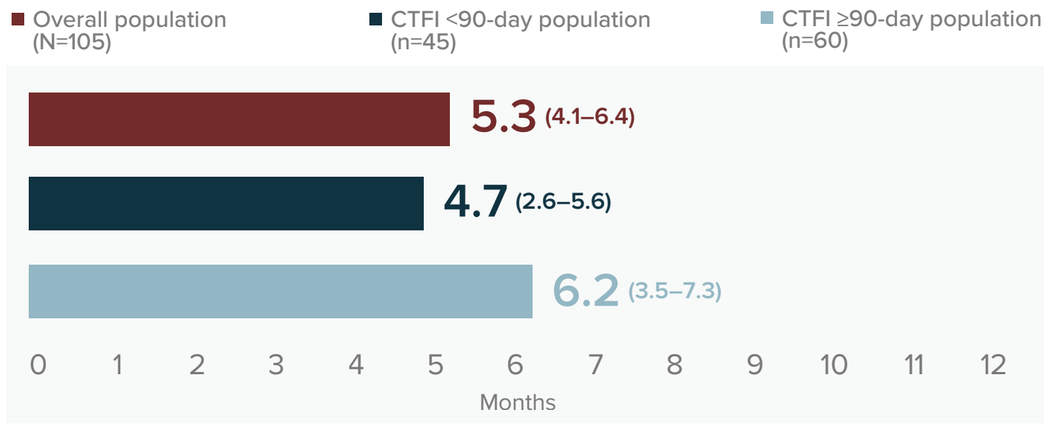
Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

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,

ZEPZELCA™ (lurbinectedin) DEMONSTRATED CLINICALLY MEANINGFUL DURATION OF RESPONSE IN…

Duration of Response by Investigator Assessment, Median in Months (95%CI)[1]



Of 8 patients who had received prior immunotherapy as first- or second-line treatment:

- Duration of response was consistent with the overall population at a median of 5.3 months (range: 2.8–6.4 months)[9]

This subgroup exploratory analysis was post hoc and not powered to determine statistical significance. Results are descriptive only.

IMPORTANT SAFETY INFORMATION

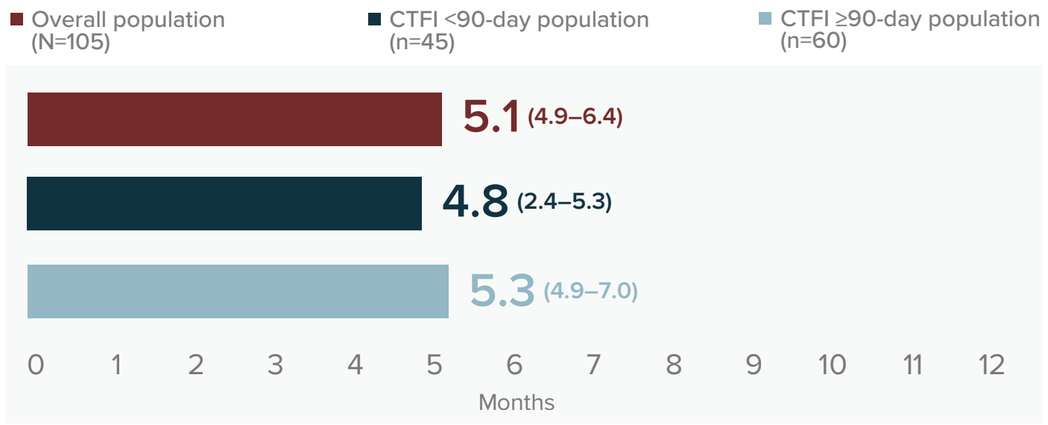
GERIATRIC USE

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%).

…PLATINUM-RESISTANT AND PLATINUM-SENSITIVE PATIENTS

Duration of Response by IRC Assessment, Median in Months (95% CI)[1]



Clinically meaningful duration of response was demonstrated **across CTFIs**[1]

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.

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ZEPZELCA™ (lurbinectedin) for injection 4 mg

ZEPZELCA™ (lurbinectedin) DEMONSTRATED A SAFETY PROFILE WITH A LOW DISCONTINUATION RATE DUE TO ADVERSE REACTIONS

Most adverse reactions were **Grade 1 or 2**[1,7]

Adverse Reactions (≥10%) in Patients With SCLC[1]

Adverse reaction	ZEPZELCA (N=105)	
	All Grades[a,b] (%)	Grades 3–4 (%)
General disorders		
Fatigue	77	12
Pyrexia	13	0
Chest pain	10	0
Gastrointestinal disorders		
Nausea	37	0
Constipation	31	0
Vomiting	22	0
Diarrhea	20	4
Abdominal pain[c]	11	1
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[d]	33	4
Metabolism and nutrition disorders		
Decreased appetite	33	1
Respiratory, thoracic, and mediastinal disorders		
Dyspnea	31	6
Cough[e]	20	0
Infections and infestations		
Respiratory tract infection[f]	18	5
Pneumonia[g]	10	7
Nervous system disorders		
Peripheral neuropathy[h]	11	1
Headache	10	1

[a]Graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) 4.0.
[b]No grade 5 adverse reactions were reported.
[c]Includes abdominal pain, abdominal pain upper, and abdominal discomfort.
[d]Includes musculoskeletal pain, back pain, arthralgia, pain in extremity, musculoskeletal chest pain, neck pain, bone pain, and myalgia.
[e]Includes cough and productive cough.
[f]Includes upper respiratory tract infection, viral upper respiratory tract infection, respiratory tract infection, and bronchitis.
[g]Includes pneumonia and lung infection.
[h]Includes neuropathy peripheral, neuralgia, paresthesia, peripheral sensory neuropathy, hypoesthesia, and hyperesthesia.

- Alopecia occurred in 1% of patients[7]

Select Laboratory Abnormalities (≥20%) Worsening From Baseline[1]

Laboratory abnormalities	ZEPZELCA (N=105)	
	All Grades[a,b] (%)	Grades 3–4 (%)
Hematology		
Decreased leukocytes	79	29
Decreased lymphocytes	79	43
Decreased hemoglobin	74	10
Decreased neutrophils	71	46
Decreased platelets	37	7
Chemistry		
Increased creatinine	69	0
Increased alanine aminotransferase	66	4
Increased glucose	52	5
Decreased albumin	32	1
Decreased sodium	31	7
Increased aspartate aminotransferase	26	2
Decreased magnesium	22	0

[a]The denominator used to calculate the rate varied from 95 to 105 based on the number of patients with a baseline value and at least one post-treatment value.
[b]Graded per NCI CTCAE 4.0.

- In the phase 2 study, 22% of patients received granulocyte colony-stimulating factor (G-CSF) for secondary prophylaxis or therapy for neutropenia, but primary prophylaxis was not allowed[1,6]

Permanent discontinuation due to an adverse reaction occurred in 1.9% of patients with SCLC (2 of 105).[1]

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

Dosage interruptions due to an adverse reaction occurred in 30.5% of patients.[1]

- Adverse reactions requiring dosage interruption in ≥3% of patients included neutropenia and hypoalbuminemia

Dosage reductions due to an adverse reaction occurred in 25% of patients.[1]

- Adverse reactions requiring dosage reductions in ≥3% of patients included neutropenia, febrile neutropenia, and fatigue

Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

ZEPZELCA™ (lurbinectedin) for injection 4 mg

ONE-HOUR DOSING, EVERY 21 DAYS MEANS MINIMAL INFUSION VISITS

The recommended dosage of ZEPZELCA™ (lurbinectedin) 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]

Premedication[1]

Consider administering the following pre-infusion medications to antiemetic prophylaxis:

- Corticosteroids (intravenous dexamethasone 8 mg or equivalent)
- Serotonin antagonists (intravenous ondansetron 8 mg or equivalent)

A Straightforward Dose-Reduction Schedule to Help Manage Adverse Reactions[1]

First dose reduction	Second dose reduction
2.6 mg/m^2 every 21 days	2 mg/m^2 every 21 days

Permanently discontinue ZEPZELCA in patients who are unable to tolerate 2 mg/m^2 or require a dose delay greater than 2 weeks.[1]

Dosage Modifications for Adverse Reactions[1]

Adverse reaction	Severity[a]	Dosage modification
Neutropenia[b]	Grade 4 or any grade febrile neutropenia	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at a reduced dose
Thrombocytopenia	Grade 3 with bleeding or Grade 4	• Withhold ZEPZELCA until platelet ≥100,000/mm^3 • Resume ZEPZELCA at a reduced dose
Hepatotoxicity and other adverse reactions	Grade 2	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at same dose
	Grade ≥3	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at a reduced dose

[a]NCI CTCAE version 4.0.
[b]Patients with isolated Grade 4 neutropenia (neutrophil count less than 500 cells/mm^3) may receive G-CSF prophylaxis rather than undergo lurbinectedin dose reduction.

- For neutrophil count <500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended[1]

IMPORTANT SAFETY INFORMATION

Myelosuppression (*continued*)

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.

PREPARATION, ADMINISTRATION, AND STORAGE

ZEPZELCA is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

Preparation and Administration[1]

- Inject 8 mL of Sterile Water for Injection USP into the vial, yielding a solution containing 0.5 mg/mL of ZEPZELCA. Shake the vial until complete dissolution
- Visually inspect the solution for particulate matter and discoloration. The reconstituted solution is a clear, colorless, or slightly yellowish solution, essentially free of visible particles
- Calculate the required volume of reconstituted solution as follows:

$$\text{Volume (mL)} = \frac{\text{Body Surface Area (m}^2\text{)} \times \text{Individual Dose (mg/m}^2\text{)}}{\text{0.5 mg/mL}}$$

- For administration through a central venous line, withdraw the appropriate amount of reconstituted solution from the vial and add to an infusion container containing at least 100 mL of diluent (0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP)
- For administration through a peripheral venous line, withdraw the appropriate amount of reconstituted solution from the vial and add to an infusion container containing at least 250 mL of diluent (0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP)
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter is observed, do not administer

Storage of Infusion Solution[1]

- If not used immediately after reconstitution or dilution, the ZEPZELCA solution can be stored prior to administration for up to 24 hours following reconstitution, including infusion time, at either room temperature/ambient light or under refrigerated (2 °C–8 °C; 36 °F–46 °F) conditions

IMPORTANT SAFETY INFORMATION

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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ZEPZELCA™ (lurbinectedin) for injection 4 mg

REIMBURSEMENT INFORMATION AND PATIENT SUPPORT

J-code issued for ZEPZELCA™ (lurbinectedin)

Permanent, product-specific HCPCS J-code for ZEPZELCA	J9223

JazzCares
Making a difference in Patients' lives, one Patient at a time

JazzCares is committed to helping your patients get access to their ZEPZELCA medication and providing personalized support throughout their treatment

Dedicated JazzCares specialists assist patients and practices with:

- Benefit investigation—helps patients understand their insurance coverage for ZEPZELCA
- Prior authorization support
- Appeals support
- Billing and coding information
- Referrals to other financial assistance

Reduction of out-of-pocket costs for ZEPZELCA for eligible patients

Savings Card—eligible, commercially insured patients can pay as little as $10 for their ZEPZELCA medication, subject to an annual maximum

Free drug program for eligible patients

Learn more about JazzCares support offerings by calling **1-833-533-JAZZ (5299)** Monday–Friday, 8 AM TO 8 PM ET, or visit **JazzCares.com**

Insurance coverage and plans may vary. The JazzCares program at Jazz Pharmaceuticals provides general information only and is not a guarantee of any coverage or reimbursement outcome. All treatment decisions rest solely with the treating physician or qualified healthcare professional. Jazz Pharmaceuticals reserves the right to terminate or modify this program at any time with or without notice. Other terms and conditions apply.

ORDERING INFORMATION

Order ZEPZELCA through our distribution partners

Specialty distributors
ZEPZELCA is available for purchase from the authorized Specialty Distributors listed below. Verify that your facility has an account with their Specialty Distributor before ordering. If not, they should contact their Specialty Distributor. The facility should also contact their Specialty Distributor with questions regarding product returns.

AmerisourceBergen

ASD Healthcare	Oncology Supply
ASD Healthcare Phone/Fax: (800) 746-6273/(800) 547-9413 Online: https://www.asdhealthcare.com/home	Oncology Supply Phone/Fax: (800) 633-7555/(800) 248-8205 Online: https://www.oncologysupply.com/

Cardinal Health

Cardinal Health
Phone/Fax: (877) 453-3972/(877) 274-9897 Online: Order Express (Hospitals) https://orderexpress.cardinalhealth.com Specialty Online (Clinics): https://specialtyonline.cardinalhealth.com

McKesson

McKesson Plasma and Biologics (MPB)	McKesson Specialty Health (MSH)
Phone/Fax: (877) 625-2566/(888) 752-7626 Online: https://connect.mckesson.com	Phone/Fax: (800) 482-6700/(800) 289-9285 Online: http://MSCS.McKesson.com

Group Purchasing Organizations (GPOs) ZEPZELCA is available through:

- ION Solutions (AmerisourceBergen®)
- Unity GPO (The US Oncology Network/McKesson)
- Onmark® GPO (McKesson)
- VitalSource™ (Cardinal Health™)

Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

ZEPZELCA™ (lurbinectedin) for injection 4 mg

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).

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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.

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.

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.

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 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 accompanying full Prescribing Information.

References: 1. ZEPZELCA (lurbinectedin). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Farago AF, Drapkin BJ, Lopez-Vilarino de Ramos JA, et al. ATLANTIS: a Phase III study of lurbinectedin/doxorubicin versus topotecan or cyclophosphamide/doxorubicin/vincristine in patients with small-cell lung cancer who have failed one prior platinum-containing line. *Future Oncol.* 2019;15(3):231-239. **3.** Christensen CL, Kwiatkowski N, Abraham BJ, et al. Targeting transcriptional addictions in small cell lung cancer with a covalent CDK7 inhibitor. *Cancer Cell.* 2014;26(6):909-922. **4.** Santamaría Nuñez G, Robles CM, Giraudon C, et al. Lurbinectedin specifically triggers the degradation of phosphorylated RNA polymerase II and the formation of DNA breaks in cancer cells. *Mol Cancer Ther.* 2016;15(10):2399-2412. **5.** Belgiovine C, Bello E, Liguori M, et al. Lurbinectedin reduces tumour-associated macrophages and the inflammatory tumour microenvironment in preclinical models. *Br J Cancer.* 2017;117(5):628-638. **6.** 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. **7.** Data on file. LUR-2020-003. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **8.** 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. **9.** 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. Appendix S3. Efficacy outcomes in patients pretreated with immunotherapy. *Lancet Oncol.* 2020;21(5):645-654. **10.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer. V.3.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 23, 2021. To view the most recent and compete version of the guideline, go online to NCCN.org.

ZEPZELCA® (lurbinectedin) for injection 4 mg

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[10*†]

- **Lurbinectedin is a category 2A recommended treatment option** for patients who relapse **≤6 months** *or* **>6 months**‡ following first-line platinum-based chemotherapy
- **Lurbinectedin is a preferred category 2A treatment option** for patients who relapse ≤6 months with ECOG PS 0–2

*See the NCCN Guidelines for SCLC for detailed recommendations, including other treatment options.
‡Other recommended regimen.

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).

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%).

Please see pages 18 and 19 for Important Safety Information and accompanying full Prescribing Information.

Learn more at **ZEPZELCApro.com**

†**Category 2A:** Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[10]
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