

Positive Quality Intervention: Lurbinectedin (Zepzelca™) for Small Cell Lung Cancer

Description: The purpose of this PQI is to evaluate the use of lurbinectedin for the treatment of adult patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy.

Background: Small cell lung cancer (SCLC), which accounts for around 15% of all lung cancer diagnoses, is typically highly aggressive with poor survival outcomes.¹ The recommended first-line treatment is a platinum-based chemotherapy regimen.² Few options exist for treatment of patients with SCLC after failure of first-line treatment. Lurbinectedin is an alkylating agent that inhibits oncogenic transcription. It is approved as second-line therapy in patients with metastatic SCLC. The United States Food & Drug Administration approval of lurbinectedin in this setting is based on a single-arm, open-label, phase 2, multi-centered basket trial in Europe and the US.³ Patients enrolled in the trial were adults (aged ≥ 18 years) with a pathologically proven diagnosis of SCLC, ECOG performance status ≤ 2 , measurable disease, absence of brain metastasis, adequate organ function, and pre-treated with only one previous chemotherapy-containing line of treatment. The primary outcome was overall response (ORR) as assessed by the investigators according to RECIST 1.1. In the 105 patients who were enrolled and treated with lurbinectedin, ORR was demonstrated in 37 patients (35.2%; 95% CI 26.2-45.2). The most common grade 3-4 adverse events included hematological abnormalities such as anemia (9%), leucopenia (29%), neutropenia (46%), and thrombocytopenia (7%). Serious treatment-related adverse events occurred in 10% of the patients, of which neutropenia and febrile neutropenia were the most common (5% patients for each). No treatment-related deaths were reported.^{3,4}

PQI Process:⁵

- Screen for drug interactions; avoid coadministration with strong/moderate CYP3A inhibitors/inducers
- Recommended dosage is 3.2 mg/m² administered over 60 minutes every 21 days until disease progression or unacceptable toxicity
- No initial dose adjustment recommended for baseline renal or hepatic impairment (limited data available)
- Initiate treatment only if baseline ANC $\geq 1,500$ cells/mm³ and platelet count is $\geq 100,000$ /mm³
- Pre-medications for antiemetic prophylaxis:
 - Corticosteroids: dexamethasone 8 mg intravenously or equivalent
 - Serotonin antagonists: ondansetron 8 mg intravenously or equivalent
- Preparation:
 - Available as a single-dose, preservative free vial with 4 mg lyophilized powder per vial
 - Inject 8 mL of SWFI into the vial, yielding a solution containing 0.5 mg/mL lurbinectedin
 - Shake the vial until complete dissolution; 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: Volume (mL) = Body Surface Area (m²) x Individual Dose (mg/m²)/0.5 mg/mL
 - 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 or 5% Dextrose)
- See supplemental Information section for adverse effects, recommendations, and dose adjustments

Patient Centered Activities:

- Counsel patient on lurbinectedin with written and verbal materials
- Ensure patient has access to supportive antiemetic medication

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- Embryo-Fetal Toxicity: advise females and males of reproductive potential of the potential risk to a fetus and to use an effective method of contraception
- Instruct patient to report any adverse events, such as fatigue, thrombocytopenia, nausea, decreased appetite, musculoskeletal pain, constipation, dyspnea, vomiting, cough, and diarrhea
- Patient Assistance: [NCODA Financial Assistance Tool](#)

References:

1. Basumallik N, Agarwal M. Small Cell Lung Cancer. 2021 Jul 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 29494065.
2. Small Cell Lung Cancer. Version 1.2021. National Comprehensive Cancer Network. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf.
3. 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.
4. Singh S, Jaigirdar AA, Mulkey F, et al. FDA Approval Summary: Lurbinectedin for the Treatment of Metastatic Small Cell Lung Cancer. *Clin Cancer Res.* 2021;27(9): 2378-2382.
5. [Zepzelca \[package insert\]](#)

Supplemental Information:

Most common adverse reactions ($\geq 20\%$) effecting laboratory values include: leukopenia, lymphopenia, anemia, neutropenia, increased creatinine, increased alanine aminotransferase, increased glucose, increased aspartate aminotransferase, decreased albumin, decreased sodium, decreased magnesium

Adverse Event Table for Lurbinectedin:

Adverse Event	Severity	Recommended Action
Neutropenia	Grade 4 or any grade febrile neutropenia	Hold until \leq Grade 1 Use G-CSF for neutrophil count < 500 cells/mm ³ Resume at reduced dose
Thrombocytopenia	Grade 3 with bleeding or Grade 4	Hold until platelets $\geq 100,00$ /mm ³ Resume at reduced dose
Hepatotoxicity	Grade 2/3/4	Hold until \leq Grade 1 Resume at reduced dose

Dose Reduction for Lurbinectedin for Adverse Reactions:

Event	Recommended Action
1 st dose reduction	2.6 mg/m ² every 21 days
2 nd dose reduction	2 mg/m ² every 21 days
3 rd dose reduction	Permanently discontinue if unable to tolerate 2 mg/m ² or dose delay greater than two weeks

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