EE152

Cost-Effectiveness Modeling of Lurbinectedin as a Second-line Therapy in Patients With Small Cell Lung Cancer (SCLC)

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Background

- Lung cancer is the leading cause of cancer death, making up approximately 20% of all cancer deaths,[1] with small cell lung cancer (SCLC) comprising 13%-15% of all lung cancer diagnoses[2]
- Left untreated, SCLC has a median survival of 2-4 months after diagnosis[3] and, despite treatment, a predicted 5-year survival rate of 7% in the United States.[4] Treatment options and survival rate for patients with SCLC have not changed substantially in the past two decades[2]
- Lurbinectedin is a selective inhibitor of oncogenic transcription that received accelerated approval from the US Food and Drug Administration (FDA) as monotherapy (3.2 mg/m^2 intravenously [IV] every 21 days) in June 2020 for the treatment of adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy[5]
  - Lurbinectedin demonstrated an overall response rate of 35.2% and a median duration of response of 5.3 months in 105 patients with relapsed SCLC from a single-arm, open-label, phase 2 basket trial (NCT02454972)[2]

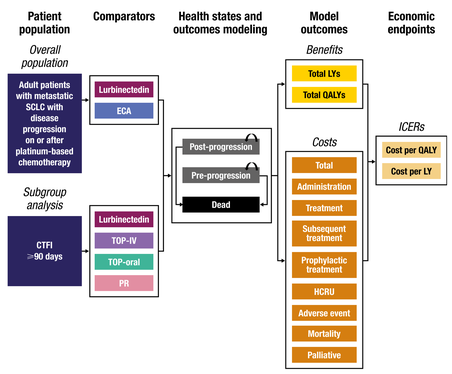
Objective

- To model the cost-effectiveness of lurbinectedin in adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy in the United States

Methods

- A cost-effectiveness model was developed to estimate the incremental cost per quality-adjusted life year (QALY) gained for lurbinectedin vs its comparators using a lifetime partitioned survival model from the US payer perspective (**Figure 1**)
  - In the overall population, the comparator was a mix of other treatment options used in SCLC from an external control arm (ECA) analysis and included platinum rechallenge (PR), topotecan (IV [TOP-IV] and oral [TOP-oral]), irinotecan, nivolumab, and paclitaxel.[6] This current study only reports lurbinectedin vs the ECA for the overall population
  - A subgroup analysis in platinum-sensitive patients (defined as chemotherapy-free interval ⩾90 days per the European Society for Medical Oncology guidelines) was derived from a published network meta-analysis[7] that compared lurbinectedin against PR, TOP-IV, and TOP-oral
- The progression-free survival (PFS; median: 3.5 months [95% CI: 2.6, 4.3]) and overall survival (OS; median: 9.3 months [95% CI: 6.3, 11.8]) for lurbinectedin were derived from patients with SCLC in the basket trial[2]
- The PFS and OS of the comparator arms were estimated using hazard ratios (HRs) from published studies that applied proportional hazard models[6]
  - In the overall population, the HRs were based on an ECA analysis comparing lurbinectedin against a mix of other second-line SCLC treatments. The median OS of the ECA was 4.6 (95% CI: 2.6, 9.1) months
  - In the platinum-sensitive subgroup analysis, lurbinectedin demonstrated significantly greater OS compared with PR (HR: 0.42; 95% CI: 0.30, 0.58), TOP-IV (HR: 0.43; 95% CI: 0.26, 0.70), and TOP-oral (HR: 0.43; 95% CI: 0.27, 0.67)
- Health-related quality of life estimates were based on the published literature.[8,9] The utility for stable disease and progressed disease was 0.81[8] and 0.69,[9] respectively
- Total cost included second-line and subsequent treatment acquisition and administration costs, serious myelosuppression-related adverse event management, primary and secondary prophylaxis (granulocyte colony-stimulating factor [G-CSF]), office visits, monitoring, and mortality cost
  - The market share of various treatments for second- and subsequent-treatment lines was based on a Jazz internal analysis of Flatiron Electronic Medical Records data
  - The rates of serious adverse events (SAEs) were estimated per pivotal trials of respective treatments[5,10-15]
    - Only myelosuppression-related SAEs were modeled: anemia, leukopenia, neutropenia, febrile neutropenia (FN), and thrombocytopenia
    - There is a lack of published data on the probabilities of hospitalization due to SAEs, so estimates were provided by a physician with extensive knowledge of SCLC to fill this data gap. The hospitalization rate for FN and other myelosuppression-related SAEs was estimated to be 95% and 10%, respectively
- G-CSF prophylactic treatment schedule followed the latest National Comprehensive Cancer Network® (NCCN®) guidelines for Supportive Care Hematopoietic Growth Factors.[16] Topotecan is associated with high risk of FN,[17] while lurbinectedin and PR are associated with intermediate risk of FN[2,18]
- Office visits and monitoring schedule were based on NCCN® clinical practice guidelines for SCLC[19]
- Costs and health outcomes were discounted at 3%

Figure 1. Cost-Effectiveness Model Conceptual Framework



CTFI, chemotherapy-free interval; ECA, external control arm; HCRU, healthcare resource use; ICER, incremental cost-effectiveness ratio; IV, intravenous; LY, life year; PR, platinum rechallenge; QALY, quality-adjusted life year; SCLC, small cell lung cancer; TOP, topotecan.

Results

Overall Population

- The incremental cost-effectiveness ratio (ICER) of lurbinectedin vs the ECA was $20,691/QALY, which is below the commonly accepted willingness-to-pay (WTP) threshold of $100,000/QALY in the United States[20]
- Higher acquisition cost of lurbinectedin compared with the ECA was partially offset by the myelosuppression prophylaxis cost (**Table 1**)

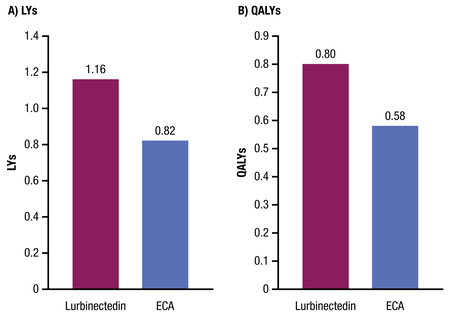
Table 1. Cost Summary for Lurbinectedin-Treated Patients vs the ECA Population (Discounted)

Cost Component	Lurbinectedin (2022 USD)	ECA (2022 USD)
PF: Second-line treatment	$39,440	$33,920
PF: Myelosuppression prophylaxis	$1875	$3132
PF: Adverse event	$3101	$2492
PD: Subsequent therapy	$8426	$8453
PD: Adverse event	$1865	$1871
PD: Medical	$2877	$2518
Mortality	$15,831	$16,019
Total costs	**$77,018**	**$72,489**

ECA, external control arm; PD, progressed disease; PF, progression free.

- Lurbinectedin-treated patients had higher LYs and QALYs compared with patients in the ECA (**Figure 2**)

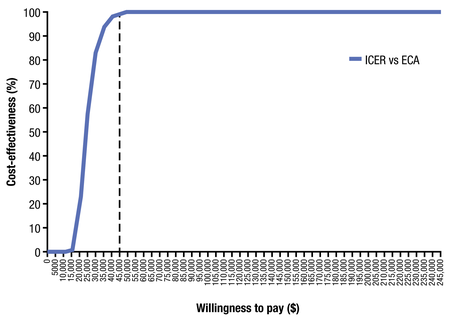
Figure 2. A) LYs and B) QALYs of Lurbinectedin-Treated Patients vs the ECA



LY, life year; QALY, quality-adjusted life year.

- In probabilistic sensitivity analysis, starting at a WTP threshold of $45,000/QALY, lurbinectedin remains 100% likely to be cost-effective compared with the ECA (**Figure 3**)
- Deterministic sensitivity analysis results have shown that the rate of primary and secondary G-CSF use are the most influential inputs on cost-effectiveness outcomes

Figure 3. Cost-Effectiveness Acceptability Curve: Overall Population



ECA, external control arm; ICER, incremental cost-effectiveness ratio.

Platinum-Sensitive Group

- The ICER for lurbinectedin vs PR, TOP-IV, and TOP-oral was $63,017/QALY, $53,835/QALY, and $22,999/QALY, respectively, which is well below the commonly accepted WTP threshold of $100,000/QALY to $150,000/QALY in the United States[20]
- Lurbinectedin incurred higher treatment costs than the comparators, which were partially offset by higher primary and secondary G-CSF use and adverse event costs in the TOP-IV and TOP-oral comparator groups (**Table 2**)

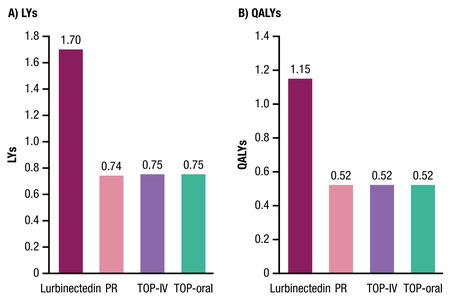
Table 2. Cost Summary for Lurbinectedin-Treated Patients vs the Platinum-Sensitive Subgroup (Discounted)

Cost Component	Lurbinectedin (2022 USD)	PR (2022 USD)	TOP-IV (2022 USD)	TOP-Oral (2022 USD)
PF: Second-line treatment	$42,407	$1337	$3559	$22,318
PF: Myelosuppression prophylaxis	$2016	$1638	$7066	$7059
PF: Adverse event	$3335	$3208	$5810	$6699
PD: Subsequent therapy	$8413	$8468	$8467	$8467
PD: Adverse event	$1862	$1874	$1874	$1874
PD: Medical	$4211	$2808	$2859	$2851
Mortality	$15,549	$16,063	$16,055	$16,056
Total costs	**$81,947**	**$42,191**	**$47,683**	**$67,312**

IV, intravenous; PD, progressed disease; PF, progression free; PR, platinum rechallenge; TOP, topotecan.

- Lurbinectedin-treated patients had higher LYs and QALYs than the patients treated with PR, TOP-IV, and TOP-oral (**Figure 4**)

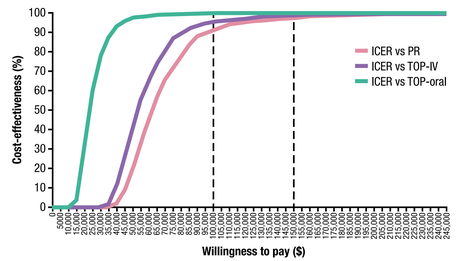
Figure 4. A) LYs and B) QALYs of Lurbinectedin-Treated Patients vs the Platinum-Sensitive Subgroup



IV, intravenous; LY, life year; PR, platinum rechallenge; QALY, quality-adjusted life year; TOP, topotecan.

- In a probabilistic sensitivity analysis, lurbinectedin was 91%, 95%, and 100% likely to be cost-effective compared with PR, TOP-IV, and TOP-oral at a WTP threshold of $100,000/QALY, respectively (**Figure 5**)

Figure 5. Cost-Effectiveness Acceptability Curve: Platinum-Sensitive Subgroup



ICER, incremental cost-effectiveness ratio; IV, intravenous; PR, platinum rechallenge; TOP, topotecan.

Limitations

- The HRs for the comparative effectiveness of lurbinectedin were derived from studies with defined follow-up time.[2,6,7] However, the HRs were applied over the lifetime of the patients in the model, beyond the follow-up time of the studies
- The HRs for the treatment benefit of lurbinectedin vs its comparators were not varied in the probabilistic sensitivity analysis and therefore lacked uncertainty
  - Future considerations include introducing uncertainty to the lurbinectedin HRs or modeling separate survival curves for all treatments instead of using HRs
- For lurbinectedin vs the ECA in the overall population, the PFS HR was assumed to be the same as OS HR, due to a lack of data on PFS. This is a conservative assumption as it is generally easier to improve PFS than OS
- Only myelosuppression-related SAEs were modeled, leading to a potential underestimation of the cost and disutility of SAEs
- No SCLC-specific utility data were found during the development of this model. The utility values for progression-free and progressed disease were from different publications studying patients with non-small cell lung cancer.[8,9] It is possible for the difference in patient population and study design of those studies to introduce bias

Conclusions

- Lurbinectedin is a cost-effective second-line treatment for patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. ICERs were well below the commonly accepted WTP threshold of $100,000/QALY to $150,000/QALY.[20] Probabilistic sensitivity analysis results showed that this conclusion still held true under real-world uncertainty
- The higher acquisition cost of lurbinectedin was partially offset by its lower myelosuppression prophylaxis cost compared with ECA, TOP-IV, and TOP-oral, as well as lower myelosuppression-related SAE management cost compared with PR

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Support and Acknowledgments: This study was supported by Jazz Pharmaceuticals. Medical writing support, under the direction of the authors, was provided by Ellen Woon, PhD, of CMC AFFINITY, a division of IPG Health Medical Communications, with funding from Jazz Pharmaceuticals, in accordance with Good Publication Practice (GPP 2022) guidelines.

Disclosures: W Su, B Rengarajan, and **D Profant** are employees of and hold stock ownership/options in Jazz Pharmaceuticals. **K Mayo** was an employee of and held stock ownership/options in Jazz Pharmaceuticals at the time of the analysis. **M Groff** and **G Tremblay** are employees of Cytel Incorporated. **AK Ganti** has received consulting fees from AstraZeneca, Flagship Biosciences, G1 Therapeutics, Jazz Pharmaceuticals, Cardinal Health, Mirati Therapeutics, BeiGene Ltd., Sanofi Genzyme, Blueprint Medicines, and Regeneron Pharmaceuticals; research support from Takeda; data and safety monitoring committee fees from Y-mAbs Therapeutics; and research funding from Merck, TAB Biosciences, Nektar Therapeutics, Mirati Therapeutics, and Iovance Biotherapeutics.

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Poster presented at ISPOR 2023 Annual Meeting, May 7-10, 2023, Boston, Massachusetts