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Real-world Outcomes of Second-line Patients With Small Cell Lung Cancer Treated With Lurbinectedin

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Introduction

- Lurbinectedin is a novel agent that inhibits oncogenic transcription through the preferential binding of guanines located in guanine-cytosine-rich regulatory areas
- Lurbinectedin is the first US Food and Drug Administration-approved treatment option for second-line (2L) relapsed/refractory small cell lung cancer (SCLC) in over 20 years, and is approved for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy[1]
- Accelerated approval was based on a single-arm, phase 2 trial (N=105), in which lurbinectedin demonstrated an overall response rate of 35.2%, median progression-free survival of 3.5 months (95% confidence interval [CI]: 2.6, 4.3 months), and a manageable safety profile[2]

Objective

- This study describes clinical characteristics, treatment patterns, and outcomes including real-world progression-free survival (rwPFS), time to discontinuation (TTD), and time to next treatment or death (TTNT/D) in patients with SCLC treated with 2L lurbinectedin monotherapy in a real-world setting

Methods

- This study used the US nationwide Flatiron Health electronic health record-derived de-identified database. The Flatiron Health database is a longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction[3,4]
- Patients with histologically confirmed SCLC aged ⩾18 years old and treated with lurbinectedin monotherapy in 2L between 15 June 2020 (approval date in the United States) and 31 December 2021 (three months prior to the end of available data within the dataset) were included in this study
- The index date was defined as the date of treatment initiation with 2L lurbinectedin monotherapy
- Stage at diagnosis was defined as the earliest stage observed using the following grouping: limited stage = Group 0–3 or limited; extensive stage = Group 4+ or extensive. Patients with both limited and extensive stage on the same day were classified as extensive
- Patients were excluded if they met any of the following criteria:
  - Patients without first-line (1L) platinum-based (carboplatin, cisplatin, oxaliplatin) chemotherapy
  - Gap in structured clinical activity (as measured by vital visits, medication administrations, and lab testing) >120 days between SCLC diagnosis date and index date
  - Participation in a clinical trial at any time prior to or during the 2L treatment with lurbinectedin (identified by use of 'clinical study drug')
  - Received lurbinectedin as 1L therapy
- Clinical characteristics and demographics were assessed in the period between initial SCLC diagnosis and index date
- Treatment patterns were assessed in the line prior to lurbinectedin initiation (1L), during the line of lurbinectedin treatment (2L), and in the line following lurbinectedin treatment (third-line [3L])
- Outcomes were assessed using Kaplan-Meier methods
- Outcomes and CTFI are defined in **Table 1**
- Results were evaluated among all patients and the subsets of patients with chemotherapy-free interval (CTFI) ⩾90 days and ⩾180 days

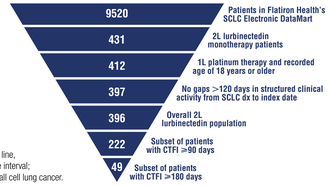
Table 1. Real-world Outcome and CTFI Definitions

Outcome	Definitions
rwPFS	The time from index to progression or death
TTD	The time from index to discontinuation due to any cause, including next treatment or death
TTNT/D	The time from index to next treatment or death
CTFI	The time from last platinum therapy dose to progression or start of 2L (in the absence of progression)

CTFI, chemotherapy-free interval; rwPFS, real-world progression-free survival; TTD, time to discontinuation; TTNT/D, time to next treatment or death.

Results

Figure 1. Patient Attrition and CTFI Subgroups



1L, first line; 2L, second line, CTFI, chemotherapy-free interval; dx, diagnosis; SCLC, small cell lung cancer.

Patient Demographics and Clinical Characteristics

- A total of 396 patients treated with lurbinectedin as 2L monotherapy were included
- Of the 396 patients, 222 had a CTFI ⩾90 days and 49 had a CTFI ⩾180 days

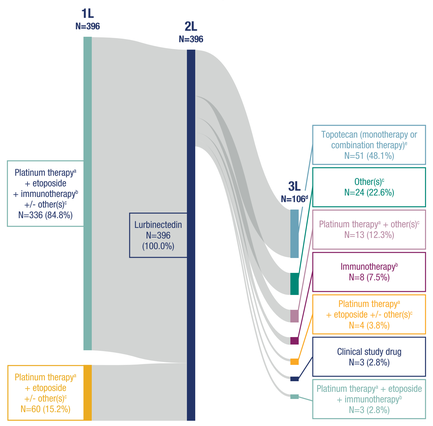
Table 2. Demographics, Clinical Characteristics, and Treatment Patterns of 2L Patients Treated With Lurbinectedin Monotherapy

	Overall	CTFI ⩾90 Days	CTFI ⩾180 Days
N (%[a])	396	222 (56.1%)	49 (12.4%)
Median (IQR) age at index, years	67.0 (61.0, 73.0)	66.0 (60.0, 73.0)	67.0 (60.0, 73.5)
ECOG Status at Index, Among Those With Recorded ECOG Status (N=340)[b]			
0	97 (28.5%)	56 (29.6%)	16 (41%)
1	171 (50.3%)	93 (49.2%)	18 (46.2%)
2	68 (20.0%)	39 (20.6%)	5 (12.8%)
3	4 (1.2%)	1 (0.5%)	0 (0.0%)
Stage at Diagnosis			
Limited stage	61 (15.4%)	39 (17.6%)	11 (22.4%)
Extensive stage	335 (84.6%)	183 (82.4%)	38 (77.6%)
Number of Cycles of Lurbinectedin in 2L[c]			
Mean (SD)	4.3 (3.2)	4.8 (3.3)	5.7 (3.6)
Median (IQR)	3.0 (2.0, 6.0)	4.0 (2.0, 7.0)	6.0 (2.0, 8.0)

2L, second line; CTFI, chemotherapy-free interval; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; SD, standard deviation.
[a]% of overall.
[b]Assessed within 30 days prior to index; percentage reported among those with a recorded ECOG status (N=340). 14.1%, 14.9% and 20.4% of patients had no recorded ECOG among the overall, CTFI ⩾90 days, and CTFI ⩾180 days groups, respectively.
[c]Defined as the number of lurbinectedin administrations/orders received from start to end of 2L.

- Median age was 67 years and 84.6% of patients had extensive-stage disease at initial diagnosis
- Among the 340 (85.9% out of 396) patients with recorded Eastern Cooperative Oncology Group (ECOG) performance status in the 30 days prior to index, 28.5% had a score of 0, 50.3% had a score of 1, and 20.0% had a score of 2
- Patients had a median of 3 lurbinectedin cycles (4 and 6 cycles for CTFI ⩾90 days and ⩾180 days, respectively)

Figure 2. Recorded 1L, 2L, and 3L Treatments for the Overall 2L Lurbinectedin Monotherapy Population



1L, first line; 2L, second line; 3L, third line.
[a]Platinum therapy = cisplatin or carboplatin.
[b]Immunotherapy = atezolizumab, bevacizumab-bvzr, durvalumab, ipilimumab, nivolumab, or pembrolizumab.
[c]Other(s) = cyclophosphamide, docetaxel, doxorubicin, gemcitabine, irinotecan, paclitaxel, temozolomide, or vincristine.
[d]There are two lurbinectedin patients who retried lurbinectedin after a 90-day gap in treatment and are excluded from the recorded 3L group.
[e]Topotecan alone or in combination with lurbinectedin, immunotherapy, or other(s).

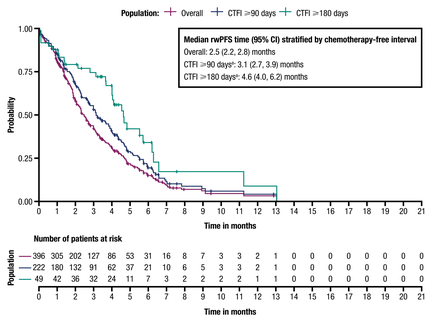
Treatment Patterns and Characteristics

- Among patients included in this study, 84.8% of patients received immunotherapy in combination with platinum therapy in the 1L setting
- 26.8% of patients had a recorded 3L treatment after their 2L lurbinectedin treatment; 288 did not have subsequent therapy

Outcomes

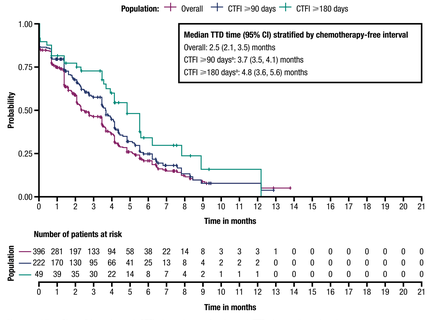
- Median rwPFS was 2.5 months (95% CI: 2.2, 2.8 months) in the overall population and was longer in the subsets of patients with CTFI ⩾90 days (3.1; 95% CI: 2.7, 3.9) and ⩾180 days (4.6; 95% CI: 4.0, 6.2) (**Figure 3**)
- Longer median rwPFS, TTD, and TTNT/D times were seen in the subset of patients with CTFI ⩾90 days and ⩾180 days across all outcomes assessed (**Figures 3, 4 and 5**)

Figure 3. rwPFS for the Overall 2L Lurbinectedin Monotherapy Population and Subsets of Patients With CTFI ⩾90 Days and ⩾180 Days[a]



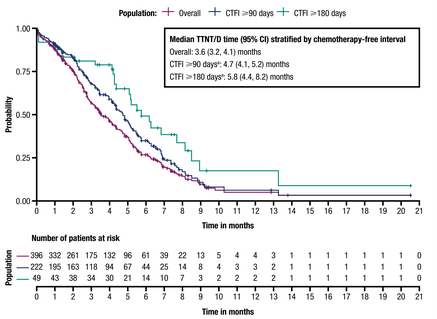
2L, second line; CI, confidence interval; CTFI, chemotherapy-free interval; rwPFS, real-world progression-free survival.
[a]Patients in the CTFI ⩾90 days group are a subset of the overall population. Patients in the CTFI ⩾180 days group are a subset of the CTFI ⩾90 days group.

Figure 4. TTD for the Overall 2L Lurbinectedin Monotherapy Population and Subsets of Patients With CTFI ⩾90 Days and ⩾180 Days[a]



2L, second line; CI, confidence interval; CTFI, chemotherapy-free interval; TTD, time to discontinuation.
[a]Patients in the CTFI ⩾90 days group are a subset of the overall population. Patients in the CTFI ⩾180 days group are a subset of the CTFI ⩾90 days group.

Figure 5. TTNT/D for the Overall 2L Lurbinectedin Monotherapy Population and Subsets of Patients With CTFI ⩾90 Days and ⩾180 Days[a]



2L, second line; CI, confidence interval; CTFI, chemotherapy-free interval; TTNT/D, time to next treatment or death.
[a]Patients in the CTFI ⩾90 days group are a subset of the overall population. Patients in the CTFI ⩾180 days group are a subset of the CTFI ⩾90 days group.

Discussion/Limitations

- Patients in this study were different from the lurbinectedin single-arm trial. In this study, a higher percentage of patients had extensive-stage disease at diagnosis and ECOG score of 2 than the phase 2 single-arm trial
- Unlike a clinical trial, the data being used are not collected for the purpose of a study and miscoding is possible, which could lead to misclassification bias

Conclusions

- Despite different clinical characteristics in the real-world population than what was observed in the single-arm trial, patients treated with lurbinectedin as 2L monotherapy in this real-world setting had a median rwPFS estimate interval within the PFS bounds observed in the phase 2 single-arm clinical trial
- Lurbinectedin provides a treatment option for relapsed SCLC patients, including those with platinum-sensitive disease

References: 1. FDA Grants Accelerated Approval to Lurbinectedin for Metastatic Small Cell Lung Cancer. US Food and Drug Administration. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-lurbinectedin-metastatic-small-cell-lung-cancer. Accessed 8 August 2022. **2.** Trigo J, et al. *Lancet Oncol.* 2020;21(5):645–654. **3.** Ma X, et al. *medRxiv.* https://doi.org/10.1101/2020.03.16.20037143. Accessed 22 August 2022. **4.** Birnbaum B, et al. https://arxiv.org/abs/2001.09765. Accessed 22 August 2022.

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