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FDA Approval Summary: Lurbinectedin for the Treatment of Metastatic Small Cell Lung Cancer

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Abstract

On June 15, 2020, the Food and Drug Administration granted accelerated approval to lurbinectedin for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. Approval was granted based on the clinically meaningful effects on overall response rate (ORR) and duration of response (DOR), and the safety profile observed in a multicenter, open-label, multi-cohort clinical trial (PM1183-B-005-14, NCT02454972), referred to as Study B-005, in patients with advanced solid tumors. The trial included a cohort of 105 patients with metastatic SCLC who had disease progression on or after platinum-based chemotherapy. The confirmed ORR determined by investigator assessment using RECIST 1.1 in the approved SCLC patient population was 35% (95% CI: 26, 45), with a median DOR of 5.3 (95% CI: 4.1, 6.4) months. The drug label includes warnings and precautions for myelosuppression, hepatotoxicity, and embryo-fetal toxicity. This is the first drug approved by the FDA in over 20 years in the second line for patients with metastatic SCLC. Importantly, this approval includes an indication for patients who have platinum-resistant disease, representing an area of particular unmet need.

Introduction

SCLC is a highly aggressive neuroendocrine lung malignancy that accounts for 15% of all lung cancers (1). It represents a major cause of cancer mortality, responsible for approximately 250, 000 deaths worldwide annually with only 7% of patients surviving five years from diagnosis (2). The majority of patients present with extensive-stage SCLC (ES-SCLC), which includes metastatic disease, and is defined as disease that extends beyond the supraclavicular areas, with malignant pleural or pericardial effusion or hematogenous spread.

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Although SCLC is initially responsive to cytotoxic chemotherapy which may be administered in approved combination with checkpoint inhibitors targeting the PD-1 pathway, nearly all tumors recur and are resistant to further treatment. Patients with ES-SCLC who progress following platinum-based therapy are generally classified as having either platinum-sensitive or -resistant disease. The chemotherapy-free interval (CTFI), defined as the length of time from last platinum dose to time of relapse or disease progression, is the strongest predictor of outcome in these patients (3,4). Patients with sensitive disease who experience disease recurrence or progression at 90 days or greater have tumor response rate of approximately 25% to additional chemotherapy, whereas patients with resistant disease exhibit tumor response rates of less than 10% (5).

Prior to 2019, patients with newly diagnosed ES-SCLC were treated with four to six cycles of platinum-based chemotherapy. In 2019, FDA approved atezolizumab in combination with carboplatin and etoposide for the first-line treatment of patients with ES-SCLC based on an improvement in overall survival (6). More recently, FDA approved durvalumab in combination with etoposide and either carboplatin or cisplatin as first-line treatment of patients with ES-SCLC (7). These recent approvals in the first-line setting affirmed the benefit of adding immunotherapy to chemotherapy for newly diagnosed ES-SCLC. Table 1 outlines first and second-line available therapies for patients with ES-SCLC.

Management of SCLC in the second-line depends on duration of remission after initial therapy. Treatment paradigms may include re-treatment with a platinum-based combination for patients with disease progression or recurrence more than 6 months after initial chemotherapy, or single-agent chemotherapy and palliative radiotherapy for patients with progression or recurrence within 6 months of completion of first-line treatment (8). Topotecan, approved in 1998, is the only FDA-approved agent for recurrent or progressive SCLC, specifically for patients with platinum-sensitive disease (9). In this setting, topotecan has shown a response rate of 24% (95% CI: 16, 32) with median DOR of 3.3 months (95% CI: 3.0, 4.1).

The FDA granted accelerated approval to lurbinectedin on June 15, 2020, for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy, representing the first approval in the immediate post-platinum setting in over 20 years. Herein, we provide a summary of FDA’s review of the marketing application that led to approval of lurbinectedin.

Regulatory History

Orphan Drug Designation was granted to lurbinectedin in 2018 for the treatment of SCLC. FDA met with Pharma Mar USA, Inc. in several multidisciplinary meetings from 2015 through 2019 to discuss the content of the new drug application (NDA) and the design of a potential confirmatory trial. The NDA was submitted on December 16, 2019, and was granted priority review due to the unmet medical need of the intended patient population.

Mechanism of Action

Lurbinectedin is an alkylating drug that binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix towards the major groove.

Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in eventual double-strand breaks and ultimately leading to cell death. Consistent with its mechanism of action, lurbinectedin had antiproliferative and cytotoxic activity in multiple tumor cell lines and displayed enhanced activity in cell lines with defects in DNA mismatch repair. Incubation with lurbinectedin also resulted in increased cell death of human monocytes and, at lower concentrations, decreased migration and chemokine production. In mouse xenograft models, administration of lurbinectedin inhibited growth of a variety of human tumors, including SCLC.

Nonclinical toxicology

Toxicological assessment of lurbinectedin was conducted in the Sprague Dawley rat, Beagle dog and Cynomolgus monkey. All three species exhibited injection site findings including hemorrhage, edema, inflammation, thrombosis, and necrosis, as well as bone marrow effects of transient leukopenia, mild anemia and decreased cellularity. Gastrointestinal (GI) tract toxicity was also common at high dose levels in all species, and in the 4-week rat study, there were signs of liver toxicity including large increases in liver enzymes and bilirubin at the high dose of lurbinectedin. Myelosuppression, GI and liver toxicity were commonly observed in clinical studies.

Clinical Pharmacology

FDA reviewed the clinical pharmacology characteristics of lurbinectedin in various studies, including the pivotal trial PM1183-B-005-14 (NCT02454972), hereafter referred to as Study B-005, and PM1183-C-004-14 (CORAIL), a supportive study in patients with ovarian cancer (10).

The approved dosing regimen is 3.2 mg/m^2 every 21 days, and the elimination half-life is 51 hours following intravenous infusion over 60 minutes. Lurbinectedin exposure-response relationships for efficacy have not been fully characterized given the limited data from Study B-005 at a single dose level in a small number of patients; however, a numerical trend for better efficacy at higher lurbinectedin exposure was observed, especially for patients with platinum-sensitive SCLC (CTFI ≥ 90 days). Higher exposure also correlated with higher probability of adverse events (AEs) including Grade 4 neutropenia and Grade ≥ 3 thrombocytopenia.

Lurbinectedin is primarily metabolized by CYP3A4, *in vitro*. As no dedicated clinical drug-interaction studies with modulators of CYP3A4 were conducted, FDA issued a post-marketing requirement (PMR) to characterize the effect of CYP3A4 modulators on lurbinectedin exposure. Furthermore, the drug label recommends to avoid coadministering lurbinectedin with strong or moderate CYP3A4 inhibitors and strong or moderate CYP3A4 inducers. When the coadministration of moderate CYP3A4 inhibitors cannot be avoided, the product label recommends to consider dose reduction if clinically indicated based on adverse events (neutropenia, thrombocytopenia, and hepatotoxicity).

No clinically significant differences in the exposure of lurbinectedin were identified based on age, sex, body weight, mild to moderate renal impairment or mild hepatic impairment. In

the pivotal trial (Study B-005), patients with hepatic function that exceeded mild impairment were excluded. Therefore, the effect of moderate or severe hepatic impairment on the pharmacokinetics of lurbinectedin has not yet been studied. As the primary elimination pathway of lurbinectedin is hepatic clearance, FDA issued a PMR to characterize the effect of varying degrees of hepatic impairment on lurbinectedin exposure. Renal excretion represents only 6% of lurbinectedin elimination. Lurbinectedin did not prolong the QT interval at the recommended dosing regimen of 3.2 mg/m^2 every 21 days.

Clinical Trial Design

The efficacy of lurbinectedin was evaluated in 105 patients with SCLC enrolled in Study B-005, a single-arm cohort in a multicenter, open-label, multi-cohort clinical trial (PM1183-B-005-14, NCT02454972). The major efficacy outcome measures were confirmed ORR determined by investigator assessment according to RECIST v 1.1 and DOR. Lurbinectedin was administered at a dose of 3.2 mg/m^2 by 60-minute intravenous infusion on day 1 of each 21-day cycle until disease progression or unacceptable toxicity.

Results

As of the January 15, 2019, data cut-off used for the safety and efficacy analyses of this NDA, Study B-005 had enrolled and treated 105 patients with SCLC who had documented disease progression after receiving only one prior chemotherapy-containing line. The efficacy population consists of all patients who received any partial or complete infusion of lurbinectedin. At the time of the database lock, treatment was discontinued by 90% (n=94) of patients, with 10% (n=11) still receiving therapy and 37% (n=39) still alive. Median follow-up time for patients in the SCLC cohort was 17.1 months.

Patient demographics and baseline disease characteristics are shown in Tables 2 and 3. Median age was 60 years (range 40–83) and 9% of patients were ≥75 years old. At initial diagnosis, the majority of patients (70%) had extensive-stage disease, and 30% had limited-stage disease. At the time of study enrollment, 102 of the 105 patients (97%) had metastatic disease (either distant or locoregional metastasis).

All patients had received prior platinum-based therapy, 57% had sensitive disease, defined as CTFI ≥ 90 days, and 43% had resistant disease defined as CTFI < 90 days. Additionally, 8% had received prior immunotherapy. Two patients were listed as receiving prior surgery, one curative and the other palliative. Prior radiotherapy was received by 72% of patients and 58% had prophylactic cranial irradiation (PCI).

Efficacy:

Efficacy results are shown in Table 4.

Safety:

Safety of single-agent lurbinectedin at a dose of 3.2 mg/m^2 was assessed in patients with a variety of advanced solid tumors, including SCLC. Five hundred and fifty-four patients received lurbinectedin in Study B-005 (n=335) and in CORAIL (n=219), a clinical trial in

patients with platinum-resistant ovarian cancer. Median duration of exposure was 3.3 months in the SCLC cohort and 3.1 months in the overall safety population (n=554).

The most common (≥20%) treatment-emergent adverse reactions (AR) that occurred on or within 30 days after the last dose of lurbinectedin are listed in Supplementary Table 1; laboratory values are presented in Supplementary Table 2. The most common Grade ≥ 3 ARs were fatigue (12%), pneumonia (7%), dyspnea (6%), respiratory traction infection (5%), and musculoskeletal pain (4%).

Permanent discontinuation due to an adverse reaction, including peripheral neuropathy and myelosuppression, occurred in 2% of patients with SCLC who received lurbinectedin. Dosage interruptions due to an adverse reaction occurred in 30% of patients; adverse reactions requiring dose interruptions in ≥ 3% of patients included neutropenia and hypoalbuminemia. Dose reductions due to an adverse reaction occurred in 25% of patients; adverse reactions requiring dosage reductions in ≥ 3% of patients included neutropenia, febrile neutropenia and fatigue.

Serious adverse reactions occurred in 34% of patients who received lurbinectedin. The most frequent serious adverse reaction (in ≥ 3% of patients) were pneumonia, febrile neutropenia, neutropenia, respiratory traction infection, anemia, dyspnea and thrombocytopenia. Fatal adverse reactions were not observed in the SCLC cohort of Study B-005.

Myelosuppression occurred at a substantial rate among patients treated with lurbinectedin. In the overall safety population, 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. Grade 3 or 4 thrombocytopenia occurred in 10% of patients, and Grade 3 or 4 anemia occurred in 17% of patients. Complications associated with bone marrow suppression including febrile neutropenia and sepsis occurred in 7% and 2% of patients, respectively. All cases of sepsis occurred in patients with solid tumors other than SCLC, and 1% of these cases were fatal. The protocol of Study B-005 permitted patients to receive G-CSF for secondary prophylaxis (i.e., after patients had an initial decrease in WBC), but not primary prophylaxis, and for isolated Grade 4 neutropenia (rather than undergo dose reduction). The drug label advises monitoring of blood counts prior to each administration of lurbinectedin, with use of G-CSF recommended for neutrophil counts less than 500 cells/mm^3.

Additionally, hepatotoxicity was observed in the overall safety population with 61% of patients experiencing increased alanine aminotransferase (ALT) and 42% experiencing increased aspartate aminotransferase (AST); however, the rates of Grade 3 and 4 elevations were low. The median time to onset of Grade 3 or higher transaminase elevation was 8 days with a median duration of 7 days. Providers are advised to monitor liver function tests prior to initiating lurbinectedin and regularly throughout treatment, as listed in the label, with recommendations to withhold, reduce the dose or permanently discontinue based on severity.

Regulatory Insights

The approval of lurbinectedin represents the first approval for metastatic SCLC in the immediate post-platinum setting. Table 1 outlines available therapies in the first and second-

line treatment of patients with ES-SCLC. Topotecan is the only other FDA-approved drug in the second-line setting and was approved over two decades ago. This accelerated approval is supported by the efficacy results of one single-arm trial, Study B-005, which demonstrated a response rate of 35% (95% CI: 26, 45) and DOR of 5.3 months (95% CI: 4.1, 6.4), constituting a meaningful advantage over available therapy. Importantly, efficacy of lurbinectedin was observed in both the platinum-resistant and platinum-sensitive populations with ORR of 22% (95% CI: 11, 37) and 45% (95% CI: 32, 58), respectively.

Furthermore, based on safety findings in 554 patients with advanced solid tumors, lurbinectedin has a safety profile that is considered acceptable to the intended population given the life-threatening nature of metastatic SCLC. Patients with SCLC experienced similar rates of AEs and dose delays due to AEs regardless of chemosensitivity. Lurbinectedin is also administered on a less frequent schedule (once every 21 days) in contrast to topotecan which is infused daily for 5 consecutive days in each 21-day cycle.

Study B-005 was initiated prior to the approval of immunotherapy (atezolizumab in 2019, and durvalumab in 2020) for front-line treatment of ES-SCLC. Accordingly, eligibility criteria required patients to have received one line of prior platinum-based chemotherapy as was considered standard management for ES-SCLC at the time of patient enrollment (2015 to 2018), and the SCLC cohort included only 8 patients who had also received prior immunotherapy (either atezolizumab or nivolumab). There were 5 partial responses observed among these 8 patients for an ORR of 63% (95% CI: 24, 91); however, due to the limited sample size, these results must be interpreted with caution. The true efficacy of lurbinectedin in the second-line in patients who have progressed on or after treatment with a checkpoint inhibitor is not yet known.

Continued approval of lurbinectedin is contingent upon verification of clinical benefit in a confirmatory study. ATLANTIS (NCT02566993) is a randomized, controlled trial in patients with SCLC who had disease progression after platinum-based chemotherapy and subsequently received either the study regimen of doxorubicin and lurbinectedin, or investigator's choice of chemotherapy (cyclophosphamide, doxorubicin and vincristine [CAV], or topotecan) as control. The primary endpoint is overall survival.

Conclusions

The favorable benefit-risk evaluation of Study B-005 supported accelerated approval of lurbinectedin in adult patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy. An additional trial, ATLANTIS, to verify the clinical benefit of lurbinectedin has completed accrual.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Pietanza MC, Byers LA, Minna JD, Rudin C. Small cell lung cancer: will recent progressive lead to improved outcomes? Clin Cancer Res 2016;21(10):2244–2255.
2. Gazdar AF, Bunn PA, Minna JD. Small-cell lung cancer: what we know, what we need to know and the path forward. Nat Rev Cancer 2017;17:725–737. [PubMed: 29077690]
3. Gong J, Salgia R. Managing patients with relapsed small-cell lung cancer. J Oncol Pract 2018;14(6):359–366. [PubMed: 29894664]
4. Lara PN, Moon J, Redman MW, Semrad TJ, Kelly K, Allen JW, et al. Relevance of platinum sensitivity status in relapsed/refractory extensive stage small cell lung cancer (ES-SCLC) in the modern era: a patient level analysis of SWOG trials. J Thorac Oncol 2016;10(1):110–115.
5. Neal JW, Gubens MA, Wakelee HA. Current management of small cell lung cancer. Clin Chest Med 2011;32:853–863. [PubMed: 22054891]
6. Drug Approval Package: TECENTRIQ (atezolizumab). Drugs@FDA [database on the Internet]. Silver Spring (MD): U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761034
7. Drug Approval Package: IMFINZI (durvalumab). Drugs@FDA [database on the Internet]. Silver Spring (MD): U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process
8. National Comprehensive Cancer Network Guidelines, version 1.2021. Small Cell Lung Cancer; 2020. Available from: https://www.nccn.org/professionals/physiciangls/pdf/sclc.pdf
9. Drug Approval Package: HYCAMTIN (topotecan). Drugs@FDA [database on the Internet]. Silver Spring (MD): U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=020671
10. Drug Approval Package: ZEPZELCA (lurbinectedin). Drugs@FDA [database on the Internet]. Silver Spring (MD): U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=213702
11. Pharmaceuticals Jazz, Inc. ZEPZELCA (lurbinectedin) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213702s000lbl.pdf

Table 1:

Summary of Condition and Available Therapies

Disease	Current Treatment Options
Metastatic SCLC	First-line treatment for patients with newly diagnosed ES-SCLC, including metastatic SCLC, consists of platinum-based chemotherapy with FDA-approved immunotherapy (atezolizumab or durvalumab) (ref 6, 7). Second-line treatment options include: • Retreatment with a platinum-based regimen (for patients with recurrence >6 months from last dose of platinum) or use of single-agent chemotherapy. • Topotecan is the only FDA-approved therapy for patients with recurrent or progressive SCLC, specifically for patients with platinum-sensitive disease (9). Prior to lurbinectedin, there was no approved therapy for patients with platinum-resistant disease that has no response to or disease progression after first-line chemotherapy.

Data from the following sources:

Drug Approval Package: TECENTRIQ (atezolizumab). Drugs@FDA [database on the Internet]. *Silver Spring (MD)*: U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761034 (ref. 6)

Drug Approval Package: IMFINZI (durvalumab). Drugs@FDA [database on the Internet]. *Silver Spring (MD)*: U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process (ref. 7)

Drug Approval Package: HYCAMTIN (topotecan). Drugs@FDA [database on the Internet]. *Silver Spring (MD)*: U.S. Food and Drug Administration. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=020671 (ref. 9)

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Table 2:

Demographics of Patients in SCLC Cohort in Study B-005

Demographic, n (%)	All SCLC (N=105)	Sensitive CTFI ≥ 90 days (N=60)	Resistant CTFI < 90 days (N=45)
Sex			
Female	42 (40%)	25 (42%)	17 (38%)
Male	63 (60%)	35 (58%)	28 (62%)
Age			
Median (min, max)	60 (40, 83)	59 (44, 79)	66 (40, 83)
< 65 yo	68 (65%)	46 (77%)	22 (49%)
≥ 65 yo	37 (35%)	14 (23%)	23 (51%)
≥ 75 yo	9 (9%)	5 (8%)	4 (9%)
Race			
White	79 (75%)	47 (78%)	32 (71%)
Asian	1 (1%)	1 (2%)	0 (0%)
Black or African American	1 (1%)	0 (0%)	1 (2%)
Other[a]	24 (23%)	12 (20%)	12 (27%)
Region			
Europe	94 (90%)	56 (93%)	38 (84%)
USA	11 (10%)	4 (7%)	7 (16%)
Baseline ECOG			
0	38 (36%)	27 (45%)	11 (24%)
1	59 (56%)	30 (50%)	29 (64%)
2	8 (8%)	3 (5%)	5 (11%)
Smoking status			
Current/former	97 (92%)	54 (90%)	43 (96%)
Never	8 (8%)	6 (10%)	2 (4%)

[a]Data on race and/or ethnicity were not collected in France and Belgium because of local regulations.

Abbreviations: SCLC: small cell lung cancer; CTFI: chemotherapy-free interval

Source: Drug Approval Package: ZEPZELCA (lurbinectedin) (Ref. 10)

Table 3:

Baseline Disease Characteristics of Patients in SCLC Cohort in Study B-005

Characteristic, n (%)	All SCLC (N=105)	Sensitive CTFI ≥ 90 days (N=60)	Resistant CTFI <90 days (N=45)
SCLC stage at diagnosis			
Extensive	73 (70%)	35 (58%)	38 (84%)
Limited	32 (30%)	25 (42%)	7 (16%)
Prior therapies			
1 line	98 (93%)	57 (95%)	41 (91%)
2 lines	7 (7%)	3 (5%)	4 (9%)
Prior radiotherapy	76 (72%)	57 (95%)	19 (42%)
Prophylactic cranial irradiation	61 (58%)	47 (78%)	14 (31%)
Prior immunotherapy	8 (8%)	3 (5%)	5 (11%)

Abbreviations: SCLC: small cell lung cancer; CTFI: chemotherapy-free interval

Source: Drug Approval Package: ZEPZELCA (lurbinectedin) (Ref. 10)

Table 4:

Overall Response Rates and Duration of Response of Patients in SCLC Cohort in Study B-005

Investigator Assessed Response	All SCLC N=105	Sensitive CTFI ≥ 90 days N=60	Resistant CTFI < 90 days N=45
Overall Response Rate (95% CI)	35% (26, 45)	45% (32, 58)	22% (11, 37)
Complete response, n (%)	0 (0)	0 (0)	0 (0)
Partial response, n (%)	37 (35)	27 (45)	10 (22)
Median DOR months (95% CI)	5.3 (4.1, 6.4)	6.2 (3.5, 7.3)	4.7 (2.6, 5.6)
≥ 6 months DOR, n (%)	13 (35)	12 (44)	1 (10)
IRC Assessed Response			
Overall Response Rate (95% CI)	30.5% (22 40)	43% (31, 57)	13% (5, 27)
Complete response, n (%)	0 (0)	0 (0)	0 (0)
Partial response, n (%)	32 (30)	26 (43)	6 (13)
Median DOR months (95% CI)	5.1 (4.9, 6.4)	5.3 (4.9, 7.0)	4.8 (2.4, 5.3)
≥ 6 months DOR, n (%)	8 (25)	8 (31)	0 (0)

Abbreviations: CI: confidence interval; CTFI: chemotherapy-free interval; DOR: duration of response; IRC: independent review committee; SCLC: small cell lung cancer.

Source: ZEPZELCA (lurbinectedin) [package insert] (Ref. 11)