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Real-World Effectiveness and Safety of Lurbinectedin for Previously Treated Extensive-Stage Small Cell Lung Cancer: Final Primary and Subgroup Analysis Results of Jazz EMERGE 402

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Objective

- We report primary results from the final data analysis of the Jazz EMERGE 402 observational trial and outcomes for select subgroups of interest with previously treated extensive-stage small cell lung cancer (ES-SCLC)

Conclusions

- Jazz EMERGE 402 enrolled a broader population of patients with previously treated ES-SCLC than the phase 2 basket trial,[1] including those who were heavily pretreated, older, had brain or hepatic metastases, had worse performance status, and had received prior immunotherapy
- The favorable effectiveness and safety profiles noted in this real-world study are consistent with the clinical trial outcomes that led to the accelerated approval of lurbinectedin monotherapy, reflected in the current lurbinectedin prescribing information
- A recent report from EMERGE 402 showed that those who had baseline brain metastases and those with platinum-resistant disease derived less overall benefit from lurbinectedin monotherapy[2]
- In this analysis of additional key subgroups, better performance status at baseline was associated with longer overall survival with lurbinectedin monotherapy
- Lurbinectedin showed a predictable and manageable safety profile with low rates of dose reductions and treatment discontinuations due to adverse events
  - Serious hematologic abnormalities were reported at lower rates than in the pivotal phase 2 basket trial of lurbinectedin[1]
  - Granulocyte colony-stimulating factor prophylaxis likely contributed to the low rates of neutropenia reported

References: 1. Trigo J, et al. *Lancet Oncol* 2020;21:645-54. **2.** Halmos B, et al. Poster presented at: European Lung Cancer Congress 2026; March 25–28, 2026; Copenhagen, Denmark. 4298P. **3.** Jazz Pharmaceuticals, Inc. ZEPZELCA® (lurbinectedin) for injection, for intravenous use. Updated February 2026. Accessed March 17, 2026. https://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf. **4.** Swissmedic Swiss Public Assessment Report. Extension of therapeutic indication Zepzelca. Updated January 2026. Accessed March 3, 2026. https://www.swissmedic.ch/dam/swissmedic/de/dokumente/zulassung/swisspar/67729-zepzelca-02-swisspar-20260127.pdf.download.pdf/SwissPAR%20Zepzelca.pdf. **5.** Paz-Ares L, et al. *Lancet*. 2025;405:2129-43. **6.** Data on file. **7.** Jazz Pharmaceuticals, Inc. To assess the effectiveness and safety of Zepzelca in adult patients with extensive-stage small cell lung cancer (SCLC). Updated February 27, 2026. Accessed April 2, 2026. https://clinicaltrials.gov/study/NCT04894591

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Introduction

- Lurbinectedin combined with atezolizumab is approved in multiple countries, including the US and Switzerland, as first-line maintenance therapy for ES-SCLC based on results from the phase 3 IMforte trial (NCT05091567), showing statistically significant and clinically meaningful progression-free survival (PFS, stratified hazard ration [HR], 0.54; 95% CI: 0.43, 0.67) and overall survival (OS, stratified HR, 0.73; 95% CI: 0.57, 0.95) benefits with the combination regimen compared with atezolizumab alone[3-5]
  - This trial enrolled patients without brain metastases who had not progressed after induction therapy with atezolizumab, carboplatin, and etoposide[3]
- Lurbinectedin is also available in 22 countries/territories, including with accelerated approvals in the US and Switzerland, as monotherapy for the treatment of adults with metastatic SCLC that has progressed on or after platinum-based chemotherapy based on results from a phase 2 basket trial (NCT02454972)[1,3,4,6]
  - This trial excluded patients with central nervous system (CNS) involvement; of those enrolled, 93% received second-line (2L) lurbinectedin treatment, and only 8% had received prior immunotherapy[1]
  - The overall response rate (ORR) was 35% (chemotherapy-free interval [CTFI] <90 days, 22%; CTFI ≥90 days, 45%), with a median duration of response (DoR) of 5.3 months (CTFI <90 days, 4.7 months; CTFI ≥90 days, 6.2 months)[1]
- Jazz EMERGE 402 (NCT04894591)[7] was a prospective, single-arm, multicenter, phase 4 observational trial to assess the effectiveness and safety of lurbinectedin monotherapy in routine practice in the US and Canada. Jazz EMERGE 402 enrolled a broader population of patients than the population in the phase 2 basket trial, including those with baseline CNS metastases and poor performance status
  - Primary outcomes and results by line of therapy, CNS metastases, and platinum sensitivity were reported recently and showed that baseline CNS metastases and platinum resistance were associated with lower ORR and OS, respectively[2]

Methods

- Jazz EMERGE 402 included adult patients with previously treated ES-SCLC who were prescribed lurbinectedin according to the local label in the US and Canada per routine treatment practice prior to study enrollment
- Data were collected at baseline and until death, withdrawal of consent, loss to follow-up, or 24 months elapsed (whichever occurred first)
- Effectiveness and safety/tolerability outcomes were assessed in all patients and effectiveness in subgroups of interest (**Table 1**)
  - Tumor responses are reported for patients who were assessed per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) with baseline measurable disease
  - 95% CIs for tumor responses were estimated using the Clopper-Pearson exact method
  - DoR, PFS, and OS were estimated using the Kaplan-Meier method, and 95% CIs for PFS probability were generated using the Greenwood formula
  - Adjusted multivariable logistic and Cox regressions were used to assess effectiveness outcomes (ORR, PFS, OS) among selected subgroups

Table 1. Study endpoints and subgroups

Primary endpoint	Key secondary endpoints	Subgroups of interest for this poster[a]
Investigator-assessed overall response rate per RECIST v1.1	Progression-free survival Duration of response Disease control rate Overall survival Incidence and severity of adverse events Reasons for treatment discontinuation or dose reduction/delay	• Age <65 vs ≥65 years • Initial diagnosis of limited- vs extensive-stage disease • ECOG PS <2 vs ≥2

[a]Subgroups by line of treatment (second- vs third-line), platinum sensitivity (second-line with CTFI <90 vs ≥90 days), and baseline brain metastasis (second-line with vs without) were previously presented.[7]
CTFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Results

Table 2. Baseline patient demographic and clinical characteristics

	All patients N = 267
Age, median, years (min–max)	67.0 (29–89)
<65 years, n (%)	101 (38)
≥65 years, n (%)	166 (62)
Sex, n (%)	
Female	136 (51)
Male	131 (49)
Geographic region, n (%)	
Canada	60 (22)
US	207 (78)
Race, n (%)[a]	
American Indian/Alaska Native	2 (1)
Asian	7 (3)
Black or African American	24 (9)
White	224 (84)
Multiple	1 (0.4)
Ethnicity, n (%)[b]	
Hispanic or Latino	7 (3)
Not Hispanic or Latino	242 (91)
SCLC stage at initial diagnosis, n (%)	
Extensive	196 (73)
Limited	69 (26)
Missing	2 (1)
ECOG PS, n (%)	
0	45 (17)
1	133 (50)
2	45 (17)
3	7 (3)
Missing	37 (14)
CTFI, n (%)	
<30 days	51 (19)
<90 days	88 (33)
≥90 days	137 (51)
≥180 days	73 (27)
Not calculated[c]	42 (16)
Metastases sites, n (%)	
CNS	67 (25)
Liver	84 (31)
Line of therapy for lurbinectedin, n (%)	
2L	169 (63)[d]
3L	78 (29)
4L or later	20 (7)

[a]Nine patients declined to state their race. [b]Eighteen patients declined to state their ethnicity. [c]Did not have a reported progression date on first-line therapy. [d]Two patients in the 2L setting received lurbinectedin in combination with another anticancer therapy.
2L, second-line; 3L, third-line; 4L, fourth-line; CNS, central nervous system; CTFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; SCLC, small cell lung cancer

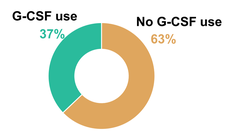
- As of the final data cutoff on July 17, 2025, 267 patients had received ≥1 cycle of lurbinectedin treatment and were followed for up to 24 months

Table 3. Lurbinectedin treatment

n (%)	All patients N = 267
Any dose modification	**45 (17)**
Dose delay	25 (9)
Dose reduction	22 (8)
Any treatment discontinuation[a]	261 (98)
Disease progression	183 (70)
Death	23 (9)
Adverse event	13 (5)
Physician decision	12 (5)
Withdrawal of consent	6 (2)
Lost to follow-up	3 (1)
Other	21 (8)

[a]Discontinuation reason per the discontinuation electronic data capture form.

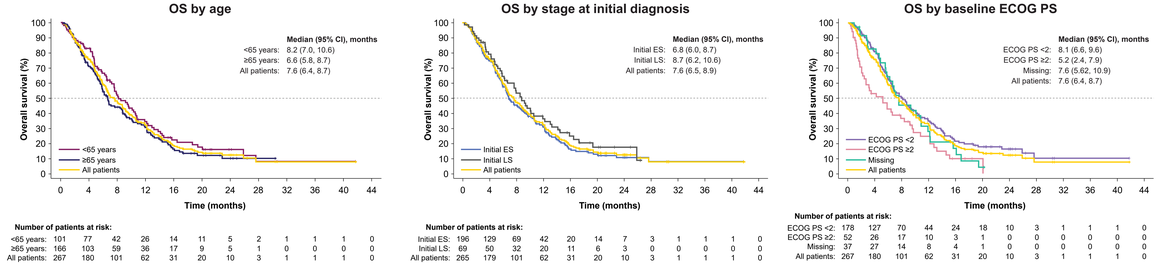
Figure 1. G-CSF prophylaxis use



G-CSF, granulocyte colony-stimulating factor.

- Median (first quartile–third quartile [Q1–Q3]) number of lurbinectedin cycles administered was 4 (2–7) with a median (Q1–Q3) duration of treatment of 91 (56–170) days
- Granulocyte colony-stimulating factor was used in 99 (37%) patients: 71 patients as a primary prophylaxis, 22 as a secondary prophylaxis, and 6 did not report the reason

Figure 2. Kaplan-Meier analysis of OS[a]



[a]Some patients had OS follow-up >24 months and were noted as protocol deviations.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; ES, extensive stage; LS, limited stage; OS, overall survival.

Table 4. Tumor responses in all patients and by subgroup[a]

	All patients n = 189[a]	Age <65 years n = 69	Age ≥65 years n = 120	Initial LS n = 54	Initial ES n = 135	ECOG PS <2 n = 127[b]	ECOG PS ≥2 n = 32[b]
ORR, n (%) [95% CI]	55 (29) [23, 36]	21 (30) [20, 43]	34 (28) [20, 37]	18 (33) [21, 47]	37 (27) [20, 36]	33 (26) [19, 35]	13 (41) [24, 59]
BOR, n (%)							
CR	8 (4)	2 (3)	6 (5)	4 (7)	4 (3)	6 (5)	1 (3)
PR	47 (25)	19 (28)	28 (23)	14 (26)	33 (24)	27 (21)	12 (38)
SD	37 (20)	15 (22)	22 (18)	9 (17)	28 (21)	28 (22)	2 (6)
PD	69 (37)	27 (39)	42 (35)	19 (35)	50 (37)	51 (40)	9 (28)
DCR,[c] n (%) [95% CI]	92 (49) [41, 56]	36 (52) [40, 64]	56 (47) [38, 56]	27 (50) [36, 64]	65 (48) [39, 57]	61 (48) [39, 57]	15 (47) [29, 65]
DoR, months, median (95% CI)	3.9 (3.0, 4.9)	4.4 (2.6, 6.4)	3.7 (2.7, 5.2)	6.2 (3.5, 7.5)	3.6 (2.6, 4.4)	4.4 (2.6, 6.3)	3.7 (2.7, 6.9)
PFS, months, median (95% CI)	3.3 (2.6, 4.1)	4.1 (2.8, 4.5)	2.9 (2.2, 3.8)	4.0 (2.4, 5.8)	3.3 (2.5, 4.1)	3.3 (2.6, 4.2)	2.6 (1.7, 5.2)
6-month PFS, % (95% CI)	24 (18, 30)	23 (14, 34)	24 (16, 32)	37 (24, 50)	18 (12, 26)	23 (16, 32)	24 (11, 40)
9-month PFS, % (95% CI)	9 (6, 15)	7 (2, 15)	11 (6, 18)	17 (8, 29)	6 (3, 12)	9 (5, 16)	10 (3, 24)

[a]All patients with measurable disease at baseline who were assessed via RECIST v1.1, including patients who received lurbinectedin as a fourth-line or later therapy and 2 patients who received lurbinectedin in combination with bevacizumab. [b]ECOG PS was missing for 30 patients. [c]Disease control was defined as a BOR of CR, PR, or SD.
BOR, best overall response; CR, complete response; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ES, extensive stage; LS, limited stage; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

- ORR, DCR, and PFS were generally similar across subgroups
- A multivariable analysis showed that Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≥2 was associated with shorter OS compared with ECOG PS <2 (HR, 1.81 [95% CI: 1.26–2.61])

Table 5. Summary of safety

n (%)	All patients (N = 267)
Any AE	162 (61)
AE leading to discontinuation	21 (8)
AE leading to dose reduction	14 (5)
Fatal AEs	32 (12)
Any SAE	107 (40)
Treatment-related SAE	29 (11)
Any TRAE	88 (33)
TRAEs occurring in ≥5% of patients, any grade	
Anemia	21 (8)
Neutropenia	19 (7)
Thrombocytopenia	15 (6)
Nausea	15 (6)
Fatigue	14 (5)
Any AESI[a]	73 (27)
Any serious AESI	19 (7)
Injection-site reaction	5 (2)
Neutropenic infection	5 (2)
Anemia	4 (1)
Neutropenia	3 (1)
Hepatic enzyme increase	2 (1)
Thrombocytopenia	2 (1)
Capillary leak syndrome	1 (0.4)
Rhabdomyolysis	1 (0.4)

[a]AESIs include grade 3/4 myelosuppression (including neutropenia, anemia, and thrombocytopenia), acute infection (in the setting of grade ≥3 neutropenia), elevated liver enzymes, injection-site reaction, capillary leak syndrome, creatine phosphokinase elevations/rhabdomyolysis, and acute myeloid leukemia/myelodysplasia.
AE, adverse event; AESI, AE of special interest; SAE, serious AE; TRAE, treatment-related AE.

- The safety profile was consistent with clinical trial experience, and no new safety signals were identified[1,5]

Limitations

- This was an observational, single-arm study, with small sample sizes in some subgroups; therefore, the findings should be interpreted with caution
- Causal relationship to effectiveness outcomes cannot be determined and may be confounded by selection bias, and uncontrolled or unobserved variables may influence outcomes
- Variation in real-world assessment practices may also affect the evaluation of effectiveness and safety