

Small Cell Lung Cancer (SCLC) – Lurbinectedin

Low Value Regimen Rationale

- Lurbinectedin received accelerated approval in 2020 for adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. The FDA approval was based on the results of a single arm phase II trial, using 2 surrogate endpoints : Overall Response Rate and Duration of Response.
- A randomized phase 3 trial- ATLANTIS – comparing lurbinectedin +doxorubicin vs Standard of Care chemotherapy failed to show an Overall Survival advantage.
- Although the dose of lurbinectedin in the ATLANTIS trial was less than the approved dose of 3.2mg/m² and it was used in combination with doxorubicin, OS was similar in the B-005 basket trial utilizing lurbinectedin 3.2mg/m². In addition, patients with CNS disease and cardiac comorbidities were excluded from lurbinectedin trials.
- In addition, lurbinectedin comes at the risk of financial toxicity at nearly 70-fold greater cost of \$42,800 dosed at 3.2mg/m² every 3 weeks compared to topotecan at \$620 for 90 days of treatment.
- More data is required to determine the true benefit for patients treated with lurbinectedin.

RECOMMENDED ALTERNATIVES

- For platinum-resistant relapse: Topotecan, Irinotecan, CAV regimen, and others.
- For platinum-sensitive relapse: Re-treatment with a platinum-based regimen. affordable utilization.

Data Summary				
	Topotecan	Cyclophosphamide, Doxorubicin, and Vincristine (CAV)	Lurbinectedin And Doxorubicin Lurbinectedin	Lurbinectedin
Trial	ATLANTIS		ATLANTIS	Study B-005
N	306		307	105
Median Age	63		63	60
Median OS, months	7.6		8.6	9.3
Median PFS, months	4		4	3.5
ORR %	29.7		31.6	30
Median DOR	3.8		5.7	5.1
Dose	Topotecan 1.5mg/m ² days 1 to 5 every 3 weeks	Cyclophosphamide 1000mg/m ² , Doxorubicin 45mg/m ² , and vincristine 2mg day 1 every 3 weeks	Doxorubicin 40mg/m ² on day 1 followed by lurbinectedin 2mg/m ² on day 1 every 3 weeks	Lurbinectedin 3.2 mg/m ² day 1 every 3 weeks
Quarterly cost	\$277	\$1,415	\$29,340	\$46,828
Grade ≥ 3 AEs (%)				
Anemia	31.1		14.5	9
Neutropenia	69.2		37	46
Thrombocytopenia	31.1		13.9	7

PATIENT SELECTION

- CNS Disease
 - Patients with CNS disease were excluded from lurbinectedin Study B-005
 - Patients with symptomatic or progressing or steroid requiring CNS involvement disease were excluded from ATLANTIS
- Patients with cardiac comorbidities were excluded from lurbinectedin trials
- Chemotherapy Treatment Free Interval (CTFI)
 - IRC assessed ORR was 13% in patients with CTFI<90 days in Study B-005
 - ORR was 20.2% (experimental) vs 18.8% (SOC) in patients with CTFI<90 days in ATLANTIS
 - NCCN Guidelines recommend rechallenge with original/similar platinum-based regimen for disease free interval >6 months and consideration for 3-6 months

References

1. Singh S, Jaigirdar AA, Mulkey F, Cheng J, Hamed SS, Li Y, Liu J, Zhao H, Goheer A, Helms WS, Wang X, Agarwal R, Pragani R, Korsah K, Tang S, Leighton J, Rahman A, Beaver JA, Pazdur R, Theoret MR, Singh H. FDA Approval Summary: Lurbinectedin for the Treatment of Metastatic Small Cell Lung Cancer. Clin Cancer Res. 2021 May 1;27(9):2378-2382. doi: 10.1158/1078-0432.CCR-20-3901. Epub 2020 Dec 7.
2. Aix SP, Ciuleanu TE, Navarro A, Cousin S, Bonanno L, Smit EF, Chiappori A, Olmedo ME, Horvath I, Grohé C, Farago AF, López-Vilariño JA, Cullell-Young M, Nieto A, Vasco N, Gómez J, Kahatt C, Zeaiter A, Carcereny E, Roubec J, Syrigos K, Lo G, Barneto I, Pope A, Sánchez A, Kattan J, Zarogoulidis K, Waller CF, Bischoff H, Juan-Vidal O, Reinmuth N, Dómine M, Paz-Ares L. Combination lurbinectedin and doxorubicin versus physician's choice of chemotherapy in patients with relapsed small-cell lung cancer (ATLANTIS): a multicentre, randomised, open-label, phase 3 trial. Lancet Respir Med. 2023 Jan;11(1):74-86. doi: 10.1016/S2213-2600(22)00309-5. Epub 2022 Oct 14. PMID: 36252599.
3. Trigo J, Subbiah V, Besse B, Moreno V, López R, Sala MA, Peters S, Ponce S, Fernández C, Alfaro V, Gómez J, Kahatt C, Zeaiter A, Zaman K, Boni V, Arrondeau J, Martínez M, Delord JP, Awada A, Kristeleit R, Olmedo ME, Wannesson L, Valdivia J, Rubio MJ, Anton A, Sarantopoulos J, Chawla SP, Mosquera-Martinez J, D'Arcangelo M, Santoro A, Villalobos VM, Sands J, Paz-Ares L. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. Lancet Oncol. 2020 May;21(5):645-654. doi: 10.1016/S1470-2045(20)30068-1. Epub 2020 Mar 27. Erratum in: Lancet Oncol. 2020 Dec;21(12):e553.