

## Lurbinectedin

### Approved indication: small cell lung cancer

#### Zepzelca (Specialised Therapeutics)

#### vials containing 4 mg powder for reconstitution

Metastatic small cell lung cancer has a poor prognosis. Although many patients will have a response to chemotherapy, the cancer soon relapses. Their median survival can then be less than a year, so there is a need for effective second-line treatments.

Lurbinectedin is a cytotoxic drug with some similarity to trabectedin. It binds to DNA, affecting DNA repair and transcription leading to cell death.

The drug has to be reconstituted and diluted before being given by intravenous infusion over an hour. Lurbinectedin is thought to be metabolised by cytochrome P450 (CYP) 3A4. It is therefore recommended that strong inhibitors of CYP3A, such as the azole antifungals, be avoided. Moderate inhibitors, such as ciprofloxacin and erythromycin, should be avoided too, but if they have to be used the dose of lurbinectedin may need to be reduced. Strong inducers of CYP3A, such as phenytoin, and moderate inducers, such as phenobarbital, should be avoided. There are no clinical drug–drug interaction studies. The effect of severe hepatic or renal disease is unknown, but no changes in dose are required in mild disease. Most of the dose is metabolised then excreted in the faeces. The half-life is 51 hours.

The activity of lurbinectedin was investigated in several different cancers. An open-label phase II trial included 105 patients with small cell lung cancer that had progressed despite platinum-based chemotherapy. They were infused with lurbinectedin every three weeks. After a median follow-up of 17.1 months, the investigators thought that 35.2% of the patients met the criteria for a partial response. The median duration of the response was 5.3 months. Although the responders tended to survive longer, the median overall survival for all patients was 9.3 months.<sup>1</sup>

The results of this trial led to the phase III ATLANTIS trial of lurbinectedin in combination with doxorubicin for the treatment of small cell lung cancer that had progressed after platinum-based chemotherapy. This trial was also open-label, but patients were

randomised to the regimen or the investigators' choice of treatment. At the time of writing the full results for the 631 patients in the ATLANTIS trial have not been published, but it is reported not to have met its primary end point. The median progression-free survival was four months with both treatments. The median overall survival was 8.6 months with lurbinectedin and doxorubicin compared with 7.6 months for the other treatments.<sup>2</sup>

Some of the toxicity of lurbinectedin can be predicted from its mechanism of action. Many patients develop myelosuppression, and neutropenia or thrombocytopenia require the dose of lurbinectedin to be modified. It should also be modified if hepatotoxicity emerges. Other adverse effects seen in the phase II trial included infections such as pneumonia, peripheral neuropathy, dyspnoea, fatigue, nausea, vomiting and diarrhoea.<sup>1</sup> Prophylactic antiemetic drugs may be given before the infusion.

Lurbinectedin has only been given provisional approval for use in Australia. More study is needed to work out how to use it and which patients may benefit. While the ATLANTIS trial did not show any survival advantage for lurbinectedin, the dose prescribed was less than that used in the phase II trial.<sup>1,2</sup>

**T** manufacturer provided the product information

### REFERENCES

1. Trigo J, Subbiah V, Besse B, Moreno V, López R, Sala MA, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol* 2020;21:645-54. [https://doi.org/10.1016/S1470-2045\(20\)30068-1](https://doi.org/10.1016/S1470-2045(20)30068-1). [Erratum in: *Lancet Oncol* 2020;21:e553]
2. Helwick C. No overall survival benefit with lurbinectedin/doxorubicin in small cell lung cancer. *ASCO Post* 2021 Sep 13. <https://ascopost.com/news/september-2021/no-overall-survival-benefit-with-lurbinectedindoxorubicin-in-small-cell-lung-cancer/> [cited 2021 Dec 1]

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, *Aust Prescr* 2014;37:27.

At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA.

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