New drugs

Eribulin

Approved indication: metastatic breast cancer
Halaven (Eisai)
vials containing 1 mg/2 mL solution for injection
Australian Medicines Handbook Appendix A

Eribulin mesilate is a synthetic analogue of halichondrin B, a product derived from a marine sponge. It inhibits the division of proliferating cells. By binding to tubulin, eribulin blocks the formation of microtubules and cells cannot undergo mitosis.

Eribulin is indicated as a monotherapy for women whose breast cancer has progressed despite previous chemotherapy (including an anthracycline and a taxane). After showing some benefit in phase II trials,[1,2] an open-label randomised phase III trial (EMBRACE) compared eribulin to other treatments chosen by the doctor (including vinorelbine, gemcitabine, capecitabine, taxanes, anthracyclines, hormone treatment).[3] The trial enrolled 762 women with heavily pre-treated (median of 4 chemotherapies) locally recurrent or metastatic disease. Treatment was continued until the disease progressed or serious toxicities occurred (median of 3.9 months for eribulin and 2.1 months for the comparators). Median overall survival was longer with eribulin than with the comparator treatments (13.1 vs 10.6 months, p=0.041). However, progression-free survival was not significantly different (3.7 vs 2.2 months, p=0.137), as determined by an independent review.[3]

The most common adverse reactions to eribulin are neutropenia (82% of patients), anaemia (58%), weakness or fatigue (54%), alopecia (45%), peripheral neuropathy (35%), nausea (35%) and constipation (25%). Other common events (≥18% of people) included headache, fever, diarrhoea, vomiting, joint and muscle pain, reduced appetite and weight loss. Abnormal liver function tests were found in 18% of women. Peripheral neuropathy was the most common reason for discontinuing treatment, with 4% of women stopping treatment because of it.

In the phase III trial, grades 3 and 4 neutropenia, leucopenia and peripheral neuropathy were more common with eribulin than with the other treatments. Febrile neutropenia occurred in 5% of women. Five women in the eribulin arm died of treatment-related adverse events which included febrile neutropenia and lung infection.[3]

As haematological toxicities are common, it is important to monitor blood counts before treatment starts and then before each dose as dose delay or reduction may be necessary. The dose should not be increased again after a reduction. Women taking anticoagulants were excluded from the phase III trial.

In a group of 26 patients, eribulin was found to prolong the QTc interval by 11 milliseconds on day 8 of treatment. ECG monitoring is therefore recommended in patients with heart failure, bradycardia (<60 beats/min), electrolyte abnormalities or those taking other drugs that prolong the QT interval.

After intravenous administration, unchanged eribulin is eliminated in the faeces (82%) and urine (9%) with an elimination half-life of about 40 hours. The recommended dose is 1.4 mg/m^2 on days 1 and 8 of a 21-day cycle. Lower doses are recommended in people with liver impairment (Child-Pugh A or B) or moderate renal impairment (glomerular filtration rate 30–59 mL/min).

Eribulin was teratogenic in rats and is not recommended in pregnancy. It is also contraindicated in breastfeeding.

This new cytotoxic drug offers another option for women with treatment-refractory breast cancer. Although eribulin appears to extend life by a median of 2.5 months over other chemotherapies, toxicities are likely to limit treatment in some patients.

☒ manufacturer declined to supply data

REFERENCES †*A

1. Vahdat LT, Pruitt B, Fabian CJ, Rivera RR, Smith DA, Tan-Chiu E, et al. Phase II study of eribulin mesylate, a halichondrin B analog, in patients with metastatic breast cancer previously treated with an anthracycline and a taxane. J Clin Oncol 2009;27:2954-61.
2. Cortes J, Vahdat L, Blum JL, Twelves C, Campone M, Roche H, et al. Phase II study of the halichondrin B analog eribulin mesylate in patients with locally advanced or metastatic breast cancer previously treated with an anthracycline, a taxane, and capecitabine. J Clin Oncol 2010;28:3922-8.
3. Cortes J, O'Shaughnessy J, Loesch D, Blum JL, Vahdat LT, Petrakova K, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet 2011;377:914-23.

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A Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

NEW DRUGS

The Transparency score (T) is explained in 'New drugs: T-score for transparency', 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 (www.fda.gov)

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu)

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm)