HALAVEN® (ERIBULIN) MEDIA BACKGROUNDER

WHAT IS HALAVEN® (ERIBULIN)?

Eribulin is a chemotherapy, discovered and developed by Eisai, approved for use in adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen (an anthracycline and a taxane in either the adjuvant or metastatic setting) for advanced disease. Halaven is also approved for the treatment of adult patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

Eribulin is a structurally-modified version of halichondrin B, a product naturally occurring in the marine sponge *Halichondria okadai*. It is the first-in-class for halichondrin chemotherapies.[2,3]

Eribulin was first approved by the European Medicines Agency (EMA) in 2011 for the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least two chemotherapeutic regimens for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.[1,4]

In June 2014 it received an indication expansion to the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.[1,4]

Halichondria okadai sea sponge

HOW DOES ERIBULIN WORK?

Eribulin is a microtubule-dynamics inhibitor which binds to high affinity sites on the growing positive ends of microtubules to inhibit the development of the mitotic spindle. This stops the cell cycle and leads to apoptosis.[5]

Eribulin has an established safety profile and side effects are expected as with other chemotherapeutic agents.[6,7]

Overall survival could be influenced by choice of treatments used after progression of the cancer, results for patients.[8] Overall survival outcomes with eribulin are maximised when eribulin is used after two previous lines of treatment.[9]

WHERE IS ERIBULIN AVAILABLE?

Eribulin is approved in approximately 66 countries around the world including the European Union, Canada, United States, Russia, Switzerland, South Korea, Japan and Singapore.[10,11]

WHO CAN BE TREATED WITH ERIBULIN?

Eribulin is a chemotherapy approved by the EMA for the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.[1] Eribulin was also approved in 2016 for the treatment of adult patients with unresectable liposarcoma, a rare cancer of connective tissues, who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.[1,4]

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WHAT IS THE EVIDENCE BEHIND ERIBULIN?

Globally, eribulin has now been used by over 200,000 patients; the three-year safety data compiled from these women is consistent with the data from the pivotal Phase III trials.

The EU licence for eribulin is based on evidence from two global Phase III trials; **EMBRACE** (Eisai Metastatic Breast Cancer Study Assessing Treatment of Physicians' Choice Versus Eribulin)[7] and **Study 301**[14] as well as a **pooled analysis** of EMBRACE and Study 301 as requested by the EMA.[15]

EMBRACE

- **Patients:** The EMBRACE trial included 762 women with locally recurrent or metastatic breast cancer to receive eribulin (n=508) or treatment of physicians' choice (TPC; n=254). Patients had received between two and five previous chemotherapy regimens (two or more for advanced disease), including an anthracycline and a taxane, unless unsuitable.[7]
- **Results:** Overall survival was significantly improved in women assigned to eribulin (median 13.2 months) compared with TPC (10.5 months; hazard ratio [HR], 0.81; 95% CI: 0.68–0.96; nominal p=0.014)[1]
- **Adverse events:** The most commonly reported adverse events (incidence of ≥ 35%) in the eribulin study arm were fatigue (asthenia; 54%), a decrease in infection-fighting white blood cells (neutropenia; 52%), hair loss (alopecia; 45%), numbness and tingling in arms and legs (peripheral neuropathy; 35%) and nausea (35%).[7]

STUDY 301

- **Patients:** Study 301 included 1,102 patients with locally advanced or metastatic breast cancer, randomised to investigate the efficacy of eribulin monotherapy (n=554), compared to capecitabine monotherapy (n=548). Patients had received up to three previous chemotherapy regimens (two or more for advanced disease), including an anthracycline and a taxane.[14]
- **Results:** The study numerically favoured eribulin, compared to capecitabine for overall survival in the intent to treat population, although the improvement was not statistically significant. Median overall survival for eribulin and capecitabine were 15.9 and 14.5 months, respectively (HR, 0.88; 95% CI: 0.77–1.00; p=0.056). Median progression free survival times for eribulin and capecitabine were 4.1 and 4.2 months respectively (HR, 1.08; 95% CI: 0.93–1.25; p=0.30). Objective response rates by independent review were 11.0% for eribulin and 11.5% for capecitabine.[14]
- **Adverse events:** Adverse events experienced were consistent with the known profile of eribulin. The most commonly reported adverse reactions (incidence of ≥ 16%) in the eribulin study arm were a decrease in infection-fighting white blood cells (neutropenia; 54%), hair loss (alopecia; 35%), numbness and tingling in arms and legs (peripheral neuropathy; 27%), nausea (22%), anaemia (19%) and fatigue (17%). An additional analysis into the quality of life (QoL) implications of chemotherapy showed that there was no statistical difference in average GHS/QoL between eribulin and capecitabine (p=0.958 [linear mixed model]).[14]

POOLED ANALYSIS (REQUESTED BY EMA)

- **Patients:** The pooled analysis included 1,644 patients (eribulin n=946; control n=698) with locally advanced or metastatic breast cancer from the EMBRACE and Study 301 patient cohorts.[15]
- **Results:** Overall survival was significantly longer in patients with eribulin versus control, with median overall survival being 15.0 months and 12.6 months respectively (HR, 0.85; 95% CI 0.76–0.94; p=0.002). Treatment with eribulin was also associated with a significantly longer progression free survival compared with the control arm; median progression free survival for eribulin and the control was 3.9 versus 3.2 months respectively (HR, 0.87; 95% CI: 0.78–0.97; p=0.017).[15]
- **Adverse events:** Adverse events experienced were consistent with the known safety profile of eribulin. The most commonly reported adverse reactions (incidence of ≥21%) in the eribulin study arm were a decrease in infection-fighting white blood cells (neutropenia; 54%), hair loss (alopecia; 39%), nausea (29%), numbness and tingling in arms and legs (peripheral neuropathy; 29%,), decrease in other white blood cells (leukopenia; 27%), fatigue (24%) and lack of energy (asthenia; 22%).[15]

References

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