

EISAI RECEIVES POSITIVE OPINION FROM EMA'S CHMP ON EXPANDING INDICATION OF ANTICANCER AGENT HALAVEN® FOR USE IN EARLIER-LINE TREATMENT OF ADVANCED BREAST CANCER

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that its U.K. subsidiary Eisai Europe Limited has received a positive opinion from the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) on the indication expansion of Halaven® (generic name: eribulin mesylate, "eribulin") to contribute to earlier-line treatment of 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.

Eribulin is currently indicated in Europe for the treatment of 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 unless patients were not suitable for these treatments. The positive opinion received from the CHMP is a recommendation for the expansion of the current indication, which is limited to patients who have previously received at least two chemotherapeutic regimens, to include patients with metastatic breast cancer who have had less prior treatment.

The CHMP's positive opinion is based on evidence from two pivotal Phase III studies, including the Phase III clinical study (Study 305: EMBRACE) of eribulin versus Treatment of Physician's Choice (TPC) in patients with locally advanced or metastatic breast cancer who had previously received at least two to five prior chemotherapeutic regimens including treatment with an anthracycline and a taxane, and a Phase III clinical study (Study 301) of eribulin versus capecitabine in women with locally advanced or metastatic breast cancer who had received prior treatment with an anthracycline and a taxane. These studies involved more than 1,800 patients, making this one of the largest data sets in metastatic breast cancer.

Although advances are being made in the treatment of breast cancer each year with the development of new diagnostic technologies and anticancer agents, the unmet medical needs of patients with metastatic breast cancer continue to remain high. Eisai remains committed to providing scientific evidence aimed at maximizing the value of Halaven as it seeks to make further contributions to address the diversified needs of, and increase the benefits provided to, patients with cancer and their families as well as healthcare providers.

[Please refer to the following notes for further information on Halaven, Study 305 and Study 301.]

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[Notes to editors]

1. About Halaven® (eribulin mesylate)

Halaven, a non-taxane, microtubule dynamics inhibitor with a novel mechanism of action, belongs to a class of antineoplastic agents, the halichondrins, which are natural products isolated from the marine sponge *Halichondria okadai*. It is believed to work by inhibiting the growth phase of microtubule dynamics without affecting the shortening phase and sequestering tubulin into nonproductive aggregates. Halaven was first approved as a treatment for breast cancer in the United States in November 2010, and is approved in more than 50 countries worldwide, including European Union member states, Japan, Singapore and Switzerland. In Japan, the drug has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. Furthermore, with the aim of maximizing value of the drug, Eisai is currently moving ahead with developments investigating the potential of Halaven as a therapy in the treatment of breast cancer with fewer prior treatments as well as soft-tissue sarcoma and non-small cell lung cancer.

2. About Study 305 (EMBRACE)

In the Phase III clinical study (Study 305, EMBRACE) of Halaven versus treatment of physician's choice (TPC) in 762 patients with locally advanced or metastatic breast cancer previously treated with an anthracycline and a taxane, Halaven indicated extended overall survival (OS) of 2.5 months (OS of 13.1 months versus 10.6 months, respectively; Hazard Ratio (HR) 0.81; $p=0.041$) when compared to selected, major existing therapies. An updated analysis of OS (not protocol-specified) in the EMBRACE study was also performed at the request of European and U.S. regulatory authorities. These results demonstrated an increase of 2.7 months in OS for Halaven compared with TPC (OS of 13.2 months versus 10.5 months, respectively; HR 0.81; $p=0.014$). The most common adverse reactions (events with an incidence rate of at least 25%) among patients treated with Halaven were asthenia (fatigue), neutropenia, alopecia (hair loss), peripheral neuropathy (numbness and tingling in arms, legs and/or other parts of the body), nausea and constipation. The most common serious side effects reported in patients receiving Halaven were neutropenia. The most common adverse reaction resulting in discontinuation of treatment with Halaven was peripheral neuropathy (5%).

3. About Study 301

Study 301 was an open-label, randomized, two-parallel-arm, multicenter study designed to evaluate Halaven versus capecitabine in 1,102 women with locally advanced or metastatic breast cancer who had up to three prior chemotherapy regimens in the (neo)adjuvant setting, and no more than two prior regimens for locally advanced and/or metastatic disease. The regimens must have included an anthracycline and a taxane. Although eribulin did not achieve a statistically significant result when compared to capecitabine in terms of overall survival (OS) and progression-free survival (PFS), the co-primary endpoints of the study, eribulin did demonstrate a trend favoring improved OS (eribulin median OS: 15.9 months, capecitabine median OS: 14.5 months; HR 0.879; 95% CI: 0.770-1.003; $p=0.056$). Additionally, a later PFS assessment carried out by an independent evaluation body concluded that there was no significant difference between the two drugs (eribulin median PFS: 4.1 months, capecitabine median PFS: 4.2 months, HR 1.079; 95% CI: 0.932-1.250; $p=0.305$). In regard to safety, adverse events (AEs) were consistent with the known side-effect profiles of both drugs. The most common AEs (events with an incidence rate of at least 20%) for Halaven and capecitabine were, respectively, neutropenia (54.2% vs. 15.9%), hand-foot syndrome (0.2% vs. 45.1%), alopecia (34.6% vs. 4.0%), leukopenia (31.4% vs. 10.4%), diarrhea (14.3% vs. 28.8%), and nausea (22.2% vs. 24.4%).