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Eisai Co., Ltd.

EISAI RECEIVES EUROPEAN COMMISSION APPROVAL OF INDICATION EXPANSION FOR ANTICANCER AGENT HALAVEN® FOR ADVANCED BREAST CANCER AFTER ONLY ONE PRIOR CHEMOTHERAPY

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today that it has received approval from the European Commission of the indication expansion of Halaven® (generic name: eribulin mesylate, “eribulin”) to contribute to earlier 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.

Halaven 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 approval received from the European Commission is for the expansion of the current indication, which was limited to patients who had previously received at least two chemotherapeutic regimens, to include patients with metastatic breast cancer who have had less prior treatment. Through this indication expansion, Halaven will now be able to contribute at an earlier stage to patients with metastatic breast cancer in countries of the European Union.

The approval is based on evidence from two pivotal Phase III studies, including the Phase III clinical study (Study 305: EMBRACE) of Halaven 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 treatments with an anthracycline and a taxane, and a Phase III clinical study (Study 301) of Halaven 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.

Over 300,000 women are diagnosed with breast cancer in Europe every year, of whom about one third subsequently develop metastatic disease^{1,2}. 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.

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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 okadaei*. 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 Halaven 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, Halaven did demonstrate a trend favoring improved OS (Halaven 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 (Halaven 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%).

References

¹ World Health Organization. Atlas of Health in Europe. 2003. World Health Organization, Regional Office of Europe, Copenhagen, Denmark.

² Cancer Research UK. Breast cancer incidence statistics.
<http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/incidence/#world>