No. 19-52

July 17, 2019
Eisai Co., Ltd.

ANTICANCER AGENT HALAVEN® APPROVED FOR TREATMENT OF LOCALLY ADVANCED OR METASTATIC BREAST CANCER IN CHINA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that Eisai received New Drug Approval for Eisai's in-house developed anticancer agent Halaven® (eribulin mesylate) for use in the treatment of patients with locally advanced or metastatic breast cancer, previously treated with at least two prior chemotherapy regimens, including an anthracycline and a taxane, from the China National Medical Products Administration (NMPA).

This approval is based on the results of Study 304,[1] which was a multicenter, open-label, randomized, parallel group Phase III clinical study, to evaluate the efficacy and safety of Halaven and vinorelbine in 530 women with locally recurrent or metastatic breast cancer, previously treated with chemotherapy regimens, including an anthracycline and a taxane. Halaven demonstrated a statistically significant extension in the study's primary endpoint of progression-free survival (PFS) over the comparator treatment vinorelbine according to independent imaging review (Hazard Ratio: 0.80; 95% Confidence Interval: 0.65-0.98; p = 0.036).
The five most common adverse events observed in the Halaven arm of this study were white blood cell count decreased, neutrophil count decreased, increased aspartate aminotransferase, increased alanine aminotransferase, and anemia, which is consistent with the known side-effect profile of Halaven.

The number of women diagnosed with breast cancer in China has increased in recent years,[2] with an estimated 368,000 new cases of breast cancer and approximately 98,000 related deaths in 2018.[3] Breast cancer is now the most frequently diagnosed cancer in Chinese women.[3]

Halaven is a halichondrin class microtubule dynamics inhibitor with a distinct binding profile. In addition to its mechanism of action of inhibiting the growth of microtubule dynamics, non-clinical studies showed Halaven's unique actions on the tumor microenvironment such as an increase in vascular perfusion and permeability in tumor cores,[4] promotion of the epithelial state, decrease in the capacity of breast cancer cells to migrate,[5] etc. For use in the treatment of breast cancer, Halaven is currently approved in over 65 countries worldwide, including the United States, Japan and countries in Europe and Asia.

Eisai positions oncology as a key therapeutic area, and is aiming to discover revolutionary new medicines with the potential to cure cancer. Lenvima® has been available as a treatment of patients with unresectable hepatocellular carcinoma who have not received prior systematic therapy in China since November 2018.* With this approval of Halaven, Eisai seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers in China.

*Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A's Chinese subsidiary MSD China have been providing information about Lenvima in China.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. **About Halaven (generic name: eribulin mesylate)**

Halaven is in the halicondrin class of microtubule dynamics inhibitors with a novel mechanism of action. Structurally, Halaven is a simplified and synthetically produced version of halichondrin B, a natural product isolated from the marine sponge *halichondria okadai*. Halaven is believed to work by inhibiting the growth phase of microtubule dynamics which prevents cell division. In addition, non-clinical studies showed Halaven's unique actions in the tumor microenvironment such as an increase in vascular perfusion and permeability in tumor cores,[4] promotion of the epithelial state, decrease in capacity of breast cancer cells to migrate,[5] and etc.

Halaven was first approved as a treatment in the United States in November 2010 for patients with metastatic breast cancer. Halaven is currently approved for use in the treatment of breast cancer in over 65 countries worldwide, including Japan and countries in Europe, the Americas and Asia. Furthermore, Halaven was first approved as a treatment for soft tissue sarcoma in the United States in January 2016, and is approved in over 60 countries including Japan and in Europe and Asia. Furthermore, Halaven has been designated as an orphan drug for soft tissue sarcoma in the United States and Japan.

Specifically, Halaven is approved for the following indications.

In the United States for the treatment of patients with:

- Metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
- Unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

In Japan for the treatment of patients with:

- Inoperable or recurrent breast cancer
- Soft tissue sarcoma

In Europe for the treatment of adult patients with:

- Locally advanced or metastatic breast cancer who have received a prior anthracycline-containing 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.
- Unresectable liposarcomas who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

2. About Study 304[1]

Conducted in China, Study 304 was a multicenter, open-label, randomized, parallel group Phase III clinical study to evaluate the efficacy and safety of Halaven and vinorelbine in 530 female patients with locally recurrent or metastatic breast cancer, previously treated with at least two and a maximum of five prior chemotherapy regimens, including an anthracycline and a taxane. Patients received either Halaven (1.4mg/m^2 administered intravenously on Day 1 and Day 8 to 264 patients) or vinorelbine (25 mg/m^2 administered intravenously on Day 1, Day 8 and Day15 to 266 patients) every 21 days. The study's primary endpoint was progression-free survival (PFS).

[1] Yuan P et al., Eribulin mesilate versus vinorelbine in women with locally recurrent or metastatic breast cancer: A randomized clinical trial *Eur J Cancer,* 2019; 112, 57-65

[2] Lei F et al., Breast cancer in China. *The Lancet Oncology,* 2014; 15(7), e279–e289

[3] Ferlay J, et al., (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. https://gco.iarc.fr/today, As of July 17, 2019

[4] Funahashi Y et al., Eribulin mesylate reduces tumor microenvironment abnormality by vascular remodeling in preclinical human breast cancer models. *Cancer Sci.,* 2014; 105, 1334-1342

[5] Yoshida T et al., Eribulin mesilate suppresses experimental metastasis of breast cancer cells by reversing phenotype from epithelial-mesenchymal transition (EMT) to mesenchymal-epithelial transition (MET) states. Br J Cancer, 2014; 110, 1497-1505