

**PHASE III STUDY (STUDY 301) RESULTS OF ANTICANCER AGENT HALAVEN[®]
VERSUS CAPECITABINE IN LOCALLY ADVANCED OR METASTATIC BREAST
CANCER PRESENTED AT 2012 SABCS**

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that the results of a Phase III study (Study 301) of Halaven[®] (eribulin mesylate) versus capecitabine in locally advanced or metastatic breast cancer were presented at the 2012 CTSC-AACR San Antonio Breast Cancer Symposium (SABCS) in the United States. The head-to-head study compared anticancer agents Halaven and capecitabine in patients with locally advanced or metastatic breast cancer who had received prior treatment that included an anthracycline and a taxane.

The multicenter, randomized, open-label study compared Halaven versus capecitabine in 1,102 patients with locally advanced or metastatic breast cancer in which prior treatment with anthracyclines and taxanes had been unsuccessful, with the majority of these patients receiving study treatment as their 1st- or 2nd-line chemotherapeutic regimen for metastatic disease. The co-primary endpoints of the study were overall survival (OS) and progression-free survival (PFS).

Results from the study demonstrated a trend that favored improved OS with Halaven compared with capecitabine, although the improvement was not statistically significant. Patients treated with Halaven had a median OS of 15.9 months versus 14.5 months with capecitabine (HR 0.879; 95% CI: 0.770-1.003; p=0.056). No difference was observed in the median PFS of the two groups in an independent review, with 4.1 and 4.2 months for Halaven and capecitabine respectively (HR 1.079; 95% CI: 0.932-1.250; p=0.305).

The study carried out a series of exploratory analyses, including one analysis based on the expression status of human epidermal growth factor receptors (HER2s), which was a pre-specified stratification factor in the study protocol, and other analyses based on hormone receptor expression status, which were not pre-specified stratification factors in the study. These analyses showed that in a subset of HER2-negative patients (n=755), the median OS was 15.9 months for Halaven and 13.5 months for capecitabine (HR 0.838; 95% CI: 0.715-0.983; nominal p=0.030). Furthermore, in triple-negative breast cancer patients (n=284), a group with extremely high unmet medical needs in which the disease is HER2-negative, estrogen receptor-negative and progesterone receptor-negative, the median OS was 14.4 months for Halaven and 9.4 months for capecitabine (HR 0.702; 95% CI: 0.545-0.906; nominal p=0.006).

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%).

The trial studied Halaven versus capecitabine, which is currently approved in Europe and the United States as an earlier-stage breast cancer therapy than Halaven. While Halaven did not statistically meet either co-primary endpoint, the data do demonstrate a trend that favored improved OS with Halaven compared with capecitabine as well as a clinically meaningful improvement in OS for Halaven in certain patient groups, such as patients with HER2-negative or triple-negative disease and further work should be undertaken.

Although advances are being made in the treatment of breast cancer each year in line with the development of new anticancer agents, the unmet medical needs of locally advanced or metastatic breast cancer patients continue to remain high. Halaven is currently approved for the treatment of breast cancer in 42 countries worldwide, including Japan, the United States, European Union (EU) member states and Singapore. Eisai remains committed to generating 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, cancer patients and their families as well as healthcare providers.

[Please refer to the following notes for further information on Halaven and Study 301 (design summary and exploratory analysis results).]

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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 okadae*. It is believed to work by inhibiting the growth phase of microtubule dynamics without affecting the shortening phase and sequestering tubulin into nonproductive aggregates.

In a Phase III clinical study (EMBRACE) conducted overseas of Halaven versus treatment of physician's choice in 762 patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane, Halaven indicated an extended OS of 2.7 months when compared to selected, major existing therapies. The most common adverse reactions (events with an incidence rate of at least 25%) among patients treated with Halaven were asthenia (fatigue), neutropenia, anemia, alopecia (hair loss), peripheral neuropathy (numbness and tingling in arms, legs and other parts of the body), nausea and constipation. The most common serious side effects reported in patients receiving Halaven were neutropenia with or without fever (4% and 2%, respectively). The most common adverse reaction resulting in discontinuation of treatment with Halaven was peripheral neuropathy (5%). Furthermore, in a Phase II clinical study conducted in Japan, Halaven was found to possess excellent anticancer effects and tolerability in patients with advanced or recurrent breast cancer who had previously undergone treatment.

Halaven was first approved as a treatment for breast cancer in the United States in November 2010, and is now approved in 42 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 on July 2011. Furthermore, with the aim of maximizing the drug's value, Eisai is currently conducting late-stage clinical trials investigating the potential of Halaven as a monotherapy in the treatment of other types of cancer such as breast cancer with fewer prior treatments, as represented by Study 301, as well as soft-tissue sarcoma and non-small cell lung cancer. The company has also commenced clinical trials of a liposome formulation that it hopes will more effectively deliver Halaven to target cancer cells.

2. Study 301 Design Summary

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, and no more than two prior regimens for advanced and/or metastatic disease. The regimens must have included an anthracycline and a taxane, either in the (neo)adjuvant setting, or for locally advanced or metastatic disease. Patients must have had documented evidence of progression during or after their most recent anticancer therapy. Patients were also randomized according to their human epidermal growth factor receptor 2 (HER2) status (positive, negative or unknown) and geographical region (Eastern Europe, North America, Latin America, Western Europe, South Africa, and Asia) at a ratio of 1:1 to receive treatment with either Halaven 1.4 mg/m²/day (administered intravenously on days 1 and 8, every 21 days) or capecitabine 2.5 g/m²/day (administered orally on days 1 to 14, every 21 days).

3. Results of Study 301 Exploratory Analyses

In this study, pre-planned exploratory analyses were conducted based on hormone receptor expression status. The exploratory analyses presented at this year's SABCS event are as follows:

Sample Group	Hazard Ratio (HR) (95% Confidence Interval [CI])	Median Overall Survival (OS) in Months	
		Halaven®	capecitabine
HER2-positive	0.965 (0.688, 1.355)	14.3	17.1
HER2-negative	0.838 (0.715, 0.983)	15.9	13.5
Estrogen receptor-positive	0.897 (0.737, 1.093)	18.2	16.8
Estrogen receptor-negative	0.779 (0.635, 0.955)	14.4	10.5
Triple negative	0.702 (0.545, 0.906)	14.4	9.4
Non-triple negative	0.927 (0.795, 1.081)	17.5	16.6