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EISAI PRESENTS NEW FINDINGS FOR ANTIBODY DRUG CONJUGATE FARLETUZUMAB ECTERIBULIN AT 2022 ASCO ANNUAL MEETING

Poster Discussion Features Investigational Safety and Efficacy Data from the Platinum-Resistant Ovarian Cancer Cohort Expansion of a Phase 1 Study Evaluating Farletuzumab Ecteribulin (MORAb-202) in Solid Tumors (Abstract: #5513)

Poster Presentation Features Analyses Based on PK/PD Modeling/Simulations for Dose Optimization of Farletuzumab Ecteribulin Including Findings for Body Surface Area-Based Dosing (Abstract: #3090)

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today new investigational data from the platinum-resistant ovarian cancer (PROC) cohort expansion of a Phase 1 study (Study 101) evaluating the antibody drug conjugate (ADC) co-developed by Eisai and Bristol Myers Squibb, farletuzumab ecteribulin (MORAb-202). The safety and efficacy findings are being featured in a poster discussion at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting (#ASCO22), a hybrid meeting in Chicago from June 3 to 7 (NCT03386942; Abstract: #5513). Farletuzumab ecteribulin is composed of Eisai's in-house developed farletuzumab, a humanized IgG1 monoclonal antibody that binds to the folate receptor alpha (FRα), and Eisai's anticancer agent eribulin, a microtubule dynamics inhibitor, using an enzymatically cleavable linker.

"We are encouraged by the clinical safety and efficacy results, as measured by the preliminary antitumor activity observed in patients with platinum-resistant ovarian cancer being treated with each dose of farletuzumab ecteribulin, and with varying levels of folate receptor alpha expression," said Shin Nishio, MD, PhD, Principal Investigator and Associate Professor, Department of Obstetrics and Gynecology, Kurume University School of Medicine, Fukuoka, Japan. "Based on the data from pre-clinical studies, farletuzumab ecteribulin has the clinical potential to elicit a bystander effect through an enzymatically cleavable linker that releases a toxic payload from the antibody, therefore acting not only on the folate receptor alpha-positive cancer cells, but also the folate receptor alpha-negative cancer cells surrounding the folate receptor alpha-positive cancer cells. As the field of targeted therapy continues to evolve, antibody drug conjugates are anticipated to become a key modality in the treatment of recurrent, platinum-resistant disease."

Ovarian cancer is typically diagnosed at advanced stages of disease, with most patients facing a poor prognosis because of high rates of recurrence and subsequent development of chemoresistance.[1] High-grade serous ovarian cancer (HGSOC) is the most common type of ovarian cancer and tends to spread before it can be detected.[2-3] Ovarian tumors express a great number of tumor-antigens that can be used to guide targeted medicines, including the FRα biomarker, which is often overexpressed in epithelial ovarian carcinomas.[4-5] FRα is considered as a marker of tumor aggressiveness and is associated with poorer response rates to treatment.[6]

“As part of our *human health care* mission, Eisai remains dedicated to exploring novel treatment approaches with the goal of addressing unmet needs of people living with cancer,” said Dr. Takashi Owa, President, Oncology Business Group at Eisai. “The data for our first antibody drug conjugate, which was discovered in-house with Eisai technology, demonstrate the company’s commitment to working to advance precision medicine to improve care for women in need of additional treatment options. We look forward to sharing further results assessing farletuzumab ecteribulin as a potential treatment for patients with platinum-resistant ovarian cancer.”

Trial Design

The primary objective of this Phase 1 study conducted in Japan (Study 101) was to determine the safety and tolerability of farletuzumab ecteribulin. Selected secondary objectives included determining the recommended dose of farletuzumab ecteribulin for future studies, pharmacokinetic characterization and an efficacy assessment, including objective response rate (ORR) and disease control rate (DCR). Doses of farletuzumab ecteribulin from 0.3 to 1.2 mg/kg, administered by intravenous (IV) fusion every 3 weeks (Q3W), were then evaluated. The dose-escalation part of Study 101 suggested that treatment with farletuzumab ecteribulin led to antitumor activity in patients with FRα-positive solid tumors, including patients with ovarian cancer. Based on the efficacy and safety results from the dose-escalation part of this study, farletuzumab ecteribulin 0.9 mg/kg (Cohort 1) and 1.2 mg/kg (Cohort 2) administered by IV fusion Q3W were selected for the expansion part of this study in patients with platinum-resistant ovarian cancer. Patients were required to have FRα-positive tumors, assessed by immunohistochemistry assay, with positive expression defined as > 5% of cells stained on a slide at 1+, 2+ or 3+ intensity level. In the expansion phase of this study, tumor assessments were performed based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) at baseline and every 6 weeks until week 36, thereafter every 8 weeks, and at treatment discontinuation (or as clinically indicated). Complete and partial responses required confirmation of the next response at ≥ 4 weeks. Interstitial lung disease (ILD)/pneumonitis assessment in 0.9 mg/kg dose group was performed by external ILD experts committee before moving to 1.2 mg/kg dose group. In the case of ILD/pneumonitis, dosing of farletuzumab ecteribulin could be modified, interrupted or permanently discontinued depending on the severity. Other management options for ILD/pneumonitis included pulmonology consult, radiographic imaging, monitoring for signs and symptoms, prednisolone administration, or treatment according to local practice guidelines.

Safety and Efficacy Results

Interstitial lung disease/pneumonitis was the most common treatment-emergent adverse event (TEAE) (Cohort 1: 37.5%; Cohort 2: 66.7%) and was of low-grade severity in most patients in Cohort 1 (Grade 1: 33.3%; Grade 2: 4.2%; Grades 3-5: 0) and Cohort 2 (Grade 1: 28.6%; Grade 2: 33.3%; Grade 3: 4.8%; Grades 4-5: 0). The next most common TEAEs of any grade after ILD were pyrexia (Cohort 1: 33.3%; Cohort 2: 42.9%, headache (Cohort 1: 12.5%; Cohort 2: 47.6%) and nausea (Cohort 1: 25.0%; Cohort 2: 33.3%). Grade ≥3 TEAEs occurred in 33.3% of patients in Cohort 1 and 28.6% of patients in Cohort 2.

Treatment with farletuzumab ecteribulin resulted in an ORR of 25.0% (6 patients) in Cohort 1 (n=24) and 52.4% (11 patients) in Cohort 2 (n=21). In patients with HGSOC, ORR was 31.6% (6 out of 19 patients) in Cohort 1 and 50.0% (10 out of 20 patients) in Cohort 2. For patients with FRα-expression levels of less than 50.0%, treatment with farletuzumab ecteribulin led to an ORR of 33.3% (2 out of 6 patients) in Cohort 1 and 50.0% (1 out of 2 patients) in Cohort 2. For patients with FRα-expression levels of greater than or

equal to 50.0%, treatment with farletuzumab ecteribulin led to an ORR of 22.2% (4 out of 18 patients) in Cohort 1 and 52.6% (10 out of 19 patients) in Cohort 2 (**Table 1**).

Table 1. Tumor Responses as Assessed by Investigator per RECIST v1.1

Parameter	Cohort 1 farletuzumab ecteribulin 0.9 mg/kg n=24	Cohort 2 farletuzumab ecteribulin 1.2 mg/kg n=21
CR, n (%)	1 (4.2)	0
PR, n (%)	5 (20.8)	11 (52.4)
SD, n (%)	10 (41.7)	9 (42.9)
PD, n (%)	8 (33.3)	1 (4.8)
ORR, n (%), (95% CI)	6 (25.0), (9.8–46.7)	11 (52.4), (29.8–74.3)
ORR by FRα status, n of n (%), (95% CI) FRα < 50% FRα ≥ 50%	 2 of 6 (33.3), (4.3-77.7) 4 of 18 (22.2), (6.4-47.6)	 1 of 2 (50.0), (1.3-98.7) 10 of 19 (52.6), (28.9-75.6)
ORR by HGSOC status, n of n (%), (95% CI) HGSOC Non-HGSOC	 6 of 19 (31.6), (12.6-56.6) 0 of 5, (0)	 10 of 20 (50.0), (27.2-72.8) 1 of 1 (100), (2.5-100)
DCR, n (%), (95% CI)	16 (66.7), (44.7–84.4)	20 (95.2), (76.2–99.9)
Median DOR, months (95% CI)	10.6 (3.9-NE)	7.6 (4.3-10.8)

Data cutoff date: October 31, 2021.
CI, confidence interval; CR, complete response; ORR, objective response rate (CR+PR); DCR, disease control rate (CR+PR+SD [≥ 5 weeks]); DOR, duration of response; FRα, folate receptor alpha; HGS, high-grade serous; NE, not estimable; PD, progressive disease; PR, partial response; RECIST v1.1; Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Poster Presentation Featuring Analyses Based on PK/PD Modeling/Simulations for Dose Optimization of Farletuzumab Ecteribulin Including Findings for Body Surface Area-Based Dosing (Abstract: #3090)

Eisai presented a poster featuring analyses from Study 101 based on PK/PD modeling/simulations for dose optimization of farletuzumab ecteribulin at the 2022 ASCO Annual Meeting. Based on the results of these simulations, body surface area-based (BSA) dosing is predicted to lower the exposure-dependent ILD risk in patients with higher body weight while maintaining clinical efficacy, compared to body weight-based dosing. BSA-based dosing is common with ADC therapies. Optimization of body surface area-based dosing is ongoing to evaluate the potential benefits and risks of treatment with farletuzumab ecteribulin in a Phase 1/2 clinical study (NCT04300556; Study 201) in the United States.

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[Notes to editors]

1. About Farletuzumab Ecteribulin (MORAb-202)

Farletuzumab ecteribulin is Eisai's first antibody drug conjugate (ADC) that is composed of Eisai's in-house developed farletuzumab, a humanized IgG1 monoclonal antibody that binds to the folate receptor alpha (FRα), and Eisai's in-house developed anticancer agent eribulin, using an enzymatically cleavable linker. Eisai has entered into an exclusive global strategic collaboration agreement with Bristol Myers Squibb for the co-development and co-commercialization of farletuzumab ecteribulin. Eisai is currently conducting a Phase 1 clinical study in Japan (NCT03386942) and a Phase 1/2 clinical study in the United States (NCT04300556), respectively, for farletuzumab ecteribulin targeting FRα-positive solid tumors. Other studies are in development by Eisai and Bristol Myers Squibb. After farletuzumab ecteribulin enters the target FRα-positive cancer cells, it is thought that the linker is enzymatically cleaved, releasing eribulin from the antibody leading to its antitumor activity. When the anticancer agent and antibody components of an ADC are separated inside a targeted antigen-positive cancer cell, it is theorized that the released anticancer agent also has a bystander effect on neighboring antigen-negative cancer cells and the component cells of the tumor microenvironment. In pre-clinical studies, farletuzumab ecteribulin demonstrated a bystander effect, with antitumor activity on the FRα-negative cancer cells surrounding the FRα-positive cancer cells.

The payload eribulin was the first in the halichondrin class of microtubule dynamics inhibitors. Structurally, eribulin is a simplified and synthetically produced version of halichondrin B, a natural product isolated from the marine sponge *Halichondria okadai*, and functions by inhibiting the growth phase of microtubule dynamics which prevents cell division.

2. About Ovarian Cancer

Ovarian cancer begins in the ovary, or related areas of the fallopian tube or peritoneum, and is characterized by uncontrolled growth of cells in these areas.[7] It is the eighth most commonly diagnosed cancer in women worldwide.[8] In 2022, nearly 20,000 new cases of ovarian cancer will be diagnosed in the U.S. and about 13,000 women will die from the disease.[2] About 90% of cases are epithelial ovarian cancer, the majority of which are high-grade serous tumors (HGSOC), which have the fewest established risk factors and worst prognosis.[2] Ovarian cancer typically presents at an advanced stage and while initial chemotherapy response rates are favorable, a majority of patients experience recurrence with the subsequent development of chemoresistance.[1] Treatment of platinum-resistant ovarian cancer is particularly challenging, with less than 15% of patients responding to subsequent chemotherapy.[9]

3. Eisai's Focus on Cancer

Eisai focuses on the development of anticancer drugs, targeting the tumor microenvironment (with experience and knowledge from existing in-house discovered compounds) and the driver gene mutation and aberrant splicing (leveraging RNA Splicing Platform) as areas (*Ricchi*) where real patient needs are still unmet, and where Eisai can aim to become a frontrunner in oncology. Eisai aspires to discover innovative new drugs with new targets and mechanisms of action from these *Ricchi*, with the aim of contributing to the cure of cancers.

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