ONO PHARMACEUTICAL CO.,LTD.

October 1, 2019

Opdivo (Nivolumab) Demonstrates Statistically Significant Overall Survival Benefit versus Chemotherapy in Patients with Esophageal Cancer in Phase III ATTRACTION-3 Study Presented at ESMO 2019

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol Myers Squibb (NYSE: BMY) announced that the results from a global multi-center, randomized, open-label Phase III ATTRACTION-3 study (ONO-4538-24/CA209-473) with Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), the human anti-human PD-1 monoclonal antibody, in patients with unresectable advanced or recurrent esophageal cancer who have been refractory to or intolerant of combination therapy with fluoropyrimidine and platinum-based drugs were presented on September 30 at the European Society of Medical Oncology (ESMO) 2019 Congress. In this study, Opdivo demonstrated a significant extension in overall survival (OS), the primary endpoint, versus chemotherapy in these patients with esophageal cancer.

In the final analysis of this study, Opdivo showed a statistically significant improvement in OS, the primary endpoint, compared with chemotherapy (docetaxel or paclitaxel) and reduced the risk of death by 23% [Hazard ratio (HR) 0.77; 95% confidence interval (CI): 0.62-0.96; p = 0.019]. Median OS was 10.9 months (95% CI: 9.2-13.3) for Opdivo and 8.4 months (95% CI: 7.2-9.9) for chemotherapy. The OS rate for Opdivo was 47% (95% CI: 40-54) at 12 months and 31% (95% CI: 24-37) at 18 months. The OS rate for chemotherapy was 34% (95% CI: 28-41) at 12 months and 21% (95% CI: 15-27) at 18 months. The survival benefit with Opdivo was found regardless of PD-L1 expression levels.

As for the other endpoints, the objective response rate (ORR) was 19% (95% CI: 14-26) among patients receiving Opdivo versus 22% (95% CI: 15-29) among those receiving chemotherapy. The median duration of response (DOR) was 6.9 months (95% CI: 5.4-11.1) for Opdivo versus 3.9 months (95% CI: 2.8-4.2) for chemotherapy. In addition, the median progression free survival (PFS) was 1.7 months (95% CI: 1.5-2.7) for Opdivo versus 3.4 months (95% CI: 3.0-4.2) for chemotherapy (HR 1.08; 95% CI: 0.87-1.34).

An exploratory analysis of patient-reported outcomes showed significant overall improvement in quality of life (QOL) with Opdivo versus chemotherapy. Treatment-related adverse events (TRAEs) of any grade occurred in 66% of patients receiving Opdivo and 95% of patients receiving chemotherapy. Grade 3 or 4 TRAEs occurred in 18% in the Opdivo group and 63% in the chemotherapy group.

These data on the study (Presentation #LBA11) were presented on September 30 from 16:42 to 16:54 CEST in a proffered paper session of Presidential Symposium at the ESMO 2019 Congress, held from September 27 to October 1 in Barcelona, Spain and simultaneously published in The Lancet Oncology.

Esophageal cancer occurs in the inner layer (mucosa) of the esophagus and grows outside (toward the deeper layer). There are two main types of esophageal cancer; squamous cell carcinoma (SCC) and adenocarcinoma. SCC is the predominant histological type, accounting for approximately 90% of all esophageal cancer in Japan. Approximately 572,000 cases of esophageal cancer are newly diagnosed per year worldwide (about 20,000 cases in Japan), and approximately 508,000 deaths are caused by the disease are reported (about 12,000 in Japan) per year*1. No available drugs have showed definitive efficacy in extension of OS as the second line treatment of patients with esophageal cancer who are refractory to the treatment with cisplatin and 5-FU*2 in Japan, an innovative drug is expected to be developed as a treatment option in this patient population.

*1: Globocan 2018. Available at: http://globocan.iarc.fr/

*2: Guideline for Diagnosis and Treatment of Carcinoma of the Esophagus 2017, The Japan Esophageal Society

About ATTRACTION-3 study (ONO-4538-24/CA209-473)

ATTRACTION-3 study is a global multi-center, randomized, open-label Phase III clinical study (ONO-4538-24/CA209-473) to evaluate the efficacy on overall survival (OS), the primary endpoint, and safety of Opdivo versus chemotherapy (docetaxel or paclitaxel) in 419 patients with esophageal cancer (unselected for PD-L1 expression level) who have been refractory to or intolerant of one prior combination therapy with fluoropyrimidine and platinum-based drug. In this study, patients received Opdivo 240 mg every two weeks intravenously (n = 210), or investigator's choice (n = 209) of docetaxel 75 mg/m^2 every 3 weeks intravenously or paclitaxel 100 mg/m^2 weekly for 6 weeks followed by 1-week no treatment period, until disease progression, or onset of unacceptable toxic effect is observed. The primary endpoint of this study is OS. The secondary endpoints include progression-free survival (PFS), objective response rate (ORR) and duration of response (DOR).

About Opdivo

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response by blocking the interaction between PD-1 and its ligands. By harnessing the body's own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers since the approval for the treatment of melanoma in Japan in July 2014. Opdivo is currently approved in more than 65 countries, including Japan, South Korea, Taiwan, China, the US and European Union.

In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in September 2014. Thereafter, Opdivo received an approval for additional indications of unresectable, advanced or recurrent non-small cell lung cancer in December 2015, unresectable or metastatic renal cell cancer in August 2016, relapsed or refractory classical Hodgkin lymphoma in December 2016, recurrent or metastatic head and neck cancer in March 2017, unresectable advanced or recurrent gastric cancer which has progressed after chemotherapy in September 2017, unresectable advanced or recurrent malignant pleural mesothelioma which has progressed after chemotherapy and adjuvant treatment of melanoma, etc. in August 2018.

In addition, ONO has submitted supplemental applications for the treatment of microsatellite instable High (MSI-H) colorectal cancer and esophageal cancer, and is conducting clinical development program including esophageal cancer, esophago-gastric junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, bladder cancer, ovarian cancer, colorectal cancer, biliary tract cancer, etc.

About the ONO and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with Bristol-Myers Squibb (BMS), ONO granted BMS its territorial rights to develop and commercialize Opdivo globally except in Japan, South Korea and Taiwan, where ONO had retained all rights to Opdivo except the US at the time. In July 2014, ONO and BMS further expanded the companies' strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agent and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

Contact
ONO PHARMACEUTICAL CO., LTD.
Corporate Communications
public_relations@ono.co.jp