ONO PHARMACEUTICAL CO.,LTD.

May 30, 2019

ONO Submits Supplemental Application of Opdivo® (Nivolumab) for Indication of Unresectable Advanced or Recurrent Esophageal Cancer in Japan for a Partial Change in Approved Items of Manufacturing and Marketing Approval

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that ONO submitted a supplemental application of Opdivo® (nivolumab) Intravenous Infusion 20mg, 100mg and 240mg ("Opdivo"), the human anti-human PD-1 monoclonal antibody in Japan for additional indication of unresectable advanced or recurrent esophageal cancer for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the result of a global multi-center, randomized, open-label Phase III ATTRACTION-3 study (ONO-4538-24/CA209-473) conducted by ONO and Bristol-Myers Squibb (NYSE: BMY) in patients with unresectable advanced or recurrent esophageal cancer who have been refractory to or intolerant of combination therapy with fluoropyrimidine and platinum-based drug. In the final analysis of this study, Opdivo demonstrated a significant improvement in overall survival (OS), the primary endpoint, compared to chemotherapy (docetaxel or paclitaxel), in this patient population.

Esophageal cancer is a malignant tumor that 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 about 90% of all esophageal cancer in Japan. It is estimated that about 572,000 new cases are diagnosed with esophageal cancer per year worldwide (about 20,000 cases in Japan) and approximately 508,000 deaths (about 12,000 in Japan) per year resulting from this disease[1)]. As there have been no available drugs showing the definitive efficacy in extension of OS in the second line treatment of esophageal cancer which failed in the treatment with cisplatin and 5-FU[2)], 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)

This 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) as the primary endpoint and safety of Opdivo versus chemotherapy (docetaxel or paclitaxel) in esophageal cancer patients (regardless of 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, Opdivo or chemotherapy was administered until disease progression, or onset of unacceptable toxicity is observed. The primary endpoint, OS was assessed for the superiority of Opdivo versus chemotherapy.

About Opdivo

Opdivo is a 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.

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 a supplemental application for the treatment of microsatellite instable High (MSI-H) CRC, 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, biliary tract cancer, etc.

Opdivo is currently approved in more than 65 countries, including Japan, South Korea, Taiwan, China, the US and European Union.

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.

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