ONO PHARMACEUTICAL CO.,LTD.

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Phase II / III (ATTRACTION-4) Study Result Evaluating Opdivo in Combination with Chemotherapy in Patients with Unresectable Advanced or Recurrent Gastric Cancer Who are Previously Untreated with the First-line Therapy Presented at ESMO 2020

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced that the result from Phase II / III clinical study (ATTRACTION-4 study/ONO-4538-37), evaluating Opdivo® (nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody in combination with chemotherapy (Opdivo combination group), versus placebo in combination with chemotherapy (control combination group) in patients with unresectable advanced or recurrent gastric cancer who are negative for human epidermal growth factor receptor 2 (HER2), and previously untreated with the first-line therapy in Japan, South Korea and Taiwan, was presented on September 21 at the European Society of Medical Oncology (ESMO) 2020. In this study, Opdivo combination group demonstrated a statistically significant improvement in one of the two primary endpoints of progression-free survival (PFS), but did not show a statistically significant improvement in overall survival (OS), the other primary endpoint versus control combination group.

In interim analysis of this study, Opdivo combination group (n=362) demonstrated a statistically significant improvement in the primary endpoint of PFS as assessed by the Independent Review Committee (IRC), compared to control combination group (n=362) [Hazard ratio (HR) 0.68; 98.51% confidence interval (CI): 0.51 - 0.90; p=0.0007]. Median PFS was 10.4 months (95% CI : 8.4 - 14.8) for Opdivo combination group versus 8.3 months (95% CI : 7.0 - 9.4) for control combination group. PFS rate at 12 months were 45.4% for Opdivo combination group versus 30.6% for control combination group. In addition, median OS, the other primary endpoint, was 17.4 months (95% CI: 15.7 - 20.8) for Opdivo combination group and 17.1 months (95% CI: 15.2 - 19.6) for control combination group. A statistically significant difference was not observed between the groups (HR 0.90; 95% CI: 0.75 - 1.08). As for secondary endpoints, objective response rate (ORR) were 57.5% for Opdivo combination group versus 47.8% for control combination group. Median duration of response (DOR) was 12.9 months for Opdivo combination group versus 8.7 months for control combination group. Grade 3 or 4 treatment-related adverse events occurred in 57.1% for Opdivo combination group and 48.6% for control combination group.

The data in this study (Abstract#LBA7) was presented on September 21 from 18:42 to 18:54 CEST in Presidential Symposium III at the ESMO 2020 (Virtual) Congress, held from September 19 to 21 in Madrid, Spain.

About ATTRACTION-4 study (ONO-4538-37)

This study is a multi-center, randomized, Phase II / III clinical study (ATTRACTION-4 study: ONO-4538-37), evaluating Opdivo in combination with chemotherapy (oxaliplatin + S-1 or capecitabine) compared to placebo in combination with chemotherapy in patients with HER2-negative, unresectable advanced or recurrent gastric cancer (including esophago-gastric junction cancer) who have been previously untreated with the first-line therapy in Japan, South Korea and Taiwan. Patients received Opdivo 360 mg or placebo every 3 weeks until disease progression or unacceptable toxicity are observed. The primary endpoints of this study are PFS as assessed by IRC and OS. The secondary endpoints are ORR, DOR, etc.

About Gastric Cancer

It is estimated that about 115,000 new cases are diagnosed with gastric cancer per year in Japan (about 1,033,000 cases worldwide) and approximately 48,000 deaths per year (about 782,000 worldwide) resulting from this disease[1)], which is the 2nd most common type of cancer after lung cancer in Japan. As there has been little progression in the standard of care of first-line chemotherapy for the HER 2-negative, unresectable, advanced, recurrent gastric cancer in the past decade in Japan, an innovative treatment option is needed in this patient population.

1) Globocan 2018; Stomach Cancer: Estimated cancer incidence, mortality and prevalence worldwide. World Health Organization. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.pdf

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 carcinoma 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 in August 2018, and microsatellite instability high (MSI-High) unresectable advanced or recurrent colorectal cancer that has progressed following chemotherapy and unresectable advanced or recurrent esophageal cancer that has progressed following chemotherapy in February 2020.

In addition, ONO is conducting clinical development program including esophago-gastric junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, ovarian cancer, bladder cancer, pancreatic cancer, biliary tract cancer, etc.

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