ONO PHARMACEUTICAL CO.,LTD.

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Phase III Study Result Evaluating Opdivo in Combination with Bevacizumab and Chemotherapy in Chemotherapy-naïve Patients with Stage IIIB/IV or Recurrent Non-squamous Non-small Cell Lung Cancer Unsuitable for Radical Radiation Presented at ESMO 2020

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced that the result from Phase III clinical study (ONO-4538-52/TASUKI-52), evaluating Opdivo® (nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody in combination treatment with bevacizumab, an anti-VEGF (vascular endothelial growth factor) humanized monoclonal antibody and chemotherapy (Opdivo combination group), versus placebo in combination with bevacizumab and chemotherapy (control combination group) in chemotherapy-naïve patients with stage IIIB/IV or recurrent non-squamous non-small cell lung cancer (NSCLC) unsuitable for radical radiation 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 the primary endpoint of progression-free survival (PFS), compared to control combination group.

In pre-specified interim analysis of this study, Opdivo combination group (n=275) 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=275) [Hazard ratio (HR) 0.56; 96.37% confidence interval (CI): 0.43 - 0.71; p<0.0001]. Median PFS was 12.1 months (96.37% CI : 9.8 - 14.0) for Opdivo combination group versus 8.1 months (96.37% CI : 7.0 - 8.5) for control combination group. PFS rate at 12 months were 50.1% for Opdivo combination group versus 30.2% for control combination group. The PFS benefit of Opdivo combination group was observed regardless of PD-L1 expression levels. As for secondary endpoints, objective response rate (ORR) were 61.5% for Opdivo combination group versus 50.5% for control combination group. Median duration of response (DOR) was 11.0 months for Opdivo combination group versus 7.0 months for control combination group. While not mature, median overall survival (OS) tended to be longer in Opdivo combination group with 25.4 months (95% CI: 21.8 - NR) against control combination group with 24.7 months (95% CI: 20.2 - NR) (HR 0.85; 95% CI: 0.63 - 1.14). Grade 3 or 4 treatment-related adverse events occurred in 73.6% for Opdivo combination group and 72.0% for control combination group.

The data in this study (Abstract#LBA54) was presented on September 21 from 15:21 to 15:33 CEST in a proffered paper session at the ESMO 2020 (Virtual) Congress, held from September 19 to 21 in Madrid, Spain.

About ONO-4538-52/TASUKI-52 study

This study is a multi-center, randomized, double-blind, placebo-controlled Phase III clinical study (ONO-4538-52/TASUKI-52), evaluating Opdivo in combination treatment with bevacizumab and chemotherapy (Opdivo combination group: n=275), versus placebo in combination with bevacizumab and chemotherapy (control combination group: n=275), in chemotherapy-naïve patients with stage IIIB/IV or recurrent non-squamous NSCLC unsuitable for radical radiation. Patients in the Opdivo

combination group received Opdivo at 360 mg, carboplatin at AUC 6, paclitaxel at 200 mg/m^2 and bevacizumab at 15 mg/kg, every 3 weeks (as one cycle). Patients in the control combination group received placebo, carboplatin at AUC 6, paclitaxel at 200 mg/m^2 and bevacizumab at 15 mg/kg, every 3 weeks (as one cycle). Patients in both groups received carboplatin paclitaxel up to 4 cycles and if deemed safe, the drugs may continue for up to a maximum of 6 cycles. Thereafter, Opdivo and bevacizumab were given in the Opdivo combination group, and placebo and bevacizumab given in the control combination group until disease progression or unacceptable toxicity are observed. The primary endpoint of this study is PFS as assessed by IRC. The secondary endpoints are OS, PFS as assessed by the study site's investigator and ORR, etc.

About Lung Cancer

Lung cancer is considered to be a form of malignant tumor that arises from cells in the trachea, bronchi and alveoli. Lung cancer is divided into two types, small cell lung cancer and NSCLC, depending on the broad histological subtypes. NSCLC is one of the most common types of lung cancer, accounting for about 85% of lung cancer[1]. NSCLC is further classified into adenocarcinoma (about 40% of lung cancer), squamous cell carcinoma (about 25%) and large cell carcinoma (about 10%) [2]. Lung cancer is the most common type of cancer with an estimated 118,000 new diagnoses per year in Japan (about 2,090,000 cases worldwide). It is estimated that approximately 81,000 deaths per year resulting from the disease in Japan (approximately 1,760,000 worldwide), showing the first leading cause of cancer-related deaths in both cases[3]. Survival rates vary depending on the stage and type of the cancer when diagnosed. For patients diagnosed with metastatic lung cancer, the five-year survival rate is about 5%.

1) American Cancer Society; What Is Non-Small Cell Lung Cancer? : https://www.cancer.org/content/cancer/en/cancer/lung-cancer/about/what-is.html
2) Non-Small Cell Lung Cancer Treatment (PDQ®)–Health Professional Version, National Cancer Institute: https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq#_12_toc
3) Globocan 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. World Health Organization. Available from: http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-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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