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ONO and BMSKK Submit Supplemental Application for Opdivo plus Yervoy in Combination Treatment with Chemotherapy in Japan to Expand the Use for First–Line Treatment of Unresectable Advanced or Recurrent Non-Small Cell Lung Cancer

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol-Myers Squibb K.K. (Shinjuku, Tokyo; President, Jean-Christophe Barland; BMSKK) announced today that the companies have submitted a supplemental application in Japan for combination therapy of Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human programmed cell death-1 (PD-1) monoclonal antibody plus Yervoy® (generic name: ipilimumab) Injection ("Yervoy"), a human monoclonal antibody against cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), in combination treatment with a limited cycle of platinum-doublet chemotherapy, to expand the use for first-line treatment of unresectable, advanced or recurrent non-small cell lung cancer, for a partial change in approved items of the manufacturing and marketing approval in Japan.

This application is based on the results from the CheckMate -9LA study, a global multi-center, randomized, open-label Phase III clinical study, conducted by ONO and Bristol Myers Squibb (NYSE: BMY; "BMS"), evaluating Opdivo plus Yervoy in combination treatment with platinum-doublet chemotherapy (2 cycles) compared to platinum-doublet chemotherapy alone for the first-line treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) regardless of PD-L1 expression and histology. In an interim analysis of this study, Opdivo plus Yervoy in combination treatment with platinum-doublet chemotherapy demonstrated a significant improvement in overall survival (OS), the primary endpoint, compared to platinum-doublet chemotherapy alone in this patient population. The safety profile of Opdivo plus Yervoy and chemotherapy was reflective of the known safety profiles of the immunotherapy and chemotherapy components in first-line NSCLC.

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 CheckMate -9LA

CheckMate -9LA is a global multi-center, randomized, open-label Phase III trial evaluating Opdivo (360 mg Q3W) plus Yervoy (1 mg/kg Q6W) combined with platinum-doublet chemotherapy (two cycles) compared to platinum-doublet chemotherapy alone as a first-line treatment in patients with advanced NSCLC regardless of PD-L1 expression and histology. Patients in the combination treatment arm were treated for up to 24 months or until disease progression or unacceptable toxicity. Patients in the control arm were treated with up to four cycles of chemotherapy and optional pemetrexed maintenance (if eligible) until disease progression or toxicity. The primary endpoint of the trial was OS in the intent to treat population. Secondary endpoints included progression-free survival (PFS), overall response rate (ORR), and efficacy measures according to biomarkers.

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 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.

About Yervoy

Yervoy is a recombinant, human monoclonal antibody, and binds to the cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Yervoy binds to CTLA-4, and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including anti-tumor

immune response. On March 25, 2011, the U.S. Food and Drug Administration (FDA) approved Yervoy 3 mg/kg monotherapy for patients with unresectable or metastatic melanoma. Yervoy is now approved in more than 60 countries. There is a broad, ongoing development program in place for Yervoy spanning multiple tumor types.

In Japan, BMSKK received an approval of Yervoy for the treatment of unresectable melanoma in July 2015. Yervoy was also approved in combination therapy with Opdivo for the treatment of unresectable melanoma in May 2018, followed by unresectable or metastatic renal cell carcinoma in August 2018.

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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