February 27, 2020

ONO Submits Supplemental Application for Approval for Opdivo® (Nivolumab) to Expand the Use for Treatment of Unresectable Advanced or Recurrent Non-small Cell Lung Cancer, in Combination Treatment with Chemotherapy in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol-Myers Squibb (NYSE: BMY; "BMS") announced today that ONO has submitted a supplemental application for Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human programmed cell death-1 (PD-1) monoclonal antibody in Japan, to expand the use for the treatment of unresectable advanced or recurrent non-small cell lung cancer (NSCLC), in combination treatment with platinum-doublet chemotherapy, for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the results from Part 1 and 2 of the CheckMate -227 study, a global multipart, randomized, open-label Phase III clinical study conducted by ONO and BMS in patients with chemotherapy-naive Stage IV or recurrent 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-227 study

This study is a global multipart, open-label, randomized Phase III clinical study, evaluating Opdivo, or Opdivo plus Yervoy, or Opdivo plus platinum-doublet chemotherapy compared to platinum doublet chemotherapy in patients with chemotherapy-naive Stage IV or recurrent NSCLC. This study consists of the following 3 Parts:

1) Part 1a: Evaluating the efficacy and safety of Opdivo, or Opdivo plus Yervoy versus chemotherapy in patients whose tumors express PD-L1 ≧1%
2) Part 1b: Evaluating the efficacy and safety of Opdivo plus Yervoy, or Opdivo plus platinum-doublet chemotherapy versus chemotherapy in patients whose tumors express PD-L1 <1%
3) Part 2: Evaluating the efficacy and safety of Opdivo plus platinum-doublet chemotherapy versus chemotherapy, regardless of PD-L1

In the combination treatment with Opdivo plus platinum-doublet chemotherapy of Part 1 and Part 2, patients received Opdivo 360 mg every 3 weeks and platinum-doublet chemotherapy based on histological subtypes every 3 weeks up to 4 cycles, and then if disease progression is not observed, patients were treated for up to 24 months until disease progression or onset of unacceptable toxicity is observed. Patients with non-squamous cancer were continuously treated with pemetrexed maintenance therapy until disease progression or onset of unacceptable toxicity is observed, unless disease progression is observed after completion of 4 cycles of chemotherapy.

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 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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