ONO PHARMACEUTICAL CO.,LTD.

March 31, 2021

ONO Submits Supplemental Application for Approval for Opdivo® (Nivolumab) to Expand its Use as Adjuvant Therapy of Resected Urothelial Cancer in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") today announced that it has submitted a supplemental application for Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody in Japan, to expand its use as adjuvant therapy of resected urothelial cancer, for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the results from a global multi-center, randomized, double-blind Phase 3 clinical study, CheckMate -274 (ONO-4538-33), evaluating Opdivo monotherapy compared to placebo as an adjuvant therapy in patients with muscle-invasive urothelial cancer at a high risk of recurrence after radical surgery. In this study, Opdivo showed a statistically significant improvement in disease-free survival (DFS), compared to placebo, both in all randomized patients and in the patients whose tumor cells express PD-L1 ≥ 1%, meeting both of the endpoints. The safety profile of Opdivo in this study was consistent with previous studies with Opdivo monotherapy.

About CheckMate -274 (ONO-4538-33) study

CheckMate -274 is a global multi-center, randomized, double-blind Phase 3 clinical study evaluating Opdivo monotherapy compared to placebo in patients with muscle-invasive urothelial cancer at a high risk of recurrence after radical surgery. In this study, patients were randomized 1:1 to receive Opdivo 240 mg or placebo every two weeks. Patients continued treatment for up to one year, until disease recurrence, unacceptable toxicity or withdrawal of consent. The primary endpoints of the study are DFS in all randomized patients and in patients whose tumors express PD-L1 ≥ 1%. Key secondary endpoints include overall survival, non-urothelial tract recurrence free survival and disease-specific survival.

About Urothelial Carcinoma

Urothelial cancer is a tumor that begins in the renal pelvis, ureter, bladder and urethra, most of which is bladder cancer. Histopathologically, urothelial cancer (transitional epithelial cancer) accounts for more than 90% of bladder cancer[1]. It is estimated that about 37,000 new cases[2] of bladder cancer are diagnosed per year in Japan (about 573,000 cases worldwide[3]) and about 11,000 deaths[2] (about 213,000 worldwide[3]) per year result from this disease. Standard treatment for bladder cancer is neoadjuvant chemotherapy followed by radical resection, but it is reported that more than 50% of patients will relapse after radical resection[4]. Since the prognosis of patients who have relapsed as metastatic cancer is poor, it is considered that there is a high medical need for postoperative adjuvant therapy for prevention of recurrence.

1) : Lynch CF, Cohen MB. Urinary System. Cancer. 1995;75:316-29.
2) : Globocan 2020. Available at: https://gco.iarc.fr/today/data/factsheets/populations/392-japan-fact-sheets.pdf

3) : Globocan 2020. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
4): Clinical Practice Guidelines for Bladder Cancer 2019 edition. The Japanese Urological Association

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 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, hepatocellular carcinoma, urothelial cancer, ovarian cancer, bladder cancer, prostate 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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