ONO PHARMA

Bristol Myers Squibb®

Press Release

Ono Pharmaceutical Co., Ltd.
Bristol-Myers Squibb K.K.

Ono and Bristol-Myers Squibb KK Submit Supplemental Application of Opdivo and Yervoy in Combination Treatment in Japan to Expand the Use for Unresectable Advanced or Recurrent Microsatellite Instability-High Colorectal Cancer

Osaka and Tokyo, Japan, September 12, 2024 - Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President: Toichi Takino; "Ono") and Bristol-Myers Squibb K.K. (Headquarters: Tokyo, Japan; President: Steve Sugino; "BMSKK") today announced the submission of supplemental application of Ono's anti-PD-1 antibody, Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo") and BMSKK's anti-CTLA-4 antibody, Yervoy® (generic name: ipilimumab) Injection ("Yervoy") in combination therapy in Japan, to expand the use for the treatment of unresectable advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer. This application is related to the additional indication 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 -8HW study, a global multi-center Phase 3 clinical study (CA209-8HW: ONO-4538-87), evaluating Opdivo plus Yervoy compared to investigator's choice of chemotherapy* in patients with unresectable advanced or recurrent MSI-High or mismatch repair deficient (dMMR) colorectal cancer. In this study, Opdivo plus Yervoy demonstrated a statistically significant and clinically meaningful improvement in one of the dual primary endpoints of progression-free survival (PFS) as assessed by Blinded Independent Central Review (BICR) compared to investigator's choice of chemotherapy in previously untreated patients with centrally confirmed MSI-High or dMMR colorectal cancer at a pre-specified interim analysis. The safety profile for the combination of Opdivo plus Yervoy remained consistent with previously reported data, with no new safety signals identified.

The study is ongoing to evaluate Opdivo plus Yervoy compared to Opdivo monotherapy in another primary endpoint of PFS in patients across all lines of therapy.

*: mFOLFOX6 (5-Fluorouracil, leucovorin and oxaliplatin), mFOLFOX6 with bevacizumab or cetuximab, FOLFIRI (5-Fluorouracil, folinic acid and irinotecan) or FOLFIRI with bevacizumab or cetuximab

With respect to the indication of colorectal cancer, Opdivo monotherapy and the combination therapy of Opdivo plus Yervoy were approved in Japan for the treatment of MSI-High unresectable advanced or recurrent colorectal cancer that has progressed following chemotherapy in February 2020 and September 2020, respectively. If this application is approved, the combination therapy of Opdivo plus Yervoy will be expected to be used as the first-line treatment in this patient population.

About CheckMate -8HW Study (CA209-8HW: ONO-4538-87)

CheckMate -8HW study is a global multi-center, randomized, open-label Phase III clinical study evaluating Opdivo plus Yervoy compared to Opdivo alone or investigator's choice of chemotherapy (mFOLFOX-6 or FOLFIRI with or without bevacizumab or cetuximab) in patients with unresectable advanced or recurrent microsatellite instability–high (MSI-High) or mismatch repair deficient (dMMR) colorectal cancer.

Approximately 830 patients were randomized to receive Opdivo plus Yervoy (Opdivo 240 mg plus Yervoy 1 mg/kg Q3W for four doses, followed by Opdivo 480 mg Q4W), Opdivo monotherapy (Opdivo 240 mg Q2W for six doses, followed by Opdivo 480 mg Q4W) or investigator's choice of chemotherapy. Patients were treated until disease progression or unacceptable toxic effects. The dual primary endpoints of the study are progression-free survival (PFS) per blinded independent central review (BICR) for Opdivo plus Yervoy compared to investigator's choice of chemotherapy in previously untreated patients with centrally confirmed MSI-High or dMMR colorectal cancer, and PFS per BICR for Opdivo plus Yervoy compared to Opdivo monotherapy in patients across all lines of therapy.

About Colorectal Cancer

Colorectal cancer (CRC) is the third most common cancer, with approximately 1,926,000 new cases diagnosed each year worldwide, and approximately 904,000 deaths are reported annually[*1]. In Japan, CRC is the most common cancer, with approximately 145,000 new cases per year, and approximately 60,000 deaths are reported each year[*1].

Approximately 5% of unresectable CRC patients have MSI-High or dMMR tumors. For unresectable advanced or recurrent MSI-High or dMMR CRC, conventional chemotherapy has not been effective enough, and the development of new therapeutic drugs is expected[*2].

*1: Globocan 2022: Available at https://gco.iarc.fr/today/en/fact-sheets-populations
*2: Guidelines 2022 for the treatment of colorectal cancer, Japanese Society for Cancer of the Colon and Rectum (JSCCR)

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, 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, 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, cancer of unknown primary in December 2021, adjuvant treatment of urothelial carcinoma in March 2022, malignant mesothelioma (excluding malignant pleural mesothelioma) in November 2023 and unresectable advanced or recurrent malignant epithelial tumors in February 2024.

In addition, Ono has submitted a supplemental application for the treatment of hepatocellular carcinoma.

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 50 countries. There is a broad, ongoing development program in place for Yervoy spanning multiple tumor types. In Japan, Yervoy was approved for the indication of unresectable malignant melanoma in July 2015.

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.

Contact:
Ono Pharmaceutical Co., Ltd.
Corporate Communications
public_relations@ono-pharma.com