ONO PHARMACEUTICAL CO.,LTD.

October 20, 2021

Opdivo® Intravenous Infusion Approved for the Treatment of Gastric Cancer, Gastroesophageal Junction Cancer and Esophageal Adenocarcinoma in Combination with Chemotherapy in Taiwan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced that Ono Pharma Taiwan Co., Ltd. ("OPTW"), a Taiwanese subsidiary of ONO, received the additional approval of Opdivo® (nivolumab) Intravenous Infusion 20 mg, 100 mg Inj. ("Opdivo"), a human anti-human PD-1 monoclonal antibody, on October 14 in Taiwan from the Taiwan Food and Drug Administration (TFDA) for the treatment of advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma, regardless of PD-L1 expression level, without human epidermal growth factor receptor 2 (HER2) overexpression, in combination with fluoropyrimidine- and platinum-containing chemotherapy.

This approval is based on the results from the global, multi-center, randomized, open-label Phase 3 CheckMate -649 study, evaluating Opdivo plus chemotherapy combination treatment compared to chemotherapy alone in patients with previously untreated, non-HER2 positive, advanced or metastatic gastric cancer (GC), gastroesophageal junction cancer (GEJC) or esophageal adenocarcinoma (EAC). In this study, Opdivo plus chemotherapy combination treatment demonstrated a statistically significant improvement of overall survival (OS) both in all randomized patients and in PD-L1 positive patients with a combined positive score (CPS) ≥ 5 versus chemotherapy. The safety profile of Opdivo plus chemotherapy in this study was consistent with the known safety profile of the individual treatments.

About CheckMate -649 Study

Checkmate -649 study is a multi-center, randomized, open-label Phase 3 clinical study evaluating Opdivo plus chemotherapy combination treatment compared to chemotherapy alone in patients with previously untreated, non-HER2 positive, advanced or metastatic GC, GEJC or EAC. Patients in the Opdivo plus chemotherapy arm received Opdivo 240 mg plus 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX) every two weeks or Opdivo 360 mg plus capecitabine and oxaliplatin (CapeOX) every three weeks. Patients in the chemotherapy arm received FOLFOX or CapeOX every two or three weeks, respectively. All patients continued treatment for two years or until disease progression, unacceptable toxicity or withdrawal of consent. The primary endpoints of the study are OS in PD-L1 positive patients with a CPS ≥ 5 and PFS as assessed by Blinded Independent Central Review (BICR) in CPS ≥ 5 patients, compared to chemotherapy alone. Key secondary endpoints are OS and PFS in PD-L1 positive patients with CPS ≥1 and in all randomized patients, and overall response rate (ORR) as assessed by BICR in PD-L1 positive patients with CPS ≥ 1 and ≥ 5, and in all randomized patients.

About Gastric Cancer, Gastroesophageal Junction Cancer and Esophageal Adenocarcinoma

- Gastric cancer (GC): In Taiwan, it is estimated that approximately 3,800 new cases diagnosed with gastric cancer per year, with approximately 2,300 deaths per year resulting from this disease[1]. There are several cancers that can be classified as GC, including certain types of cancers that form

in the gastroesophageal junction, the area of the digestive tract where the esophagus and stomach connect. As there has been little progression in the standard of care of first-line chemotherapy for the HER2 negative unresectable, advanced, recurrent GC in the past decade in Taiwan, a new treatment option is needed in this patient population.

- Esophageal cancer: In Taiwan, it is estimated that approximately 2,800 new cases diagnosed with esophageal cancer per year, with approximately 1,900 deaths per year resulting from this disease[1]. Esophageal cancer is a malignant tumor that occurs in the inner layer (mucosa) of the esophagus and grows outside (toward the deeper layer). There are two main histological types of esophageal cancer; squamous cell carcinoma (SCC) and adenocarcinoma, accounting for about 90% with SCC of all esophageal cancer in Taiwan[1].

1: Cancer Registry Annual Report, 2018 Taiwan

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 has submitted supplemental applications for the adjuvant treatment of urothelial cancer and cancer of unknown primary, and is conducting clinical development program including hepatocellular carcinoma, ovarian cancer, bladder cancer, prostate cancer, pancreatic cancer, biliary tract cancer, etc.

About 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 their 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.

About Ono Pharma Taiwan Co., Ltd.

Ono Pharma Taiwan Co., Ltd. (OPTW), in Taipei, Taiwan, was established as an ONO's wholly-owned subsidiary in December 2014. OPTW has marketed specialty products such as anti-cancer agent, including Opdivo. OPTW is committed to developing and marketing its products created internally for further penetration into the Taiwanese market.

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