ONO PHARMACEUTICAL CO.,LTD.

July 19, 2022

Opdivo® Intravenous Infusion Approved in Taiwan for the First-line Treatment of Advanced or Metastatic Esophageal Squamous Cell Carcinoma in Two Combination Treatments of Opdivo + Yervoy and Opdivo + Chemotherapy

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 ("Opdivo"), a human anti-human PD-1 monoclonal antibody, on July 15, 2022 in Taiwan from the Taiwan Food and Drug Administration (TFDA) for the first-line treatment of patients with advanced or metastatic esophageal squamous cell carcinoma, in the following two combination treatments:

1) Opdivo + Yervoy® (ipilimumab), an anti-CTLA-4 monoclonal antibody, and
2) Opdivo + chemotherapy (fluoropyrimidine- and platinum-containing chemotherapy)

These approvals are based on results from the global multi-center, randomized, open-label Phase 3 CheckMate -648 study (ONO-4538-50/CA209648), evaluating Opdivo plus Yervoy and Opdivo plus chemotherapy*, compared to chemotherapy* alone in patients with previously untreated unresectable advanced or recurrent metastatic esophageal squamous cell carcinoma (ESCC). In this study, both Opdivo-based treatment combinations (Opdivo plus Yervoy and Opdivo plus chemotherapy) demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS), compared to chemotherapy at the pre-specified interim analysis in patients with tumor cell PD-L1 expression ≥1%, as well as in the all-randomized patient population. The safety profiles of Opdivo plus Yervoy and Opdivo plus chemotherapy were consistent with the known safety profiles of the individual components.

*: Fluorouracil and cisplatin combination therapy (FP therapy)

About CheckMate -648 Study (ONO-4538-50/CA209648)

CheckMate -648 is a global multi-center, randomized, open-label Phase 3 study, evaluating Opdivo plus Yervoy and Opdivo plus chemotherapy (fluorouracil and cisplatin combination therapy) versus chemotherapy (fluorouracil and cisplatin combination therapy) alone in patients with previously untreated unresectable advanced or recurrent metastatic esophageal squamous cell carcinoma (ESCC). The primary endpoints of the study are overall survival (OS) and progression-free survival (PFS) as assessed by the blinded independent central review (BICR) in patients whose tumors express PD-L1 ≥1% for both Opdivo-based combination therapies versus chemotherapy. The secondary endpoints of the study include OS and PFS as assessed by the BICR in the all-randomized patient population.

In the Opdivo plus Yervoy arm, patients received treatment with Opdivo at 3 mg/kg every 2 weeks and Yervoy at 1 mg/kg every 6 weeks up to 24 months or until disease progression or unacceptable toxicity. In the Opdivo plus chemotherapy arm, patients received treatment with Opdivo at 240 mg every 2 weeks, fluorouracil 800 mg/m²/day on Day 1 through Day 5 (for 5 days), and cisplatin 80 mg/m² on Day 1 of four-week cycle. Patients received Opdivo for up to 24 months or until disease progression or unacceptable toxicity, and chemotherapy until disease progression or unacceptable toxicity.

About Esophageal Cancer

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. In Taiwan, SCC is the predominant type accounting for about 90% of all esophageal cancer. It is estimated that there are about 2,830 new cases* per year diagnosed with esophageal cancer and approximately 1,980 deaths* per year resulting from this disease in Taiwan.

*: Cancer Registry Annual Report, 2019 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, 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, and adjuvant treatment of urothelial carcinoma in March 2022.

In addition, ONO is conducting clinical development program including hepatocellular carcinoma, ovarian cancer, bladder cancer, prostate cancer, pancreatic 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. (Taipei, Taiwan, "OPTW") is an ONO's wholly-owned subsidiary established in in December 2014. OPTW has established its own sales organization in Taiwan and marketed Opdivo, an anti-PD-1 antibody/ anti-neoplastic drug since 2016. OPTW is committed to bringing more innovative new products to meet unmet medical needs to patients in Taiwan as soon as possible.

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