ONO PHARMACEUTICAL CO.,LTD.

March 22, 2023

Opdivo® Intravenous Infusion Approved in Combination with Yervoy in Taiwan for the Treatment of Hepatocellular Carcinoma Previously Treated with Sorafenib

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO: Gyo Sagara; "ONO") announced that Ono Pharma Taiwan Co., Ltd., a Taiwanese subsidiary of ONO, received the approval of Opdivo® (nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody, in combination with Yervoy on March 21, 2023 in Taiwan from the Taiwan Food and Drug Administration (TFDA), for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib.

This approval is based on the results from the Opdivo + Yervoy cohort of Phase 1/2 CheckMate -040 trial, in patients with advanced hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. In this Opdivo + Yervoy cohort, overall response rate (ORR) as assessed by Blinded Independent Central Review (BICR) using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) was 33% (16/49 patients); 8% (4/49) had a complete response (CR) and 24% (12/49) had a partial response (PR). Duration of response (DOR) ranged from 4.6 to more than 30.5 months, with 88% lasting at least six months, 56% at least 12 months and 31% at least 24 months. Opdivo + Yervoy of this trial showed an acceptable safety profile without new safety signals.

About CheckMate -040 Trial

CheckMate -040 is an open-label Phase 1/2 trial that included an Opdivo + Yervoy cohort in patients with HCC who progressed on or were intolerant to sorafenib. The trial included both PD-L1 positive and negative patients. Key eligibility criteria included histologic confirmation of HCC and Child-Pugh Class A cirrhosis status. Additional eligibility criteria included those who were infected or uninfected with active Hepatitis C virus (HCV) or active Hepatitis B virus (HBV). Patients with active autoimmune disease, brain metastasis, a history of hepatic encephalopathy, clinically significant ascites, infection with Human Immunodeficiency Virus (HIV), or active co-infection with HBV/HCV or HBV/Delta Hepatitis Virus (HDV) were excluded. Patients with known fibrolamellar HCC, sarcomatoid HCC, and mixed cholangiocarcinoma/HCC were also excluded. Patients were treated with Opdivo 1 mg/kg IV and Yervoy 3 mg/kg IV every three weeks for four doses, followed by Opdivo 240 mg every two weeks until disease progression or unacceptable toxicity. The major efficacy outcome was ORR as assessed by BICR using RECIST v1.1 and mRECIST. DOR was also assessed.

About Hepatocellular Carcinoma

Liver cancer is the second most frequent cause of cancer death worldwide. In 2020, it is estimated that approximately more than 905,000 cases are newly diagnosed with liver cancer per year, with approximately more than 830,000 deaths resulting from the disease per year worldwide.[1)] Hepatocellular carcinoma (HCC) is the most common type of liver cancer, and accounts for 90% of primary liver cancer.[2)] In Taiwan, it is estimated that approximately 10,980 cases are newly diagnosed with HCC per year, with approximately more than 7,770 deaths, including liver cancer and intrahepatic cholangiocarcinoma.[3)]

1)： Globocan 2020: World. World Health Organization. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
2)： Eunsun K., et al. Hepatocellular carcinoma: old friends and new tricks. *Experimental & Molecular Medicine Cancer.* 2020. Dec;52(12):1898-1907. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8080814/
3)： Cancer Registry Annual Report, 2020 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, prostate 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.

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 marketed Opdivo, an anti-PD-1 antibody/anti-neoplastic drug in Taiwan since 2016. OPTW is committed to bringing more innovative new products to meet unmet medical needs to patients in Taiwan as soon as possible.

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