April 21, 2020

Ono and Takeda Announce Results from Phase 3 CheckMate -9ER Study for Opdivo® (Nivolumab) and CABOMETYX® (Cabozantinib) Combination Therapy in Patients with Previously Untreated Advanced or Metastatic Renal Cell Carcinoma

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Takeda Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO, Christophe Weber; "Takeda") today announced the top-line result from CheckMate -9ER, a global, multi-center, randomized, open-label Phase 3 study evaluating ONO's Opdivo® (nivolumab, "Opdivo"), a human anti-human PD-1 (programmed cell death-1) monoclonal antibody, and Takeda's CABOMETYX® (cabozantinib s-malate, "cabozantinib") a tyrosine kinase inhibitor, which Takeda has licensed from Exelixis, Inc. (California, US, "Exelixis") for development and commercialization in Japan, in patients with previously untreated advanced or metastatic renal cell carcinoma (RCC).

In this study, Opdivo and cabozantinib combination treatment demonstrated a significant benefit in its primary endpoint of progression-free survival (PFS) at final analysis, compared to sunitinib, as well as its secondary endpoints of overall survival (OS) at a pre-specified interim analysis, and objective response rate (ORR).

The safety profiles of Opdivo and cabozantinib observed in the study reflect the known safety profiles of the immunotherapy and tyrosine kinase inhibitor components in previously untreated RCC.

About Checkmate -9ER Study

CheckMate -9ER study is a global, multi-center, randomized, open-label Phase 3 study evaluating Opdivo in combination with cabozantinib in patients with previously untreated advanced or metastatic RCC, versus sunitinib alone. The primary endpoint of the study was PFS per blinded independent central review (BICR). The secondary efficacy endpoints were OS, objective response rate (ORR). The primary efficacy analysis is comparing the doublet combination versus sunitinib in all randomized patients.

Since August 2018, ONO and Takeda has participated in Japan in this global study which has been ongoing under the collaboration among Bristol-Myers Squibb (New York, US), Exelixis and their other partner, Ipsen Pharma SAS (France).

Kidney Cancer

Kidney cancer is a malignant tumor arising from the renal parenchyma and is the most common cancer among renal malignant tumor. Among kidney cancer, RCC constitutes 90% of all kidney cancer patients[1]. It is estimated that about 24,000 new cases are diagnosed with kidney cancer per year in Japan (about 403,000 cases worldwide) and approximately 8,260 deaths (about 175,000 worldwide) per year resulting from this disease[2].

1 : The epidemiology of renal cell carcinoma. Euro Urol. 2011;60;615-621.
2 : Globocan 2018. Available at: http://gco.iarc.fr/today/fact-sheets-populations

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 cancer 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 and adjuvant treatment of melanoma 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, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, ovarian cancer, bladder 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.

About CABOMETYX

In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced RCC and for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. CABOMETYX tablets have also received regulatory approvals in the European Union and additional countries and regions worldwide. In Japan, the product was approved for the treatment of curatively unresectable or metastatic RCC as CABOMETYX® tablets 20mg and 60mg in March 2020 by the Ministry of Health, Labor and Wealth. In addition, a supplemental application was submitted for the treatment of unresectable HCC that has progressed following chemotherapy in January 2020.

About the Takeda and Exelixis Collaboration

In January 2017, Takeda entered into an agreement with Exelixis for the commercialization and further clinical development of cabozantinib for all future indications in Japan.

Exelixis retains exclusive rights to develop and commercialize cabozantinib in the United States and has licensed exclusive rights to commercialize cabozantinib outside of the US and Japan to Ipsen Pharma SAS.

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