ONO PHARMACEUTICAL CO.,LTD.

October 9, 2018

Opdivo® (Nivolumab) Intravenous Infusion Approved for Indication of Previously Untreated Intermediate and Poor Risk Advanced Renal Cell Carcinoma in Combination with Ipilimumab, and Change in Administration Method for Intravenous Infusion Duration in South Korea

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced that Ono Pharma Korea Co., Ltd. ("OPKR"), a Korean subsidiary of ONO, received the approval of Opdivo® (nivolumab) Intravenous Infusion 20 mg, 100 mg Inj. ("Opdivo"), a human anti-human PD-1 monoclonal antibody, on October 5 by the Ministry of Food and Drug Safety (MFDS) in South Korea, for indication of previously untreated intermediate and poor risk advanced renal cell carcinoma in combination with ipilimumab (Yervoy®) ("Yervoy"), and the change in administration method for intravenous infusion duration to "infuse intravenously over 30 minutes every 2 weeks" from the current "infuse intravenously over 60 minutes every 2 weeks".

This approval allows Opdivo to be used for the treatment of patients with previously untreated intermediate and poor risk advanced renal cell carcinoma in combination with Yervoy. In addition, the administration method is changed to "infuse intravenously over 30 minutes every 2 weeks" from the current "infuse intravenously over 60 minutes every 2 weeks", leading to shortened intravenous infusion duration.

About renal cell carcinoma

Kidney cancer is a malignant tumor arising from the renal parenchyma and is the most common cancer among renal malignant tumor. Globally, about 270,000 cases of kidney cancer are diagnosed yearly and 116,000 people die from the disease*[1]. Among kidney cancer, renal cell carcinoma (RCC) constitutes almost 90%*[1] of all patients[1]. In South Korea, it is estimated that there are about 4,500 patients of RCC newly diagnosed yearly*[2].

*1: The epidemiology of renal cell carcinoma. Euro Urol. 2011;60;615-621.
*2: National cancer center, Annual Report of Cancer Statistics in Korea in 2015, (published 2017.12.21)

OPKR is committed to taking measures necessary for proper use of Opdivo by collecting clinical data on the safety and efficacy of Opdivo. In South Korea, OPKR and BMS Pharmaceutical Korea Limited continue to co-promote the sales of Opdivo, based on the strategic collaboration agreement made between ONO and Bristol-Myers Squibb in July 2014.

Outline of Opdivo® Intravenous Infusion 20 mg, 100 mg

Product name	Opdivo® 20 mg, 100 mg Inj.
Generic name (INN)	Nivolumab
Indication	1. Unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab 2. Locally advanced or metastatic non-small cell lung cancer refractory to existing platinum-based chemotherapy 3. Advanced renal cell carcinoma 3.1 Advanced renal cell carcinoma after prior anti-angiogenic therapy as a single agent 3.2 Previously untreated intermediate and poor risk advanced renal cell carcinoma in combination with ipilimumab 4. Classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and pre/post-transplantation brentuximab vedotin 5. Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after platinum-based therapy 6. Locally advanced or metastatic urothelial carcinoma with disease progression during or following platinum-containing chemotherapy or disease progression within 12 months of neo-adjuvant or adjuvant treatment with platinum-containing chemotherapy 7. Advanced or recurrent gastric or gastroesophageal junction adenocarcinoma after two or more prior chemotherapy regimens
Dosage and administration	1. Melanoma: As monotherapy, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes every 2 weeks. In combination with ipilimumab, infuse intravenously at 1 mg/kg (body weight) of nivolumab over 30 minutes, followed by intravenous infusion of ipilimumab at 3 mg/kg (body weight) on the same day, every 3 weeks for the first 4 doses. Thereafter, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes every 2 weeks. 2. Renal cell carcinoma: As monotherapy, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes every 2 weeks. In combination with ipilimumab, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes, followed by intravenous infusion of ipilimumab at 1 mg/kg (body weight) on the same day, every 3 weeks for the first 4 doses. Thereafter, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes every 2 weeks. 3. Non-small cell lung cancer, classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, gastric or gastroesophageal junction adenocarcinoma: Infuse intravenously at 3 mg/kg (body weight) of nivolumab over 30 minutes every 2 weeks.
Approval date	October 5, 2018
Manufacturer	Ono Pharmaceutical Co., Ltd.
Importer/distributor	Ono Pharma Korea Co., Ltd.
Distribution collaboration	BMS Pharmaceutical Korea Limited

* Underlined parts show the revised ones due to this approval.

About Ono Pharma Korea Co., Ltd.

Ono Pharma Korea Co., Ltd. (OPKR), in Seoul, Korea, was established as an ONO's wholly-owned subsidiary in December 2013. OPKR has started to market specialty products such as anti-cancer agents, including Opdivo. OPKR has been committed to developing and marketing its products created internally for further penetration into the South Korean market.

About Opdivo

Opdivo is a 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.

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, and unresectable advanced or recurrent gastric cancer which has progressed after chemotherapy in September 2017, and unresectable advanced or recurrent malignant pleural mesothelioma which has progressed after chemotherapy and adjuvant treatment of melanoma, etc. in August 2018. In addition, ONO is conducting clinical development program including esophageal cancer, esophago-gastric junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, ovarian cancer, biliary tract cancer, etc.

In abroad, BMS has a robust clinical development program for Opdivo monotherapy and in combination with other Immuno-Oncology and non-Immuno-Oncology therapies across more than 350 clinical trials. BMS is studying Opdivo in approximately 50 types of cancer, across solid tumors and hematologic malignancies, and is utilizing its translational medicine capabilities to tailor approaches with the goal of providing maximal benefit for individual patients.

Opdivo is currently approved in more than 60 countries, including Japan, South Korea, Taiwan, the US and European Union.

About ONO and BMS Collaboration

In 2011, through a collaboration agreement made between ONO and 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.

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