ONO PHARMACEUTICAL CO.,LTD.

June 15, 2023

ONO Submits Supplemental Application of Opdivo® in Japan to Expand its Use for Treatment of Unresectable Advanced or Recurrent Malignant Epithelial Tumors

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO: Gyo Sagara; "ONO") today announced that it has submitted a supplemental application of Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody in Japan, to expand its use for the treatment of unresectable advanced or recurrent malignant epithelial tumors, for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the result from the investigator-initiated Phase 2 clinical trial (NMSC-PD1 Study: KCTR-D014), conducted under the initiative of the Keio University Hospital, in patients with malignant epithelial tumors.

Malignant epithelial tumors are a general term for skin cancers that are systematically classified as epithelial tumors, and include squamous cell carcinoma, basal cell carcinoma, extramammary Paget's disease, skin appendage cancers (sweat gland carcinoma, sebaceous carcinoma, hair follicle carcinoma), etc.[1), 2)]

The number of patients with malignant epithelial tumors is estimated to be 25,000 to 38,315 patients[3), 4)]. More than 90% of patients are expected to be cured by local treatment mainly with surgical therapy[5), 6)]. On the other hand, the number of patients with unresectable advanced or recurrent malignant epithelial tumors is reported to be 933 cases per year[7)] with its poor prognosis in Japan. As standard treatment for unresectable advanced or recurrent malignant epithelial tumors has not yet been established in Japan, a drug development is eagerly desired.

Opdivo was designated as an orphan drug for the indication of unresectable advanced or recurrent malignant epithelial tumors on May 23, 2023, and is accepted for priority review by the Ministry of Health, Labor and Welfare (MHLW).

1) General Rules for Clinical and Pathological Studies on Malignant Neoplasms of the Skin (2nd edition), Japanese Skin Cancer Society. August 2010
2) Outlines of Various Rare Cancer (Skin Cancer), Rare Cancer Center, National Cancer Center. April 28, 2014 (updated on December 13, 2022) https://www.ncc.go.jp/jp/rcc/about/skin_tumor/index.html (available only in Japanese)
3) Patient Survey 2020, Ministry of Health, Labour and Welfare. 2023
4) P-Market patient number analysis (August 2021 - July 2022). JMDC Inc.
5) Japanese Guidelines for Skin Cancer (3rd edition). 2022 Japanese Dermatological Association/Japanese Skin Cancer Society
6) Japanese Guidelines for Skin Cancer (2nd edition). 2015 Japanese Dermatological Association
7) Fujisawa Y, et al. J Dermatol Sci. 2018 Dec;92(3):230-6.

About NMSC-PD1 Study

This study is an investigator-initiated, multi-center, unblinded, non-comparative Phase 2 clinical trial evaluating the efficacy and safety of Opdivo in patients with malignant epithelial tumors. Patients received Opdivo at 480 mg every four weeks. The primary endpoint of the study is objective response rate (Central Judgment). Secondary endpoints include objective response rate (Physician Judgment at Medical Institution), disease control rate (DCR), overall survival (OS) and progression-free survival (PFS), etc.

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.

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