

December 17, 2015

ONO receives manufacturing and marketing approval partial amendment approval for OPDIVO[®] (generic name: nivolumab) for treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer in Japan

ONO PHARMACEUTICAL CO.,LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; “ONO”) announced today that ONO has received a manufacturing and marketing approval partial amendment approval for the human anti-human PD-1 (programmed cell death-1) monoclonal antibody “OPDIVO[®] 20mg, 100mg Inj.” (OPDIVO) for the treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) in Japan.

Lung cancer is a form of malignant tumor that arises from cells in the trachea, bronchi, and alveoli. It is one of the leading causes of cancer-related death, responsible for approximately 1.6 million deaths worldwide each year. In Japan, NSCLC is the most common type of lung cancer, accounting for about 85% of lung cancer cases. Of patients with NSCLC, about 80% have non-squamous NSCLC, and about 20% squamous NSCLC, so there is an unmet need for new treatments for patients with NSCLC that cannot be removed by surgery and has become resistant to existing treatments, as they have an extremely poor prognosis, and currently available therapeutic options do not produce a significant improvement.

OPDIVO is the world’s first immune checkpoint inhibitor blocking the PD-1/PD-1 ligand pathway proven to extend overall survival (OS) in patients with advanced NSCLC previously treated with chemotherapy. The interim analysis of an open-label, randomized phase III study (CheckMate-017) which was conducted in patients with advanced squamous NSCLC outside of Japan showed that OPDIVO improved OS, with a 41% reduction in the risk of death, compared with standard of care (docetaxel). OPDIVO demonstrated the 1 year OS rate of 42% (95% CI, 34 to 50) versus 24% (95% CI, 17 to 31) for docetaxel, with a median OS of 9.2 months (95% CI: 7.3, 13.3) versus 6.0 months (95% CI: 5.1, 7.3), respectively. Also, the interim analysis of an open-label, randomized phase III study (CheckMate-057) which was conducted in patients with advanced non-squamous NSCLC outside of Japan showed that OPDIVO improved OS, with a 27% reduction in the risk of death or disease progression, compared with standard of care (docetaxel). The 1 year OS rate was

51% (95% CI, 45 to 56) with OPDIVO versus 39% (95% CI, 33 to 45) with docetaxel, and the median OS was 12.2 months (95% CI: 9.7, 15.0) in the OPDIVO group versus 9.4 months (95% CI: 8.0, 10.7) in the docetaxel group.

Furthermore, the analysis of a phase II study (ONO-4538-05) which was conducted in patients with squamous NSCLC in Japan showed that overall response rate (ORR) in OPDIVO group was 25.7% (95%CI: 14.2, 42.1), and the analysis of a phase II study (ONO-4538-06) which was conducted in patients with non-squamous NSCLC in Japan showed that ORR in OPDIVO group was 19.7% (95%CI: 12.3, 30.0), resulting in finding the same efficacy as the clinical study outside of Japan.

In addition, clinical results from CheckMate -017 and -057 study were presented at 2015 annual meeting of the American Society of Clinical Oncology with publication in The New England Journal of Medicine.

In Japan, OPDIVO is the first human anti-human PD-1 monoclonal antibody to receive regulatory approval for the treatment of patients with unresectable melanoma anywhere in the world in July 2014.

Also, outside of Japan, Bristol Myers Squibb, with whom ONO collaborates in Japan, Korea and Taiwan, currently has regulatory approval for OPDIVO in more than 40 countries globally. In the USA, OPDIVO is approved for treatment of metastatic squamous and non-squamous NSCLC after progression on or after platinum-based chemotherapy OPDIVO or other first line therapy, respectively. Also, in the USA, OPDIVO is approved for the treatment of unresectable or metastatic melanoma as a single agent and as a single agent following disease progression following Yervoy[®] (generic name: ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor. OPDIVO is also approved in combination with Yervoy for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma, the first combination of a PD-1 immune checkpoint inhibitor with a CTLA4 immune checkpoint inhibitor. Furthermore, OPDIVO is approved for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy in November this year.

In the EU, OPDIVO is approved for the treatment of advanced (unresectable or metastatic) melanoma in adults regardless of BRAF status and for the treatment of locally advanced or metastatic squamous NSCLC after prior chemotherapy.

Accumulating further clinical data is important in ensuring that OPDIVO will be used more properly and effectively, so ONO is committed to taking actions necessary for the proper use of OPDIVO by implementing a post-marketing use-results survey (all-case surveillance) and collecting clinical data on the safety and efficacy of OPDIVO pursuant to the conditions for its approval.

Product name	OPDIVO® Intravenous Infusion 20 mg/100 mg
Generic name (JAN)	Nivolumab (recombinant)
Indication	<u>1. Unresectable melanoma</u> <u>2. Unresectable, advanced or recurrent non-small cell lung cancer</u>
Dosage and administration	<u>1. Unresectable melanoma</u> The recommended dose for adults is 2 mg/kg (body weight) of nivolumab administered as an intravenous infusion every 3 weeks. <u>2. Unresectable, advanced or recurrent non-small cell lung cancer</u> The recommended dose for adults is 3 mg/kg (body weight) of nivolumab administered as an intravenous infusion every 2 weeks.
Manufacturer/distributor	ONO PHARMACEUTICAL CO., LTD.
Co-promotion	Bristol-Myers KK
Conditions for approval	<u>1. ONO is required to perform properly based on medicine risk management plan.</u> <u>2. Because of the very limited number of patients treated with OPDIVO in Japanese clinical trials, ONO is required to perform a post-marketing use-results survey covering all cases until data on a certain minimum number of patients have been accumulated.</u> Through these activities, ONO should identify the characteristics of patients to be treated with OPDIVO and collect safety and efficacy data as soon as possible, thereby taking actions necessary to ensure the proper use of OPDIVO.

* According to this manufacturing and marketing approval partial amendment approval, revised parts are underlined.

Photograph of product



About ONO PHARMACEUTICAL CO., LTD.

ONO PHARMACEUTICAL CO., LTD., headquartered in Osaka, Japan, is an R&D-oriented pharmaceutical company committed to creating innovative medicines in specific areas. It focuses especially on the diabetes and oncology areas. For more information, please visit the company's website at <http://www.ono.co.jp/eng/index.html>.

About the ONO PHARMACEUTICAL and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with ONO PHARMACEUTICAL, Bristol-Myers Squibb expanded its territorial rights to develop and commercialize OPDIVO globally except in Japan, South Korea and Taiwan, where ONO had retained all rights to the compound at the time. In July 2014, ONO and Bristol-Myers Squibb further expanded the companies' strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

Contact

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