

February 29, 2016

ONO Receives Approval for OPDIVO® (Nivolumab) for a Partial Change in Approved Items for Treatment of Unresectable Melanoma in Japan

ONO PHARMACEUTICAL CO.,LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; “ONO”) announced today that ONO has received approval for a partial change in approved items of the manufacturing and marketing authorization of OPDIVO® Intravenous Infusion 20mg, 100mg (“OPDIVO”), the human anti-human PD-1 (programmed cell death-1) monoclonal antibody for the treatment of unresectable melanoma in Japan.

OPDIVO has been approved for the treatment of unresectable melanoma in Japan. The approval for a partial change granted this time allows OPDIVO to be given in patients who have not been previously treated with chemotherapy at the dosage and administration of 3 mg/kg (body weight) every 2 weeks as an intravenous infusion. Also, this supplemental approval includes additional application for dosage and administration of intravenous infusion at 3 mg/kg (body weight) every 2 weeks, in addition to the current dosage and administration of intravenous infusion at 2 mg/kg every 3 weeks in patients with unresectable melanoma who have been treated with chemotherapy.

This partial change approval is based on data from the Japanese Phase II study (ONO-4538-08) and the global Phase III study (CA209-066) conducted by Bristol-Myers Squibb. The Japanese Phase II study was a multicenter, open-label, uncontrolled study intended to evaluate the efficacy and safety of OPDIVO in patients with untreated, unresectable stage III/IV or recurrent malignant melanoma. In this study, subjects received continuous intravenous infusions of OPDIVO over approximately 60 minutes at a dose of 3 mg/kg every 2 weeks. The primary endpoint of efficacy was the overall response rate (ORR) (central assessment). The ORR (central assessment) in the OPDIVO group in the study was 29.2% (90% CI [16.7, 45.9]).

The global Phase III (CA209-066) randomized double blind study conducted by Bristol-Myers Squibb, comparing OPDIVO, an investigational PD-1 immune checkpoint inhibitor, to the chemotherapy dacarbazine (DTIC) in patients with treatment naïve BRAF wild-type advanced melanoma (n=418). The study met the primary endpoint of overall survival (OS) with the median OS not reached for OPDIVO vs. 10.8 months for DTIC. The one-year survival rate was 73% for OPDIVO vs. 42% for DTIC and there was a 58% decrease in the risk of death for patients treated with OPDIVO (Hazard Ratio for death [HR]: 0.42, P<0.0001).

The Japanese Phase II study (ONO-4538-08) in patients with untreated or recurrent malignant melanoma demonstrated similar efficacy of OPDIVO to that in the global Phase III study (CA209-066), indicating the similar clinical usefulness of OPDIVO in Japanese and non-Japanese patients.

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment producing cells (melanocytes) which are related deeply with the skin color, and said to be the most metastatic and deadliest form of the disease.

OPDIVO is the first human anti-human PD-1 monoclonal antibody to receive regulatory approval for the indication of unresectable melanoma in July 2014 in Japan anywhere in the world. Also, OPDIVO received a supplemental approval for the indication of unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) in December 2015. Outside of Japan, Bristol Myers Squibb, with whom ONO collaborates in Japan, South Korea and Taiwan, currently has regulatory approval for OPDIVO in more than 40 countries globally.

In Japan, ONO and Bristol-Myers Squibb (and BMS Japan subsidiary BMKK) have formed a strategic partnership that includes co-development, co-commercialization, and co-promotion of multiple immunotherapies for patients with cancer.

ONO believes that accumulating further clinical data is important in ensuring that OPDIVO can be used more properly and effectively. 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 approval.

Product name	OPDIVO® Intravenous Infusion 20 mg/100 mg
Generic name (JAN)	Nivolumab (recombinant)
Indication	1. Unresectable melanoma 2. Unresectable, advanced or recurrent non-small cell lung cancer
Dosage and administration	1. Unresectable melanoma <u>Chemotherapy-naive patients: Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks.</u> <u>Chemotherapy-treated patients: Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks or 2 mg/kg (body weight) of nivolumab every 3 weeks.</u> 2. Unresectable, advanced or recurrent non-small cell lung cancer Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks.
Manufacturer/distributor	ONO PHARMACEUTICAL CO., LTD.
Co-promotion	Bristol-Myers KK
Conditions for approval	1. Design and appropriately implement a Risk Management Plan. 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. 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 the approval for partial change in approved items of the manufacturing and marketing approval, revised parts are underlined.

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 oncology and diabetes areas. For more information, please visit the company's website at <http://www.ono.co.jp/eng/index.html>.

About the ONO and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with ONO, 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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