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Chugai Obtains Approval for Additional Indication and Formulation for Tecentriq in PD-L1-Positive Triple Negative Breast Cancer

- The first approved immune checkpoint inhibitor in Japan for the treatment of PD-L1-positive triple-negative breast cancer

TOKYO, September 20, 2019 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it has obtained regulatory approval for its humanized anti-PD-L1 monoclonal antibody, Tecentriq® [generic name: atezolizumab (genetical recombination)] from the Ministry of Health, Labour and Welfare (MHLW) for an additional indication of PD-L1-positive, hormone receptor-negative and HER2-negative inoperable or metastatic breast cancer. It has also obtained approval for an additional formulation of Tecentriq 840 mg. Tecentriq 840 mg was developed to provide an optimal formulation for breast cancer for which approved dosage is 840 mg once every 2 weeks.

VENTANA OptiView PD-L1 (SP142), a pathological testing kit marketed by Roche Diagnostics K.K., should be used to detect PD-L1 expression. An expanded use of VENTANA OptiView PD-L1 (SP142) as a companion diagnostic of Tecentriq was approved on August 20, 2019 to allow physicians to identify patients with PD-L1-positive breast cancer who could benefit from Tecentriq.

“We are very pleased that Tecentriq has been approved as the first immune checkpoint inhibitor for the treatment of PD-L1-positive triple-negative breast cancer (TNBC) in Japan,” said Dr. Yasushi Ito, Chugai’s Executive Vice President, Co-Head of Project & Lifecycle Management Unit. “This approval provides a novel cancer immunotherapy-based treatment for TNBC, a rapidly-progressing cancer with limited therapeutic options. We are committed to contribute to patients through the treatment.”

This approval is based on the results from the phase III IMpassion130 study. Tecentriq in combination with *nab*-paclitaxel (albumin-bound) met primary endpoint with a significant reduction in the risk of disease worsening or death (PFS) compared with *nab*-paclitaxel (albumin-bound) alone in the intention-to-treat (ITT) population (median PFS=7.2 vs 5.5 months; hazard ratio [HR]=0.80, 95%CI: 0.69-0.92, p=0.0025) and in people who were tested positive for PD-L1 expression (median PFS=7.5 vs 5 months; hazard ratio [HR]=0.62, 95% CI: 0.49-0.78, p<0.0001). Tecentriq and *nab*-paclitaxel (albumin-bound) showed a clinically meaningful improvement in the co-primary endpoint of overall survival (OS) in the PD-L1-positive population (median OS=25.0 vs 18.0 months; HR=0.71, 95% CI: 0.54-0.93) at the second interim analysis. OS results in the PD-L1-positive population were not formally tested due to the hierarchical design of the study as statistical significance was not met for OS in the intention-to-treat (ITT) population (median OS=21.0 vs 18.7 months; HR=0.86, 95% CI: 0.72-1.02, p=0.078). Follow-up will continue until the next planned analysis. The safety profile of Tecentriq in combination with chemotherapy was consistent with the known safety profiles of the individual medicines, and no new safety signals were identified.

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About the IMpassion130 study

The IMpassion130 study is a Phase III, multicenter, randomized, double-blind study evaluating the efficacy, safety and pharmacokinetics of Tecentriq plus *nab*-paclitaxel (albumin-bound) compared with *nab*-paclitaxel (albumin-bound) in people with unresectable locally advanced or metastatic TNBC who have not received prior systemic therapy for metastatic breast cancer. The co-primary endpoints are PFS per investigator assessment (RECIST 1.1) and OS in the ITT population and in the PD-L1-positive population.

<Reference>

Roche's Tecentriq in combination with Abraxane improves outcomes as an initial treatment for people with PD-L1-positive metastatic triple-negative breast cancer (Press release issued by Roche on October 20, 2018)
https://www.roche.com/media/releases/med-cor-2018-10-20.htm

Chugai Files for Additional Indication and Additional Formulation of Anti-PD-L1 Antibody TECENTRIQ® for Breast Cancer (Press release issued by Chugai on December 21, 2018)
https://www.chugai-pharm.co.jp/english/news/detail/20181221153000_582.html

Roche presents data from across its breast cancer portfolio at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting (Press release issued by Roche on June 3, 2019)
https://www.roche.com/media/releases/med-cor-2019-06-03.htm

Free Offering of Tecentriq 840 mg prior to the Listing in the NHI Reimbursement Price List

Under the system for healthcare services provided combining insurance-covered and non-covered services provided by MHLW, Chugai will offer Tecentriq for free to respond to requests for emergency use from patients with PD-L1-positive, hormone receptor-negative and HER2-negative inoperable or metastatic breast cancer with very limited treatment options. In the context of proper use, Tecentriq will be offered for free only to medical institutions participated in the clinical study of IMpassion130 study for development of the drug as clinical sites on condition that; 1) they would use the drug in accordance with the approved indications and dosage and administration and 2) they would corporate with us in implementing various safety measures to promote proper use, including activities based on Early Post-Marketing Phase Vigilance conducted by Chugai during the free offering period. The offering will start immediately after the date of regulatory approval and end on the day before the listing in the NHI reimbursement price list.

Sites for implementation of free offering of the drug	Medical institutions participated in the clinical study of IMpassion130 study in Japan
Period for implementation of free offering of the drug	From date of regulatory approval through the day before the listing in the NHI reimbursement price list

As a top pharmaceutical company in the field of oncology in Japan, Chugai is committed to contribute to patients and medical professionals by offering Tecentriq as a new treatment option and accordingly, to improve access of medications and their proper use.

Prescribing Information *The underlined parts were newly added.

Product name	Tecentriq® Intravenous Infusion 840 mg Tecentriq® Intravenous Infusion 1200 mg
Generic name	atezolizumab (genetical recombination)
Indications	Tecentriq® Intravenous Infusion 840 mg ・ PD-L1-positive, hormone receptor-negative and HER2-negative inoperable or metastatic breast cancer Tecentriq® Intravenous Infusion 1200 mg ・ Unresectable, advanced or recurrent non-small cell lung cancer ・ Extensive-stage small cell lung cancer
Dosage and administration	・ In case of patients with untreated unresectable, advanced or recurrent non squamous non-small cell lung cancer. The usual adult is 1200 mg atezolizumab (genetical recombination) in combination with carboplatin, paclitaxel and bevacizumab (genetical recombination) by intravenous infusion over 60 minutes once every 3 weeks. If the initial infusion is well tolerated, subsequent infusions can be delivered over 30 minutes. ・ In case of patients with unresectable, advanced or recurrent non squamous non-small cell lung cancer who has undergone chemotherapy. The usual adult dosage is 1200 mg atezolizumab (genetical recombination) administered by intravenous infusion over 60 minutes once every 3 weeks. If the initial infusion is well tolerated, subsequent infusions can be delivered over 30 minutes. ・ In case of patients with extensive-stage small cell lung cancer. The usual adult dosage is 1200 mg atezolizumab (genetical recombination) in combination with carboplatin and etoposide by intravenous infusion over 60 minutes once every 3 weeks. If the initial infusion is well tolerated, subsequent infusions can be delivered over 30 minutes. ・ In case of patients with PD-L1-positive, hormone receptor-negative and HER2-negative inoperable or metastatic breast cancer. The usual adult dosage is 840 mg atezolizumab (genetical recombination) in combination with *nab*-paclitaxel (albumin-bound) administered by intravenous infusion over 60 minutes once every 2 weeks. If the initial infusion is well tolerated, subsequent infusions can be delivered over 30 minutes.
Drug price	Tecentriq® Intravenous Infusion 840 mg Not listed in the NHI price list Tecentriq® Intravenous Infusion 1200 mg JPY 625,567/per vial
Conditions for approval	・ A risk management plan should be created and appropriately implemented. ・ In case of patients with unresectable, advanced or recurrent non squamous non-small cell lung cancer who has undergone chemotherapy.

	Because the number of participants in Japanese clinical trials was very limited, post-marketing drug use surveillance of all patients receiving Tecentriq treatment should be conducted until data for a certain number of patients have been accumulated, in order to understand background information on people using Tecentriq as well as to collect safety and efficacy data on Tecentriq promptly, and take necessary measures for the appropriate use of Tecentriq.

About Triple-Negative Breast Cancer

In Japan, 86,500 women (2018 predicted value) are estimated to be afflicted with breast cancer each year. 14,800 women in Japan (2018 predicted value) die as a result of the disease. Triple-negative breast cancer accounts for 15% of all breast cancer cases and, is more common in women under the age of 50, compared with other forms of breast cancer. Triple-negative breast cancer is defined by the lack of expression of hormone receptors (estrogen and progesterone receptors) and the overexpression of human epidermal growth factor receptor 2 (HER2). In general, triple-negative breast cancer has a high tumor-proliferative capacity and shorter overall survival, compared with other forms of breast cancer.

About approval status of Tecentriq in Japan

Tecentriq was launched in April 2018 with an indication of unresectable, advanced or recurrent NSCLC, followed by an approval for the additional dosing for the treatment of untreated unresectable, advanced or recurrent NSCLC in December 2018. In addition, an approval of extensive-stage small cell lung cancer has been obtained in August 2019.

Sources

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Inquiry for free offering of Tecentriq 840 mg prior to the listing in the NHI reimbursement price list

For healthcare providers/patients and their families
Medical Information Dept.
Tel: 0120-14-0564 (Toll free, domestic call only, 9:00AM to 5:30PM Monday to Friday)

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