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Translation

Anti-Cancer Agent, Tarceva®
Condition for Approval (All Patients Surveillance) Partially Removed in Japan for "Nonresectable Recurrent and Advanced Non-small Cell Lung Cancer which is Aggravated Following Chemotherapy"

February 7, 2012 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Head Office: Chuo-ku, Tokyo; President: Osamu Nagayama (hereafter, "Chugai")] announced today that it has received yesterday a notification from the Japanese Ministry of Health, Labour and Welfare (MHLW) that the condition for approval has been partially removed for the anti-cancer agent erlotinib hydrochloride [brand name: Tarceva® Tablet 25mg, 100mg and 150mg hereafter, "Tarceva®"] for the indication of "nonresectable recurrent and advanced non-small cell lung cancer which is aggravated following chemotherapy."

Tarceva® was originally approved in 2007 for "nonresectable recurrent and advanced non-small cell lung cancer which is aggravated following chemotherapy." At the time of approval, condition for approval was set as "1; a post-marketing surveillance of all patients who receive Tarceva® should be conducted until the data of a certain number of patients are accumulated in order to identify the background of the patients, and safety and efficacy data should be collected and necessary measures for appropriate use of Tarceva® should be taken" and "2; take necessary safety measures to ensure that Tarceva® will be handled by doctors, medical institutions and pharmacists who have sufficient experience in diagnosis and chemotherapy in lung cancer and who can control risks, especially risk of interstitial lung disease, associated with Tarceva®." This time, Chugai received the notice to lift condition 1, but will continue with condition 2.

Safety (3,488 patients) and efficacy (3,453 patients) data with "nonresectable recurrent and advanced non-small cell lung cancer which is aggravated following chemotherapy" was submitted to the Japanese MHLW by Chugai as the aggregate analysis results of the post-marketing surveillance of all patients. Based on the results, it has been determined that the post marketing surveillance, which was the condition for the approval of Tarceva®, had been conducted properly, and that necessary measures for proper use of the drug are in place.

Among the indications of this drug, surveillance of all patients with "pancreatic cancer not amenable to curative resection" is ongoing and new patients are continued to be enrolled.

Chugai, as a leading pharmaceutical company in the field of oncology, will continuously provide innovative and useful pharmaceutical products and information with the aim of "the realization of cancer care that brings about hope for patients when coping with cancer," and will continue to make efforts to provide information on the proper use of our products while giving the highest priority to the safety of patients.

Note: Tarceva® Tablet 150mg is not approved for pancreatic cancer.

[References]

Objective of all patient surveillance

The objective of the surveillance is to obtain information on the safety (adverse reactions) of the drug and to ensure the safe use of the drug for those patients with "nonresectable recurrent and advanced non-small cell lung cancer which is aggravated following chemotherapy," who receive treatment with Tarceva®. The all patient surveillance started from December 18, 2007, and completed on March 31, 2011.

Aggregate analysis results

Of 3,743 patients with "nonresectable recurrent and advanced non-small cell lung cancer which is aggravated following chemotherapy" who were enrolled between December 18, 2007 and June 30, 2008, those subjected to data aggregation (background data aggregation: 3,488 patients, safety data aggregation: 3,488 patients, effective data aggregation: 3,453 patients) were included in this surveillance and data on these patients was analyzed.

The incidence of adverse reactions was 81.8% (2,852 patients) in 3,488 patients of safety analysis set, in which the incidence of serious adverse reactions accounted for 13.1% (458 patients, including 68 fatal cases). The most common adverse reactions with incidence of more than 5% included 63.0% of rashes such as acneiform, 23.5% of diarrhoea, 8.3% of stomatitis, 6.6% of dry skin, 6.4% of decreased appetite, 6.0% of paronychia and 5.2% of hepatic function disorder. The tendency of the adverse reactions was similar to that at the approval point.

In Asian patients, it is reported that many ILD-like events are observed as the adverse reaction of EGFR tyrosine kinase inhibitors such as "Tarceva®." In 3,488 patients of safety analysis set, the ILD-like events were reported in 189 cases (physicians' report). Each ILD-like event was evaluated based on the internal findings, the chest radiographic findings and the pathological findings (when specimen was available), by the Proper Use Exploratory Committee consisting of external specialist. This committee decided that 31 cases were "not ILD," and the incidence of "ILD" was finally determined to be 4.5% (158 cases). There were 55 fatal cases by ILD (1.6%).

The results of these surveillances have been presented at domestic and international meetings[1, 2, 3, 4, 5] and provided to healthcare professionals in various forms of information including package insert, interview form and guidance for proper use of the drug.

1. The 7th Annual Meeting of Japanese Society of Medical Oncology (March 20, 2009)
2. The 49th Annual Meeting of The Japanese Respiratory Society (June 12, 2009)
3. The 50th Annual Meeting of The Japan Lung Cancer Society (November 13, 2009)
4. The 8th Annual Meeting of Japanese Society of Medical Oncology (March 18, 2010)
5. The 51st Annual Meeting of The Japan Lung Cancer Society (November 4, 2010)
6. Joint 16th ECCO (European Cancer Organisation) - 36th ESMO (European Society for MedicalOncology) - 30th ESTRO (European Society for Radiotherapy & oncology) Multidisciplinary Cancer Congress (September 26, 2011)