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Roche Group

Translation

Results of Japanese Phase II Clinical Trial for Non-Small Cell Lung Cancer with *EGFR* Mutations was Published Online on "The Lancet Oncology"

August 29, 2014 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that the results of the phase II clinical trial (JO25567 study) conducted in Japan were published on the electronic version of "The Lancet Oncology", one of the most prestigious medical journals in the oncology field around the world, on August 28, 2014. The aim of the JO25567 study was to compare the efficacy and safety between combination therapy with erlotinib hydrochloride (hereafter, "erlotinib") and bevacizumab (genetical recombination) (hereafter, "bevacizumab") and erlotinib monotherapy as the first-line treatment of non-small cell lung cancer with *EGFR* mutations.
http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(14)70381-X/abstract

The JO25567 study published in "The Lancet Oncology" is a randomized phase II clinical trial conducted by Chugai in Japan. The subjects were 154 Japanese chemotherapy-naïve patients with stage IIIB/IV or recurrent non-squamous non-small cell lung cancer who have *EGFR* mutations (exon 19 deletion mutation, L858R point mutation). The primary endpoint of this study was progression-free survival assessed by an independent review committee. Overall survival, response rate, quality of life (QOL) and safety were defined as the secondary endpoints.

The median progression-free survival, which was the primary endpoint, was 16.0 months in combination with erlotinib and bevacizumab, and 9.7 months in erlotinib monotherapy, showing a statistically significant increase in the combination therapy [hazard ratio, 0.54 (95% confidence interval, 0.36-0.79, p = 0.0015)]. The response rate was 69% (52 subjects, 95% confidence interval, 58-80%) in the combination therapy and 64% (49 subjects, 95% confidence interval, 52-74%) in the monotherapy. Regarding safety, grade 3/4 adverse events were skin disorder, an adverse event characteristic to the use of erlotinib (in 25% of patients on the combination therapy and in 19% on monotherapy). Grade 3/4 hypertension, which is an adverse event characteristic to the use of bevacizumab, was observed in 60% of the combination therapy and 10% of the monotherapy. Similarly, proteinuria was observed in 8% of the combination therapy and none in the monotherapy. No new safety findings were observed and the safety profile was consistent with those seen in previous reports. The combination with bevacizumab did not lower the QOL.

The results of the JO25567 study have been presented at the 50th annual meeting of American Society of Clinical Oncology (held in May-June 2014).

As the top pharmaceutical company in the field of oncology, Chugai will promote the appropriate use in combination with bevacizumab and erlotinib so that it will be a new therapeutic option for patients suffering from *EGFR* mutation-positive non-small cell lung cancer.

About erlotinib

Erlotinib is a once-daily, oral treatment for advanced or metastatic NSCLC and pancreatic cancer. It has been shown to potently inhibit EGFR, a protein involved in the growth and development of cancers.

In Japan, erlotinib received approval for “unresectable recurrent/advanced NSCLC that has become aggravated after chemotherapy” in October 2007 and “pancreatic cancer not amenable to curative resection” in July 2011 and “chemotherapy-naïve, unresectable, recurrent/advanced non-small cell lung cancer with *EGFR* mutations” in June 2013.

The brand name is Tarceva® Tablet 25mg, Tarceva® Tablet 100mg and Tarceva® Tablet 150mg in Japan. Tarceva® Tablet 150mg is not approved for pancreatic cancer.

Tarceva® is a registered trademark of OSI Pharmaceuticals, LLC, a member of the Astellas global group of companies.

About bevacizumab

Bevacizumab is an antibody drug that binds specifically to VEGF, which plays an important role in the vascularization needed for the growth and metastasis of tumors, and impedes its activity. Bevacizumab received approval for the treatment of metastatic colorectal cancer in the U.S. in February 2004 and is recommended as one of the standard treatments in several guidelines. In Japan, it received approval for “unresectable advanced or recurrent colorectal cancer” in April 2007, “unresectable advanced or recurrent non-squamous non-small cell lung cancer” in November 2009, “inoperable or recurrent breast cancer” in September 2011, “malignant glioma” in June 2013 and “ovarian cancer” in November 2013.

The brand name is Avastin® for intravenous infusion 100mg/4mL and Avastin® for intravenous infusion 400mg/16mL in Japan.

Avastin® is a registered trademark of Genentech, Inc. (USA).