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Translation

Anti-Cancer Agent "Avastin®," Obtained Approval for Additional Indication of Ovarian Cancer

November 22, 2013 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that it gained approval by the Japanese Ministry of Health, Labour and Welfare (MHLW) on November 22, 2013, for "Ovarian cancer," as new additional indication for the anti-cancer agent / anti-VEGF humanized monoclonal antibody, "AVASTIN® I.V. Infusion 100 mg/4 mL and 400 mg/16 mL" [generic name: bevacizumab (genetic recombinant) for Infusion] (hereafter, "Avastin®"). In Japan, Avastin® is currently marketed for the indications of "unresectable advanced or recurrent colorectal cancer," "unresectable advanced or recurrent non-squamous non-small cell lung cancer," "inoperable or recurrent breast cancer" and "malignant glioma."

On December 13, 2010, Chugai received a request from the MHLW to develop "Avastin®" for the treatment of ovarian cancer, as a result of the evaluation by the "5th Review Committee on Unapproved Drugs and Indications with High Medical Needs" held on October 6, 2010. Chugai filed an application for approval on October 5, 2012.

This approval was mainly based on the phase III study (GOG-0218 study conducted in the US, Japan and other countries) in front line therapy for the patients with ovarian cancer. The GOG-0218 study investigated efficacy and safety of "Avastin®" when administered in combination with carboplatin/paclitaxel, a standard chemotherapy, and then continued "Avastin®" monotherapy as a continued therapy. The GOG-0218 study met its primary endpoint to significantly prolong the progression free survival in patients with ovarian cancer who received "Avastin®" as compared with those who received the standard chemotherapy alone. Avastin® was well tolerated and its safety profile was consistent with the previously reported data of "Avastin®."

The GOG-Japan, a subsidiary organization of the Japanese Gynecologic Oncology Group (JGOG; President: Kazunori Ochiai, Professor, Jikei University), participated in the GOG-0218 study, which was an investigator-initiated clinical trial for registration. The result of Japanese ovarian cancer patients who participated in the GOG-0218 study was included in the application materials for approval.

Professor Ochiai said, ""Avastin®" was the first anti-cancer agent in Japan to be approved based on an investigator-initiated global clinical trial, and its approval is a result of the cooperation of patients who have participated in the study, as well as the efforts of all the people concerned, such as GOG-Japan's investigators, the Clinical Trials Coordinating Center of the Kitasato University Research Center for Clinical Pharmacology, the U.S. NCI and Chugai. This approval can be regarded as innovative accomplishment, and will be welcome news for ovarian cancer patients whose treatment options have so far been limited. We believe that the approval of "Avastin®" has the potential to improve on the current clinical practice in Japan."

"Avastin®" is approved in Europe for the treatment of advanced stages of breast cancer, colorectal cancer, non-small cell lung cancer, renal cell cancer and ovarian cancer, and is available in the US for the treatment of colorectal cancer, non-small cell lung cancer, renal cell cancer and recurrent glioblastoma. "Avastin®" is approved for ovarian cancer (Front line therapy) in 110 countries including 28 EU countries (as of August 7, 2013).

The number of patients newly diagnosed with ovarian cancer in Japan continues to rise each year and is estimated to become, on annual average, approximately 8,500 during 2010-2014*.

As the top pharmaceutical company in the field of oncology, Chugai is convinced that "Avastin®" can contribute to the treatment of patients with "ovarian cancer," a disease with high unmet medical need, by providing a new therapeutic option.

* T. Sobue, et al., Cancer White Paper 2012, Shinoharashinsha Inc.

About "Avastin®"

"Avastin®" 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. "Avastin®" 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 and "malignant glioma" in June 2013.

About the "Review Committee on Unapproved Drugs and Indications with High Medical Needs"

The "Review Committee on Unapproved Drugs and Indications with High Medical Needs" was established for the purpose of "enhancing development by the pharmaceutical companies of drugs and indications that have been approved in western countries but not yet approved in Japan, through activities such as evaluating medical needs and confirming the applicability of "application based on evidence in the public domain" and investigating the need for studies that should be additionally conducted."

Drug Information

The underlined descriptions are newly added.

Brand name: Avastin® for intravenous infusion 100 mg/4 mL
Avastin® for intravenous infusion 400 mg/16 mL

Generic name: bevacizumab (genetic recombination)

Indications, dosage and administration:

Indications	Dosage and Administration
Unresectable advanced or recurrent colorectal cancer	The usual adult dosage is 5 mg/kg (body weight) or 10 mg/kg (body weight) of bevacizumab (recombinant) per intravenous infusion in combination with other antineoplastic agents. The administration interval of AVASTIN should be 2 weeks or longer.
	The usual adult dosage is 7.5 mg/kg (body weight) of bevacizumab (recombinant) per intravenous infusion in combination with other antineoplastic agents. The administration interval of AVASTIN should be 3 weeks or longer.
Unresectable advanced or recurrent non-squamous non-small cell lung cancer	The usual adult dosage is 15 mg/kg (body weight) of bevacizumab (recombinant) per intravenous infusion in combination with other antineoplastic agents. The administration interval of AVASTIN should be 3 weeks or longer.
<u>Ovarian cancer</u>	
Inoperable or recurrent breast cancer	The usual adult dosage is 10 mg/kg (body weight) of bevacizumab (recombinant) per intravenous infusion in combination with paclitaxel. The administration interval of AVASTIN should be 2 weeks or longer.
Malignant glioma	The usual adult dosage per intravenous infusion of bevacizumab (recombinant) is 10 mg/kg (body weight) every 2 weeks or 15 mg/kg (body weight) every 3 weeks. The administration interval of AVASTIN should be appropriately extended on the basis of patient condition.

Drug prices: Avastin® for intravenous infusion 100 mg/4 mL JPY 45,563/vial
Avastin® for intravenous infusion 400 mg/16 mL JPY 173,511/vial