



Anti-Cancer Agent “Avastin[®],” Obtained Approval for Additional Indication of Advanced or Recurrent Cervical Cancer

TOKYO, May 23, 2016 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it gained approval by the Japanese Ministry of Health, Labour and Welfare (MHLW) on May 23, 2016, for “advanced or recurrent cervical 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] (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,” “malignant glioma” and “ovarian cancer.” On September 14, 2015, Avastin for advanced or recurrent cervical cancer has been designated as orphan drug and priority review product.

This approval was obtained based on the results of overseas phase III studies (The GOG-0240 study) and Japanese phase II study (The JO29569 study).

The GOG-0240 study evaluated the efficacy and safety profile of standard chemotherapies (paclitaxel and cisplatin or paclitaxel and nogitecan) with or without Avastin in 452 patients with persistent, recurrent or metastatic cervical cancer.

- The study met its primary endpoint of improving overall survival (OS) with a statistically significant 26 percent reduction in the risk of death, representing a median gain in survival of 3.9 months, compared with those who received chemotherapy alone [16.8 months vs. 12.9 months; HR=0.74, stratified log-rank test, one-sided p=0.0066 (significance level: 0.0140)]
- The study showed that patients who received Avastin plus chemotherapy had a significant improvement of progression free survival (PFS) compared with those who received chemotherapy alone [8.3 months vs. 6.0 months; HR=0.66, stratified log-rank test, p<0.0001].
- The study showed that patients who received Avastin plus chemotherapy had a significantly higher rate of tumor shrinkage (objective response rate, ORR) compared with those who received chemotherapy alone [45.4% (95% CI: 38.8-52.1%) vs. 33.8% (95% CI 27.6-40.4%); Chi-squared test, p=0.0117].
- The safety profile in the study was consistent with previous reports of Avastin, except for an increase in gastrointestinal-vaginal fistulas observed in patients who received Avastin plus chemotherapy compared to those who received chemotherapy alone (8.3% vs. 0.9% respectively). All patients with gastrointestinal-vaginal fistulas had a history of prior pelvic radiation.

The JO29569 study evaluated the tolerability, safety and efficacy of Avastin plus paclitaxel and cisplatin. Within eight Japanese patients with advanced or recurrent cervical cancer enrolled in the study, seven patients were evaluated, and one patient was excluded before the start of the study. As a result, the tolerability of Avastin plus chemotherapy was confirmed, and the harmful phenomenon to become the problem was not accepted, and no new safety finding were observed.

“We are proud that Avastin received an approval for cervical cancer as the sixth indication in Japan, which will contribute to the treatment of many cancer patients,” said Chugai’s Director and Executive Vice President, Dr. Yutaka Tanaka. “We believe that Avastin would bring great news for the treatment of advanced or recurrent cervical cancer, which has limited treatment options and has not seen any progress for the last ten years.”

Avastin is approved in Europe for the treatment of advanced stages of breast cancer, colorectal cancer, non-small cell lung cancer, renal cell cancer, ovarian cancer and cervical cancer, and is available in the US for the treatment of colorectal cancer, non-small cell lung cancer, renal cell cancer, recurrent glioblastoma, cervical cancer and recurrent ovarian cancer. Avastin is approved for cervical cancer in 67 countries (as of January, 2016).

The number of patients newly diagnosed as cervical cancer in Japan continues to rise each year and the annual average in 2015-2019 is estimated to be approximately 10,600.*

As the top pharmaceutical company in the field of oncology in Japan, Chugai is convinced that Avastin can contribute to the treatment of patients with “advanced or recurrent cervical cancer,” a disease with high unmet medical need, by providing a new therapeutic option.

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

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.
Ovarian cancer	
<u>Advanced or recurrent cervical 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 41,738/vial
 Avastin® for intravenous infusion 400 mg/16 mL JPY 158,942/vial

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