Pharmaceuticals and Medical Devices Agency

PMDA Risk Communication

Japan's view on Avastin (bevacizumab) for breast cancer indication

30 November 2011

Pharmaceuticals and Medical Devices Agency (PMDA)

Information for patients
who are currently receiving therapy with Avastin (bevacizumab)

MHLW/PMDA is aware of media reports of removing breast cancer from the indication of Avastin's product labeling in the U.S.
In Japan, Avastin's indication for breast cancer was approved in September 2011 based on careful assessments of all available relevant information including the situation in the U.S. The process leading to approval is briefly described below.
Consult your healthcare professional if you have any questions or concerns about the medication.

The US Food and Drug Administration announced that it is revoking its accelerated approval of the breast cancer indication for Avastin on 18 November 2011. In Japan, Avastin's indication for breast cancer was approved on 16 September 2011. [1)] (Note: It has been approved with indications for treatment of "unresectable or recurrent breast cancer," requiring concomitant use with paclitaxel in "Dosage and Administration" section in the package insert.)

PMDA has mainly evaluated the results of three overseas controlled clinical trials and a domestic clinical trial in patients who have not been treated with chemotherapy for their form of unresectable or recurrent breast cancer.

Main clinical trials:

- E2100 trial and domestic Phase Ⅱ trial: evaluating Avastin in combination with paclitaxel.
- AVADO trial: evaluating Avastin in combination with docetaxel
- RIBBON1 trial: evaluating Avastin in combination with capecitabine, taxanes or anthracyclines.

In conclusion of the review, MHLW/PMDA concluded Avastin in combination with paclitaxel showed favorable benefit/risk ratio as compared with paclitaxel alone because in the E2100 trial Avastin in combination with paclitaxel improved progression-free survival, which means that the drug provided a meaningful increase in the amount of time from when the treatment was started until the tumor grows, though no significant survival benefit was showed.
MHLW/PMDA considered that the combination therapy of Avastin with paclitaxel has clinical significance as one of therapies for unresectable or recurrent breast cancer, as long as the drug is used properly in accordance with the “Precautions” of the package insert.

In February 2008, US-FDA approved Avastin for use in combination with paclitaxel for treatment of breast cancer based on the result of E2100 trial. After that, however, the procedure of revoking Avastin’s approval for breast cancer indication was started since both the AVADO trial and the RIBBON1 trial which were underway at the time of approval of Avastin showed no significant survival effect and so on.

In Japan, PMDA reviewed all available clinical trial results including the AVADO trial and the RIBBON1 trial evaluated by US-FDA. Furthermore, Avastin’s approval for breast cancer indication has been determined after taking everything into consideration including the ongoing discussions about the approval revoking in the U.S.
Thus the U.S. announcement was not based on new efficacy or safety information obtained after approval in Japan.

In Europe, Avastin has been approved for treatment of breast cancer in combination with paclitaxel based on the result from the E2100 trial since March 2007, and still remains on the market as an approved treatment.

The marketing authorization holder of Avastin has a plan to conduct a new clinical trial for treatment of Avastin in patients with breast cancer. MHLW/PMDA will continue to review the safety issue when new information is available and will update the public when further appropriate measure should be taken.

PMDA encourages people to use the drug properly.

1) Press Announcement from the FDA
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm280536.htm

2) Review report of AVASTIN® 100mg/4mL Intravenous Infusion and AVASTIN® 400mg/16mL Intravenous Infusion on July 14, 2011
http://www.info.pmda.go.jp/shinyaku/P201100161/450045000_21900AMX00910_A100_1.pdf