Genentech
A Member of the Roche Group

IMPORTANT DRUG WARNING

10/04/2011

Higher incidence of new cases of ovarian failure observed in premenopausal women treated with Avastin® (bevacizumab)

Dear Healthcare Provider:

Genentech, a member of the Roche Group, would like to inform you of important new safety information in women receiving AVASTIN (bevacizumab).

Genentech has revised the Product Information for Avastin to include this information. The current Avastin Package Insert is enclosed.

Summary
In study NSABP C-08, a randomized, active-controlled trial evaluating the safety and efficacy of Avastin in combination with mFOLFOX6 chemotherapy for the adjuvant treatment of patients with colon cancer, an approximately 15-fold increase in the incidence of new cases of ovarian failure was observed in premenopausal women treated with Avastin plus mFOLFOX6 as compared to mFOLFOX6 alone.

Fertility preservation strategies should be discussed with women of child-bearing potential prior to starting treatment with Avastin.

Further information
Repeat dose safety studies in animals have shown that bevacizumab, or specific VEGF blockade, results in a dose-dependent reversible inhibition of ovarian function, which may have an adverse effect on female fertility. At the request of the FDA, Genentech conducted a study on the effects of Avastin on ovarian function in premenopausal women.

Study NSABP C-08 is a randomized, active-controlled trial of mFOLFOX6 alone or in combination with Avastin as adjuvant treatment for stage II/III colon cancer that enrolled 2687 patients with colon cancer, of whom 1344 were women. The incidence of ovarian failure (defined as amenorrhoea lasting 3 or more months, FSH levels ≥30 mIU/mL and a negative serum β-HCG pregnancy test) was evaluated in a subset of 179 premenopausal women.

The incidence of new cases of ovarian failure (defined as not having ovarian failure at randomization, but having ovarian failure during protocol treatment) was 2% (2/84) in the mFOLFOX6-treated group and 34% (32/95) in the mFOLFOX6 plus Avastin-treated group. Age did not appear to be correlated with the risk of developing ovarian failure. After Avastin treatment was discontinued, ovarian function recovered in 22% of evaluable women who had no missing data during the post-treatment period in the mFOLFOX6 plus Avastin group. Recovery of ovarian function is defined as resumption of menses, a positive serum β -HCG pregnancy test, or a FSH level < 30 mIU/mL at all time points during the post-treatment period. Long term effects of the treatment with bevacizumab on fertility are unknown.

Avastin is not approved for use in combination with mFOLFOX as adjuvant treatment of patients with colon cancer.

Avastin is indicated for the treatment of metastatic renal cell carcinoma in combination with interferon alfa, also for the first-line treatment of unresectable, locally advanced, recurrent or metastatic non–squamous non–small cell lung cancer in combination with carboplatin and paclitaxel, and also for the first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil–based chemotherapy.

Call for reporting
Healthcare professionals should report any serious adverse events suspected to be associated with the use of AVASTIN to Genentech at 1-888-835-2555. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), online (https://www.accessdata.fda.gov/scripts/medwatch/) or mailed, using the MedWatch for FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

The current Avastin Package Insert is enclosed. For further information or any questions on ovarian failure associated with the use of Avastin, please contact Genentech Medical Information/Communications Department at (800) 821-8590.

Sincerely,

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Chief Medical Officer
Genentech, Inc.

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