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NCCN Guidelines Panel: Breast Cancer

On behalf of Genentech, I respectfully request the NCCN Breast Cancer Guideline Panel to review the enclosed data for the use of Avastin® (Bevacizumab) in patients with metastatic breast cancer (MBC).

Specific Changes: Consider the recently presented data for updating of the options for chemotherapy agents used in combination with Avastin for the 1st and 2nd line treatment of MBC.

FDA Clearance: FDA has not approved Avastin for 2nd line treatment of MBC. Avastin is indicated for the treatment of HER2-negative MBC in combination with paclitaxel in patients who have not received chemotherapy. Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

Rationale: Results were recently presented at the 46th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois in June 2010.¹⁻⁴ Study results included the following:

- A meta-analysis of results from 3 pivotal phase III studies of Avastin with or without chemotherapy in the treatment of previously untreated MBC. The pooled analysis showed a significant improvement in the primary endpoint, progression-free survival. The safety profile was consistent with previous experience with Avastin.^{1,2}
- Additional sub-group analyses from RIBBON-2, a randomized, double-blind, placebo-controlled Phase III study that evaluated chemotherapy with or without Avastin in MBC patients who have been previously treated with chemotherapy.^{3,4}

Additionally, the results from the multicenter, randomized Avastin with Docetaxel Study (AVADO) were published in the Journal of Clinical Oncology.⁵ The results demonstrated a significant improvement in the primary endpoint of PFS. No new safety concerns related to Avastin were reported.

The following enclosures are included for your review (copyright-paid where applicable):

- O'Shaughnessy J, Miles D, Gray RJ, et al. A meta-analysis of overall survival data from three randomized trials of bevacizumab and first-line chemotherapy as treatment for patients with metastatic breast cancer. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology in Chicago, IL; June 4-8, 2010. ASCO Oral Presentation #1005.
- Brufsky A, Rivera RR, Hurvitz SA, et al. Progression-free survival in patient subgroups in RIBBON-2, a Phase III trial of chemotherapy plus or minus bevacizumab for second-line treatment of HER2-negative, locally recurrent or metastatic breast cancer. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology in Chicago, IL; June 4-8, 2010. ASCO Poster #1021.
- Miles DW, Chan A, Dirix LY, et al. Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol. E-pub Date: 2010. DOI # 10.1200/JCO.2008.21.6457.
- Avastin Prescribing Information

Cited References

1. O'Shaughnessy J, Miles D, Gray RJ, et al. A meta-analysis of overall survival data from three randomized trials of bevacizumab (BV) and first-line chemotherapy as treatment for patients with metastatic breast cancer (MBC). *J Clin Oncol* 2010;28. ASCO Abstract #1005.
2. O'Shaughnessy J, Miles D, Gray RJ, et al. A meta-analysis of overall survival data from three randomized trials of bevacizumab and first-line chemotherapy as treatment for patients with metastatic breast cancer. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology in Chicago, IL; June 4-8, 2010. ASCO Oral Presentation #1005.
3. Brufsky A, Rivera RR, Hurvitz SA, et al. Progression-free survival (PFS) in patient subgroups in RIBBON-2, a Phase III trial of chemotherapy (chemo) plus or minus bevacizumab (BV) for second-line treatment of HER2-negative, locally recurrent or metastatic breast cancer (MBC). *J Clin Oncol* 2010;28. ASCO Abstract #1021.
4. Brufsky A, Rivera RR, Hurvitz SA, et al. Progression-free survival in patient subgroups in RIBBON-2, a Phase III trial of chemotherapy plus or minus bevacizumab for second-line treatment of HER2-negative, locally recurrent or metastatic breast cancer. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology in Chicago, IL; June 4-8, 2010. ASCO Poster #1021.
5. Miles DW, Chan A, Dirix LY, et al. Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol*. E-pub Date: 2010. DOI # 10.1200/JCO.2008.21.6457.