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NCCN Guidelines Panel: Ovarian Cancer

On behalf of Genentech, I respectfully request the NCCN Ovarian Cancer Guideline Panel to review the enclosed data for the use of Avastin® (Bevacizumab) in the treatment of patients with platinum-sensitive recurrent ovarian, primary peritoneal or fallopian tube cancer.

Specific Changes: Consider the recently presented data on Avastin in combination with carboplatin and gemcitabine in the treatment of platinum-sensitive recurrent ovarian, primary peritoneal or fallopian tube cancer for your updating purposes.

FDA Clearance: FDA has not approved Avastin for the treatment of ovarian cancer. Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

Rationale: Results were recently presented at the 47th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois in June 2011. OCEANS is a Phase III, multicenter open-label trial comparing carboplatin and gemcitabine to carboplatin and gemcitabine in combination with Avastin followed by maintenance Avastin in patients with platinum-sensitive recurrent ovarian cancer.¹

Aghajanian et al. reported a statistically significant improvement in the primary endpoint, progression-free survival (PFS). An interim overall survival (OS), a secondary endpoint, was also reported but the data is immature at this time. The safety profile was consistent with previous reports of Avastin and there were no new safety signals.

Phase II and Phase III data on the use of Avastin in relapsed or recurrent ovarian cancer and front-line ovarian cancer, respectively, have previously been reported.²⁻¹⁶

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

- Aghajanian C, Finkler NJ, Rutherford T, et al. OCEANS, a phase III, multicenter, randomized, blinded, placebo-controlled trial of carboplatin and gemcitabine plus bevacizumab in patients with platinum-sensitive recurrent ovarian, primary peritoneal, or fallopian tube cancer. Presented at the 2011 American Society of Clinical Oncology Annual Meeting in Chicago, IL; June 3-7, 2011. ASCO Oral Presentation #LBA5007
- Avastin Prescribing Information

Cited References

1. Aghajanian C, Finkler NJ, Rutherford T, et al. OCEANS, a Phase III, multicenter, randomized, blinded, placebo-controlled trial of carboplatin and gemcitabine plus bevacizumab in patients with platinum-sensitive recurrent ovarian, primary peritoneal, or fallopian tube cancer. Presented at the 2011 American Society of Clinical Oncology Annual Meeting in Chicago, IL; June 3-7, 2011. ASCO Oral Presentation #LBA5007.

2. Kristensen G, Perren T, Qian W, et al. ICON7: A Phase III gynaecologic cancer intergroup (GCIG) trial of adding bevacizumab to standard chemotherapy in women with newly diagnosed epithelial ovarian, primary peritoneal, or fallopian tube cancer: Interim analysis on overall survival. Presented at the American Society of Clinical Oncology 2011 Annual Meeting in Chicago, IL; June 3-7, 2011. ASCO Oral Presentation.
3. Perren T, Swart AM, Pfisterer J, et al. ICON7: A Phase III gynaecologic cancer interGroup (GCIG) trial of adding bevacizumab to standard chemotherapy in women with newly diagnosed epithelial ovarian, primary peritoneal or fallopian tube cancer. Presented at the 35th European Society for Medical Oncology in Milan, Italy; October 8-12, 2010. ESMO Oral Presentation.
4. Burger RA, Brady MF, Bookman MA, et al. Phase III trial of bevacizumab in the primary treatment of advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer: a gynecologic oncology group (GOG) study. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology in Chicago, IL; June 4-8, 2010. ASCO Oral Presentation #LBA1.
5. Garcia AA, Hirte H, Fleming G, et al. Phase II clinical trial of bevacizumab and low-dose metronomic oral cyclophosphamide in recurrent ovarian cancer: a trial of the California, Chicago, and Princess Margaret Hospital phase II consortia. *J Clin Oncol* 2008;26:76-82.
6. McGonigle KF, Muntz HG, Vuky J, et al. Phase II prospective study of weekly topotecan and bevacizumab in platinum-resistant ovarian, fallopian tube or primary peritoneal cancer. *Gynecol Oncol* 2009;112:S145. SGO Abstract #286.
7. Muggia FM, Boyd L, Liebes L, et al. Pegylated liposomal doxorubicin (PLD) with bevacizumab (B) in second-line treatment of ovarian cancer (OC): pharmacokinetics (PK), safety, and preliminary outcome results. *J Clin Oncol* 2009;27. ASCO Abstract #5548.
8. Wenham R, LaPolla J, Lin H, et al. A phase II trial of docetaxel and bevacizumab in recurrent ovarian cancer within 12 months of prior platinum-based chemotherapy. *Gynecol Oncol* 2010;116:S61-S62. SGO Abstract #155.
9. Chambers SK, Clouser MC, Roe DJ, et al. Phase II trial of bevacizumab and erlotinib in women with refractory ovarian cancer. Presented at the 100th Annual Meeting of the American Association for Cancer Research in Denver, CO; April 18-22, 2009. AACR Abstract #3582.
10. Nimeiri HS, Oza AM, Morgan RJ, et al. Efficacy and safety of bevacizumab plus erlotinib for patients with recurrent ovarian, primary peritoneal, and fallopian tube cancer: a trial of the Chicago, PMH, and California Phase II consortia. *Gynecol Oncol* 2008;110:49-55.
11. Burger RA, Sill MW, Monk BJ, et al. Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: a Gynecologic Oncology Group Study. *J Clin Oncol* 2007;25:5165-5171.
12. Cannistra SA, Matulonis UA, Penson RT, et al. Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer. *J Clin Oncol* 2007;25:5180-5186.
13. Burger RA, Brady MF, Bookman MA, et al. Safety and subgroup efficacy analyses in GOG-0218, a Phase III trial of bevacizumab in the primary treatment of advanced epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer: a gynecologic oncology group study. Presented at the 35th European Society for Medical Oncology in Milan, Italy; October 8-12, 2010. ESMO Poster #978PD.
14. Burger RA, Brady MF, Bookman MA, et al. Safety and subgroup efficacy analyses in GOG218, a Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian cancer (EOC), primary peritoneal cancer (PPC) or fallopian tube cancer (FTC): a Gynecologic Oncology Group study. *Ann Oncol* 2010;21 (suppl 8):viii307. ESMO Abstract #978PD.
15. Burger RA, Brady MF, Rhee J, et al. Independent radiologic review of GOG218, a Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian (EOC), primary peritoneal (PPC) or Fallopian tube cancer (FTC). *J Clin Oncol* 2011;29. ASCO Abstract #5023.
16. Burger RA, Brady MF, Rhee J, et al. Independent radiologic review of GOG218, a Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian (EOC), primary peritoneal (PPC) or fallopian tube cancer (FTC). Presented at the 2011 American Society of Clinical Oncology Annual Meeting in Chicago, IL; June 3-7, 2011. ASCO Poster #5023.