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NCCN Guidelines Panel: Ovarian Cancer

Dear NCCN Ovarian Cancer Panel,

Please find the enclosed references[1,2,4,5] for your review regarding Avastin® (bevacizumab).

Request(s):

1) On June 13, 2018, the Food and Drug Administration (FDA) approved Avastin in combination with carboplatin and paclitaxel, followed by Avastin as a single agent for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.[3] Consider the enclosed information on the use of Avastin in patients with ovarian cancer for your drug information updating needs.

2) Consider the enclosed results from the MITO16BMaNGO OV2B-ENGOT OV17 study on the use of Avastin and chemotherapy in patients with recurrent platinum-sensitive ovarian cancer who had received first-line therapy with Avastin presented on June 5th at the 2018 American Society of Clinical Oncology annual conference.

Rationale:

1) Efficacy and updates to the prescribing information were based upon efficacy results from the GOG-0218 study. GOG-0218 was a Phase III, multi-center, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of Avastin in women with stage III or stage IV epithelial, fallopian tube, or primary peritoneal cancer following initial surgical resection. Patients were randomized 1:1:1 to one of the following treatment arms: carboplatin and paclitaxel (CP) followed by placebo, Avastin concurrently with CP followed by placebo, and Avastin concurrently with CP followed by Avastin. The trial met its primary endpoint of progression-free survival (PFS).[1] Disease progression was defined using Response Evaluation Criteria in Solid Tumors (RECIST), the Gynecologic Cancer Intergroup criteria (GCIG) for progression based on rising CA-125 levels, global deterioration of health or death from any cause.[1]

   As per the prescribing information, efficacy was based upon pre-specified investigator-assessed PFS in which patients who progressed on the basis of CA-125 criteria were censored as required by regulatory agencies.[1,2,3] In this pre-planned analysis, patients who received Avastin in combination with chemotherapy, and continued the use of Avastin alone for up to 22 cycles, had a median PFS of 18.2 months compared to 12.0 months in patients who received chemotherapy alone (HR=0.62; 95% CI 0.52 - 0.75, p<0.001).[3] Of note, the primary analysis presented in the GOG-0218 publication had a data cutoff of February 2010. However, the data cutoff in the prescribing information censored for CA-125 is September 2009.[1,3]

   Adverse events were consistent with those seen in previous trials of Avastin across tumor types for approved indications.[3] Hypertension of grade 2 or greater was significantly more common in the Avastin containing arms than in the chemotherapy only arm. The most common (≥5%) adverse events across all treatment arms were hypertension grade ≥2, pain grade ≥2, neutropenia ≥grade 4, and venous thromboembolic event.[1,3]

2) MITO16BMaNGO OV2B-ENGOT OV17[4] was a Phase III, randomized, open-label trial conducted to evaluate the safety and efficacy of Avastin plus platinum-based chemotherapy in patients with recurrent platinum-sensitive ovarian cancer who were previously treated with Avastin during first line. Patients were randomized to 6 cycles of platinum-based chemotherapy with or without Avastin.

   With a median follow-up of 20.3 months, the study met its primary end-point of investigator assessed PFS as defined by RECIST 1.1 criteria, with a median PFS of 8.8 months without Avastin and 11.8 months with Avastin (HR 0.51, 95% CI: 0.41-0.64, p<0.001).

   The rate of treatment-related grade 3-4 adverse events which were significantly higher in the Avastin containing arm included, hypertension, proteinuria, and thrombocytopenia.

FDA Clearance:

- Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: http://www.gene.com/download/pdf/avastin_prescribing.pdf

Thank you for your consideration and I hope this information is helpful to you. If you have any questions, please contact me directly.

Respectfully submitted,
Ayesha Ahmed, PharmD

References

1. Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 2011;365:2473-2483. http://www.ncbi.nlm.nih.gov/pubmed/22204724.
2. Burger RA, Brady MF, Bookman MA, et al. Supplement to: incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 2011;365:2473-2483.
3. Avastin (bevacizumab) [package insert]. Genentech, Inc.; South San Francisco, CA. 2018. https://www.gene.com/download/pdf/avastin_prescribing.pdf.
4. Pignata S, Lorusso D, Joly F, et al. Chemotherapy plus or minus bevacizumab for platinum-sensitive ovarian cancer patients recurring after a bevacizumab containing first line. The randomized Phase 3 trial MITO16B - MaNGO OV2B - ENGOT OV17. Presented at the American Society of Clinical Oncology Annual Meeting in Chicago, IL; June 1–5, 2018. ASCO Oral Presentation. https://meetinglibrary.asco.org/record/161812/slide
5. Pignata S, Lorusso D, Joly F, et al. Chemotherapy plus or minus bevacizumab for platinum-sensitive ovarian cancer patients recurring after a bevacizumab containing first line treatment: The randomized phase 3 trial MITO16BMaNGO OV2B-ENGOT OV17. Presented at the American Society of Clinical Oncology Annual Meeting in Chicago, IL; June 1–5, 2018. ASCO Abstract #5506. https://meetinglibrary.asco.org/record/161812/abstract