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Submitted by:
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NCCN Guidelines Panel: Ovarian Cancer

On behalf of Genentech, Inc., I respectfully request the NCCN Ovarian Cancer Guideline Panel to review the following enclosed full publication of the GOG-0213 trial for:

- **Avastin® (bevacizumab): Platinum-Sensitive Ovarian Cancer**
    - Coleman RL, Brady MF, Herzog TJ, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy andsecondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, Phase 3 trial [supplementary appendix appears online]. *Lancet Oncol.* E-pub Date: [published online ahead of print] April 2017.

Specific Changes:

- Please consider the above publication for your updating purposes.

FDA Clearance:

- Avastin either in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by Avastin as a single agent was FDA-approved for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer on December 6, 2016.
- Please refer to the full prescribing information for FDA-approved indications and safety information.
    - Full Avastin® prescribing information available at: https://www.gene.com/download/pdf/avastin_prescribing.pdf

Rationale:

- The GOG-0213 Phase III trial supported the FDA approval of Avastin in combination with carboplatin and paclitaxel in patients with platinum-sensitive ovarian cancer. The study results were previously presented and are now published in the Lancet Oncology.
- Randomized, Phase 3, multi-centered, open-label trial which compared the efficacy and safety of adding Avastin to chemotherapy (carboplatin plus paclitaxel), followed by Avastin maintenance in 674 patients with platinum-sensitive, recurrent ovarian, primary peritoneal, and fallopian tube cancer. The primary endpoint was overall survival (OS) and the secondary endpoints included investigator-assessed progression-free survival (PFS).
    - *Efficacy*:
        - Based on stratification by treatment-free interval (TFI) the hazard ratio (HR) for overall survival (OS) was 0.829 (95% CI, 0.683-1.005; p=0.056), with a median of 42.2 months in the Avastin plus chemotherapy arm vs 37.3 months in the chemotherapy alone arm.

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        - After review of the audited electronic case-report forms, a discrepancy in TFI was identified for 45 patients, 20 in the Avastin plus chemotherapy arm and 25 in the chemotherapy alone arm.
            - A post-hoc sensitivity analysis using the electronic case report forms led to an adjusted HR for OS of 0.823 (95% CI, 0.68-0.996; p=0.0447).
        - Both HR's are represented in the Avastin Prescribing Information.
        - There was a significant improvement in progression free survival (PFS) for patients treated with Avastin plus chemotherapy vs. chemotherapy alone (HR 0.628; 95% CI, 0.534-0.739; p<0.0001) with a median of 13.8 months vs 10.4 months, respectively.
    - *Safety*:
        - In the Avastin plus chemotherapy arm, 317 patients (96%) experienced at least 1 Grade ≥3 AE vs 282 patients (86%) in the chemotherapy alone arm. Treatment related AEs of special interest for Avastin are provided in Table 3. One patient experienced a Grade 4 intracranial hemorrhage that was related to Avastin treatment. There were 3% treatment-related deaths in the Avastin plus chemotherapy arm and 1% in the chemotherapy only arm.
- The GOG-0213 study results were previously submitted in abstract form.
- An additional study evaluating the use of Avastin in patients with pSOC, OCEANS, was previously submitted.

Respectfully submitted,

Krupa Parekh, Pharm.D