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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 enclosed recent key Avastin® (bevacizumab) presentations from the 2013 European Cancer Congress (ECC). Presentations that have copyright consent are enclosed for your review.

- **ICON7 Trial:** Front-line treatment of ovarian cancer

Oza AM, Perren TJ, Swart AM, et al. ICON7: final overall survival results in the GCIG Phase III randomized trial of bevacizumab in women with newly diagnosed ovarian cancer. Presented at the European Cancer Congress in Amsterdam, Netherlands; September 27-October 1, 2013. ECC Oral Presentation.

Oza AM, Perren TJ, Swart AM, et al. ICON7: final overall survival results in the GCIG Phase III randomized trial of bevacizumab in women with newly diagnosed ovarian cancer. Presented at the European Cancer Congress in Amsterdam, Netherlands; September 27-October 1, 2013. ECC Abstract #6. <http://eccamsterdam2013.ecco-org.eu/Scientific-Programme/Abstract-search.aspx#>.

- **AURELIA Trial:** Platinum-resistant ovarian cancer

Witteveen P, Lortholary A, Fehm T, et al. Final overall survival results from AURELIA, an open-label randomised phase III trial of chemotherapy with or without bevacizumab for platinum-resistant recurrent ovarian cancer. Presented at the European Cancer Congress in Amsterdam, Netherlands; September 27-October 1, 2013. ECC Oral Presentation.

Specific Changes: No specific changes are requested. Please consider the recently presented key Avastin data for your updating purposes.

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

Rationale: The ICON7¹ and AURELIA² trial results were previously published and submitted. Final overall survival (OS) results were presented at the European Cancer Congress in October, 2013.

ICON7 Trial

- At a median follow up of 49 months, the final analysis of OS, a secondary endpoint, showed no significant difference in patients treated with Avastin + chemotherapy compared with those treated with chemotherapy alone (HR=0.99, 95% CI 0.85-1.14; p=0.85). No new safety concerns were observed with long-term follow up.

AURELIA Trial

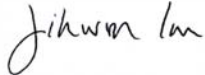
- Overall survival was a secondary endpoint. After a median follow up of 27.4 months, the final OS analysis showed a median OS of 16.6 months in the Avastin + chemotherapy arm and

13.3 months in the chemotherapy alone arm (HR=0.85; 95% CI 0.66-1.08; p=0.174). The study was not powered to detect a statistically significant difference in OS.

- In the updated safety results, Grade ≥ 3 adverse events that occurred more frequently in the Avastin arm compared with the chemotherapy alone arm included hypertension, proteinuria, gastrointestinal (GI) perforation, fistula/abscess formation, wound-healing complication, arterial thromboembolic events, and reversible posterior leukoencephalopathy syndrome.

Additional Phase III trials have been conducted to evaluate Avastin in patients with ovarian cancer.³⁻⁵

Respectfully submitted,



Supplemental References

1. Perren TJ, Swart AM, Pfisterer J, et al. A Phase 3 trial of bevacizumab in ovarian cancer. N Engl J Med 2011;365:2484-2496. <http://www.ncbi.nlm.nih.gov/pubmed/22204725>.
2. Pujade-Lauraine E, Hilpert F, Weber B, et al. AURELIA: a randomized Phase III trial evaluating bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer. Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Oral presentation #LBA5002. <http://www.asco.org>.
3. 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>.
4. 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.
5. Aghajanian C, Blank SV, Goff BA, et al. OCEANS: a randomized, double-blind, placebo-controlled Phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol 2012;30:2039-45. <http://www.ncbi.nlm.nih.gov/pubmed/22529265>.