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NCCN Guidelines Panel: Malignant Pleural Mesothelioma

On behalf of Genentech, Inc., I respectfully request the NCCN Malignant Pleural Mesothelioma (MPM) Guideline Panel to review the enclosed recent presentation for:

- Avastin® (bevacizumab): First-line treatment of MPM

Zalcman G, Mazieres J, Margery J, et al. Bevacizumab 15mg/kg plus cisplatin-pemetrexed (CP) triplet versus CP doublet in malignant pleural mesothelioma (MPM): results of the IFCT-GFPC 0701 "MAPS" randomized Phase 3 trial. Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, Illinois; May 29–June 2, 2015. ASCO Oral presentation.

Specific Changes:

Please consider the Zalcman, et al. Avastin presentation for your updating purposes.

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

- Full Avastin prescribing information available at:
http://www.gene.com/download/pdf/avastin_prescribing.pdf

Rationale:

- In a Phase III randomized, open-label trial, Avastin in combination with pemetrexed and cisplatin (CP) followed by Avastin maintenance significantly improved the primary outcome measure of median overall survival by 2.75 months from 16.07 to 18.82 months (stratified HR=0.76, 95%CI [0.61-0.94], p=0.0127) vs. CP alone in chemotherapy-naïve malignant pleural mesothelioma patients.
- Progression-free survival was also significantly improved in the Avastin arm by 2 months from 7.48 to 9.59 months (stratified HR=0.61; 95%CI [0.50-0.75], p<0.0001).
- Adverse events of any grade that were significantly more common in the Avastin group included hypertension, pulmonary embolism, venous thrombosis, arterial thrombosis, epistaxis, hemorrhage (1 death), and proteinuria.
- There was no significant difference in overall Grade 3/4 adverse events, however there were significantly more Grade 1/2 adverse events for the Avastin group. This did not lead to a significant difference in quality of life between the two groups.
- Additional data on the use of Avastin to treat mesothelioma have been reported.¹⁻⁴

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Respectfully submitted,



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Supplemental References

1. Kindler HL, Karrison TG, Gandara DR, et al. Multicenter, double-blind, placebo-controlled, randomized phase II trial of gemcitabine/cisplatin plus bevacizumab or placebo in patients with malignant mesothelioma. *J Clin Oncol* 2012;30:2509-2515.
2. Ceresoli GL, Zucali PA, Mencobono M, et al. Phase II study of pemetrexed and carboplatin plus bevacizumab as first-line therapy in malignant pleural mesothelioma. *Br J Cancer*. 2013 Aug 6;109(3):552-8. doi: 10.1038/bjc.2013/bjc.2013.368. Epub 2013 Jul 16.
3. Dowell JE, Dunphy FR, Taub RN, et al. A multicenter, phase II study of cisplatin, pemetrexed and bevacizumab in patients with advanced malignant mesothelioma. *Lung Cancer*. 2012 Sep;77(3):567-71. doi:10.1016/j.lungcan.2012.05.111. Epub 2012 Jul 4.
4. Jackman DM, Kindler HL, Yeap BY, et al. Erlotinib plus bevacizumab in previously treated patients with malignant pleural mesothelioma. *Cancer*. 2008 Aug 15;113(4):808-14: 10.1002/cncr.23617

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