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NCCN Guidelines Panel: Non-small Cell Lung Cancer

On behalf of Genentech, I respectfully request the NCCN Non-small Cell Lung Cancer Guideline Panel to review the enclosed data for Tarceva[®] (erlotinib) in the first-line treatment of patients with advanced non-small-cell lung cancer (NSCLC).

Specific Changes: Consider the published data on the use of Tarceva[®] (erlotinib) in first-line treatment of patients with NSCLC for your updating purposes.^{1,2}

FDA Clearance: Tarceva is not FDA-approved as first-line treatment for NSCLC. Tarceva is FDA-approved as a single agent for treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.³ It is also FDA-approved as a single agent for maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. Tarceva is approved for first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine. Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

Rationale: Mok et al. presented the FASTACT-2 trial, a Phase III study of previously untreated Asian patients with Stage IIIb/IV NSCLC.¹ This trial evaluated intercalated Tarceva with chemotherapy (gemcitabine/platinum; GC-Tarceva) followed by Tarceva maintenance until disease progression versus chemotherapy alone (GC-placebo). In the chemotherapy arm, patients who progressed could be initiated on Tarceva. The primary endpoint was progression-free survival (PFS), which was significantly prolonged with the GC-Tarceva treatment arm versus GC-placebo. Adverse events were similar across both treatment arms, though the GC-Tarceva arm experienced a higher incidence of skin rash and diarrhea.

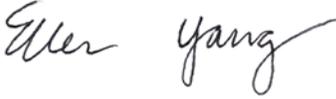
The OPTIMAL study is a Phase III, randomized, open-label, multicenter trial that compared Tarceva to platinum-based doublet chemotherapy (gemcitabine plus carboplatin) as first-line treatment for Chinese patients with activating EGFR mutations in advanced or recurrent Stage III or IV NSCLC.² Per a previous submission, the primary endpoint of PFS was significantly improved in Tarceva-treated patients compared to chemotherapy-treated patients. At the American Society of Clinical Oncology 2012 Annual Meeting, Zhou et al. presented overall survival data, which did not differ significantly between the two treatment arms.

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

- Mok T, Wu Y-L, Thongprasert S, et al. A randomized placebo-controlled Phase III study of intercalated erlotinib with gemcitabine/platinum in 1st-line advanced non-small-cell lung cancer (NSCLC): FASTACT-2. Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Poster #7519.
- Zhou C, Wu Y-L, Liu X, et al. Preliminary overall survival (OS) results from OPTIMAL (CTONG0802), a Phase III trial of erlotinib (E) versus carboplatin plus gemcitabine (GC) as first-

line treatment for Chinese patients with *EGFR* mutation-positive advanced non-small cell lung cancer (NSCLC). Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Poster #7520.

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Cited References

1. Mok T, Wu Y-L, Thongprasert S, et al. A randomized placebo-controlled Phase III study of intercalated erlotinib with gemcitabine/platinum in 1st-line advanced non-small-cell lung cancer (NSCLC): FASTACT-2. Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Poster #7519.
2. Zhou C, Wu Y-L, Liu X, et al. Preliminary overall survival (OS) results from OPTIMAL (CTONG0802), a Phase III trial of erlotinib (E) versus carboplatin plus gemcitabine (GC) as first-line treatment for Chinese patients with *EGFR* mutation-positive advanced non-small cell lung cancer (NSCLC). Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Poster #7520.
3. Tarceva Prescribing Information