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Date of Request:	May 14, 2018
NCCN Guidelines Panel:	Non-Small Cell Lung Cancer

Dear Sir or Madam:

On behalf of AstraZeneca, this letter is a formal request to the National Comprehensive Cancer Network (NCCN) Panel for Non-Small Cell Lung Cancer (NSCLC) to review the enclosed Lancet Oncology publication¹ for:

IRESSA (gefitinib): NSCLC (ADJUVANT/CTONG 1104)

Specific Changes: There are no specific changes being requested. We are providing data on IRESSA in NSCLC for your review and consideration.

FDA Status: IRESSA is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. Limitation of Use: Safety and efficacy of IRESSA have not been established in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

Please refer to the enclosed prescribing information for the full FDA-approved indication and safety information.²

Rationale: The ADJUVANT/CTONG1104 study is a randomized, open-label, phase III trial conducted at 27 centers in China. The trial evaluated the efficacy and safety of gefitinib versus vinorelbine plus cisplatin in patients with completely resected EGFR mutation-positive stage II-IIIa (N1-N2) NSCLC. The primary endpoint was disease-free survival (DFS) in the intention-to-treat (ITT) population. The median DFS was 28.7 months [95% CI 24.9–32.5] in the gefitinib group compared to 18.0 months [95% CI 13.6–22.3] in the vinorelbine plus cisplatin group; (hazard ratio [HR] 0.60, 95% CI 0.42–0.87; p=0.0054). In the safety population, the most commonly reported grade 3 or worse adverse events in the gefitinib group (n=106) were raised alanine aminotransferase and aspartate aminotransferase (two [2%] patients with each event versus none with vinorelbine plus cisplatin). In the vinorelbine plus cisplatin group (n=87), the most frequently reported grade 3 or worse adverse events were neutropenia (30 [34%] patients versus none with gefitinib), leukopenia (14 [16%] versus none), and vomiting (eight [9%] versus none). The overall survival (OS) data are not yet mature.¹

Sincerely,

Nabil Chehab

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Reference(s):

¹ Zhong, W-Z, Wang Q, Mao W-M et al., Gefitinib versus Vinorelbine plus Cisplatin as Adjuvant Treatment for Stage II-IIIa (N1-N2) *EGFR*-Mutant NSCLC (ADJUVANT/CTONG 1104): a Randomized, Open-Label, Phase 3 Study [article and supplementary appendix]. *Lancet Oncol.* 2018; 19:139-148.

² IRESSA Prescribing Information.