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Date of Request:	April 18, 2018
NCCN Guidelines Panel:	Non-Small Cell Lung Cancer (NSCLC)

Dear Sir or Madam:

On behalf of AstraZeneca, the purpose of this letter is to inform the National Comprehensive Cancer Network (NCCN) Panel for Non-Small Cell Lung Cancer (NSCLC) of the Food and Drug Administration (FDA) approval of TAGRISSO® (osimertinib) for the first-line treatment of patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test. This approval was based on data from the FLAURA study which is a randomized, double-blind, phase 3 trial evaluating the efficacy and safety of osimertinib compared to standard of care (SoC) EGFR tyrosine kinase inhibitors gefitinib or erlotinib in patients with previously untreated, EGFR mutation-positive metastatic NSCLC; see attached New England Journal of Medicine publication and supplement.[1] Additional data recently presented at The European Lung Cancer Conference on April 13, 2018 demonstrates improvements in post-progression outcomes in the osimertinib group compared to the standard of care group.[2]

- In 556 patients randomized 1:1, post-progression outcomes were as follows:[2]
  - Progression-free survival 2 (PFS2, time from randomization to second progression on subsequent treatment or death) in the osimertinib group was not calculable (NC) (95% CI, 23.7-NC) and in the SoC group was 20.0 months (95% CI, 18.2-NC).
  - Time to first subsequent therapy or death was 23.5 months (95% CI, 22.0-NC) in the osimertinib group and 13.8 months (95% CI, 12.3-15.7) in the SoC group; HR: 0.51 (95% CI, 0.40-0.64; p<0.0001).
  - The most frequent first subsequent therapy in the osimertinib group was platinum-based chemotherapy (56% of patients that progressed) and osimertinib in the SoC group (43% of patients that progressed; patients had to be T790M mutation-positive to receive osimertinib).

Specific Change: We respectfully request that osimertinib be updated to category 1 recommendation for the first-line treatment of metastatic EGFR mutation-positive NSCLC based on the attached TAGRISSO® Prescribing Information which can also be accessed here.[3,4]

FDA Status: TAGRISSO is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test. TAGRISSO is also indicated for the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

Sincerely,

Nabil Chehab

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Reference(s):

[1] Soria J-C, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated *EGFR*-mutated advanced non-small-cell lung cancer [article and supplementary appendix]. *N Engl J Med*. 2018;378:113-125.
[2] Planchard D, Boyer M, Lee JS, et al. Osimertinib vs standard of care (SoC) EGFR-TKI as first-line therapy in patients with untreated EGFRm advanced NSCLC: FLAURA post-progression outcomes [presentation]. Presented at: European Lung Cancer Conference, April 11-14, 2018; Geneva, Switzerland.
[3] TAGRISSO Prescribing Information.
[4] AstraZeneca website: https://www.azpicentral.com/tagrisso/tagrisso.pdf#page=1. Accessed April 18, 2018.