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. 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.

- In 556 patients randomized 1:1, post-progression outcomes were as follows:
  - 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.

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

Nabil Chehab, Ph.D.
Medical Lead, EGFR Lung Team, US Medical Affairs
AstraZeneca Pharmaceuticals LP
Reference(s):


3 TAGRISSO Prescribing Information.