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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 data provided as additional evidence in support of TAGRISSO® (osimertinib) in the NSCLC guideline for the first-line treatment of metastatic epidermal growth factor receptor (EGFR) mutation-positive NSCLC.

Specific change: We respectfully request the inclusion of the enclosed data as additional evidence for the first-line treatment of metastatic NSCLC patients harboring uncommon EGFR mutations.¹ Additionally, we also respectfully request that you consider the addition of treatment recommendations that includes osimertinib for the uncommon mutations (G719X, L861Q and S768I) in a separate algorithm from the listing of the common sensitizing mutations (exon 19 deletions and L858R).

FDA Status: Osimertinib is not FDA-approved for the treatment of patients with metastatic NSCLC having uncommon mutations in the *EGFR* gene.²

Rationale: This request is based on clinical evidence from a phase II, open label, multicenter trial evaluating the efficacy and safety of osimertinib in patients with metastatic NSCLC having uncommon mutations which was presented at the Annual Society for Clinical Oncology congress on June 3, 2018.¹

The study analyzed 36 patients who received osimertinib at 80 mg orally, once daily. Of these 36 patients, 61.1% were treatment-naïve, 30.6% received osimertinib as second-line therapy and 8.3% received osimertinib as third-line therapy. The three most frequently observed mutations in patients enrolled in this study were G719A/C/D/S/X (52.8%), L861Q (25.0%), and S768I (22.2%). The primary endpoint of the study was overall response rate (ORR).¹

Efficacy Results:

- At the time of data cut-off, the ORR was 50.0% (95% CI 32.8-67.2)
- The median progression-free survival (PFS) was 9.5 months (range 1.0-20.1)
- The disease control rate (DCR) was 88.9% (95% CI 78.1-99.7)
- The median duration of response (DoR) was 7.0 months (95% CI 4.7-9.3)
- Three out of 9 patients (33%) had either complete (n=1) or partial (n=2) response to brain metastasis

Safety Results:

- The most common all-causality adverse events (AEs) occurring in $\geq 20\%$ of patients were rash (30.6%, any grade [0% Grade ≥ 3]) and anorexia (22.2%, any grade [0% Grade ≥ 3]).

Sincerely,

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Reference(s):

1. Ahn M-J, Cho JH, Sun J-M, et al. An open-label, multicenter, phase II single arm trial of osimertinib in non-small cell lung cancer patients with uncommon EGFR mutation (KCSG-LU15-09). Presented at ASCO; June 1-5, 2018; Chicago, IL. *J Clin Oncol.* 2018;36:suppl. Abstract 9050.
2. TAGRISSO Prescribing Information.