Tagrisso® (osimertinib) – Expanded indication

- On February 19, 2024, AstraZeneca announced the FDA approval of Tagrisso (osimertinib), in combination with pemetrexed and platinum-based chemotherapy, for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.

- This is the fourth approval for Tagrisso for NSCLC. Tagrisso is also approved:

    - As adjuvant therapy after tumor resection in adult patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
    - For first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
    - For the treatment of adult 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 therapy.

- The approval of Tagrisso for the expanded indication was based on FLAURA2, a randomized, open-label study in 557 patients with EGFR exon 19 deletion or exon 21 L858R mutation-positive locally advanced or metastatic NSCLC, who had not received previous systemic treatment for advanced disease. Patients were randomized to (1) Tagrisso with pemetrexed and investigator's choice of cisplatin or carboplatin or (2) Tagrisso alone. The primary endpoint was progression-free survival (PFS). Overall survival (OS) was a key secondary outcome measure. Additional efficacy outcome measures included objective response rate (ORR) and duration of response (DOR).

    - Median PFS was 25.5 months for Tagrisso with pemetrexed and platinum-based chemotherapy vs. 16.7 months for Tagrisso alone (hazard ratio [HR] 0.62, 95% CI: 0.49, 0.79; $p < 0.0001$).
    - The ORR was 77% (95% CI: 71, 82) for Tagrisso with pemetrexed and platinum-based chemotherapy vs. 69% (95% CI: 63, 74) for Tagrisso alone.
    - The median DOR was 24.9 months (95% CI: 22.1, not estimable) for Tagrisso with pemetrexed and platinum-based chemotherapy vs. 17.9 months (95% CI: 15.2, 20.9) for Tagrisso alone.
    - While OS results were immature at the current analysis, with 45% of pre-specified deaths for the final analysis reported, no trend towards a detriment was observed.

- The most common adverse reactions (> 20%), including laboratory abnormalities, with Tagrisso in combination with pemetrexed and platinum-based chemotherapy were leukopenia, thrombocytopenia, neutropenia, lymphopenia, rash, diarrhea, stomatitis, nail toxicity, dry skin, and increased blood creatinine.

- The recommended dose of Tagrisso for the new approval is 80 mg tablet orally once daily until disease progression or unacceptable toxicity due to Tagrisso.

    - Refer to the Tagrisso drug label for dosing for its other uses.