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Tagrisso with the addition of chemotherapy approved in the US for patients with EGFR-mutated advanced lung cancer

Approval based on FLAURA2 results which showed Tagrisso plus chemotherapy extended median progression-free survival by nearly 9 months vs. standard of care

AstraZeneca's *Tagrisso* (osimertinib) with the addition of chemotherapy has been approved in the US for the treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC).

The approval following a Priority Review by the Food and Drug Administration (FDA) was based on the results from the FLAURA2 Phase III trial published in *The New England Journal of Medicine*. *Tagrisso* with the addition of chemotherapy reduced the risk of disease progression or death by 38% compared to *Tagrisso* monotherapy which is the 1st-line global standard of care (hazard ratio [HR] 0.62; 95% confidence interval [CI] 0.49-0.79; p<0.0001). Median progression-free survival (PFS) by investigator assessment was 25.5 months for patients treated with *Tagrisso* plus chemotherapy, an 8.8-month improvement versus *Tagrisso* monotherapy (16.7 months).

PFS results from blinded independent central review (BICR) were consistent with the results by investigator assessment, showing 29.4 months median PFS with *Tagrisso* plus chemotherapy, a 9.5-month improvement over *Tagrisso* monotherapy (19.9 months) (HR 0.62; 95% CI 0.48-0.80; p=0.0002).

Each year in the US, there are over 200,000 people diagnosed with lung cancer, and 80-85% of these patients are diagnosed with NSCLC, the most common form of lung cancer.[1-3] Approximately 70% of people are diagnosed with advanced NSCLC.[4] Additionally, about 15% of NSCLC patients in the US have an EGFR mutation.[5]

Pasi A. Jänne, MD, PhD, medical oncologist at Dana-Farber Cancer Institute and principal investigator for the trial, said: "This approval based on the unprecedented data from FLAURA2 brings a critical new treatment option to patients with advanced EGFR-mutated non-small cell lung cancer. Now, with the choice of two highly effective osimertinib-based options, physicians can better tailor treatment to an individual's needs and help ensure the best possible outcome for each patient."

Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca, said: "This important new treatment option can delay disease progression by nearly nine additional months, establishing a new benchmark with the longest reported progression-free survival benefit in the 1st-line advanced setting. This approval reinforces *Tagrisso* as the backbone of EGFR-mutated lung cancer treatment either as monotherapy or in combination with chemotherapy. This news is especially important for those with a poorer prognosis, including patients whose cancer has spread to the brain and those with L858R mutations."

Laurie Ambrose, President and CEO, GO2 for Lung Cancer, said: "We are so excited to see this continued progress advancing more personalized treatment options for our community. The more we can target the right treatments for the right people at the right time, the better outcomes will be for our community - a goal we all collectively share."

Results from a prespecified exploratory analysis of patients in the FLAURA2 trial with brain metastases at baseline showed *Tagrisso* plus chemotherapy reduced the risk of central nervous system (CNS) disease progression or death by 42% compared to *Tagrisso* alone (HR 0.58; 95% CI 0.33-1.01) as assessed by BICR. With two years of follow up, 74% of patients treated with *Tagrisso* plus chemotherapy had not experienced CNS disease progression or death versus 54% of patients treated with *Tagrisso* monotherapy.

While the overall survival (OS) results remained immature at the second interim analysis (41% maturity), no trend towards a detriment was observed (HR 0.75; 95% CI 0.57-0.97). The trial continues to assess OS as a key secondary endpoint.

The safety profile of *Tagrisso* with the addition of chemotherapy was generally manageable and consistent with the established profiles of the individual medicines. Adverse event (AE) rates were higher in the *Tagrisso* plus chemotherapy arm, driven by well-characterised chemotherapy-related AEs. Discontinuation rates for *Tagrisso* due to AEs were low in both arms of the trial (11% for *Tagrisso* plus chemotherapy and 6% for monotherapy).

In December 2023, osimertinib (*Tagrisso*) with the addition of chemotherapy was added to the NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®) as a NCCN Category 1 Other Recommended regimen for patients with NSCLC whose tumours have EGFR exon 19 deletion or exon 21 L858R mutations based on the data from FLAURA2.[6]

The US regulatory submission was reviewed under Project Orbis, which provides a framework for concurrent submission and review of oncology medicines among participating international partners. As part of Project Orbis, *Tagrisso* in combination with chemotherapy is also under review by regulatory authorities in Australia, Canada, and Switzerland. Regulatory applications are also under review in several other countries based on the FLAURA2 results.

Tagrisso is approved as monotherapy in more than 100 countries including in the US, EU, China and Japan. Approved indications include for 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC, locally advanced or metastatic EGFR T790M mutation-positive NSCLC, and adjuvant treatment of early-stage EGFRm NSCLC.

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As part of AstraZeneca's ongoing commitment to treating patients as early as possible in lung cancer, *Tagrisso* is also being investigated in the neoadjuvant setting in the NeoADAURA Phase III trial with results expected later this year, and in the early-stage adjuvant resectable setting in the ADAURA2 Phase III trial.

Notes

Lung cancer

Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths.[7] Lung cancer is broadly split into NSCLC and small cell lung cancer.[2] The majority of all NSCLC patients are diagnosed with advanced disease.[4]

Patients with EGFRm NSCLC are particularly sensitive to treatment with an EGFR-tyrosine kinase inhibitor (EGFR-TKI) which blocks the cell-signalling pathways that drive the growth of tumour cells.[8]

FLAURA2

FLAURA2 is a randomised, open-label, multi-centre, global Phase III trial in the 1st-line treatment of patients with locally advanced (Stage IIIB-IIIC) or metastatic (Stage IV) EGFRm NSCLC. Patients were treated with *Tagrisso* 80mg once daily oral tablets with the addition of chemotherapy (pemetrexed (500mg/m2) plus cisplatin (75mg/m2) or carboplatin (AUC5)) every three weeks for four cycles, followed by *Tagrisso* with pemetrexed maintenance every three weeks.

The trial enrolled 557 patients in more than 150 centres across more than 20 countries, including in the US, Europe, South America and Asia. The primary endpoint is PFS. The trial is ongoing and will continue to assess the secondary endpoint of OS.

Tagrisso

Tagrisso (osimertinib) is a third-generation, irreversible EGFR-TKI with proven clinical activity in NSCLC, including against CNS metastases. *Tagrisso* (40mg and 80mg once-daily oral tablets) has been used to treat more than 800,000 patients across its indications worldwide and AstraZeneca continues to explore *Tagrisso* as a treatment for patients across multiple stages of EGFRm NSCLC.

There is an extensive body of evidence supporting the use of *Tagrisso* in EGFRm NSCLC. *Tagrisso* is the only targeted therapy to improve patient outcomes in both early-stage disease in the ADAURA Phase III trial and late-stage disease in the FLAURA Phase III trial and FLAURA2 Phase III trial.

The Company is also researching ways to address tumour mechanisms of resistance through the SAVANNAH and ORCHARD Phase II trials, and the SAFFRON Phase III trial, which test *Tagrisso* plus savolitinib, an oral, potent and highly selective MET TKI, as well as other potential new medicines.

AstraZeneca in lung cancer

AstraZeneca is working to bring patients with lung cancer closer to cure through the detection and treatment of early-stage disease, while also pushing the boundaries of science to improve outcomes in the resistant and advanced settings. By defining new therapeutic targets and investigating innovative approaches, the Company aims to match medicines to the patients who can benefit most.

The Company's comprehensive portfolio includes leading lung cancer medicines and the next wave of innovations, including *Tagrisso* and *Iressa* (gefitinib); *Imfinzi* (durvalumab) and *Imjudo* (tremelimumab); *Enhertu* (trastuzumab deruxtecan) and datopotamab deruxtecan in collaboration with Daiichi Sankyo; *Orpathys* (savolitinib) in collaboration with HUTCHMED; as well as a pipeline of potential new medicines and combinations across diverse mechanisms of action.

AstraZeneca is a founding member of the Lung Ambition Alliance, a global coalition working to accelerate innovation and deliver meaningful improvements for people with lung cancer, including and beyond treatment.

AstraZeneca in oncology

AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

Contacts

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