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Tagrisso with the addition of chemotherapy recommended for approval in the EU by CHMP for patients with EGFR-mutated advanced lung cancer

Recommendation 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 pemetrexed and platinum-based chemotherapy has been recommended for approval in the European Union (EU) for 1st-line treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC) whose tumours have exon 19 deletions or exon 21 (L858R) mutations.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on the results from the FLAURA2 Phase III trial, which were also published in *The New England Journal of Medicine*.

Results showed *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).

While overall survival (OS) remained immature at the second interim analysis (41% maturity), an encouraging trend towards an OS benefit was observed with *Tagrisso* plus chemotherapy versus *Tagrisso* alone (HR 0.75; 95% CI 0.57-0.97). The trial continues to assess OS as a key secondary endpoint.

Each year in Europe, there are more than 450,000 people diagnosed with lung cancer.[1] Among those with NSCLC, the most common form of lung cancer, about 10-15% of patients in Europe have tumours with an EGFR mutation.[2,3] Additionally, the majority of patients with NSCLC are diagnosed with advanced disease.[4]

David Planchard, MD, PhD, thoracic oncologist at Gustave Roussy Institute of Oncology and principal investigator for the trial, said: "The FLAURA2 results build on the established efficacy of osimertinib monotherapy in patients with EGFR-mutated lung cancer, demonstrating a meaningful nine-month improvement in progression-free survival with the addition of chemotherapy. Today's positive recommendation is a vital step towards providing patients in Europe with an additional treatment option capable of extending the time before their disease progresses. This expands on the already approved use of osimertinib as monotherapy, providing physicians with options to tailor treatments that best suit their patients' specific disease needs."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "Today's news reinforces the importance of *Tagrisso* as the backbone therapy in EGFR-mutated lung cancer. If approved in Europe, patients will have the option to be treated with *Tagrisso* alone, or with chemotherapy, which is especially important when caring for patients whose disease has spread to the brain or those with L858R mutations."

The safety profile of *Tagrisso* plus 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 of *Tagrisso* due to AEs were 11% for *Tagrisso* plus chemotherapy and 6% for monotherapy.

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. *Tagrisso* with the addition of chemotherapy is also approved in the US and several other countries for the 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC.

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.[5] Lung cancer is broadly split into NSCLC and small cell lung cancer.[3] Each year there are an estimated 2.4 million people diagnosed with lung cancer globally, with 80-85% of patients diagnosed with NSCLC, the most common form of lung cancer.[3,5-6] The majority of all NSCLC patients are diagnosed with advanced disease.[7]

Approximately 10-15% of NSCLC patients in the US and Europe, and 30-40% of patients in Asia have EGFRm NSCLC.[8-10] 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.[11]

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

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 central nervous system (CNS) metastases. *Tagrisso* (40mg and 80mg once-daily oral tablets) has been used to treat nearly 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 early-stage disease in the ADAURA Phase III trial, locally advanced stages in the LAURA Phase III trial and late-stage disease in the FLAURA Phase III trial and FLAURA2 Phase III trial.

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.

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
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

References

1. Ferlay J, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *Eur J Cancer.* 2018;103:356-387.
2. Sanden SV, et al. Prevalence of Epidermal Growth Factor Receptor Exon 20 Insertion Mutations in Non-small-Cell Lung Cancer in Europe: A Pragmatic Literature Review and Meta-analysis. *Targeted Onc.* 2022;17:153-166.
3. LUNGevity Foundation. Types of Lung Cancer. Available at: https://lungevity.org/for-patientscaregivers/lung-cancer-101/types-of-lung-cancer. Accessed May 2024.
4. Cagle PT, et al. Lung Cancer Biomarkers: Present Status and Future Developments. *Archives Pathology Lab Med.* 2013;137:1191-1198.
5. World Health Organization. International Agency for Research on Cancer. Lung Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/cancers/15-trachea-bronchus-and-lung-fact-sheet.pdf. Accessed May 2024.
6. American Cancer Society. What Is Lung Cancer? Available at: https://www.cancer.org/cancer/lung-cancer/about/what-is.html. Accessed May 2024.

7. Cancer.Net. Lung Cancer - Non-Small Cell: Statistics. Available at: https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics. Accessed May 2024.
8. Keedy VL, et al. American Society of Clinical Oncology Provisional Clinical Opinion: Epidermal Growth Factor Receptor (EGFR) Mutation Testing for Patients with Advanced Non-Small-Cell Lung Cancer Considering First-Line EGFR Tyrosine Kinase Inhibitor Therapy. *J Clin Oncol*. 2011;29:2121-27.
9. Szumera-Ciećkiewicz A, et al. EGFR Mutation Testing on Cytological and Histological Samples in Non-Small Cell Lung Cancer: a Polish, Single Institution Study and Systematic Review of European Incidence. *Int J Clin Exp Pathol*. 2013;6:2800-2812.
10. Ellison G, et al. EGFR Mutation Testing in Lung Cancer: a Review of Available Methods and Their Use for Analysis of Tumour Tissue and Cytology Samples. *J Clin Pathol*. 2013;66:79-89.
11. Cross DA, et al. AZD9291, an Irreversible EGFR TKI, Overcomes T790M-Mediated Resistance to EGFR Inhibitors in Lung Cancer. *Cancer Discov*. 2014;4(9):1046-1061.

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