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Tagrisso approved in Japan for 1st-line treatment of EGFR-mutated non-small cell lung cancer

1st-line Tagrisso offers a potential new standard of care for Japanese lung cancer patients

AstraZeneca today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has approved *Tagrisso* (osimertinib) for the 1st-line treatment of patients with inoperable or recurrent epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer (NSCLC), following priority review. The approval is based on results from the global Phase III FLAURA trial which included Japanese patients and which were published in the *New England Journal of Medicine*.

Dave Fredrickson, Executive Vice President, Head of the Oncology Business Unit, said: "*Tagrisso* is already approved in Japan for the treatment of patients with EGFR T790M mutation-positive inoperable or recurrent NSCLC that is resistant to existing 1st-line EGFR-inhibitor medicines. Today's approval moves the use of *Tagrisso* to the 1st-line setting, replacing older medicines which, given the high prevalence of the EGFR mutation in Japan, offers an important new treatment option for these patients."

The FLAURA trial compared *Tagrisso* to current 1st-line EGFR tyrosine kinase inhibitors (TKIs), erlotinib or gefitinib in previously-untreated patients with locally-advanced or metastatic EGFR-mutated (EGFRm) NSCLC. In the trial, *Tagrisso* demonstrated superior progression-free survival (PFS) of 18.9 months compared with 10.2 months for the comparator arm (see table below), and this benefit was consistent across all subgroups including in patients with or without central nervous system (CNS) metastases, an important benefit for lung cancer patients.

FLAURA trial efficacy results according to investigator assessment

Efficacy parameter	***Tagrisso* (N=279)**	**EGFR-TKI comparator (gefitinib or erlotinib) (N=277)**
PFS		
Number of events (62% maturity)	136 (49)	206 (74)
Median PFS (95% confidence interval [CI])	18.9 months (15.2, 21.4)	10.2 months (9.6, 11.1)
Hazard ratio (HR [95% CI]); p-value	0.46 (0.37, 0.57); p < 0.0001	
Objective response rate (ORR)		
Response rate (95% CI)	80% (75, 85)	76% (70, 81)
Odds ratio (95% CI); p-value	1.3 (0.9, 1.9); p=0.2421	
Duration of response (DoR)		
Median DoR (95% CI)	17.2 months (13.8, 22.0)	8.5 months (7.3, 9.8)

Safety data for *Tagrisso* in the FLAURA trial were in line with those observed in prior clinical trials. *Tagrisso* was generally well tolerated, with Grade 3 or higher adverse events (AEs) occurring in 34% of patients taking *Tagrisso* and 45% in the comparator arm. The most common adverse reactions in patients treated with *Tagrisso* were rash/acne (54.5%), diarrhoea (49.5%), dry skin/eczema (33.3%) and nail disorder including paronychia (32.6%) (at the time of supplementary approval).

Tagrisso has now received approval in 40 countries for the 1st-line treatment of patients with metastatic EGFRm NSCLC, including the US, Japan and in Europe. Other global health authority reviews and submissions are ongoing.

About EGFRm NSCLC

Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths, more than breast, prostate and colorectal cancers combined. Lung cancer is broadly split into NSCLC and small cell lung cancer (SCLC), with 80-85% classified as NSCLC. Approximately 10-15% of NSCLC patients in the US and Europe, and 30-40% of patients in Asia have EGFRm NSCLC. These patients are particularly sensitive to treatment with EGFR-TKIs which block the cell-signalling pathways that drive the growth of tumour cells. Approximately 25% of patients with EGFRm NSCLC have brain metastases at diagnosis, increasing to approximately 40% within two years of diagnosis. The presence of brain metastases often reduces median survival to less than 8 months.

About *Tagrisso*

Tagrisso (osimertinib) is a third-generation, irreversible EGFR-TKI designed to inhibit both EGFR-sensitising and EGFR T790M-resistance mutations, with clinical activity against CNS metastases. *Tagrisso* 40mg and 80mg once-daily oral tablets have now received approval in 39 countries, including the US, Japan and in Europe, for 1st-line EGFRm advanced NSCLC, and more than 75 countries, including the US, Japan, China and in Europe, for 2nd-line use in patients with EGFR T790M mutation-positive advanced NSCLC. *Tagrisso* is also being developed in the adjuvant setting (ADAURA), in the locally-advanced unresectable setting (LAURA), and in combination with other treatments.

About the FLAURA trial

The FLAURA trial assessed the efficacy and safety of *Tagrisso* 80mg orally once daily vs. standard-of-care EGFR-TKIs (either erlotinib [150mg orally, once daily] or gefitinib [250mg orally, once daily]) in previously-untreated patients with locally-advanced or metastatic EGFRm NSCLC. The trial was double-blinded and randomised, with 556 patients across 29 countries.

About AstraZeneca in Lung Cancer

AstraZeneca has a comprehensive portfolio of approved and potential new medicines in late-stage clinical development for the treatment of lung cancer across all stages of disease and lines of therapy. We aim to address the unmet needs of patients with EGFRm NSCLC with our approved medicines, *Iressa* and *Tagrisso,* and with the Phase III ADAURA and LAURA trials.

Our Immuno-Oncology portfolio includes *Imfinzi*, an anti-PDL1 antibody, which is in development as monotherapy (ADJUVANT, PACIFIC2, MYSTIC and PEARL trials) and in combination with tremelimumab and/or chemotherapy (MYSTIC, NEPTUNE, CASPIAN, and POSEIDON trials).

About AstraZeneca in Oncology

AstraZeneca has a deep-rooted heritage in oncology and offers a quickly-growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020, and a broad pipeline of small molecules and biologics in development, we are committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms - Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates - and by championing the development of precision combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

About AstraZeneca
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

For more information, please visit www.astrazeneca.com and follow us on Twitter @AstraZeneca.

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