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Tagrisso granted Breakthrough Therapy Designation in the US for the adjuvant treatment of patients with Stage IB-IIIA EGFR-mutated lung cancer

Designation based on unprecedented results from the Phase III ADAURA trial where Tagrisso reduced the risk of disease recurrence or death by c. 80%

AstraZeneca's *Tagrisso* (osimertinib) has been granted Breakthrough Therapy Designation (BTD) in the US for the adjuvant treatment of patients with early-stage (IB, II and IIIA) epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC) after complete tumour resection with curative intent.

The Food and Drug Administration's (FDA) BTD is designed to accelerate the development and regulatory review of potential new medicines that are intended to treat a serious condition and address a significant unmet medical need. The new medicine needs to have shown encouraging early clinical results that demonstrate substantial improvement on a clinically significant endpoint over available medicines.

While up to 30% of patients with NSCLC may be diagnosed early enough to have potentially curative surgery, disease recurrence is common in early-stage disease and nearly half of patients diagnosed in Stage IB, and over three quarters of patients diagnosed in Stage IIIA, experience recurrence within five years.[1-6]

José Baselga, Executive Vice President, Oncology R&D said: "Patients with early-stage EGFRm lung cancer often experience recurrence even after successful surgery and adjuvant chemotherapy, yet there are currently no approved targeted treatments to improve outcomes. The Phase III ADAURA trial with *Tagrisso* demonstrated an unprecedented level of clinical benefit in these patients, and we are working closely with the FDA to deliver this potentially curative treatment to patients as quickly as possible."

The FDA granted the BTD based on data from the Phase III ADAURA trial, which were also recently presented during the plenary session of the American Society of Clinical Oncology ASCO20 Virtual Scientific Program.

In the trial *Tagrisso* demonstrated a statistically significant and clinically meaningful improvement in disease-free survival (DFS) in the adjuvant treatment of Stage IB-IIIA EGFRm NSCLC patients, reducing the risk of disease recurrence or death by 79% (HR 0.21; 95% CI 0.16-0.28; p<0.0001) in a key secondary endpoint. In April 2020, an Independent Data Monitoring Committee recommended for the trial to be unblinded two years early based on its determination of overwhelming efficacy.

Tagrisso is approved for the 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC and for the treatment of locally advanced or metastatic EGFR T790M mutation-positive NSCLC in the US, Japan, China, the EU and many other countries around the world.

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, with 80-85% classified as NSCLC.[8] The majority of all NSCLC patients are diagnosed with advanced disease while approximately 25-30% present with resectable disease at diagnosis.[1-3] A significant portion of patients with resectable NSCLC eventually develop recurrence despite complete tumour resection and adjuvant chemotherapy.

Approximately 10-15% of NSCLC patients in the US and Europe, and 30-40% of patients in Asia have EGFRm NSCLC.[9-11] These patients are particularly sensitive to treatment with EGFR-tyrosine kinase inhibitors (TKIs) which block the cell-signalling pathways that drive the growth of tumour cells.[12]

ADAURA

ADAURA is a randomised, double-blinded, global, placebo-controlled Phase III trial in the adjuvant treatment of 682 patients with Stage IB, II, IIIA EGFRm NSCLC following complete tumour resection and adjuvant chemotherapy as indicated. In the experimental arm, patients were treated with *Tagrisso* 80mg once-daily oral tablets for three years or until disease recurrence. The trial enrolled in more than 200 centres across more than 20 countries, including the US, in Europe, South America, Asia and the Middle East. The primary endpoint DFS in Stage II and IIIA patients and a key secondary endpoint is DFS in Stage IB, II and IIIA patients. The data readout was originally anticipated in 2022. The trial will continue to assess OS.

Tagrisso

Tagrisso (osimertinib) is a third-generation, irreversible EGFR-TKI with clinical activity against CNS metastases. *Tagrisso* 40mg and 80mg once-daily oral tablets have received approval in the US, Japan, China, the EU and many countries around the world for 1st-line EGFRm advanced NSCLC and EGFR T790M mutation-positive advanced NSCLC. *Tagrisso* is also being developed in the Stage III, unresectable setting (LAURA), in the neoadjuvant resectable setting (NeoADAURA), in combination with chemotherapy (FLAURA2) and in combination with potential new medicines to address resistance to EGFR-TKIs (SAVANNAH, ORCHARD).

AstraZeneca in lung cancer

AstraZeneca has a comprehensive portfolio of approved and potential new medicines in late-stage development for the treatment of different forms of lung cancer spanning different histologies, several stages of disease, lines of therapy and modes of action. AstraZeneca aims to address the unmet needs of patients with EGFRm tumours as a genetic driver of disease, which occur in 10-15% of NSCLC patients in the US and the EU and 30-40% of NSCLC patients in Asia, with the approved medicines *Iressa* (gefitinib) and *Tagrisso*, and its ongoing Phase III trials LAURA, NeoADAURA, and FLAURA2.[9-11]

AstraZeneca is committed to addressing tumour mechanisms of resistance through the ongoing Phase II trials SAVANNAH and ORCHARD which test *Tagrisso* in combination with savolitinib, a selective inhibitor of c-MET receptor tyrosine kinase, along with other potential new medicines. *Enhertu* (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate (ADC) is in development for metastatic non-squamous HER2-overexpressing or HER2-mutated NSCLC including trials in combination with other anticancer treatments. In addition, DS-1062, a trophoblast cell-surface antigen 2 (TROP2)-directed ADC, is in early development for advanced NSCLC where TROP2 is overexpressed in the majority of patients.[13]

An extensive late-stage Immuno-Oncology programme focuses on lung cancer patients without a targetable genetic mutation which represents up to three-quarters of all patients with lung cancer.[14] *Imfinzi*, an anti-PDL1 antibody, is in development for patients with advanced disease (Phase III trials POSEIDON and PEARL) and for patients in earlier stages of disease including potentially curative settings (Phase III trials MERMAID-1, AEGEAN, ADJUVANT BR.31, PACIFIC-2, PACIFIC-4, PACIFIC-5, and ADRIATIC) both as monotherapy and in combination with tremelimumab and/or chemotherapy. *Imfinzi* is also in development in the Phase II trials NeoCOAST, COAST and HUDSON in combination with potential new medicines from the early-stage pipeline including *Enhertu*.

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 seven new medicines launched between 2014 and 2020, and a broad pipeline of small molecules and biologics in development, the Company is committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers.

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

AstraZeneca
AstraZeneca (LSE/STO/NYSE: AZN) 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 & 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 Twitter @AstraZeneca.

Contacts
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