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Datopotamab deruxtecan application in the EU for patients with advanced nonsquamous non-small cell lung cancer voluntarily withdrawn

AstraZeneca and Daiichi Sankyo have voluntarily withdrawn the marketing authorisation application (MAA) in the EU for datopotamab deruxtecan (Dato-DXd) for the treatment of adult patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) based on the TROPION-Lung01 Phase III trial.

The decision to withdraw the MAA was informed by feedback from the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA). AstraZeneca and Daiichi Sankyo will continue to work to bring datopotamab deruxtecan to patients with lung cancer in the EU who can benefit and are committed to unlocking the potential of this medicine in lung cancer through our robust clinical development programme which includes seven pivotal trials in various lung cancer settings.

AstraZeneca and Daiichi Sankyo's application in the EU for datopotamab deruxtecan for the treatment of hormone receptor (HR)-positive, HER2-negative metastatic breast cancer based on the TROPION-Breast01 Phase III trial remains under review.

Datopotamab deruxtecan is a specifically engineered TROP2-directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo and being jointly developed by AstraZeneca and Daiichi Sankyo.

Notes

Advanced non-small cell lung cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[1] In Europe, nearly half a million lung cancer cases were diagnosed in 2022.[1] Lung cancer is broadly split into small or non-small cell lung cancer, the latter accounting for about 80% of cases.[2] While immunotherapy and targeted therapies have improved outcomes in the 1st-line setting, most patients eventually experience disease progression and receive chemotherapy.[3-5] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[3-5]

TROP2 is a protein broadly expressed in the majority of NSCLC tumours.[6] There is currently no TROP2-directed ADC approved for the treatment of lung cancer.[7,8]

TROPION-Lung01

TROPION-Lung01 is a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy and safety of datopotamab deruxtecan versus docetaxel in adult patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations who require systemic therapy following prior treatment. Patients with actionable genomic alterations were previously treated with an approved targeted therapy and platinum-based chemotherapy. Patients without known actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

The dual primary endpoints of TROPION-Lung01 are progression-free survival (PFS) as assessed by blinded independent central review (BICR) and overall survival (OS). Key secondary endpoints include investigator-assessed PFS, objective response rate, duration of response, time to response, and disease control rate as assessed by both BICR and investigator, and safety.

TROPION-Lung01 enrolled approximately 600 patients in Asia, Europe, North America, Oceania and South America. For more information visit ClinicalTrials.gov.

Primary results from TROPION-Lung01, as presented at the European Society for Medical Oncology 2023 Congress, showed datopotamab deruxtecan demonstrated a statistically significant improvement in PFS over docetaxel. OS results were presented at the IASLC 2024 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer and simultaneously published in the *Journal of Clinical Oncology* in September 2024.

Datopotamab deruxtecan (Dato-DXd)

Datopotamab deruxtecan (Dato-DXd) is an investigational TROP2-directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, datopotamab deruxtecan is one of six DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programmes in AstraZeneca's ADC scientific platform. Datopotamab deruxtecan is comprised of a humanised anti-TROP2 IgG1 monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Datopotamab deruxtecan has been granted Breakthrough Therapy Designation by the US Food and Drug Administration for the treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor-mutated (*EGFR*m) NSCLC with disease progression on or after treatment with an *EGFR*-tyrosine kinase inhibitor and platinum-based chemotherapy. AstraZeneca and Daiichi Sankyo have submitted a Biologics License Application for datopotamab deruxtecan for this potential indication.

Datopotamab deruxtecan clinical development programme

A comprehensive global clinical development programme is underway with more than 20 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple cancers, including NSCLC, triple-negative breast cancer (TNBC) and HR-positive, HER2-negative breast cancer. The programme includes seven Phase III trials in lung cancer and five Phase III trials in breast cancer evaluating datopotamab deruxtecan as a monotherapy and in combination with other anticancer treatments in various settings.

Daiichi Sankyo collaboration

AstraZeneca and Daiichi Sankyo entered into a global collaboration to jointly develop and commercialise *Enhertu* (trastuzumab deruxtecan) in March 2019 and datopotamab deruxtecan in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of *Enhertu* and datopotamab deruxtecan.

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* (osimertinib) and *Iressa* (gefitinib); *Imfinzi* (durvalumab) and *Imjudo* (tremelimumab); *Enhertu* 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's innovative medicines are sold in more than 125 countries and 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.

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