AstraZeneca

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Trastuzumab deruxtecan recommended for approval in the EU by CHMP for HER2-positive metastatic breast cancer

Recommendation based on positive results from the DESTINY-Breast01 trial, which showed durable responses in patients with previously treated disease

AstraZeneca and Daiichi Sankyo Company, Limited (Daiichi Sankyo)'s trastuzumab deruxtecan has been recommended for conditional marketing authorisation in the European Union (EU) as a monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens.

In Europe, approximately 520,000 cases of breast cancer in women are diagnosed annually, with roughly one in five cases being HER2 positive.[1-2] The impact of the disease is significant, with breast cancer responsible for more than 137,000 deaths per year.[1]

Following review of the application under its accelerated assessment procedure, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the registrational DESTINY-Breast01 Phase II trial, which were published in The New England Journal of Medicine, and the results from the Phase I trial published in The Lancet Oncology.[3,4] In the DESTINY-Breast01 trial, trastuzumab deruxtecan demonstrated clinically meaningful and durable activity in patients who had received two or more prior anti-HER2 medicines.

An updated analysis from DESTINY-Breast01 was presented lastweek at the 2020 San Antonio Breast Cancer Symposium, reinforcing the durable efficacy and long-term safety and tolerability profiles of trastuzumab deruxtecan.

José Baselga, Executive Vice President, Oncology R&D, said: “The durable responses demonstrated in the DESTINY-Breast01 trial have never been seen before in this patient setting. If approved by the European Commission, physicians in Europe will have an important new treatment option for patients with previously treated HER2-positive metastatic breast cancer.”

Gilles Gallant, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo, said: “We are encouraged by the CHMP positive opinion given the significant unmet need for patients with HER2-positive metastatic breast cancer. Trastuzumab deruxtecan is already available for patients with HER2-positive metastatic breast cancer in the US and Japan, and we are now one step closer to bringing this important new medicine to patients in Europe.”

HER2-positive breast cancer

Approximately 520,000 cases of breast cancer are diagnosed in Europe annually, with an estimated one in five cases considered HER2 positive.[1-2]

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumours, including breast, gastric, lung and colorectal cancers. HER2 overexpression may be associated with a specific HER2 gene alteration known as HER2 amplification and is often associated with aggressive disease and a poor prognosis in breast cancer.[5]

There remain significant unmet clinical needs for patients with HER2-positive metastatic breast cancer. The disease remains incurable with patients eventually progressing after currently available treatment options.[6,7]

DESTINY-Breast01

DESTINY-Breast01 is a registrational Phase II, single-arm, open-label, global, multicentre, two-part trial testing the safety and efficacy of trastuzumab deruxtecan in patients with HER2-positive unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine. The primary endpoint of the trial is objective response rate, as determined by independent central review. Secondary objectives include duration of response, disease control rate, clinical benefit rate, progression-free survival and overall survival.

Trastuzumab deruxtecan

Trastuzumab deruxtecan is a HER2-directed antibody drug conjugate (ADC). It is the lead ADC in the oncology portfolio of Daiichi Sankyo and the most advanced programme in AstraZeneca's ADC scientific platform.

ADCs are targeted cancer medicines that deliver cytotoxic chemotherapy ('payload') to cancer cells via a linker attached to a monoclonal antibody that binds to a specific target expressed on cancer cells. Trastuzumab deruxtecanis comprised of a HER2 monoclonal antibody attached to a topoisomerase I inhibitor payload by a tetrapeptide-based linker.

Trastuzumab deruxtecan is approved under the brand name *Enhertu* (5.4mg/kg)in the US and Japan for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting based on the DESTINY-Breast01 trial.In September 2020, *Enhertu* (6.4mg/kg) was

approved in Japan for patients with HER2-positive unresectable advanced or recurrent gastric cancer that progressed after chemotherapy based on the DESTINY-Gastric01 trial.

Development programme

A comprehensive development programme is underway globally, with nine registrational trials evaluating the efficacy and safety of trastuzumab deruxtecan monotherapy across multiple HER2 cancers, including breast, gastric and lung cancers. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

In October 2020, trastuzumab deruxtecan was granted Priority Review from the US Food and Drug Administration for the treatment of patients with HER2-positive metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma. In May 2020, trastuzumab deruxtecan received a Breakthrough Therapy Designation (BTD) and Orphan Drug Designation (ODD) for gastric cancer, including GEJ adenocarcinoma.

In May 2020, trastuzumab deruxtecan also received a BTD for the treatment of patients with metastatic non-small cell lung cancer whose tumours have a HER2 mutation and with disease progression on or after platinum-based therapy.

Daiichi Sankyo collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialise trastuzumab deruxtecan (a HER2-directed ADC) in March 2019, and datopotamab deruxtecan (DS-1062; a TROP2-directed ADC) in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for manufacturing and supply of trastuzumab deruxtecan and datopotamab deruxtecan.

AstraZeneca in breast cancer

Driven by a growing understanding of breast cancer biology, AstraZeneca is

starting to challenge, and redefine, the current clinical paradigm for how breast cancer is classified and treated to deliver even more effective treatments to patients in need – with the bold ambition to one day eliminate breast cancer as a cause of death.

AstraZeneca has a comprehensive portfolio of approved and promising compounds in development that leverage different mechanisms of action to address the biologically diverse breast cancer tumour environment. AstraZeneca aims to continue to transform outcomes for HR-positive breast cancer with foundational medicines *Faslodex* (fulvestrant) and *Zoladex* (goserelin) and the next-generation SERD and potential new medicine AZD9833. PARP inhibitor, *Lynparza* (olaparib) is a targeted treatment option for metastatic breast cancer patients with an inherited BRCA mutation. AstraZeneca with MSD (Merck & Co., Inc. in the US and Canada) continue to research *Lynparza* in metastatic breast cancer patients with an inherited BRCA mutation and are exploring new opportunities to treat these patients earlier in their disease state. Building on the first approval of *Enhertu,* a HER2-directed antibody-drug conjugate*,* in previously treated HER2-positive metastatic breast cancer, AstraZeneca and Daiichi Sankyo are exploring its potential in earlier lines of treatment and in new breast cancer settings. To bring much needed treatment options to patients with triple-negative breast cancer, an aggressive form of breast cancer, AstraZeneca is testing immunotherapy durvalumabin combination with other oncology medicines, including *Lynparza* and *Enhertu*, investigating the potential of AKT kinase inhibitor, capivasertib, in combination with chemotherapy, and collaborating with Daiichi Sankyo to explore the potential of TROP2-directed ADC, datopotamab deruxtecan (DS-1062).

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 six scientific platforms – Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response, Antibody Drug

Conjugates, Epigenetics, and Cell Therapies – 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/Nasdaq: 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

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

References

1.GLOBALCAN 2018 Breast Cancer Fact Sheet. World Health Organization. Accessed: December 2020.

2.DeKoven M, et al. Treatment pattern by hormone receptors and HER2 status in patients with metastatic breast cancer in the UK, Germany, France, Spain and Italy (EU-5): results from a physician survey. *J Comp Eff Res*. 2012 Sep;1(5):453–63.

3.Tamura, K, et al. Trastuzumab deruxtecan (DS-8201a) in patients with advanced HER2-positive breast cancer previously treated with trastuzumab emtansine: a dose-expansion, phase 1 study. *Lancet Oncol*. 2019;20(6):816-826.

4.Modi, S et al. Trastuzumab deruxtecan in previously treated HER2-positive

breast cancer. *N Engl J Med*. 2020; 382:610-621; DOI: 10.1056/NEJMoa1914510.

5.Iqbal N, et al. Human Epidermal Growth Factor Receptor 2 (HER2) in cancers: Overexpression and therapeutic implications. *Mol Biol Int*. 2014;852748.

6.de Melo Gagliato D, et al. Mechanisms of resistance and sensitivity to anti-HER2 therapies in HER2+ breast cancer. *Oncotarget*. 2016;7(39):64431-46.

7.National Comprehensive Cancer Network (NCCN). NCCN Guidelines Version 3.2020. Breast Cancer. December 2020.

Om AstraZeneca

AstraZeneca är ett globalt, innovationsdrivet bioläkemedelsföretag med fokus på forskning, utveckling och marknadsföring av receptbelagda läkemedel, primärt för behandling av sjukdomar inom tre huvudsakliga terapiområden: cancer, kardiovaskulära sjukdomar, njursjukdomar och metabola sjukdomar och sjukdomar i andningsvägarna. AstraZeneca bedriver verksamhet i över 100 länder och dess innovativa läkemedel används av miljontals patienter över hela världen.

Mer information finns på: www.astrazeneca.com och www.astrazeneca.se. Du kan även följa oss på twitter https://twitter.com/AstraZenecaSE

Kontaktpersoner

Christina Malmberg Hägerstrand
Presskontakt
Presschef, AstraZeneca AB och Norden-Baltikum
christina.malmberghagerstrand@astrazeneca.com
+46 8 552 531 06
+46 72 855 93 29

Jacob Lund
Presskontakt
Kommunikationsdirektör AstraZeneca Norden, Baltikum och ordförande Leif Johanssons kontor
jacob.lund@astrazeneca.com
08 553 260 20 Mobil: 072 560 21 57