Phase 3 study of trastuzumab deruxtecan (T-DXd) with or without pertuzumab vs a taxane, trastuzumab and pertuzumab in first-line, human epidermal growth factor receptor 2–positive metastatic breast cancer: DESTINY-Breast09

Sara M. Tolaney,1 Romualdo Barroso-Sousa,2 Zefei Jiang,3 Yeon Hee Park,4 Mothaffar Rimawi,5 Cristina Saura,6 Andreas Schneeweiss,7 Masakazu Toi,8 Tinghui Yu,9 Jagdish Shetty,9 Pia Herbolsheimer,9 Sibylle Loibl10

1 Dana-Farber Cancer Institute, Boston, MA, USA; 2 Oncology Center, Hospital Sírio-Libanês, Brasília, Brazil; 3 The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China; 4 Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 5 Baylor College of Medicine, Houston, TX, USA; 6 Vall d’Hebron University Hospital, Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain; 7 National Center for Tumor Diseases, Heidelberg, Germany; 8 Kyoto University, Kyoto, Japan; 9 AstraZeneca Pharmaceuticals, Gaithersburg, MD, USA; 10 DBF Forschungs GmbH, Neu-Isenburg, Germany; Centre for Haematology and Oncology Bethanien, Frankfurt, Germany

Background

The current standard-of-care (SOC) treatment for patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer (mBC) is a first-line (1L) regimen of a taxane, trastuzumab, and pertuzumab (THP)1

Many patients ultimately develop treatment resistance
More treatment options are needed in the 1L setting to address treatment resistance and improve clinical outcomes in patients with HER2-positive mBC

Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate (ADC) composed of an anti-HER2 antibody, a tetrapeptide-based cleavable linker, and a topoisomerase I inhibitor payload2,3

Structure of T-DXd

T-DXd has shown efficacy in heavily pretreated patients with HER2-positive mBC

In the primary analysis of the DESTINY-Breast01 phase 2 trial, T-DXd demonstrated antitumor activity in patients with HER2-positive mBC, with a response to treatment seen in 112 of 184 patients (60.9%)1

Data from the DESTINY-Breast01 trial supported global approval of T-DXd for the treatment of unresectable or metastatic HER2-positive breast cancer that has progressed on ≥2 prior therapies1

Combining T-DXd with pertuzumab may further enhance the efficacy seen with T-DXd monotherapy and may be a more efficacious option for 1L treatment of HER2-positive mBC

Previously, a study combining pertuzumab with the ADC trastuzumab emtansine showed that pertuzumab facilitated internalization of the ADC2

Here we describe DESTINY-Breast09, an open-label, phase 3 trial evaluating the efficacy and safety of T-DXd alone or in combination with pertuzumab compared with the SOC for 1L treatment of patients with HER2-positive mBC1

For more information, please visit ClinicalTrials.gov (NCT04784715)

DESTINY-Breast09: A Phase 3, Open-Label Trial of T-DXd Alone or in Combination With Pertuzumab for First-Line Treatment of Human Epidermal Growth Factor Receptor 2–Positive Metastatic Breast Cancer

Study Design and Population

Patient population (N=1134)

− Advanced and/or HER2-positive breast cancer
− HER2-positive (IHC 3+ or ISH+) by central confirmation
− No previous chemotherapy or HER2-targeted therapy for advanced or metastatic breast cancer
− Patients will be stratified by prior treatment status (de novo vs recurrent), HR status (positive vs negative), and PIK3CA mutation status (detected vs not detected)

Combination Arm

Arm A: T-DXd + placebo
Arm B: T-DXd + pertuzumab
Arm C: THP

Countries with participating study sites

Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Denmark, Germany, Hungary, India, Israel, Italy, Japan, Mexico, Peru, Philippines, Romania, Russia, Saudi Arabia, South Africa, South Korea, Spain, Sweden, Taiwan, Turkey, United Kingdom, United States

Enrollment Start: 2020 April 1 | Currently Recruiting Patients

Key Inclusion Criteria

− Age ≥ 21 years
− Pathologically documented advanced or metastatic breast cancer that is locally amenable to treatment (i.e., respectively centrally confirmed as HER2-positive (IHC 3+ or ISH+) in the metastatic setting. HR status must be documented by local testing
− No prior chemotherapy or HER2-targeted therapy for advanced or metastatic breast cancer except for 1 previous line of endocrine therapy in the metastatic setting. Patients who have received chemotherapy or HER2-targeted therapy in the neoadjuvant or adjuvant setting are eligible if time from treatment to metastatic diagnosis is ≥6 months
− Adequate tumor tissue sample from the metastatic setting available for assessment of HER2 and PIK3CA status by central laboratory
− Protocol-defined adequate organ and bone marrow function
− LVEF ≥50% within 28 days before randomization

Key Exclusion Criteria

− Inability for any of the agents used in the study
− Spleen involvement or clinically active CNS metastases. Patients with clinically inactive BMMs or treated BMMs that are no longer symptomatic may be included in the study
− Active or prior documented IDL pneumonitis or suspected IDL pneumonitis that cannot be ruled out by imaging at screening
− Any substance abuse or other medical conditions that, in the investigator’s opinion, may interfere with the patient’s participation or study results
− Prior randomization or treatment in a previous 1L T-DXd study regardless of treatment arm assignment

Key Study Endpoints

1. PFS by BICRA

2. PFS by investigatora

3. HRQOL using the EORTC QLQ-BR45

4. Pharmacokinetics, including serum concentrations of T-DXd and pertuzumab

5. Immunogenicity assessed by presence of ADA for T-DXd and pertuzumab

6. Safety and tolerability
− ORR by BICRA and investigatora
− DOR by BICRA and investigatora
− DFS2 by investigator

7. HRQOL using the EORTC QLQ-C30

8. Time to deterioration in EORTC QLQ-C30 scores

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References


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http://www.clinicaltrials.gov/ct2/show/NCT04784715

For more details on DESTINY-Breast09, please visit https://clinicaltrials.gov/ct2/show/NCT04784715

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