

TROPION-Breast06: Multicenter, multinational, open-label, single-arm, phase 3b study of datopotamab deruxtecan (Dato-DXd) in patients with locally advanced inoperable or metastatic HR+/HER2 IHC 0 breast cancer refractory to endocrine therapy

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Plain language summary



Why are we performing this research?

- Patients with hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer may have tumors with no HER2 expression (also known as immunohistochemistry [IHC] 0), or tumors with a small amount of HER2 expression (HER2-low). For those with HER2 IHC 0, who no longer respond to hormone therapy, treatment options are limited.^{1,2}
- Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate, which is a chemotherapy (DXd) joined to an antibody (datopotamab), connected via a cleavable linker.³ Based on results from the TROPION-Breast01 study, Dato-DXd is approved for the treatment of patients with HR-positive/HER2-negative breast cancer (including patients with tumors that have no HER2 expression and those with a small amount of HER2 expression) that had spread (i.e. were metastatic), who had already received chemotherapy and hormone therapy.^{4,5}
- In the TROPION-Breast01 study, Dato-DXd was effective, slowed down cancer progression and had manageable side effects.⁶
- Building upon these results, this study, known as TROPION-Breast06, will assess Dato-DXd in patients with HR-positive/HER2 IHC 0 breast cancer, that cannot be treated with surgery or is metastatic, who have not received prior chemotherapy, and whose tumor no longer responds to hormone therapy.



How are we performing this research?

Approximately 100 patients will receive Dato-DXd through an intravenous injection every three weeks. Patients will be monitored for how well the treatment controls the cancer, how long it works, and what side effects occur.



Who will participate in this study?

Eligible patients enrolled into this study:

- Have HR-positive/HER2 IHC 0 breast cancer that cannot be treated with surgery or is metastatic.
- Have tried hormone therapy but it no longer works.
- Have not received chemotherapy or antibody-drug conjugates for metastatic breast cancer.



Where can I access more information?

For more information about TROPION-Breast06, please visit <https://clinicaltrials.gov/study/NCT07205822>. You may also speak to your doctor about clinical studies.

1. Tolaney SM, et al. ESMO Open 2024;9:103691. 2. Chaitinikun S, et al. Breast Cancer Res Treat 2020;183:729–39. 3. Okajima D, et al. Mol Cancer Ther 2021;20:2329–40. 4. US FDA. DATROWAY® Prescribing Information 2025. 5. EMA. DATROWAY® Summary of Product Characteristics 2025. 6. Bardia A, et al. J Clin Oncol 2024;43:285–96.



TROPION-Breast06 (NCT07205822): An open-label, single-arm, phase 3b study

- HR+/HER2 IHC 0* locally advanced inoperable or metastatic breast cancer
- Progressed on and not suitable for further ET
- No prior treatment with any TROP2-targeted therapy or any agent targeting Topo-I (including ADCs)
- No prior CT for metastatic breast cancer

N≈100

Dato-DXd 6 mg/kg IV Q3W*

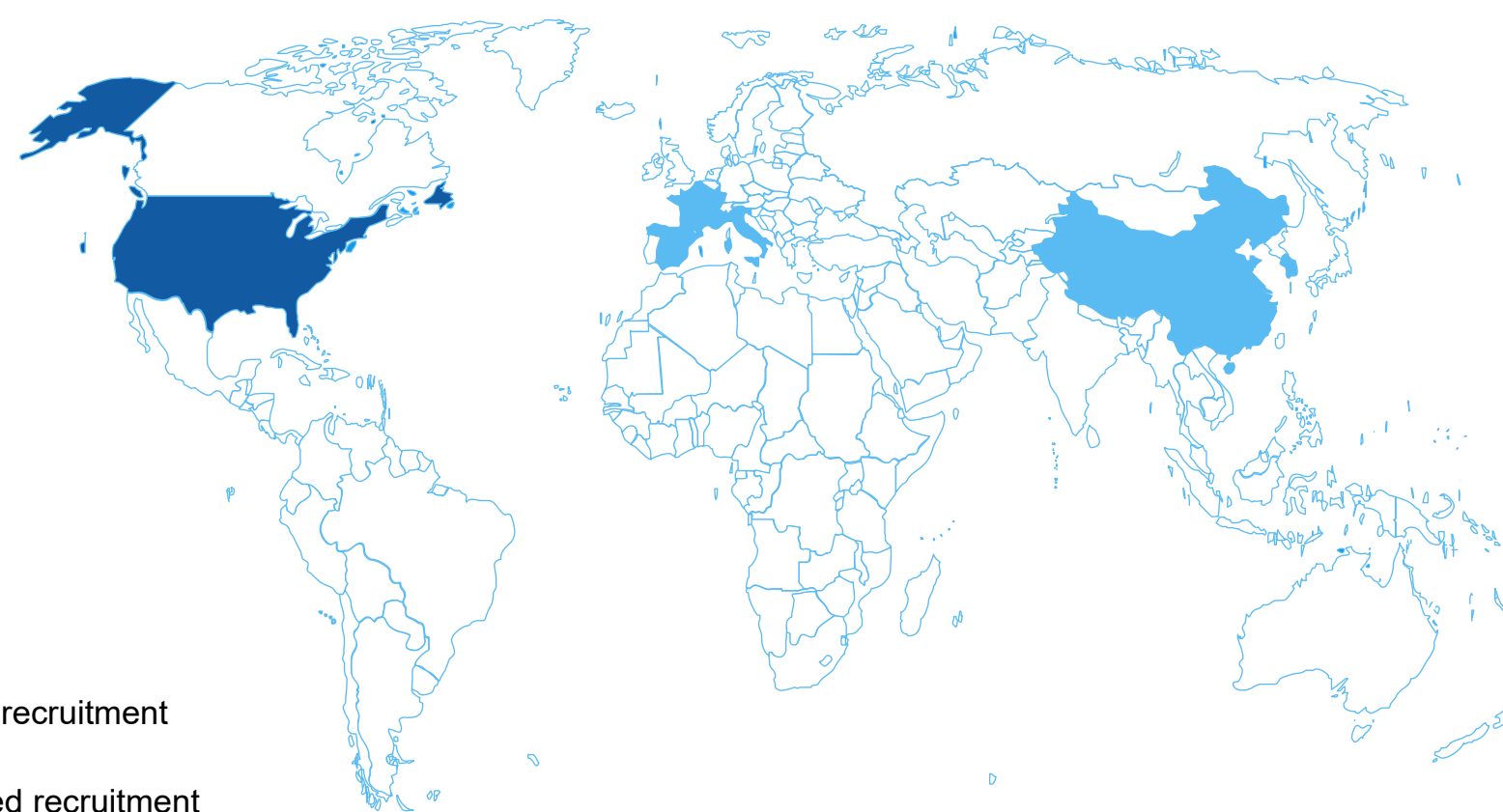
Primary Endpoint

Investigator-assessed PFS per RECIST v1.1

- A daily oral care plan for oral mucositis/stomatitis prophylaxis will be given to all patients
- Patients will complete daily diaries to collect information about oral care and adherence to prophylaxis and symptom severity
- Prophylaxis for ocular surface events will be strongly advised

*As per ASCO/CAP guidelines on local laboratory results. HR+ defined as: either ER and/or PgR positive (ER or PgR ≥1%); HER2 IHC 0 defined as: no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells.^{8,9}
†Participants will receive study intervention until RECIST v1.1-defined radiological progression by investigator, unacceptable toxicity or the patient withdraws from the study.

Enrollment start: October 2025 | Enrollment is ongoing



- Active recruitment
- Planned recruitment

Countries with participating study sites (~40 sites)

China, France, Italy, Republic of Korea, Spain, USA



Key inclusion criteria

- Age ≥18 years with inoperable or metastatic HR+/HER2 IHC 0 breast cancer per ASCO/CAP guidelines by local testing^{8,9}
 - HR+ defined as: either ER and/or PgR positive (ER or PgR ≥1%)
 - HER2 IHC 0 defined as: no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells
- Progressed on and not suitable for further ET per investigator assessment
- ECOG PS 0 or 1
- Measurable disease per RECIST v1.1; baseline biopsy mandatory (archival samples are permitted if obtained no earlier than 6 weeks prior to screening; bone biopsies are not permitted)
- Adequate bone marrow reserve and organ function within 7 days prior to first dose of study treatment



Key exclusion criteria

- Evidence of severe or uncontrolled systemic diseases
 - Including active bleeding diseases and significant cardiac or psychological conditions
- History of allogenic organ transplant
- History of substance abuse
- Persistent toxicities caused by previous anticancer therapy, excluding alopecia, not yet improved to grade ≤1 or baseline
- Spinal cord compression or brain metastases unless treated, no longer symptomatic and radiologically stable
- Leptomeningeal carcinomatosis or metastasis
- Clinically significant corneal disease
- Active infection with hepatitis B or C, HIV or tuberculosis
- Suspected, current or history of non-infectious ILD/pneumonitis that required steroids or other severe pulmonary function compromise
- Prior exposure to TROP2-targeted therapy, any treatment (including ADC) with a Topo-I-targeted therapy or any chemotherapy in the metastatic setting
- Contraindication to the use of steroid-containing mouthwash



Key study endpoints

- 1° **Primary endpoint**
 - Investigator-assessed PFS per RECIST v1.1
- 2° **Secondary endpoints**
 - Proportion of patients with oral mucositis/stomatitis, ocular surface events and treatment-related grade ≥3 adverse events
 - CBR
 - Proportion of patients with a confirmed CR or PR or who have SD per RECIST 1.1 (investigator-assessed) for at least 24 weeks following first dose of study treatment
 - ORR
 - DoR
 - OS
 - Safety and tolerability



Background

- Patients with endocrine-refractory HR+/HER2- (IHC 0, IHC 1+, or IHC 2+/ISH-) metastatic breast cancer have limited treatment options; while CT is a mainstay of treatment, limited efficacy contributes to poor patient outcomes and highlights the need for more durable and effective therapeutic options.^{1,2}
- Dato-DXd is a TROP2-directed ADC composed of a humanized anti-TROP2 IgG1 monoclonal antibody conjugated to a highly potent topoisomerase I inhibitor payload via a tetrapeptide-based, tumor-selective cleavable linker.³
- Dato-DXd is approved in multiple countries for the treatment of adults with unresectable or metastatic HR+/HER2- (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received prior ET and CT for unresectable or metastatic disease, based on the results of the phase 3 TROPION-Breast01 study.⁴⁻⁶
 - In this study, treatment with Dato-DXd reduced the risk of disease progression or death by 37% compared with CT (hazard ratio, 0.63 [95% CI, 0.52–0.76]; p<0.0001). Median PFS by BICR was 6.9 months with Dato-DXd versus 4.9 months with CT and Dato-DXd demonstrated a manageable safety profile.⁴
- In the phase 3 DESTINY-Breast06 study, the HER2-directed ADC, trastuzumab deruxtecan, significantly improved outcomes compared with CT in patients with HR+/HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) unresectable or metastatic breast cancer.⁷
- TROPION-Breast06 aims to build upon the results of TROPION-Breast01, by assessing the efficacy and safety of Dato-DXd in the endocrine-refractory setting prior to CT for patients with HR+/HER2 IHC 0 (defined as no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells) inoperable or metastatic breast cancer.

Abbreviations

ADC, antibody-drug conjugate; ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CAP, College of American Pathologists; CBR, clinical benefit rate; CI, confidence interval; CT, chemotherapy; CR, complete response; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; ET, endocrine therapy; HER2-, human epidermal growth factor receptor 2-negative; HIV, human immunodeficiency virus; HR+, hormone receptor-positive; IgG1, immunoglobulin G1; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; ORR, objective response rate; OS, overall survival; OSE, ocular surface events; PFS, progression-free survival; PR, partial response; PgR, progesterone receptor; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; Topo-I, topoisomerase I; TROP2, trophoblast cell surface protein-2.

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Disclosures

Komal Jhaveri reports consultant/advisory board role for Arivins, AstraZeneca, Bicycle Therapeutics, Blueprint Medicines, Daiichi Sankyo, Eisai, Genentech, Gilead, Halda Therapeutics, Lilly/Loxo Oncology, Menarini/Stemline, Merck Pharmaceuticals, Novartis, Olema Pharmaceuticals, Pfizer, Rayzebio, Scorpion Therapeutics and Zymeworks, and research funding support (Institution) from AstraZeneca, Bicycle Therapeutics, Blueprint Medicines, BridgeBio Oncology Therapeutics, Eisai, Genentech, Gilead, Lilly/Loxo Oncology, Merck Pharmaceuticals, Novartis, Pfizer, PUMA Biotechnology, Rayzebio, Scorpion Therapeutics and Zymeworks.

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