



TUXEDO-4

Trastuzumab-deruxtecan in HER2-low metastatic breast cancer patients with newly diagnosed or progressing brain metastases: The TUXEDO-4 phase II trial

IMPORTANT:

- The document contains the summary of a clinical trial, and its sole purpose is to communicate the results of it to the general public.
- This document is not intended to promote recruitment or provide medical advice.
- The results reflected in this document may contradict those of other trials.
- It is not recommended to make decisions based on the information collected in this document; it should always be consulted with a medical professional beforehand.

ABOUT THIS SUMMARY

SPONSOR: MEDICA SCIENTIA INNOVATION RESEARCH S.L.

CANCER TYPE: HER2-low metastatic breast cancer with brain metastases, with/without type II

PHASE: leptomeningeal disease
PHASE II

MEDICINE(S) STUDIED: Trastuzumab-deruxtecan

DATES OF STUDY: Ongoing, accrual started on June 5, 2024

TITLE OF THIS STUDY: Trastuzumab-deruxtecan in HER2-low metastatic breast cancer patients with newly diagnosed or progressing brain metastases: The TUXEDO-4 phase II trial

PATIENTS NUMBER: 27

PHARMACEUTICAL PARTNER: Daiichi Sankyo

DATE OF THIS REPORT: October 26th, 2024

CLINICAL TRIALS.GOV: [NCT06048718](https://clinicaltrials.gov/ct2/show/study/NCT06048718)

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What was the purpose of this study?

Breast cancer is a disease in which normal breast cells grow and divide uncontrollably. There are different types of breast cancer based on the presence of molecules called 'human epidermal growth factor receptor 2' (HER2) proteins on the breast cancer cell surface. HER2-negative breast cancer is the most common type of breast cancer and does not have HER2 proteins. HER2-positive is an aggressive breast cancer and is characterized by high levels of HER2. And HER2-low breast cancer has lower quantity of HER2. This is important to help doctors determine the best treatment option for each patient.

Additionally, breast cancer cells can produce metastases, which means that they can leave the original tumor site and invade other areas of the body to develop new tumors. Among all cancers that form lumps in the body, metastatic breast cancer is the second most common cause of brain metastases (BMs), and the leading cause of leptomeningeal disease (LMD), which are metastases in the leptomeninges, thin tissue layers that cover the brain and the spinal cord.

Patients with BMs and/or LMD have very limited treatment options because the blood-brain barrier, a locked layer of cells that protects our brain from dangerous substances and avoid damage, is impenetrable for most drugs. The group of treatments called 'antibody-drug conjugates' (ADCs) cannot cross this barrier either but has shown promising results in this type of patients. ADCs are targeted therapies made up of laboratory-made proteins called 'antibodies' that bind cancer cells and potent drugs to destroy them.

Trastuzumab deruxtecan (T-DXd) is a novel ADC that attaches to HER2 proteins from cancer cells through the antibody trastuzumab and uses a medicine called deruxtecan, which kill cancer cells by blocking the DNA duplication. T-DXd has demonstrated to work in HER2-positive metastatic breast cancer patients, either with or without BMs and/or LMD, as well as in HER2-low metastatic breast cancer patients.

TUXEDO-4 is a medical study that will evaluate the effectiveness of T-DXd in HER2-low breast cancer patients with recently diagnosed or getting-worse BMs, and with or without a category of LMD called 'type II LMD', which is characterized a typical LMD diagnosis, but excluding the presence of tumor cells in the watery liquid that protects and surrounds their brain and spinal cord (called 'cerebrospinal fluid').

What do researchers want to find out?

The researchers mainly want to evaluate the percentage of patients whose brain tumors shrink or disappear after receiving T-DXd.

Other key measures will include how well T-DXd works on tumors outside the brain, and the percentage of patients who will have complete disappearance of tumors, those who will have partial shrinkage of tumors, and those who will have tumors that will not grow.

Who took part of this study?

- (a) Male or female patients ≥ 18 years.
- (b) Radiologically documented metastatic disease.
- (c) Locally documented HER2-low status: -HER2 IHC score by local standard + or ++/ISH-.
- (d) Asymptomatic untreated or progressing BMs after local treatment.
- (e) Measurable disease by RANO-BM criteria.
- (f) Presenting with ≥ 1 brain lesion measurable (≥ 10 mm per local radiological assessment).
- (g) With or without untreated type II LMD per EANO-ESMO criteria.
- (h) Able to provide a fresh tumor biopsy sample a baseline or an FFPE since last progression.
- (i) ≥ 1 line of systemic treatment in the advanced setting.
- (j) No prior treatment with T-DXd.
- (k) Have not received any investigational agent within 28 days prior to initiation of treatment.
- (l) ECOG PS ≤ 2 , LVEF $\geq 50\%$.
- (m) Life expectancy ≥ 12 weeks.

When and where did the studies take place?

The enrollment began in June 2024 and the estimated trial completion is July 2026. During the study, nine Austrian and Spanish sites will recruit a total of 27 patients in two phases. Thirteen patients will be treated in the first one. If 3 or more patients out of 13 respond to T-DXd, 14 more patients will be recruited in the second phase.

Austria and Spain

Where I can find more information?

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

For more details, please visit:

<https://www.medsir.org/tuxedo-4-clinical-trial>

The full scientific report of this study is available online at:

<https://clinicaltrials.gov/study/NCT06048718>

Thank you who took part in the study

If you took part in this study, **Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co**, as the Sponsor, extends its gratitude for your participation. This overview will outline the findings of the study. If you have any queries regarding the study or its outcomes, please reach out to the doctor or staff at your study location.

Thank you who took part in the study

ABOUT Oncoclínicas & Co

Oncoclínicas&Co is the largest group dedicated to cancer treatment in Latin America, with a specialized and innovative model focused on the entire oncology care journey, combining operational efficiency, humanized care, and high specialization through a medical team composed of over 2,700 specialist physicians with an emphasis on oncology. With its mission to democratize cancer treatment, it offers a comprehensive system that integrates outpatient clinics with high-complexity cancer centers. The company operates 145 units across 39 Brazilian cities, allowing high-quality access in all regions it serves, aligned with world-class standards.

Focusing on technology, precision medicine, and genomics, Oncoclínicas performed approximately 635,000 treatments in 2023. It is the exclusive partner in Brazil of the Dana Farber Cancer Institute, affiliated with Harvard Medical School, one of the world's leading cancer research and treatments centers. The company also owns Boston Lighthouse Innovation, a bioinformatics firm based in Cambridge, United States, and holds shares in Medsir, a company dedicated to the development and management of clinical trials for independent cancer research, based in Barcelona, Spain. Recently, Oncoclínicas

expanded its operations to Saudi Arabia through a joint venture with the Al Faisaliah Group, bringing its mission to beat cancer to a new continent and providing advanced oncology care on a global scale by combining oncological hyperspecialization with innovative treatment approaches.

The company is part of the IDIVERSA index, launched by B3, highlighting companies committed to gender and racial diversity. For more information, visit: visit www.grupooncoclinicas.com

ABOUT MEDSIR

Founded in 2012, MEDSIR works closely with its partners to drive innovation in oncology research. Based in Spain and the United States, the company manages all aspects of clinical trials, from study design to publication, utilizing a global network of experts and integrated technology to streamline the process. The company offers proof-of-concept support and a strategic approach that helps research partners experience the best of both worlds from industry-based clinical research and investigator-driven trials. To promote independent cancer research worldwide, MEDSIR has a strategic alliance with Oncoclínicas, the leading oncology group in Brazil with the greatest research potential in South America. Learn how MEDSIR brings ideas to life: www.medsir.org