



DEMETHER

DEMETHER: A single-arm phase II trial to evaluate the efficacy and safety of subcutaneous pertuzumab and trastuzumab maintenance after induction treatment with trastuzumab deruxtecan (T-DXd) for previously untreated HER2-positive advanced breast cancer.

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-positive Advanced Breast Cancer

PHASE: PHASE II

MEDICINE(S) STUDIED: pertuzumab and trastuzumab + T-DXd

DATES OF STUDY: Ongoing (accrual started on June, 2024)

TITLE OF THIS STUDY: DEMETHER: A single-arm phase II trial to evaluate the efficacy and safety of subcutaneous pertuzumab and trastuzumab maintenance after induction treatment with trastuzumab deruxtecan (T-DXd) for previously untreated HER2-positive advanced breast cancer

PATIENTS NUMBER: 165

SCIENTIFIC PARTNER: Hoffmann-La Roche

PHARMACEUTICAL PARTNER: Roche Pharma S.A.

DATE OF THIS REPORT: October 26th, 2024

CLINICAL TRIALS.GOV: [NCT06172127](https://clinicaltrials.gov/ct2/show/study/NCT06172127)

The content for this document was finalised by **Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co** on the 25th of October of 2024. The information in this summary does not include additional information available after this date.

What was the purpose of this study?

Breast cancer (BC) occurs when normal cells in the breast undergo changes that cause them to become abnormal and multiply uncontrollably, leading to the formation of a tumor. There are many types of breast cancer, and they can differ from each other based on specific proteins or receptors found on the surface of the cancer cells. One important protein is called HER2.

About 15 to 20% of breast cancers are HER2-positive, meaning they have high levels of this protein. These cancers tend to grow faster and can be more aggressive, while those without HER2 may behave differently. When breast cancer spreads to other parts of the body (this is called metastatic cancer), it cannot be cured. However, there are many treatments available that can help control the disease and reduce symptoms, allowing patients to live longer and feel better.

Currently, the first treatment option for patients with metastatic HER2-positive breast cancer is a combination of chemotherapy, and two targeted medicines called monoclonal antibodies (which are pertuzumab and trastuzumab), followed by maintenance pertuzumab and trastuzumab until the cancer gets worse. These two drugs target the HER2 protein on cancer cells, blocking signals that promote cancer cell growth and survival. If this treatment doesn't work, the next option is a medicine called trastuzumab deruxtecan (T-DXd).

T-DXd is a conjugated drug: on one side, trastuzumab is an antibody that specifically targets HER2 proteins on cancer cells, and on the other side, deruxtecan is a chemotherapy drug attached to the antibody. This combination allows T-DXd to deliver chemotherapy directly to the cancer cells, minimizing the damage to normal cells and, in turn, reducing side effects while shrinking tumors and potentially prolonging survival.

The results of T-DXd for patients with metastatic breast cancer have been impressive, leading to questions about whether it should be the first treatment option. Another important question is how a treatment can be effective while also being less harmful to the patient. The main goal of the DEMETHER study is to find out how well a combination treatment works for previously untreated HER2-positive metastatic breast cancer patients. This treatment includes T-DXd followed by pertuzumab and trastuzumab (known as PHESGO), which will be given as ongoing care after initial treatment.

After 6-cycles of these induction therapy with T-DXd, patients will be treated with a PHESGO maintenance therapy. The study will assess how many patients live without their cancer getting worse for a year and how many are still alive after three years. This treatment combination is designed to be less intensive, aiming to reduce side effects and improve the quality of life for patients.

What do researchers want to find out?

DEMETHER study is assessing the effectiveness of a short induction phase with T-DXd followed by a maintenance phase with subcutaneous trastuzumab and pertuzumab in previously untreated HER2-positive advanced breast cancer patients. The main goal is to analyze if this novel approach helps people live longer without their disease getting worse after one year, improves overall survival after three years, and provides better safety and quality of life for patients. If positive, this trial could provide a de-escalation strategy from standard chemotherapy, long-term T-DXd administration, and their related side effects.

Who took part of this study?

- (a) Pts aged ≥ 18 years with centrally-confirmed HER2-positive ABC;
- (b) No prior chemotherapy and/or HER2-targeted therapy for advanced disease. Participants who have received chemotherapy and/or HER2-targeted therapy in the neo(adjuvant) setting are eligible if ≥ 12 months from completion of systemic treatment to metastatic diagnosis;
- (c) ECOG performance status of 0-1;
- (d) Evaluable disease according to RECIST v.1.1.

When and where did the studies take place?

The study began in July 2024 and is expected to be completed by May 2029. It is a multicenter study, and as of October 2024, 12 centers have already been activated in Spain, with additional sites in Spain and other countries currently in the process of being activated

Countries

Spain, Italy, Germany, UK, France, US, Brazil

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/demether-clinical-trial>

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

<https://clinicaltrials.gov/study/NCT06172127>

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