Lay Language Summary

# METSGain

Gene expression changes associated to distant recurrence in HER2+ early breast cancer in the context of a chemotherapy de-escalation strategy within the PHERGain clinical 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.

**MEDICINE(S) STUDIED:** HER2 + Early Breast Cancer

**DATES OF STUDY:** 2023 - Currently

**TITLE OF THIS STUDY:** Gene expression changes associated to distant recurrence in HER2+ early breast cancer in the context of a chemotherapy de-escalation strategy within the PHERGain clinical trial.

**DATE OF THIS REPORT:** March 2024

**SCIENTIFIC PARTNER:** REVEAL GENOMICS S.L.

The content for this document was finalised by **MEDSIR** on the 11th of March of 2024. The information in this summary does not include additional information available after this date.

# Context

Approximately one in five breast cancers are identified as HER2-positive (HER2+). HER2, short for "Human Epidermal growth factor Receptor 2", is a type of protein found on the surface of both normal and cancer cells. This protein is essential in regulating cell growth, but when its levels are excessively high, such as in cancer, cells grow and multiply in an aberrant manner. For this reason, HER2+ breast cancer is known for its aggressive nature.

Early breast cancer (EBC), defined as a cancer that has not spread beyond the breast, accounts for a significant portion of diagnosed cases. Approved treatment for HER2+ EBC includes chemotherapy combined with therapies that specifically target HER2, like trastuzumab and pertuzumab. While chemotherapy kills cancer cells by stopping them from dividing, trastuzumab and pertuzumab work by binding HER2 and blocking the signals stimulating cancer cell growth. The development of HER2-targeted therapies has greatly improved the outlook for patients with this type of breast cancer.

Invasive disease-free survival (iDFS), which measures the time a patient remains free from invasive cancer after initial treatment, is a key indicator of treatment success. It also informs about the probability of the cancer coming back (recurrence) and spreading beyond the breast (distant recurrence or metastasis). Developing tools that can predict this probability is really important to make the best decisions about treatment.

The main objective of the METSGain study was to evaluate how well a genetic tool named HER2DX can predict the development of distant recurrences in HER2+ EBC patients treated with HER2-targeted therapy.

## What is *HER2DX?*

HER2DX is a genetic tool validated for its use in patients with HER2+ EBC. This test analyzes the expression of 27 genes associated with cancer, along with clinical details about the tumor, like its size and lymph node involvement (an indicator of cancer cells spread). Using this personalized information, a special algorithm calculates two independent scores: one predicts the likelihood (high, medium, or low) for the patient to respond well to the treatment before surgery (HER2DX pCR-score), and the other estimates the risk (high or low) that the cancer will reappear (HER2DX risk-score).

This test was developed by Reveal Genomics, a biotechnology company dedicated to creating advanced diagnostic tools.

## *What is the PHERGain study, and what makes it relevant?*

The PHERGain clinical trial was designed to evaluate the feasibility of treating HER2+ EBC patients only with anti-HER2 treatments, eliminating chemotherapy from their treatment.

Briefly, there were two groups of participants: group A (receiving usual treatment of chemotherapy along with trastuzumab and pertuzumab) and group B (only receiving trastuzumab and pertuzumab). Following 2 cycles of treatment, participants in group B that were not responding to anti-HER2 therapy alone started receiving also chemotherapy. After more cycles of treatment, all participants underwent surgery to remove the remaining breast tumor. Post-surgery, participants in group B that were still on the initial treatment were evaluated for pathological response (presence or absence of cancer cells).

Those participants with no remaining cancer cells continued the chemotherapy-free treatment, while those participants with presence of remanent cancer cells were switched to chemotherapy plus anti-HER2 therapy. Then, participants were regularly monitored for the following 3 years to detect any signs of tumor recurrence.

The PHERGain study demonstrated that it is possible to identify around 1/3 of patients with HER2+ EBC that can safely omit chemotherapy. With an adaptive treatment strategy that allowed for a patient's treatment to be changed based on how they respond, this approach could reduce the toxicity associated with chemotherapy while maintaining high treatment efficacy *(for a lay language summary with more details about the design and the results of the PHERGain trial at ASCO 2023 – click here)*.

## *What is the purpose and main results of the METSGain study?*

But could it be also possible to anticipate the likelihood of distant recurrences? METSGain study hypothesized that changes in HER2DX risk-score and differences in gene expression between treatment initiation (baseline, BL) and after surgery (residual disease, RD) could predict the risk of distant recurrences and provide relevant information about the process of metastasis.

The main objective of the study was to determine the association between the HER2DX risk-score in RD with the probability of having distant recurrences. Secondary objectives included assessing whether alterations in gene expression from BL to RD were associated with the development of metastases.

Initially, tumor samples from 6 participants who experienced distant recurrences and 8 participants who did not from group B of the PHERGain study were collected and analyzed at RD using HER2DX. Then, HER2DX risk-scores at RD were compared with the actual outcomes of 3-year iDFS reported in the PHERGain study. Results from this analysis showed that all participants who developed metastasis during the 3-year follow-up period had a high-risk score at the moment of surgery (RD). On the other hand, among the 8 participants without metastasis, 50% of them had a low-risk score at RD. Therefore, having a low-risk score after surgery was associated with a better 3-year iDFS.

Interestingly, when comparing gene expression from BL to RD, it was observed that those participants that had more changes in their genes were the ones that did not experienced metastases. These results suggest that during the time between treatment initiation and surgery there are gene expression rearrangements that may determine the development of recurrences.

Altogether, METSGain study demonstrated that HER2DX risk-score measurement after treatment and tumor surgery (at RD) can provide additional information about distant metastases happening in the future. The predictive potential of HER2DX in HER2+ EBC will be further studied to understand its impact in managing metastatic disease.

# Where can I find more information about the study?

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.

## Thank you to the people who took part in the study

If you took part in this study, **MEDSIR**, 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.

## 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.

## About REVEAL GENOMICS®

REVEAL GENOMICS, S.L. is a biotechnology start-up seeking to change the way biomarkers are used in oncology. It is focused on developing innovative diagnostic tools to define the best therapeutic options for patients with cancer. The company uses pioneering techniques, sophisticated computer applications, and machine learning to reveal new cancer research data.
REVEAL GENOMICS, S.L. is a spin-off company of Hospital Clínic of Barcelona, IDIBAPS, the University of Barcelona (U.B.), and the Vall d'Hebron Institute of Oncology (VHIO).