LAY/PUBLIC ABSTRACT

Human epidermal growth factor receptor 2 positive (HER2+) tumors are highly aggressive and account for 15-20% of all breast cancers. When the cancer has spread to other parts of the body, it is called metastatic disease or stage IV. For patients with HER2+ metastatic breast cancer (MBC), survival has been historically low, with less than 50% of these patients who lived longer than 2 years. However, the development of highly effective drugs targeting HER2 has radically changed the natural history of HER2+ MBC, revolutionizing both how we take care these patients and their survival. Now, in 2023, more than 50% of patients with HER2+ MBC is alive 5 years after diagnosis.

Despite these achievements, the paradigm of treatment for MBC is still non-curative. Patients are treated indefinitely, and if tests show that the tumor is growing, the treatment plan is switched to a different one. But there is a subset of patients who do very well and remain on first-line therapy without evidence of tumor growth for many years. This is very rare for stage IV MBC, and we are calling these patients “exceptional responders". However, even these patients are treated indefinitely. The treatments are usually well tolerated, but they may cause severe toxicity, are expensive, and require regular IV infusions and visits. Small studies have shown that some patients had long-lasting responses and did well even after stopping treatment, but strong data supporting this approach are lacking. What is important and unknown is how to identify earlier during the initial course of treatment which individuals will have an “exceptional response”.

The term "Minimal Residual Disease" (MRD) means finding microscopic traces of cancer in the blood of patients with no evidence of tumor on scans. For patients with stage I-III tumors, where treatments as chemotherapy and anti-HER2 therapy can lead to a cure, many studies have shown that the detection of MRD in the blood is associated with higher chances of the tumor coming back. But MRD has not been studied in HER2+ MBC before, where it could help us make treatment decisions. If we do not find any trace of tumor in the blood (MRD-negative), it could mean that individuals might safely stop treatment. On the other hand, patients with traces of tumor in blood (MRD-positive) would be more likely to have their tumor to grow again if treatment is interrupted. Also, if we monitor MRD, we might be able to predict if the tumor is coming back even before scans can detect it. This would help us change treatment early. But before we start offering this test to patients, we need to understand if MRD can predict who will have a prolonged response from treatment and who will not, and whether changing treatments based on MRD results can provide an impact on patients’ lives.

In this study, we want to demonstrate that MRD can predict which patients with HER2+ MBC will respond exceptionally to anti-HER2 treatment. We identified a group of 55 patients with exceptional response to first-line anti-HER2 treatment (they have been on it for more than 3 years and have not needed to switch) and 70 patients with “conventional response” (they derived a clinical benefit for less than 3 years).
We are planning to use in this study a very sensitive MRD test called "MAESTRO". This test looks for alterations called mutations in the tumor's DNA that are specific for that person's tumor. We are using pieces of tumor that we collected before to specially design this MRD test. Then, we are using previous blood samples we collected and stored to check if MRD is in each sample or not, and how much there is.

In the first part of this study, we will understand if the MRD test shows a meaningful difference between “exceptional responders” and “conventional responders”. In the second part, we will learn if the MRD test results are associated with specific variables such as patients’ age, tumor stage, prior treatments, or where the cancer has spread. We are also comparing how the MRD changes over time to how the tumor is changing in scans. This could help us understand how to predict which patients will more likely have a prolonged benefit from the treatment for HER2+ MBC.

In 2023, we have a unique opportunity to push back on the way we treat HER2+ MBC. With medicines that target HER2 as well as sensitive and specialized tests, we are now able to optimize the chance of success for patients. Through this study, we are seeking to understand if MRD can be used to identify which patients will achieve an exceptional response to treatment earlier during their initial course of treatment. If MRD can be used with this purpose, then in the future we can explore whether these patients might be considered cured, and if treatment may be safely reduced or stopped. We may also learn that MRD changes can help us in guiding treatment, such as by switching a medication before observing tumor growth at scans, which may translate in improving patients’ quality of life and survival chances.