# Promising advances in the treatment of metastatic breast cancer

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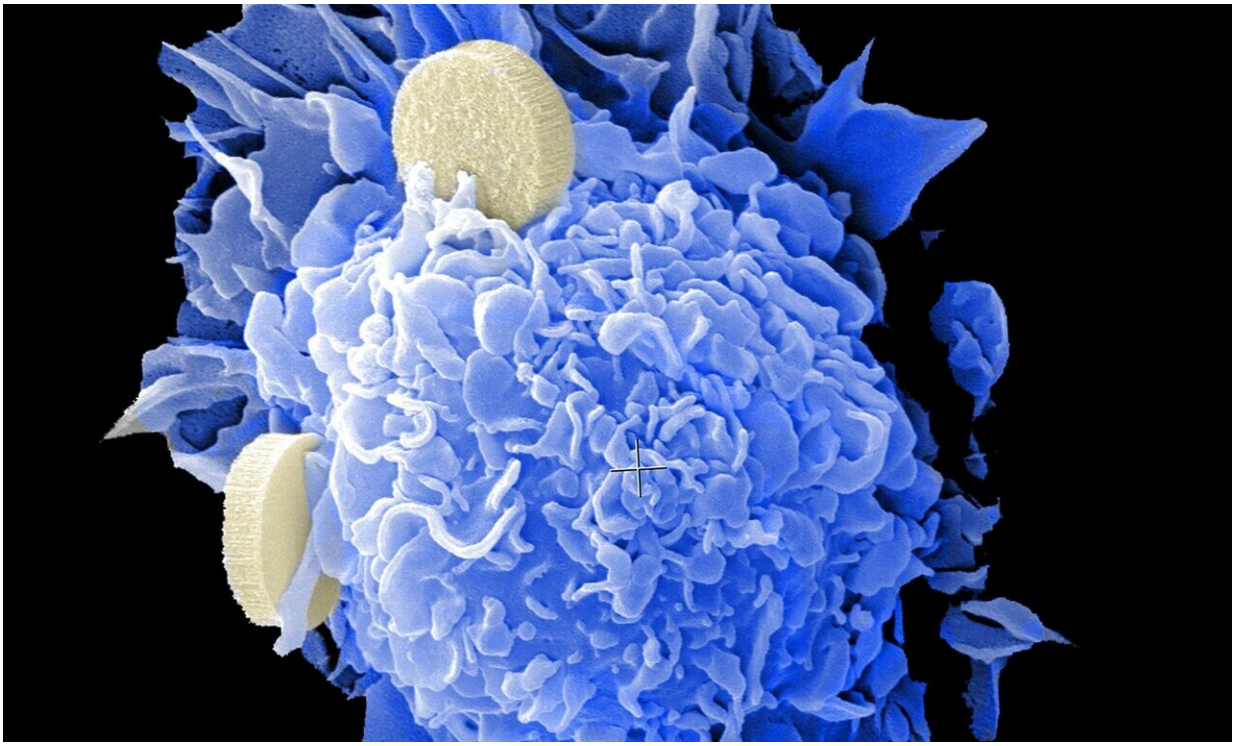

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During the virtual 2021 Annual Congress of the European Society for Medical Oncology (ESMO), 16-21 September, research (co) led by VHIO investigators revealed promising advances in the treatment of metastatic breast cancer. Among these, a trio of Late-Breaking studies selected by ESMO as oral presentations, were presented and discussed

by VHIO faculty.

## Expanding the therapeutic arsenal against metastatic breast cancer

At the meeting's first Presidential Symposium co-chaired by ESMO and ESMO Congress President, Solange Peters (Lausanne, Switzerland), and ESMO's President Elect, Andrés Cervantes (Valencia, Spain), Javier Cortés presented the positive results of the randomized phase III DESTINY-Breast03 study.

This pioneering study was designed to compare the anti-tumor activity as well as the safety and efficacy of antibody-drug conjugate (ADC), trastuzumab deruxtecan, versus trastuzumab emtansine in patients with unresectable or metastatic HER2-positive metastatic breast cancer (MBC), previously treated with trastuzumab and taxane.

"This antibody-drug conjugate has achieved spectacular clinical activity in this particular patient population. We are confident that our results will lead to a paradigm shift in the treatment of patients with HER2-positive metastatic breast cancer," observed Javier Cortés, PI of this multi-center study, Director of the International Breast Cancer Center, Quirón Group (Madrid & Barcelona, Spain), and an Associate Translational Investigator at VHIO.

The DESTINY-Breast 03 trial compared the clinical activity of treatment with trastuzumab deruxtecan in patients with HER2-positive MBC who had received prior lines of therapy versus standard treatment with ADC, trastuzumab emtansine, which was approved based on progression-free survival and interim overall survival findings in the phase III EMILIA trial.

A total of 524 patients participated in the trial, who were randomized into two groups to receive each of the treatments. Results show that progression-free survival (PFS) in patients who received standard therapy with trastuzumab emtansine was 6.8 months. In patients who were administered trastuzumab deruxtecan PFS has still not been reached and more than half of these patients have been two years without disease progression.

"In 16% of these patients we observed that all evidence of cancer had disappeared. This could potentially mean that some of these patients might be cured," said Javier Cortés.

While the results of this phase III trial are limited to HER2-positive MBC patients, treatment with trastuzumab deruxtecan is also being assessed in patients with HER2-negative breast cancer, as well as other tumor types including colorectal and lung cancer. He added, "This antibody-drug conjugate is showing extremely promising activity. Based on evidence reported thus far, trastuzumab deruxtecan promises a paradigm shift in cancer therapy. In breast cancer, no other study has ever achieved such remarkable results".

The DESTINY-Breast03 investigators also reported that only 1% of patients did not respond to this therapy. In around 80% of patients they observed an improvement in tumor shrinkage of at least 50%.

## Promising advances in the treatment of breast cancer

Presented during a Proffered Paper Session, Cristina Saura, Head of the Vall d'Hebron University Hospital's Breast Cancer Unit, Medical Oncology Department, and Principal Investigator of VHIO's Breast Cancer Group, revealed primary outcomes of the phase III TULIP study. This multi-center, open-label randomized clinical trial compared the efficacy and safety of the antibody-drug conjugate (ADC), [Vic-]

trastuzumab duocarmazine, to physician's choice in the treatment of patients with HER2-positive metastatic breast cancer (MBC) who had received at least two previous lines of therapy or ado-trastuzumab emtansine treatment in the metastatic setting.

TULIP enrolled a total of 437 patients with a median age of 56 years and a median of 4 prior MBC therapies. Conducted at 83 sites, including VHIO, the study's primary endpoint was progression-free survival (PFS).

The TULIP investigators reported a statistically significant improvement over physician's choice treatment. "We observed progression-free survival of 7 months in patients treated with trastuzumab duocarmazine versus 4.9 months in patients who received physician's choice. Our findings also showed a trend towards better overall survival for patients treated in the experimental arm," said Cristina Saura. She continued, "Although this progression-free survival rate may seem modest, one of the major challenges in combating cancer is resistance to therapies. Expanding the array of available treatment options to tackle progressive disease in patients is therefore essential."

These results are positive, but adverse events (AE) were reported. The most frequently occurring AEs for trastuzumab duocarmazine were conjunctivitis, keratitis, and fatigue. Pulmonary toxicity, which is well described in other ADCs including trastuzumab deruxtecan, occurred less frequently compared with the other AEs observed in TULIP. Ocular toxicity was also reported.

"While all adverse events will naturally need to be considered in approving this next generation antibody-drug conjugate as a contender in the treatment of patients with HER2-positive metastatic breast cancer, they are manageable. In the instance of ocular toxicity, other studies are being performed to control this particular side effect of this therapy," concluded Cristina Saura.

Mafalda Oliveira, Medical Oncologist and Clinical Investigator of the Vall d'Hebron University Hospital's Breast Cancer Unit, and VHIO's Breast Cancer Group, both directed by Cristina Saura, presented results from the POSEIDON international, multicenter randomized phase II trial; a study that derived from the Cancer Core Europe (CCE) consortium. This study assessed the efficacy and safety of adding a PI3K inhibitor, taselisib, to hormonal therapy, tamoxifen, in patients with hormone receptor positive and HER2-negative metastatic breast cancer after prior endocrine treatment.

In total 152 patients were enrolled in the clinical trial, with a median follow-up of 26.4 months. The POSEIDON investigators observed that the addition of taselisib to tamoxifen led to an increase in median progression-free survival (PFS) from 3.2 months to 4.8 months.

"While results of this treatment combination show promise, poor tolerability was observed. Adverse events were more common with taselisib compared with placebo, 44% versus 5%, respectively. That said, our findings further confirm the potential of combining PI3K inhibitors with hormonal therapy as a strategy to revert treatment resistance in this patient population," said Mafalda Oliveira.

She concluded that "future studies are warranted to seek out biomarkers that can help identify patients most likely to benefit from these therapies."

**More information:** Conference: www.esmo.org/meetings/esmo-congress-2021

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