Liquid biopsy that isolates and captures the number of circulating tumor cells (CTC) in patient blood can be used to predict early treatment response and overall survival in patients with metastatic breast cancer, according to a study presented at the San Antonio Breast Cancer Symposium, held virtually December 8-11, 2020.

The findings were predictive for all tumor subtypes analyzed, including luminal-like, HER2-positive, and triple-negative tumors (Abstract GS4-08).

“These results provide clinical validation of CTC monitoring as an early treatment response marker in advanced breast cancer and suggests the potential for clinical utility,” said Wolfgang Janni, MD, PhD, Professor and Director of the Women’s Clinic at Ulm University Hospital in Ulm, Germany.

Responses to breast cancer treatment are typically monitored by conventional imaging, but this method requires time—about 3 months, depending on the subtype—before changes can be detected.

In a press briefing, Janni said CTC wouldn’t replace conventional imaging but could offer valuable early clinical insights about the status of treatment efficacy for aggressive disease, or some newer therapies such as immune checkpoint inhibitors.

“We can have very similar information by imaging later on, but I think there are clinical situations in which we’d love to have early information and I think we should think of using CTCs in this situation,” he said.

Carlos Arteaga, MD, Director of the Simmons Comprehensive Cancer Center and Associate Dean of Oncology Programs at UT Southwestern Medical Center, added his thoughts: “This is a very large pooled analysis that really instructs use of a non-invasive approach that may provide an advantage over conventional imaging methods that can take up to 3 months before changes can be detected in breast tumor tissue.” Arteaga, Co-Director of the SABCS, did not participate in this study, but was asked to comment about the study.

First discovered for their diagnostic potential in 2004, CTCs—shed into the bloodstream from the primary tumor—have increasingly been used to help guide treatment decisions and track a patient’s progress.

In this study, Janni and a large international team sought to assess the technique as a tool for early treatment monitoring and its ability to predict overall survival in patients in a variety of advanced breast cancer subtypes.

The team analyzed globally pooled datasets from peer-reviewed and published studies of 4,079 patients with metastatic breast cancer, all of whom had undergone baseline and follow-up CTC measurements using the CellSearch test, currently the only FDA-approved test for CTC measurement.

The median time interval between the two CTC assessments was 29 days, with changes in CTC levels between baseline and follow-up analyzed to determine if they were associated with overall survival.

Of the 2,961 patients who were CTC-positive at baseline, 1,855 remained CTC-positive after initiating treatment (positive/positive), while 1,106 patients converted to CTC-negative (positive/negative). Of the 1,118 patients who were CTC-negative at baseline, 813 remained CTC-negative (negative/negative) while 305 had become CTC-positive (negative/positive).

Median overall survival was greatest for patients who were negative/negative (47 months), followed by positive/negative (32.2 months), negative/positive (29.67 months), and positive/positive (17.87 months).

“Patients with an initial CTC-positive status and evidence of CTC response had a significantly increased overall survival of 32 months compared to 18 months in patients without CTC response, which translates into a hazard ratio of .49 and indicates early treatment response,” said Janni.

Compared to patients who were negative/negative, the risk of death was 215 percent greater for those who were positive/positive, 74 percent greater for negative/positive, and 52 percent greater for positive/negative. For patients who were CTC-positive at baseline, those who remained CTC-positive at follow-up had a 51 percent greater risk of death from those who converted to CTC-negative.

Similar trends were found when CTC dynamics were analyzed by breast cancer subtype, including for hormone receptor-positive, HER-2 positive, and triple-negative breast cancers. In patients with luminal-like tumors (ER-positive/HER-2 negative), the risk of death was 287 percent greater for those who were positive/positive, 101 percent greater for negative/positive, 101 percent greater for negative/positive, and 67 percent greater for positive/negative compared to the negative/negative group.

In patients with HER-2 positive tumors, the negative/positive group and positive/positive group showed significantly worse overall survival compared to the negative/negative group; with triple-negative patients, the positive/positive group had a significantly shorter overall survival compared to the negative/negative group.

“I really think this type of study will help us in the adjuvant setting where we may potentially have a chance to add treatments, alter treatments, so that we can prevent metastatic diseases all together,” stated Virginia G. Kaklamani, MD, Professor of Medicine in the Division of Hematology/Oncology at UT Health San Antonio and the leader of the Breast Cancer Program at UT Health San Antonio MD Anderson Cancer Center. Kaklamani, Co-Director of the symposium, did not participate in this study, but was asked to comment about its findings during a press briefing. 

Warren Froelich is a contributing writer.