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To interview Wolfgang Janni, please contact Julia Gunther at julia.gunther@aacr.org or 770-403-7690. For a photo of Janni, click here.

Circulating Tumor Cell Dynamics May Predict Treatment Response and Prognosis in Patients with Metastatic Breast Cancer

SAN ANTONIO – Early circulating tumor cell dynamics were associated with overall survival in patients with metastatic breast cancer, according to a meta-analysis presented at the 2020 San Antonio Breast Cancer Symposium, held Dec. 8-11.

"With the increasing number of treatment options available to patients with metastatic breast cancer, being able to predict and monitor treatment responses rapidly will be critical to aiding treatment decisions," said Wolfgang Janni, MD, PhD, a 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—approximately three months, depending on the subtype—before changes can be detected, Janni explained. "We were interested in determining whether treatment response and prognosis could be predicted earlier using a simple blood test."

In this study, Janni and colleagues investigated the potential of circulating tumor cells (CTCs), which are shed from the primary tumor into the bloodstream, to predict overall survival. They analyzed global 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. The median time from baseline to follow-up was 29 days. Changes in CTC levels between baseline and follow-up were analyzed to determine whether 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), and 1,106 patients had 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). 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 than those who converted to CTC-negative.

Similar trends were found when CTC dynamics were analyzed by breast cancer subtype, including for hormone receptor-positive, HER2-positive, and triple-negative breast cancers. CTC dynamics were associated with overall survival for all breast cancer subtypes.

"These data indicate that CTC dynamics can predict the trajectory of the disease a little more than four weeks after initiating treatment," said Janni. "This provides an advantage over conventional imaging methods and can help physicians determine very early on whether a treatment should be continued. It is also very reassuring that CTC dynamics predicted outcomes for all breast cancer subtypes."

A limitation of the study is that information about the type of treatment received was not available for many patients. “A strength of our study is that we have individual patient data from around the world, but this is also a limitation because different sources provided varying levels of details regarding treatment,” Janni explained. The absence of these data precluded determining whether the predictive value of CTC dynamics varies by treatment.

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Abstract

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Clinical utility of repeated circulating tumor cell (CTC) enumeration as early treatment monitoring tool in metastatic breast cancer (MBC) - a global pooled analysis with individual patient data

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Background:
Several studies suggest clinical utility of serial circulating tumor cell (CTC) enumeration as a means of assessing response status in metastatic breast cancer (MBC). The aim of this study is to conduct a comprehensive pooled analysis comprising globally available data to further define and explore the role of CTC enumeration as a tool for early treatment monitoring in patients with MBC with a focus on the predictive power in different breast cancer subtypes and clinical settings.
Methods:
In a global effort, peer-reviewed published studies with data on repeated CTC assessments (CellSearch® technology; Menarini Silicon Biosystems; Bologna, Italy) in MBC patients were screened and investigators were asked to provide individual patient data for this pooled analysis. 2761 cases from 32 data sets with data on both baseline and one follow up CTC assessments were included in the analysis (median time interval between the two CTC assessments 35 days). Data were analyzed using log rank tests and Cox regressions to evaluate the association between serial CTC enumeration results and overall survival (OS) in the full patient cohort and defined subgroups.
Results:
588 (21.3%) patients had no CTCs at both time points (neg/neg), 236 (8.5%) patients were CTC negative at baseline and CTC positive at follow up (neg/pos), 712 (25.8%) patients converted from CTC positive at baseline to CTC negative (pos/neg), and 1225 (44.4%) patients had at least one CTC at both time points (pos/pos). Log rank tests showed significant differences in OS between these four CTC change groups ($p < 0.0001$ for all pairwise comparisons except for the comparison between neg/pos and pos/neg, $p = 0.015$). Median OS for the neg/neg, neg/pos, pos/neg and pos/pos group was 45.6, 26.1, 34.6, and 17.6 months, respectively. Hazard ratios (HR) (reference group neg/neg) were 1.38 (95% CI 1.16 - 1.64) for the pos/neg group, 1.78 (95% CI 1.43 - 2.22) for the neg/pos group, and 3.06 (95% CI 2.63 - 3.56) for the pos/pos group. Results were similar if a cutoff of 5 CTCs was used for CTC positivity (pos/neg group: HR 1.43, 95% CI 1.25 - 1.63; neg/pos group: HR 2.39, 95% CI 1.91 - 2.99; pos/pos group: HR 3.54, 95% CI 3.12 - 4.02).
In total, 2586 patients could be assigned to different tumor subtypes based on known hormone receptor (ER) and HER2 status of the primary tumor: 1513 (58.5%) patients had a luminal-like tumor (ER positive, HER2 negative), 682 (26.4%) patients had a HER2-positive tumor, and 391 (15.1%) patients had a triple-negative tumor. In patients with luminal-like tumors, the hazard ratios were 1.67 (95% CI 1.29 - 2.17), 2.01 (95% CI 1.45 - 2.77), and 3.87 (95% CI 3.09 - 4.83) for the pos/neg, neg/pos, and pos/pos group, respectively. In patients with HER2-positive tumors, the neg/pos group (HR 1.68, 95% CI 1.12 - 2.53) and the pos/pos group (HR 2.11, 95% CI 1.58 - 2.83) showed significantly worse OS compared to the neg/neg group, while in triple-negative patients, the pos/pos group had a significantly shorter OS compared to the neg/neg group (HR 2.99, 95% CI 2.11 - 4.24).
The results will be up-dated by inclusion of additional large data sets (CALGB 40502, CALGB 40503, COMET, SWOG S0500, TBCRC 001) for the analysis to be presented at SABCS 2020.
Conclusion:
This large pooled analysis confirms that at a median of 35 days after treatment initiation, follow-up CTC assessments strongly predict overall survival. These results suggest potential clinical utility of CTC monitoring as early response marker in MBC, especially in luminal-like tumors.

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audience of academic investigators and private physicians from over 80 countries to attain information through abstract presentations, panel discussions, research findings, and state-of-the-art educational sessions. UT Health San Antonio, with co-sponsors the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine and the American Association for Cancer Research, supports SABCS, which provides education and accessibility to the latest information regarding the prevention, diagnosis, and treatment of premalignant breast cancer and breast disease. For more information on SABCS, visit www.sabcs.org.