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Strong evidence supports prognostic value of circulating tumor cells in breast cancer

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French researchers have reported the strongest proof yet that evidence of 'circulating tumor cells' found in samples of a patient's blood is strongly linked to poor outcomes such as a short time to disease progression.

At the IMPAKT Breast Cancer Conference in Brussels, Dr François-Clement Bidard and colleagues from Institut Curie in Paris say their new findings set the scene for interventional trials designed to see if improved outcomes can be achieved by modifying treatment based on circulating tumor cell counts.

"We needed to do this study to confirm data provided by earlier small studies," Dr Bidard said. "Now we are certain that circulating tumor cells (CTC) are prognostic at baseline, and that CTC changes under treatment may be an early indicator of chemotherapy efficiency."

"In metastatic breast cancer, it is time now for interventional randomized trials which will try to demonstrate that CTC-based strategies of treatment lead to a better clinical outcome, or at least to a benefit in the cost/efficacy ratio of treatment," Dr Bidard said.

The French team conducted a prospective study in 267 patients who were receiving first-line chemotherapy for metastatic breast cancer. For each patient they performed a count of circulating tumor cells, plus an analysis of other blood markers, in 7.5ml of blood. They took their measurements at the beginning of treatment and at several later time points.

Of 260 patients who were evaluable for CTC levels at baseline, 170 (65%) had at least one circulating tumor cell per 7.5 ml blood sample, and 115 (44%) had five or more, the researchers found.

At the end of the study, a multivariate analysis of their results showed that several factors, including CTC counts, were correlated with disease progression and overall survival.

"This is the first study that has been prospectively designed and statistically powered for reporting CTC-associated outcome as primary endpoint in a homogeneous population of metastatic breast cancer patients treated first line," Dr Bidard said.

The study results also add evidence to an ongoing discussion about how many CTCs per blood sample should be used to define patients at 'high risk' for a poor outcome.

"Generally, the more CTC you have, the worse it is," Dr Bidard said. "However, to define a 'high risk group', a threshold is needed. We report that the relative risk of the high-risk group vs low-risk group does not significantly change whether you define it as having a threshold of 1 CTC or 5 CTC. In both cases, their relative risks of shorter progression-free survival compared to the low-risk group are statistically the same."

"Our data suggest that using the lower threshold of 1 CTC is feasible and is not affected by any major loss of specificity of CTC detection. This supports the use of this low threshold in other studies conducted in non-metastatic breast cancer patients."

Commenting the study, which he was not involved in, Prof Fortunato Ciardiello, from Seconda Università di Napoli, Naples, Italy, noted that circulating tumor cells have been suggested in recent times as a useful prognostic marker for several cancers, including breast cancer.

"This study is very relevant, since it gives a prospective evaluation of the role of CTC in a large series of metastatic breast cancer patients receiving first-line treatment. It represents a significant contribution confirming the prognostic role of CTC and gives important insights to establish a clinically useful threshold level for defining patients with high or low circulating tumor cells."

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