CIRCULATING TUMOR CELLS IN BREAST CANCER

Kheira REKAI[1], Terki Khadidja[2]

Establishment university hospital of Oran, 31000 , Algeria

Keyword: Circulating Tumor Cells , Breast Cancer , neoadjuvant , adjuvant

Breast cancer is the first cancer in women, ranking second among the deadliest cancers in the world.
According to the World Health Organization (WHO), ten million new cases were diagnosed in 2000. This number increased to Fifteen million in 2015 (1)
The vast majority of patients die as a result of distant metastasis and not because of the primary tumor. Metastasis is likely to be caused by circulating tumor cells (CTC) that have detached from the primary tumor and circulate in the vascular system before nesting in a new site, or organ, to colonize and form secondary tumors. (2-3)
The diagnosis of breast cancer usually requires a tissue biopsy. Although used to assess the hormone receptor status and the human epidermal growth factor receptor (HER2), these interventions are invasive, cannot be done regularly and repeatedly, and provide little information for assessment metastatic potential or therapeutic efficacy.
For several years, the CTC count by liquid biopsy has been suggested as a prognostic and predictive biomarker in order to guide the management decisions of cancer patients.
Liquid biopsies are tests done on a blood sample to find cancer cells from a tumor that circulate in the blood, or pieces of DNA from tumor cells. These procedures are easy and safe, and multiple samples can be collected non-invasively. Thus, the possibility of following the evolution of cancer from blood samples has enormous potential for therapeutic adjustment with a view to personalized medicine and could improve the prognosis and quality of life of patients.
The CellSearch test is a system for detecting and counting CTCs. This test is based on the recognition of specific antigens expressed by cancer cells, which allows them to be isolated and enriched from a blood sample. The quantitative approach is based on a positivity threshold of a certain number of CTCs in a defined volume of blood.
The CTC count by the CellSearch system was evaluated as a stratification, prognostic and predictive biomarker in patients with breast cancer and candidates for neoadjuvant, adjuvant or systemic therapy in cases of metastatic cancer.

1.CIRCULATING TUMOR CELLS IN ADJUVANT SITUATION

The validity and clinical utility of the CTC count in patients with breast cancer who are candidates for adjuvant therapy should be confirmed.
Study findings are based on the presence of CTCs in a blood sample. Reproducibility must be assessed and detection methods must be standardized.
In addition, if the prognostic value of CTC counts is established, studies will need to compare current methods of stratifying primary tumors in breast cancer patients, such as Mammaprint or Oncotype DX, with tests CellSearch. Currently, the CTC count in the context of adjuvant therapy does not yet have any validity or clinical consensus utility. (13-14)
Randomized clinical trials, which include therapeutic components dependent on changes in CTC count, are needed to establish the usefulness of this biomarker in the management of patients. The French STIC CTC Metabreast and CirCe01 studies, the European TREAT-CTC study and the German DETECT III and IV studies, which aim to establish the place of CTCs in the therapeutic management of patients, are currently in progress [Bidard et al . 2013b].
International organizations such as ASCO and ESMO do not recommend the use of CTC count tests in the management of breast cancer. (12)

2.CIRCULATING TUMOR CELLS IN A NEO ADJUVANT SITUATION

The evidence regarding the use of the CellSearch test as a clinical tool in patients with early breast cancer who are candidates for neoadjuvant therapy does not allow its usefulness to be judged, among other things because the attribution of a value prognosis for CTC count before and after treatment is not significant.

The results of the REMAGUS02 study suggest that the presence of CTC may be a prognostic factor for overall survival.

Despite these results, large-scale studies with longer follow-up and a standardized methodology will be necessary to determine whether such an association exists. Clinical validity should also

RFERENCES

[1] Bibliothèque et Archives nationales du Québec, 2016 - Bibliothèque et Archives Canada, 2016 ISSN 1915-3104 INESSS (PDF)

[2] Aktas B, Tewes M, Fehm T, Hauch S, Kimmig R, Kasimir-Bauer S. Stem cell and epithelial-mesenchymal transition markers are frequently overexpressed in circulating tumor cells of metastatic breast cancer patients. Breast Cancer Res 2009;11(4):R46.

[3] Alunni-Fabbroni M, Muller V, Fehm T, Janni W, Rack B. Monitoring in metastatic breast cancer: Is imaging outdated in the era of circulating tumor cells? Breast Care (Basel) 2014;9(1):16-21.

[4] Banys-Paluchowski M, Schneck H, Blassl C, Schultz S, Meier-Stiegen F, Niederacher D, et al. Prognostic relevance of circulating tumor cells in molecular subtypes of breast cancer. Geburtshilfe Frauenheilkd 2015;75(3):232-7.

[5] Bidard FC et Pierga JY. Clinical utility of circulating tumor cells in metastatic breast cancer. J Clin Oncol 2015;33(14):1622.

[6] Bidard FC, Belin L, Delaloge S, Lerebours F, Ngo C, Reyal F, et al. Time-dependent prognostic impact of circulating tumor cells detection in non-metastatic breast cancer: 70-month analysis of the REMAGUS02 study. Int J Breast Cancer 2013a;2013:130470. .

[7] Coumans FA, Ligthart ST, Uhr JW, Terstappen LW. Challenges in the enumeration and phenotyping of CTC. Clin Cancer Res 2012;18(20):5711-8.

[8] Hall CS, Karhade M, Laubacher BA, Kuerer HM, Krishnamurthy S, DeSnyder S, et al. Circulating tumor cells and recurrence after primary systemic therapy in stage III inflammatory breast cancer. J Natl Cancer Inst 2015b;107(11):djv250.

[9] Hayes DF et Cristofanilli M. Re: Anti-epithelial cell adhesion molecule antibodies and the detection of circulating normal-like breast tumor cells. J Natl Cancer Inst 2009;101(12):894-5; author reply 896-7.

[10] Mego M, Giordano A, De Giorgi U, Masuda H, Hsu L, Giuliano M, et al. Circulating tumor cells in newly diagnosed inflammatory breast cancer. Breast Cancer Res 2015;17:2.

[11] Cristofanilli M, Budd GT, Ellis MJ, Stopeck A, Matera J, Miller MC, et al. Circulating tumor cells, disease progression, and survival in metastatic breast cancer. N Engl J Med 2004;351(8):781-91

[12] Giuliano M, Giordano A, Jackson S, Hess KR, De Giorgi U, Mego M, et al. Circulating tumor cells as prognostic and predictive markers in metastatic breast cancer patients receiving first-line systemic treatment. Breast Cancer Res 2011;13(3):R67.

[13] Saijo N. Critical comments for roles of biomarkers in the diagnosis and treatment of cancer. Cancer Treat Rev 2012;38(1):63-7.

[14] Seronie-Vivien S. Les cellules tumorales circulantes : un nouveau challenge pour la biologie clinique oncologique. Ann Biol Clin (Paris) 2014;72(2):153-77.