Publications
Circulating Cancer Biomarkers

Year of publication 2018


Journal of the National Cancer Institute: DOI: 10.1093/jnci/djy018

Summary
We conducted a meta-analysis in nonmetastatic breast cancer patients treated by neoadjuvant chemotherapy (NCT) to assess the clinical validity of circulating tumor cell (CTC) detection as a prognostic marker.

Year of publication 2017


Circulating tumor cell count and thrombosis in metastatic breast cancer.

Summary
Essentials Tumor cells circulating in blood (CTC) may favor thrombotic events in cancer patients. We assessed the impact of CTC on the risk of thrombosis in metastatic breast cancer. Baseline CTC detection was the only independent factor associated with the risk of thrombosis. CTC detection under therapy may be the hidden link between tumor progression & thrombosis.

Year of publication 2016

H Bonnefoi, T Grelley, O Tredan, M Saghatchian, F Dalenc, A Mailliez, T L'Haridon, P Cottu, S

**A phase II trial of abiraterone acetate plus prednisone in patients with triple-negative androgen receptor positive locally advanced or metastatic breast cancer (UCBG 12-1).**

*Annals of Oncology: official journal of the European Society for Medical Oncology / ESMO*: 812-8  
DOI: [10.1093/annonc/mdw067](https://doi.org/10.1093/annonc/mdw067)

**Summary**

Several expression array studies identified molecular apocrine breast cancer (BC) as a subtype that expresses androgen receptor (AR) but not estrogen receptor α. We carried out a multicentre single-arm phase II trial in women with AR-positive, estrogen, progesterone receptor and HER2-negative (triple-negative) metastatic or inoperable locally advanced BC to assess the efficacy and safety of abiraterone acetate (AA) plus prednisone.


**Bevacizumab plus neoadjuvant chemotherapy in patients with HER2-negative inflammatory breast cancer (BEVERLY-1): a multicentre, single-arm, phase 2 study.**

*The Lancet. Oncology*: [DOI: S1470-2045(16)00011-5](https://doi.org/10.1016/S1470-2045(16)00011-5)

**Summary**

Addition of bevacizumab to standard chemotherapy in the neoadjuvant setting in patients with HER2-negative metastatic breast cancer improves progression-free survival and the proportion of patients achieving pathological complete response. In the BEVERLY-1 (UCBG-0802) trial we aimed to assess the addition of bevacizumab to neoadjuvant and adjuvant chemotherapy in the treatment of patients with HER2-negative inflammatory breast cancer.

Emeline Tabouret, François Bertucci, Jean-Yves Pierga, Thierry Petit, Christelle Levy, Jean-Marc Ferrero, Mario Campone, Joseph Gligorov, Florence Lerebours, Henri Roché, Thomas Bachelot, Steven van Laere, Naoto T Ueno, Yves Toiron, Pascal Finetti, Daniel Birnbaum, Jean-Paul Borg, Patrice Viens, Olivier Chinot, Anthony Gonçalves (2016 Feb 28)
**MMP2 and MMP9 serum levels are associated with favorable outcome in patients with inflammatory breast cancer treated with bevacizumab-based neoadjuvant chemotherapy in the BEVERLY-2 study.**

*Oncotarget*: DOI: 10.18632/oncotarget.7612

**Summary**

Addition of bevacizumab to trastuzumab-based neoadjuvant chemotherapy in HER2-positive inflammatory breast cancer (IBC) was associated with favorable outcome in the BEVERLY-2 phase II trial. Circulating levels of matrix metalloproteinases (MMP) 2 and 9 were correlated to high response rate and prolonged survival in high-grade glioma treated with bevacizumab. We examined the prognostic impact of MMP2 and MMP9 serum levels in BEVERLY-2 patients.

Francesca Riva, Oleksii I Dronov, Dmytro I Khomenko, Florence Huguet, Christophe Louvet, Pascale Mariani, Marc-Henri Stern, Olivier Lantz, Charlotte Proudhon, Jean-Yves Pierga, Francois-Clement Bidard (2016 Feb 10)

**Clinical applications of circulating tumor DNA and circulating tumor cells in pancreatic cancer.**

*Molecular oncology*: 481-93 : DOI: 10.1016/j.molonc.2016.01.006

**Summary**

Pancreatic ductal adenocarcinoma (PDAC) is the most frequent pancreatic cancer type and is characterized by a dismal prognosis due to late diagnosis, local tumor invasion, frequent distant metastases and poor sensitivity to current therapy. In this context, circulating tumor cells and circulating tumor DNA constitute easily accessible blood-borne tumor biomarkers that may prove their clinical interest for screening, early diagnosis and metastatic risk assessment of PDAC. Moreover these markers represent a tool to assess PDAC mutational landscape. In this review, together with key biological findings, we summarize the clinical results obtained using “liquid biopsies” at the different stages of the disease, for early and metastatic diagnosis as well as monitoring during therapy.

Francois-Clement Bidard, Charlotte Proudhon, Jean-Yves Pierga (2016 Jan 27)

**Circulating tumor cells in breast cancer.**

*Molecular oncology*: 418-30 : DOI: 10.1016/j.molonc.2016.01.001

**Summary**

Over the past decade, technically reliable circulating tumor cell (CTC) detection methods allowed the collection of large datasets of CTC counts in cancer patients. These data can be used either as a dynamic prognostic biomarker or as tumor material for “liquid biopsy”. Breast cancer appears to be the cancer type in which CTC have been the most extensively studied so far, with level-of-evidence-1 studies supporting the clinical validity of CTC count in
both early and metastatic stage. This review summarizes and discusses the clinical results obtained in breast cancer patients, the issues faced by the molecular characterization of CTC and the biological findings about cancer biology and metastasis that were obtained from CTC.

**Pooled Analysis of the Prognostic Relevance of Circulating Tumor Cells in Primary Breast Cancer.**

**Summary**

Although unequivocal evidence has shown the prognostic relevance of circulating tumor cells (CTC) in the peripheral blood of patients with metastatic breast cancer, less evidence is available for the prognostic relevance of CTCs at the time of primary diagnosis.

Year of publication 2015

**Circulating tumor DNA for triple-negative breast cancer diagnosis and treatment decisions.**

**Summary**

Triple-negative breast cancer (TNBC) is a highly aggressive disease characterized by a high number of relapses and poor overall survival. The heterogeneity of the disease and the limited treatment options compared to other breast cancer subtypes mainly explain these clinical outcomes. New biomarkers are urgently needed to improve the management of TNBC. Circulating tumor DNA, identified by tumor-related molecular alterations, could be used in the context of non-invasive “liquid biopsy” and help in TNBC diagnosis and treatment decisions. In this review, we discuss the key issues related to the potential of circulating tumor DNA to improve the management of this disease and the future steps to overcome before its implementation into clinical routine within the next 5 years.

Xavier Pivot, Thomas Suter, Jean Marc Nabholtz, Jean Yves Pierga, Marc Espie, Alain Lortholary, David Khayat, Iris Pauporte, Gilles Romieu, Andrew Kramar, Pierre Fumoleau (2015 Jul 12)
**Cardiac toxicity events in the PHARE trial, an adjuvant trastuzumab randomised phase III study.**  

**Summary**

This article reports the cardiac toxicity according to 6- versus 12-month durations of adjuvant trastuzumab in PHARE randomised trial (NCT00381901).

F-C Bidard, C Y Ng, P Cottu, S Piscuoglio, L Escalup, R A Sakr, F Reyal, P Mariani, R Lim, L Wang, L Norton, V Servois, B Sigal, A Vincent-Salomon, B Weigelt, J-Y Pierga, J S Reis-Filho (2015 May 9)

**Response to dual HER2 blockade in a patient with HER3-mutant metastatic breast cancer.**  

**Summary**

HER3 activating mutations have been shown in preclinical models to be oncogenic and ligand-independent, but to depend on kinase-active HER2.

Francois-Clement Bidard, Jean-Yves Pierga (2015 Apr 15)

**Clinical utility of circulating tumor cells in metastatic breast cancer.**  

**Summary**


**Circulating tumor cell thresholds and survival scores in advanced metastatic breast cancer: the observational step of the CirCe01 phase III trial.**  
*Cancer letters* : 213-8 : [DOI : 10.1016/j.canlet.2015.02.010]

**Summary**

The clinical validity of circulating tumor cell (CTC) count changes during chemotherapy in metastatic breast cancer patients has been validated, but its clinical utility remains to be demonstrated. We report here the non-randomized run-in phase of the CirCe01 trial which was designed to evaluate CTC changes and thresholds to other palliative prognostic scores.
and establish CTC thresholds to be used in the randomized part of the study. CTC count (CellSearch®) and other prognostic parameters (serum albumin level, lymphocyte level, LDH level, prognostic inflammatory and nutritional index (PINI) and Barbot’s score) were assessed in 56 metastatic breast cancer patients before the first cycle of third line chemotherapy. Early changes of CTC count were correlated with treatment outcome. Independent prognostic markers in multivariate analysis were: low serum albumin (HR = 11.1), poor performance status (HR = 3.8), ≥5 CTC/7.5 ml (HR = 3.8) and triple negative subtype (HER2+ and hormone positive vs triple negative: both HR = 0.2). Among patients with ≥5 CTC/7.5 ml at baseline, a composite criteria (<5 CTC/7.5 ml or relative decrease ≥-70% of the baseline CTC count) showed better prognostication for PFS (p=0.002).

Year of publication 2014

Pathological response and circulating tumor cell count identifies treated HER2+ inflammatory breast cancer patients with excellent prognosis: BEVERLY-2 survival data.
Clinical cancer research : an official journal of the American Association for Cancer Research : 1298-304 : DOI : 10.1158/1078-0432.CCR-14-1705

Summary

The BEVERLY-2 single-arm phase II trial assessed the efficacy and safety of combining neoadjuvant chemotherapy with bevacizumab and trastuzumab for the treatment of HER2-positive inflammatory breast cancer (IBC). Here, we report the results of a preplanned survival analysis at 3 years of follow-up, along with the association between outcome and circulating biomarkers and pathologic complete response (pCR).

Use of [(18)F]-FDG PET to predict response to neoadjuvant trastuzumab and docetaxel in patients with HER2-positive breast cancer, and addition of bevacizumab to neoadjuvant trastuzumab and docetaxel in [(18)F]-FDG PET-predicted non-responders (AVATAHER): an open-label, randomised phase 2 trial.
The Lancet. Oncology : 1493-502 : DOI : 10.1016/S1470-2045(14)70475-9

Summary
An effective and well tolerated treatment is needed for patients with early HER2-positive breast cancer who do not achieve a pathological complete response after neoadjuvant therapy. The AVATAHER trial aimed to predict pathological complete response early with the use of PET and to investigate whether the addition of bevacizumab could improve the proportion of patients achieving a pathological complete response in patients unlikely to respond to treatment.