Maintrac®

Células Epiteliais Tumorais Circulantes Vivas
(CETCs / CTCs)

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O que é o Maintrac ?

Em linha com a medicina de precisão, o Maintrac é um exame de sangue que permite quantificar células (CETCs / CTCs) que saíram do tumor e entraram na corrente sanguínea, antes, durante e depois da terapia.

(1) monitora a eficácia do tratamento, através da contagem de células VIVAS do tumor presentes no organismo;

(2) define a droga mais eficaz para aquele paciente especificamente;

(3) detecta o câncer e sua reincidência precocemente.

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Maintrac –
Contagem de Células Tumorais:

Após coleta (15ml de sangue) a amostra chega em 72 horas em nosso laboratório na Bavária (Alemanha). A contagem é feita de forma semiautomática, detectando células de qualquer tipo de câncer, exceto linfoma ou leucemia.

O processo se repete após 2 ciclos da terapia. De acordo com a variação do número de células tumorais, o médico já sabe se o tratamento está sendo eficaz ou não.

No caso de aumento, é recomendado que seja feito **o Maintrac – Teste de Substâncias** e alteração da terapia. Se há diminuição, o médico tem informação segura para definição sobre a continuação da terapia.

Vide o cronograma de testes no próximo slide.

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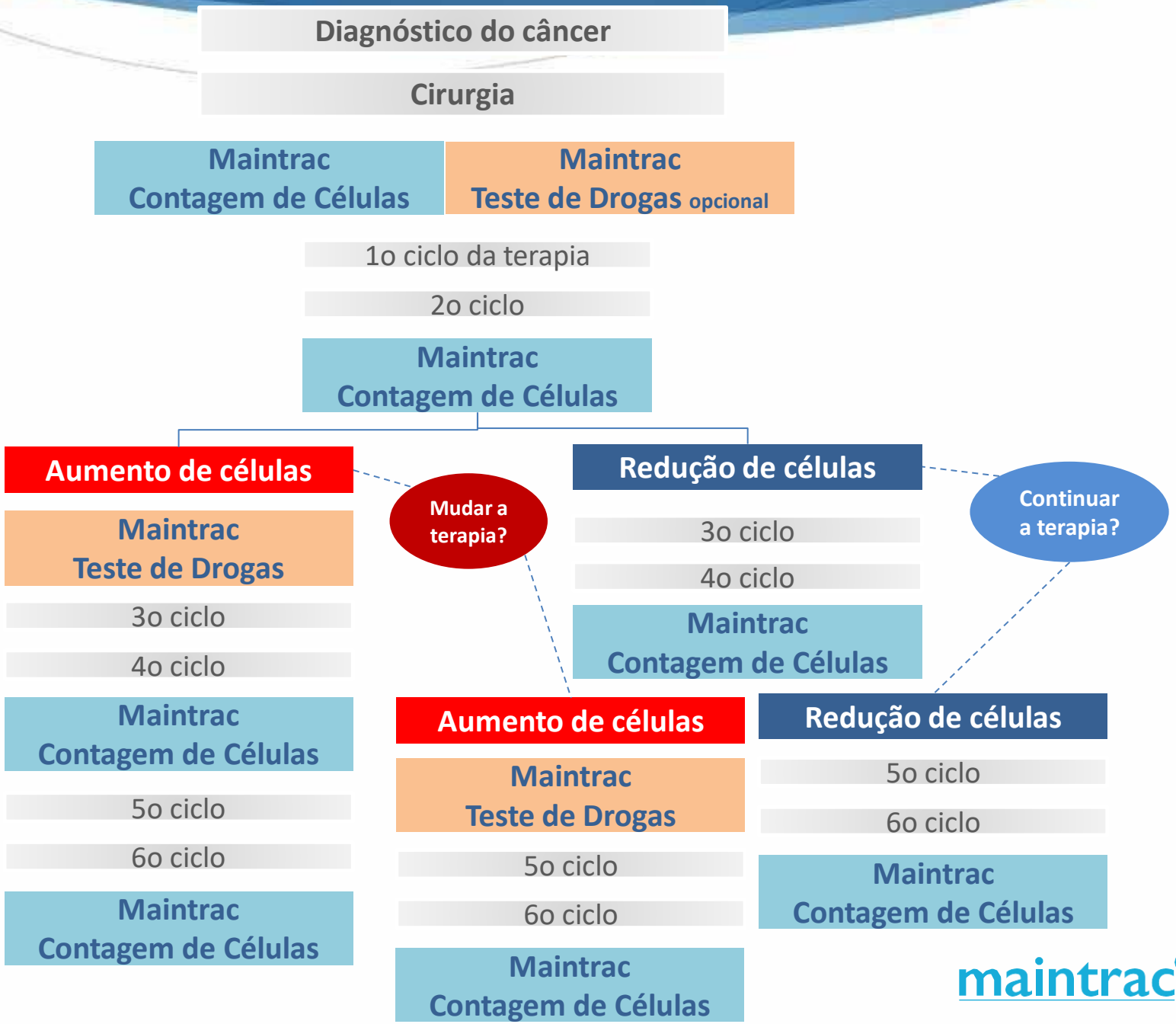
Cronograma e tipos de testes

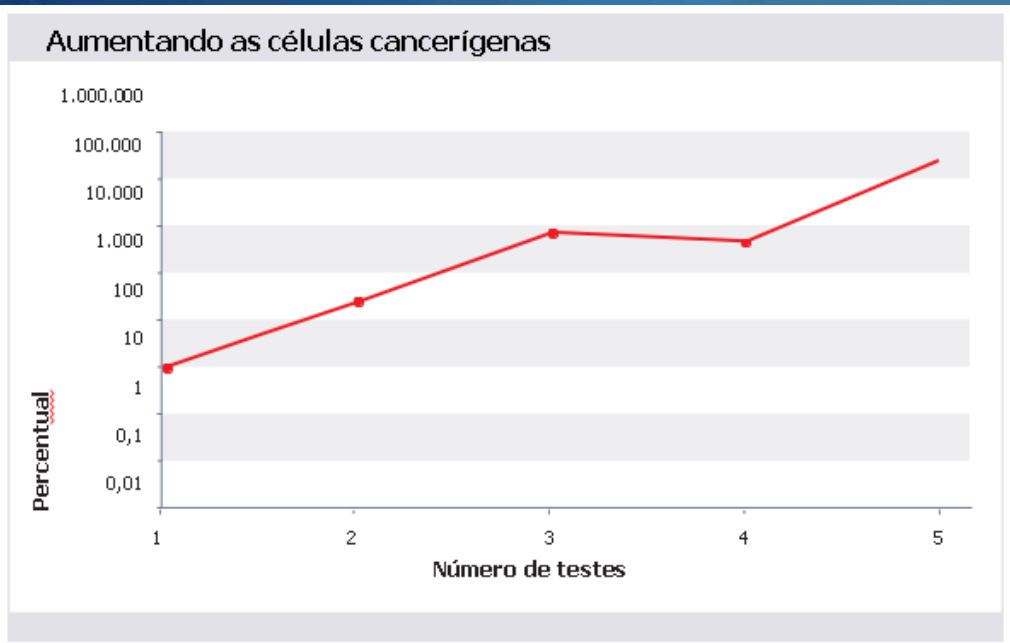


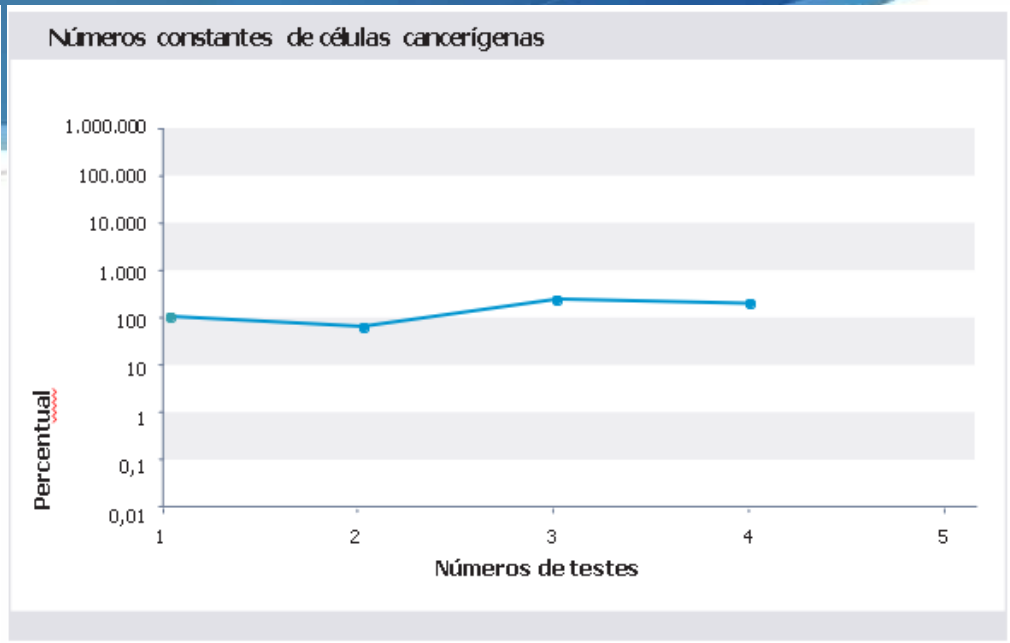
Método humanizado: informação do organismo de cada pessoa especificamente.

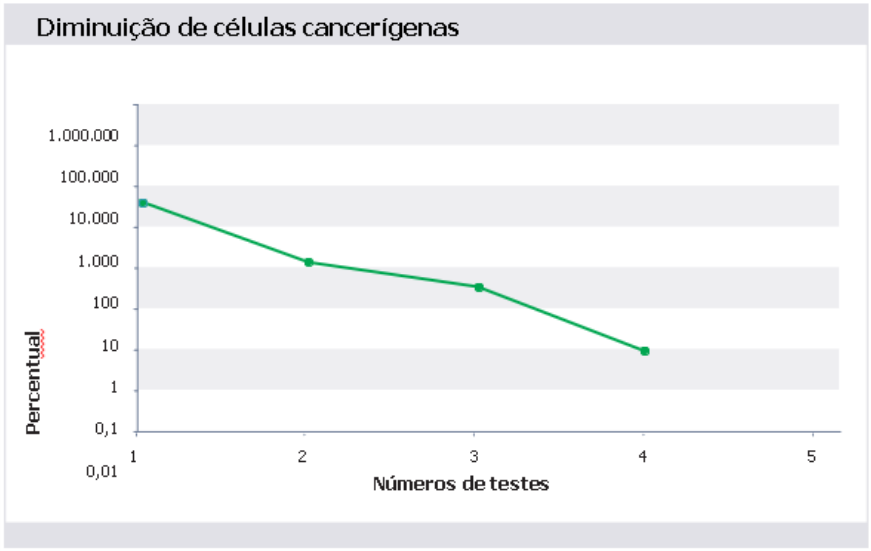
A Medicina de precisão consegue oferecer tratamentos mais eficazes (por serem personalizados), sem prejudicar a qualidade de vida do paciente.

Resposta rápida e precisa sobre a condição do paciente, possibilitando os ajustes necessários para melhores resultados

Dinâmica dos resultados do Maintrac Contagem de Células







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Diferença entre o Maintrac e testes tradicionais de biópsia líquida

A detecção quantitativa das células é determinada pela coloração delas - com precisão, evitando o desperdício de células na contagem.

SEM Fixação

SEM Isolamento

SEM Enriquecimento

A detecção precoce se baseia no fato do Maintrac® ser altamente sensível, porque as células da amostra de sangue são analisadas em tempo real.

Em outros métodos, as células tendem a ser fixadas, isoladas ou enriquecidas.

Isso permite uma determinação quantitativa de CETCs / CTCs mesmo nos estágios iniciais da doença, e não apenas quando um estágio metastático foi atingido.

SEM Células perdidas!

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Diferença entre o Maintrac e testes tradicionais de biópsia líquida

O Maintrac CTC identifica e enumera células tumorais VIVAS no sangue.

O Maintrac identifica a validade das células iniciadoras do câncer, cultivando-as de pacientes em grupos (ou esferas tumorais) e também células produtoras de tumores em membranas CA.

Todas as outras tecnologias (biópsia líquida) analisam fragmentos celulares, como DNA, RNA e proteínas. O DNA tumoral na corrente sanguínea é denominado ctDNA e é derivado de células mortas, pois o DNA é intracelular. Por isso, a interpretação e correlação com os resultados ainda precisariam ser validados/confirmados.

A biópsia líquida Maintrac CTC estuda as células tumorais vivas.

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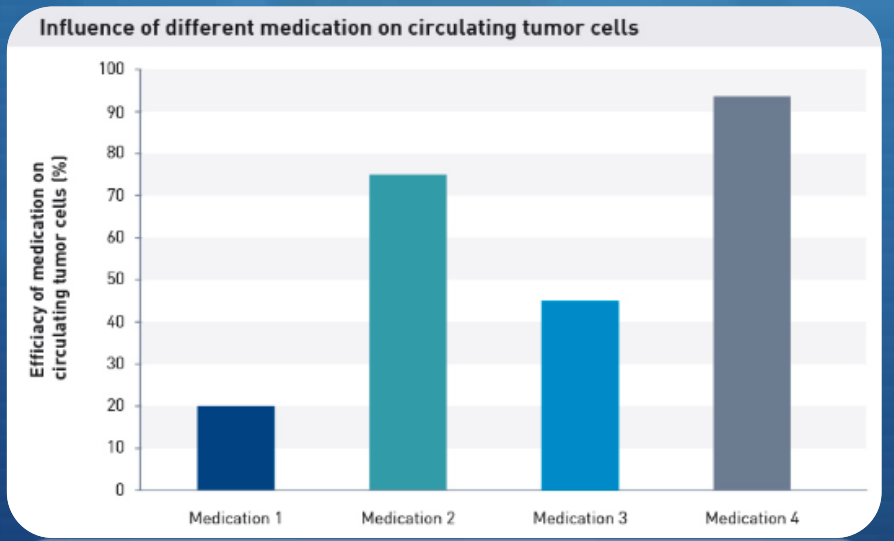
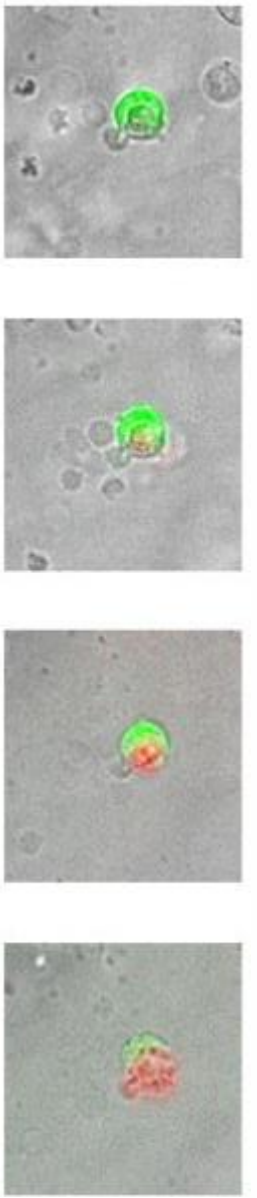
Maintrac – Teste de Substâncias

Cada medicamento fará um efeito diferente em cada paciente. O Maintrac é recomendado antes ou durante o tratamento.

Para avaliação da eficácia, medicamentos são testados diretamente nas CETC/CTC. Uma dose diária é misturada ao sangue do paciente em um tubo de ensaio (in vitro). A taxa de morte por CETC/CTC é comparada com uma amostra sem adição de medicação. Os resultados mostram o medicamento mais adequado para destruir as células tumorais do sangue.





Exemplo de uma CETC/CTC morrendo em contato com o medicamento

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O aumento de células tumorais epiteliais circulantes (CETC/CTC) ao longo da radioterapia adjuvante é um preditor de resultados menos favoráveis em pacientes com câncer de mama em estágio inicial

Mol Clin Oncol, 2022 Oct; 15(4):201.
doi: 10.3892/mco.2021.2363

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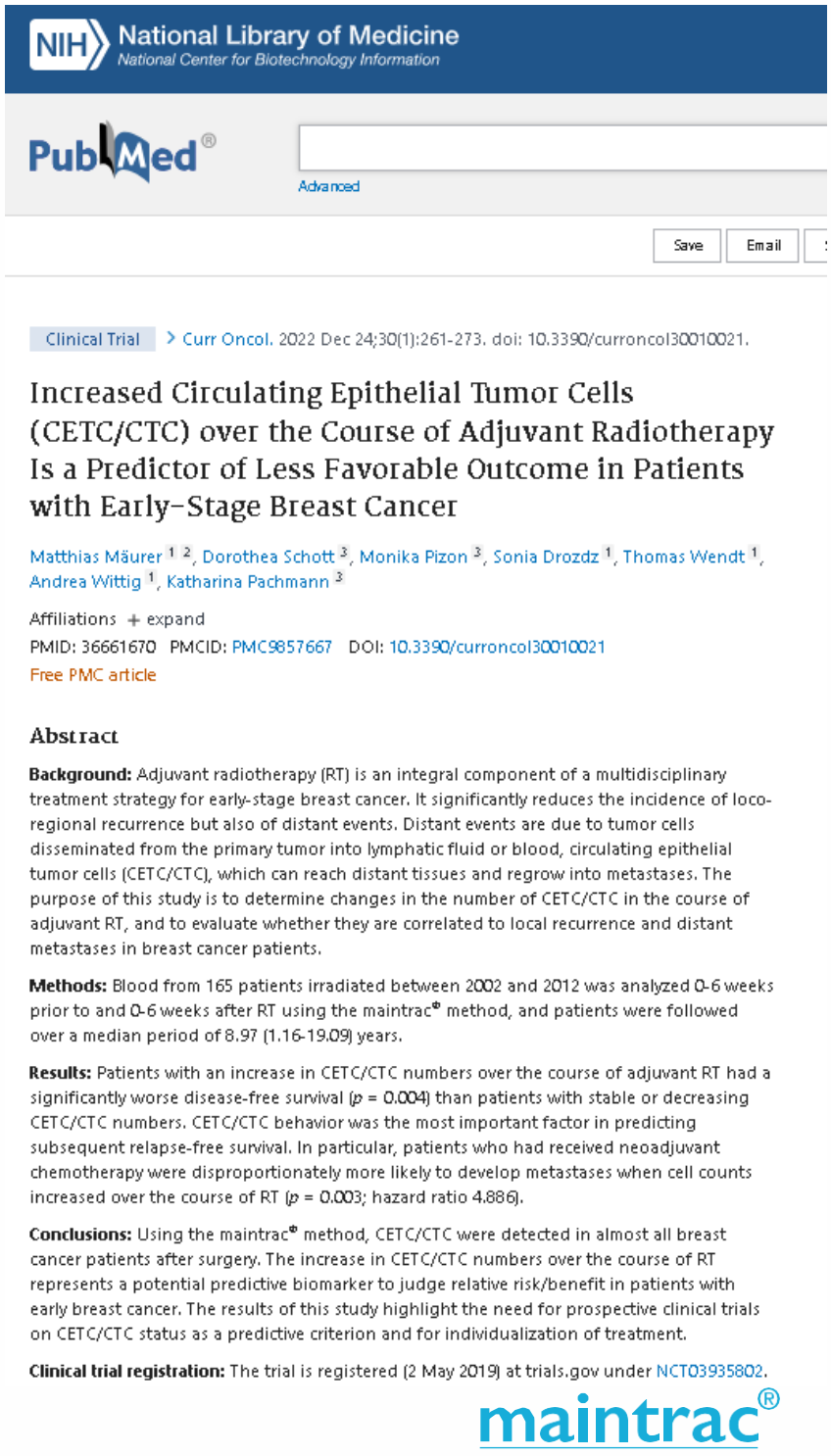

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Clinical Trial > Curr Oncol. 2022 Dec 24;30(1):261-273. doi: 10.3390/curroncol30010021.

Increased Circulating Epithelial Tumor Cells (CETC/CTC) over the Course of Adjuvant Radiotherapy Is a Predictor of Less Favorable Outcome in Patients with Early-Stage Breast Cancer

Matthias Mäurer [1,2], Dorothea Schott [3], Monika Pizon [3], Sonia Drozdz [1], Thomas Wendt [1], Andrea Wittig [1], Katharina Pachmann [3]

Affiliations + expand

PMID: 36661670 PMCID: PMC9857667 DOI: 10.3390/curroncol30010021
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Abstract

Background: Adjuvant radiotherapy (RT) is an integral component of a multidisciplinary treatment strategy for early-stage breast cancer. It significantly reduces the incidence of loco-regional recurrence but also of distant events. Distant events are due to tumor cells disseminated from the primary tumor into lymphatic fluid or blood, circulating epithelial tumor cells (CETC/CTC), which can reach distant tissues and regrow into metastases. The purpose of this study is to determine changes in the number of CETC/CTC in the course of adjuvant RT, and to evaluate whether they are correlated to local recurrence and distant metastases in breast cancer patients.

Methods: Blood from 165 patients irradiated between 2002 and 2012 was analyzed 0-6 weeks prior to and 0-6 weeks after RT using the maintrac® method, and patients were followed over a median period of 8.97 (1.16-19.09) years.

Results: Patients with an increase in CETC/CTC numbers over the course of adjuvant RT had a significantly worse disease-free survival ($p = 0.004$) than patients with stable or decreasing CETC/CTC numbers. CETC/CTC behavior was the most important factor in predicting subsequent relapse-free survival. In particular, patients who had received neoadjuvant chemotherapy were disproportionately more likely to develop metastases when cell counts increased over the course of RT ($p = 0.003$; hazard ratio 4.886).

Conclusions: Using the maintrac® method, CETC/CTC were detected in almost all breast cancer patients after surgery. The increase in CETC/CTC numbers over the course of RT represents a potential predictive biomarker to judge relative risk/benefit in patients with early breast cancer. The results of this study highlight the need for prospective clinical trials on CETC/CTC status as a predictive criterion and for individualization of treatment.

Clinical trial registration: The trial is registered (2 May 2019) at trials.gov under NCT03935802.

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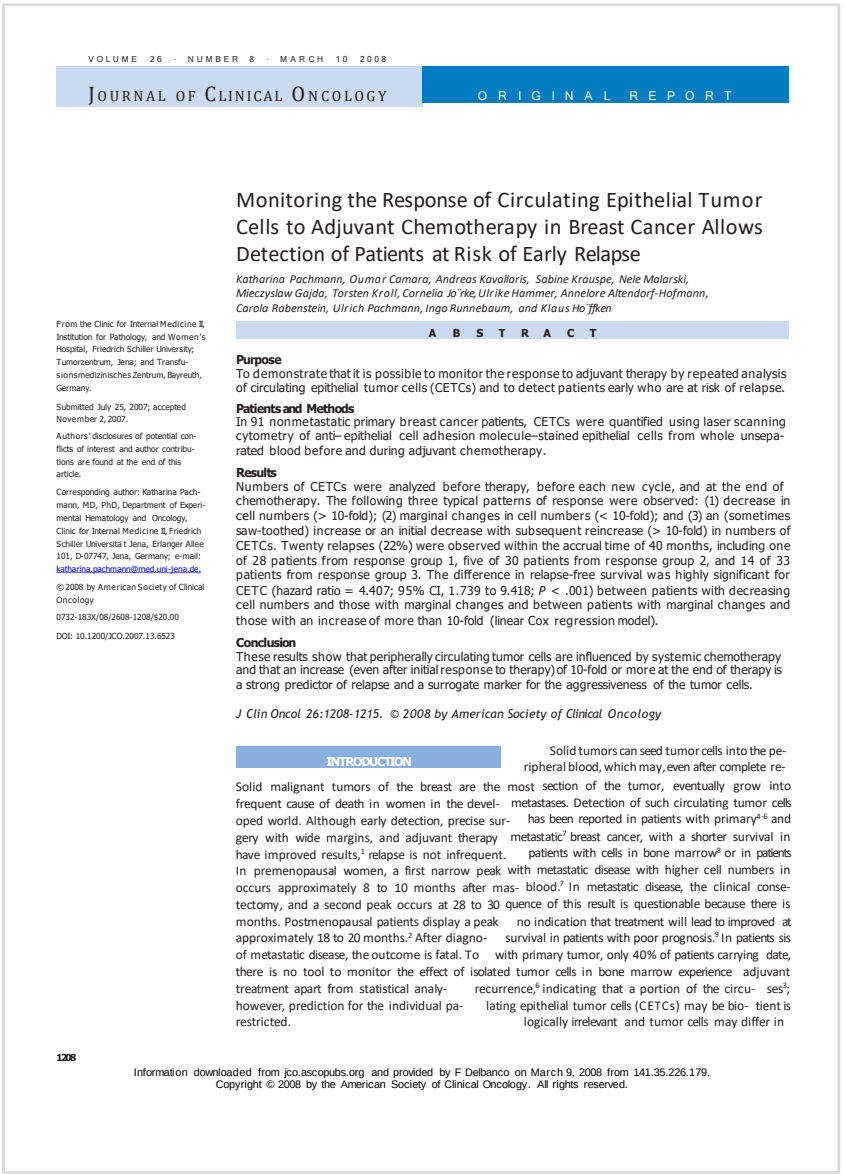
Monitorar a resposta das células tumorais epiteliais circulantes (CETC) à quimioterapia adjuvante no câncer de mama permite a detecção de pacientes com risco de recorrência precoce

J Clin Oncol 2008, 26 (8): 1208-1215



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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Monitoring the Response of Circulating Epithelial Tumor Cells to Adjuvant Chemotherapy in Breast Cancer Allows Detection of Patients at Risk of Early Relapse

Katharina Pachmann, Oumar Camara, Andreas Kavallaris, Sabine Krauspe, Nele Malarski, Mieczyslaw Gajda, Torsten Kroll, Cornelia Jo¨rke, Ulrike Hammer, Annelore Altendorf-Hofmann, Carola Rabenstein, Ulrich Pachmann, Ingo Runnebaum, and Klaus Ho¨ffken

From the Clinic for Internal Medicine II, Institution for Pathology, and Women's Hospital, Friedrich Schiller University; Tumorzentrum, Jena; and Transfusionsmedizinisches Zentrum, Bayreuth, Germany.

Submitted July 25, 2007; accepted November 2, 2007.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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0732-183X/08/2608-1208/$20.00

DOI: 10.1200/JCO.2007.13.6523

A B S T R A C T

Purpose
To demonstrate that it is possible to monitor the response to adjuvant therapy by repeated analysis of circulating epithelial tumor cells (CETCs) and to detect patients early who are at risk of relapse.

Patients and Methods
In 91 nonmetastatic primary breast cancer patients, CETCs were quantified using laser scanning cytometry of anti–epithelial cell adhesion molecule–stained epithelial cells from whole unseparated blood before and during adjuvant chemotherapy.

Results
Numbers of CETCs were analyzed before therapy, before each new cycle, and at the end of chemotherapy. The following three typical patterns of response were observed: (1) decrease in cell numbers (> 10-fold); (2) marginal changes in cell numbers (< 10-fold); and (3) an (sometimes saw-toothed) increase or an initial decrease with subsequent reincrease (> 10-fold) in numbers of CETCs. Twenty relapses (22%) were observed within the accrual time of 40 months, including one of 28 patients from response group 1, five of 30 patients from response group 2, and 14 of 33 patients from response group 3. The difference in relapse-free survival was highly significant for CETC (hazard ratio = 4.407; 95% CI, 1.739 to 9.418; $P < .001$) between patients with decreasing cell numbers and those with marginal changes and between patients with marginal changes and those with an increase of more than 10-fold (linear Cox regression model).

Conclusion
These results show that peripherally circulating tumor cells are influenced by systemic chemotherapy and that an increase (even after initial response to therapy) of 10-fold or more at the end of therapy is a strong predictor of relapse and a surrogate marker for the aggressiveness of the tumor cells.

J Clin Oncol 26:1208-1215. © 2008 by American Society of Clinical Oncology

INTRODUCTION

Solid malignant tumors of the breast are the most frequent cause of death in women in the developed world. Although early detection, precise surgery with wide margins, and adjuvant therapy have improved results,[1] relapse is not infrequent. In premenopausal women, a first narrow peak occurs approximately 8 to 10 months after mastectomy, and a second peak occurs at 28 to 30 months. Postmenopausal patients display a peak approximately 18 to 20 months.[2] After diagnosis of metastatic disease, the outcome is fatal. To there is no tool to monitor the effect of however, prediction for the individual restricted.

Solid tumors can seed tumor cells into the peripheral blood, which may, even after complete resection of the tumor, eventually grow into metastases. Detection of such circulating tumor cells has been reported in patients with primary[4-6] and metastatic[7] breast cancer, with a shorter survival in patients with cells in bone marrow[8] or in patients with metastatic disease with higher cell numbers in blood.[7] In metastatic disease, the clinical consequence of this result is questionable because there is no indication that treatment will lead to improved survival in patients with poor prognosis.[9] In patients with primary tumor, only 40% of patients carrying isolated tumor cells in bone marrow experience adjuvant recurrence,[6] indicating that a portion of the circulating epithelial tumor cells (CETCs) may be biologically irrelevant and tumor cells may differ in

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Teste de quimiossensibilidade de células tumorais epiteliais circulantes (CETC) in vitro: correlação com sensibilidade in vivo e resultado clínico

Journal of Cancer Therapy, 2013

Journal of Cancer Therapy, 2013, 4, 597-605
doi:10.4236/jct.2013.42077 Published Online April 2013 (http://www.scirp.org/journal/jct)

Scientific Research

Chemosensitivity Testing of Circulating Epithelial Tumor Cells (CETC) *in Vitro*: Correlation to *in Vivo* Sensitivity and Clinical Outcome

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Received February 25th, 2013; revised March 26th, 2013; accepted April 2nd, 2013

ABSTRACT

Background: Chemotherapy is a mainstay of tumor therapy, however, it is predominantly applied according to empirically developed recommendations derived from statistical relapse rates occurring years after the treatment in the adjuvant situation and from progression-free interval data in the metastatic situation, without any possibility of individually determining the efficacy in the adjuvant situation and with loss of time and quality of life in the metastatic situation if the drugs chosen are not effective. Here, we present a method to determine the efficiency of chemotherapeutic drugs using tumor cells circulating in blood as the part of the tumor actually available in the patient's body for chemosensitivity testing. Methodology/Principal Findings: After only red blood cell lysis, omitting any enrichment (analogous to other blood cell enumeration methods, including rare CD34 cells), the white cells comprising the circulating epithelial tumor cells (CETC) are exposed to the drugs in question in different concentrations and for different periods of time. Staining with a fluorescence-labeled anti-epithelial antibody detects both vital and dying tumor cells, distinguishing vital from dying cells through membrane permeability and nuclear staining with propidium iodide. Increasing percentages of dying tumor cells are observed dependent on time and concentration. The sensitivity can vary during therapy and was correlated with decrease or increase in CETC and clinical outcome. Conclusions/Significance: Thus, we are able to show that chemosensitivity testing of circulating tumor cells provides real-time information about the sensitivity of the tumor present in the patient, even at different times during therapy, and correlates with treatment success.

Ensaios de membrana corioalantóica de pintinho (CAM) como modelo de Xenoenxertos derivados de pacientes, de células-tronco cancerígenas circulantes (cCSCs) em pacientes com câncer de mama

Cancers (Basel), 2022

cancers

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Article

Chick Chorioallantoic Membrane (CAM) Assays as a Model of Patient-Derived Xenografts from Circulating Cancer Stem Cells (cCSCs) in Breast Cancer Patients

Monika Pizon [1,*], Dorothea Schott [1], Ulrich Pachmann [1], Rainer Schobert [2], Marek Pizon [3], Marta Wozniak [4], Rafal Bobinski [5] and Katharina Pachmann [1]

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Simple Summary: Circulating cancer cells—and in particular their very rare subpopulation, circulating cancer stem cells (cCSCs)—are responsible for recurrence and metastasis. In this study, we present a novel process in which patient-derived xenograft (PDX) can be harvested on chorioallantoic membrane (CAM) from circulating cancer stem cells. In our opinion, the CAM-based PDX model using circulating cancer stem cells can provide a fast, low-cost, easy-to-use, and efficient preclinical platform for drug screening, therapy optimization, and biomarker discovery.

Abstract: Background: cCSCs are a small subset of circulating tumor cells with cancer stem cell features: resistance to cancer treatments and the capacity for generating metastases. PDX are an appreciated tool in oncology, providing biologically meaningful models of many cancer types, and potential platforms for the development of precision oncology approaches. Commonly, mouse models are used for the in vivo assessment of potential new therapeutic targets in cancers. However, animal models are costly and time consuming. An attractive alternative to such animal experiments is the chicken chorioallantoic membrane assay. Methods: In this study, primary cultures from cCSCs were established using the sphere-forming assay. Subsequently, tumorspheres were transplanted onto the CAM membrane of fertilized chicken eggs to form secondary microtumors. Results: We have developed an innovative in vitro platform for cultivation of cCSCs from peripheral blood of cancer patients. The number of tumorspheres increased significantly with tumor progression and aggressiveness of primary tumor. The number of tumorspheres was positively correlated with Ki-67, Her2 status, and grade score in primary breast tumors. The grafting of tumorspheres onto the CAM was successful and positively correlated with aggressiveness and proliferation capacity of the primary tumor. These tumors pathologically closely resembled the primary tumor. Conclusions: The number of tumorspheres cultured from peripheral blood and the success rate of establishing PDX directly reflect the aggressiveness and proliferation capacity of the primary tumor. A CAM-based PDX model using cCSC provides a fast, low-cost, easy to handle, and powerful preclinical platform for drug screening, therapy optimization, and biomarker discovery.

Keywords: CAM-assay; cCSCs; tumorspheres; PDX; breast cancer

check for updates

Citation: Pizon, M.; Schott, D.; Pachmann, U.; Schobert, R.; Pizon, M.; Wozniak, M.; Bobinski, R.; Pachmann, K. Chick Chorioallantoic Membrane (CAM) Assays as a Model of Patient-Derived Xenografts from Circulating Cancer Stem Cells (cCSCs) in Breast Cancer Patients. *Cancers* **2022**, *14*, 1476. https://doi.org/10.3390/cancers14061476

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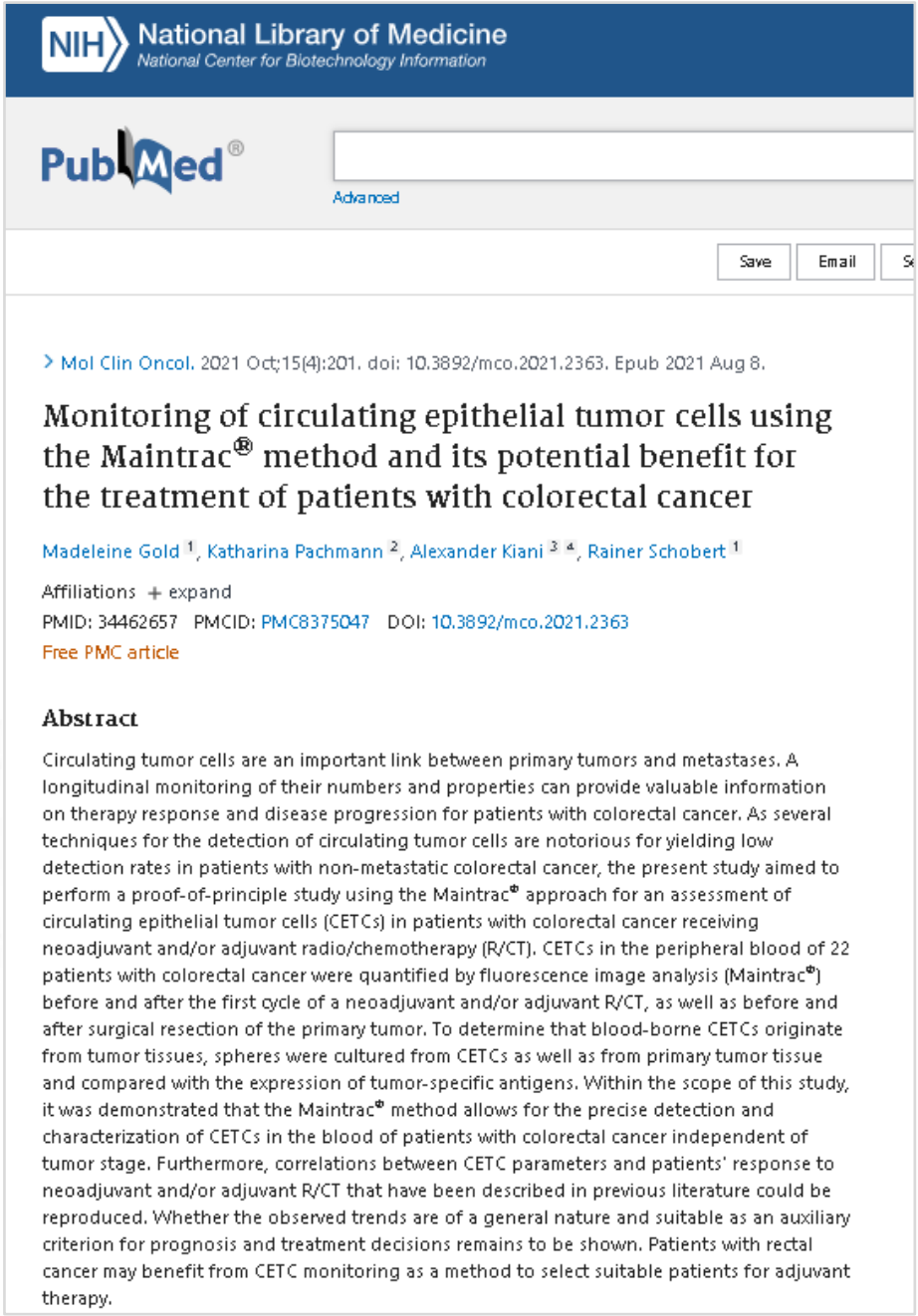
Monitoramento de células tumorais epiteliais circulantes pelo método Maintrac® e seu potencial benefício no tratamento de pacientes com câncer colorretal

Curr Oncol, 2021 Dec 24 ; 30(1):261-273. doi: 10.3390



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> Mol Clin Oncol. 2021 Oct;15(4):201. doi: 10.3892/mco.2021.2363. Epub 2021 Aug 8.

Monitoring of circulating epithelial tumor cells using the Maintrac® method and its potential benefit for the treatment of patients with colorectal cancer

Madeleine Gold [1], Katharina Pachmann [2], Alexander Kiani [3 4], Rainer Schobert [1]

Affiliations + expand

PMID: 34462657 PMCID: PMC8375047 DOI: 10.3892/mco.2021.2363

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Abstract

Circulating tumor cells are an important link between primary tumors and metastases. A longitudinal monitoring of their numbers and properties can provide valuable information on therapy response and disease progression for patients with colorectal cancer. As several techniques for the detection of circulating tumor cells are notorious for yielding low detection rates in patients with non-metastatic colorectal cancer, the present study aimed to perform a proof-of-principle study using the Maintrac® approach for an assessment of circulating epithelial tumor cells (CETCs) in patients with colorectal cancer receiving neoadjuvant and/or adjuvant radio/chemotherapy (R/CT). CETCs in the peripheral blood of 22 patients with colorectal cancer were quantified by fluorescence image analysis (Maintrac®) before and after the first cycle of a neoadjuvant and/or adjuvant R/CT, as well as before and after surgical resection of the primary tumor. To determine that blood-borne CETCs originate from tumor tissues, spheres were cultured from CETCs as well as from primary tumor tissue and compared with the expression of tumor-specific antigens. Within the scope of this study, it was demonstrated that the Maintrac® method allows for the precise detection and characterization of CETCs in the blood of patients with colorectal cancer independent of tumor stage. Furthermore, correlations between CETC parameters and patients' response to neoadjuvant and/or adjuvant R/CT that have been described in previous literature could be reproduced. Whether the observed trends are of a general nature and suitable as an auxiliary criterion for prognosis and treatment decisions remains to be shown. Patients with rectal cancer may benefit from CETC monitoring as a method to select suitable patients for adjuvant therapy.

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O valor de monitorar o comportamento da circulação Células tumorais no final da terapia endócrina em Pacientes com câncer de mama

Cancers (Basel). 2018 Nov; 10(11): 407.

cancers MDPI

Cancers (Basel). 2018 Nov; 10(11): 407.
Published online 2018 Oct 29. doi: 10.3390/cancers10110407

PMCID: PMC6266844
PMID: 30380648

The Value of Monitoring the Behavior of Circulating Tumor Cells at the End of Endocrine Therapy in Breast Cancer Patients

Katharina Pachmann[1,*] and Stefan Schuster[2]

Abstract

Go to: ▸

After five years of endocrine therapy, patients with ER+ (estrogen receptor positive) breast cancer face the question of the benefit of further treatment. Ten years of endocrine therapy has been demonstrated to improve survival compared to five years. However, the individual benefit of continuation remains unclear. Therefore, markers for predicting benefit from endocrine treatment and extended endocrine treatment are desperately needed. In this study the dynamics over time of the tumor cells circulating in peripheral blood of patients, circulating tumor cells/ circulating epithelial tumor cells (CTC/CETC), as the systemic part of the tumor were investigated in 36 patients with ER+ primary breast cancer. CTC/CETCs were monitored serially during and after endocrine therapy. After termination of endocrine therapy 12 patients showed an increase in CTC/CETCs, with 8 of 12 suffering relapse. No change or a reduction was observed in 24 patients, with 2 of 24 suffering relapse. Initial tumor size was marginally prognostic ($p = 0.053$) but not nodal status nor the mere number of CTC/CETCs. Only the trajectory of CTC/CETCs was a statistically significant predictor of relapse free survival (increasing cell numbers: mean = 940 days vs. stable/decreasing cell numbers mean not reached). Individual cases demonstrated that an increase of CTC/CETCs after discontinuation of tamoxifen therapy could be stopped by resuming the endocrine therapy.

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→

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O dia da coleta do sangue (15ml) é agendado em laboratório local, no consultório ou na casa do paciente.

→

No mesmo dia da coleta, a transportadora recolhe a amostra e entrega no laboratório na Alemanha em 72 horas.

→

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