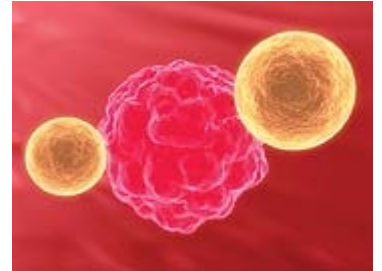


Circulating Tumor Cell Assays: A Major Advance in Cancer Treatment

By Steven Nemeroff, ND

CIRCULATING TUMOR CELLS PREDICT TREATMENT EFFECTIVENESS

One of the most exciting potential uses of CTC technology is to allow doctors to evaluate treatment effectiveness during the early phase of therapy. Historically, cancer treatment decisions have been based on the results of large studies comparing the effectiveness of different treatment regimens. These studies have shown which treatments are statistically likely to produce the best results for a large number of people. However, these treatment guidelines do not predict how an *individual* person with cancer will respond to a given treatment.



For many cancer patients, the course of the disease, and the response to treatment, can be highly unpredictable. One person might have an excellent response to a given chemotherapy regimen, while for another person the same regimen might not have any effect at all. For this reason, it is extremely important to have the ability to quickly evaluate a person's response to treatment. Ideally, doctors would obtain this information during the early course of therapy. If the cancer is not responding to treatment then appropriate treatment changes can be made. Another very important consideration is the significant toxicity that is associated with cancer treatment. If it can be determined that a treatment is ineffective during the early stage of therapy, then the treatment can be discontinued before it can cause severe toxicity.

Up until now, doctors have often had to wait at least a few months before they can assess the effectiveness of treatment. This inability to evaluate a treatment's efficacy during the early phase of therapy can have disastrous consequences for the person with cancer. Those three months of waiting to know if the treatment is working can make the difference between altering therapy to reflect the lack of response, or continuing with an ineffective treatment and allowing the cancer to progress. This waiting may become a thing of the past, as recent studies have demonstrated that CTC testing can reliably predict the response to treatment during the early phase of therapy.

In an important study,¹¹ 163 women with metastatic breast cancer were tested for CTC at baseline and at four different times during the course of treatment. The researchers discovered that those patients with less than 5 CTC at the first measurement had a median overall survival of greater than 18.5 months. Those with 5 or more CTC had a median overall survival of only 7 months. As early as 4 weeks into therapy, CTC testing determined which patients were not responding and whose cancer would continue to progress with ineffective treatment.

The authors of this study concluded that "detection of elevated CTC at any time during therapy is an accurate indication of subsequent rapid disease progression and mortality for metastatic breast cancer patients."

In a related study,¹⁰ 138 women with metastatic breast cancer had CTC measured 4 weeks after the start of therapy. The median overall survival for those with 5 or more CTC was 8.5 months. Those with a CTC count less than 5 had a substantially greater median overall survival time of 22.6 months! Also, 84% of those with a CTC count less than 5 were alive after one year, compared to only 38% for those with a CTC count of 5 or more. The findings of these studies illustrate the tremendous potential of CTC testing to accurately predict the effectiveness of treatment during the early stage of therapy.

CIRCULATING TUMOR CELLS PREDICT RISK OF RELAPSE

One of the most important questions a person has after they receive treatment for their breast cancer is, "What is the likelihood that I will have a relapse?" Although statistical predictions for relapse can be made for large groups of people, this is a question that doctors are not able to answer with great accuracy for the individual woman with breast cancer.

However, a growing number of studies have revealed that CTC testing can accurately predict the likelihood of recurrence in breast cancer patients after they receive treatment.



In 2006, scientists in Spain measured the presence of CTC in 84 high-risk breast cancer patients after they received initial chemotherapy.¹² The researchers found dramatic differences in the relapse rates between those who tested positive for CTC, as compared to those that did not have any CTC detected in their blood. The group testing positive for CTC had a 269% increased risk of relapse, and a **300% increased risk of death**, compared to the group testing negative for CTC! Further analysis showed a striking 53 month difference in the time to relapse between the groups.

In a related study,¹³ German scientists in 2008 studied 25 women with breast cancer that had not metastasized. They measured CTC levels before and after the patients received chemotherapy. The results showed that relapse occurred in **less than 10%** of patients whose CTC levels indicated a decline, no change, or minor increase when compared to baseline CTC levels. There was a substantially higher relapse rate of 40% in the group with a CTC increase at the end of therapy.

The same German scientists then completed a study of 91 non-metastatic breast cancer patients receiving chemotherapy.¹⁴ Measurements of CTC were taken before, during, and after the completion of chemotherapy. After a follow-up period of 40 months, 20 of the women had experienced a relapse. The investigators determined that the group with a greater than 10-fold decrease in CTC after treatment had a relapse rate of only 3.6%! The group that experienced a greater than 10-fold increase in CTC after treatment experienced an alarming relapse rate of 42.4%. The results of this study can have far-reaching implications for breast cancer patients in the future, as those with a greater than 10-fold increase in CTC after therapy are at much higher risk of relapse and might be candidates for more aggressive treatment. These researchers concluded that “...circulating tumor cells are influenced by systemic chemotherapy and that an increase... 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.”

SUMMARY

A number of studies have demonstrated the impressive ability of CTC testing to provide essential information for cancer patients at various stages during their evaluation and treatment. CTC testing can improve prognostic accuracy, predict risk of relapse after treatment, and allow doctors to monitor treatment effectiveness in real time.

As we look into the future of cancer assessment and treatment, it's easy to see how CTC testing will allow us to move beyond the traditional focus on the primary tumor. Major advances can occur as medical science focuses on CTC and targets treatments against the specific characteristics of these cells. Fortunately, the person dealing with cancer does not have to wait for the future, as CTC testing is available now for those who want to take advantage of this new technology and benefit from the vital information this testing provides.

To inquire about laboratories that offer circulating tumor cell (CTC) assay blood tests in the United States, call 1-800-208-3444. (Information about the more advanced CTC/molecular analysis tests available in Germany appears in the **next article**.)

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

References

1. Meng S, Tripathy D, Shete S, et al. HER-2 gene amplification can be acquired as breast cancer progresses. Proc Natl Acad Sci USA. 2004 Jun 22;101(25):9393-8.
2. Wülfing P, Borchard J, Buerger H, et al. HER2-positive circulating tumor cells indicate poor clinical outcome in stage I to III breast cancer patients. Clin Cancer Res. 2006 Mar 15;12(6):1715-20.
3. Cristofanilli M, Broglio KR, Guarneri V, et al. Circulating tumor cells in metastatic breast cancer: biologic staging beyond tumor burden. Clin Breast Cancer. 2007 Feb;7(6):471-9.
4. Moreno JG, Miller MC, Gross S, et al. Circulating tumor cells predict survival in patients with metastatic prostate cancer. Urology. 2005 Apr;65(4):713-8.
5. Tombal B, Van Cangh PJ, Loric S, et al. Prognostic value of circulating prostate cells in patients with a rising PSA after radical prostatectomy. Prostate. 2003 Aug 1;56(3):163-70.

6. Pound CR, Partin AW, Eisenberger MA, et al. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA*. 1999;281:1591-7.

7. Halabi S, Small EJ, Hayes DF, et al. Prognostic significance of reverse transcriptase polymerase chain reaction for prostate-specific antigen in metastatic prostate cancer: a nested study within CALGB 9583. *J Clin Oncol*. 2003 Feb 1;21(3):490-5.

8. Danila DC, Heller G, Gignac GA, et al. Circulating tumor cell number and prognosis in progressive castration-resistant prostate cancer. *Clin Cancer Res*. 2007 Dec 1;13(23):7053-8.

9. Olsson CA, De Vries GM, Benson MC, et al. The use of RT-PCR for prostate-specific antigen assay to predict potential surgical failures before radical prostatectomy: molecular staging of prostate cancer. *Br J Urol*. 1996 Mar;77(3):411-7.

10. Budd GT, Cristofanilli M, Ellis MJ, et al. Circulating tumor cells versus imaging--predicting overall survival in metastatic breast cancer. *Clin Cancer Res*. 2006 Nov 1;12(21):6403-9.

11. Hayes DF, Cristofanilli M, Budd GT, et al. Circulating tumor cells at each follow-up time point during therapy of metastatic breast cancer patients predict progression-free and overall survival. *Clin Cancer Res*. 2006 Jul 15;12(14 Pt 1):4218-24.

12. Quintela-Fandino M, Lopez JM, Hitt R, et al. Breast cancer-specific mRNA transcripts presence in peripheral blood after adjuvant chemotherapy predicts poor survival among high-risk breast cancer patients treated with high-dose chemotherapy with peripheral blood stem cell support. *J Clin Oncol*. 2006 Aug 1;24(22):3611-8.

13. Pachmann K, Dengler R, Lobodasch K, et al. An increase in cell number at completion of therapy may develop as an indicator of early relapse : Quantification of circulating epithelial tumor cells (CETC) for monitoring of adjuvant therapy in breast cancer. *J Cancer Res Clin Oncol*. 2008 Jan;134(1):59-65.

14. Pachmann K, Camara O, Kavallaris A, et al. Monitoring the response of circulating epithelial tumor cells to adjuvant chemotherapy in breast cancer allows detection of patients at risk of early relapse. *J Clin Oncol*. 2008 Mar 10;26(8):1208-15.

All Contents Copyright © 1995-2010 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.

Copyright of Life Extension is the property of Life Extension Foundation and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.