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EGFR and HER2-neu predict response to metronomic chemotherapy

From: **Rich Reilly** (richreilly@hotmail.com)
Sent: Sun 10/25/09 9:08 PM
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EGFR and HER2-neu predict response to metronomic chemotherapy

Published date : 31/07/2007

MedWire News: Serum levels of the human epidermal growth factor receptors 1 (EGFR) and 2 (Her2-neu) have been shown to predict response to metronomic chemotherapy in women with metastatic breast cancer.

Research published in the journal Cancer shows that low serum levels of EGFR before the start of chemotherapy and elevated HER2-neu levels 2 months post-treatment are associated with a reduced response rate and worse prognosis in terms of progression-free survival (PFS) and overall survival (OS).

Italian researchers from the European Institute of Oncology in Milan prospectively evaluated the prognostic and predictive role of serum EGFR and serum HER2-neu in a phase III trial of advanced breast cancer patients treated with low-dose "metronomic" chemotherapy.

In the trial, 178 women were randomized to receive oral cyclophosphamide (50 mg, once daily) and methotrexate (2.5 mg, twice daily) on days 1 and 4 every week with or without oral thalidomide (200 mg, once daily). No differences in PFS or OS were noted among the two treatment arms, so the patients were treated as a single cohort.

Serum levels of EGFR and HER2-neu were assessed before and after 2 months' treatment. Although elevated (>15 ng/ml) HER2-neu at baseline was not associated with response rates, values at 2 months were. HER2-neu levels at 2 months were significantly higher than at baseline in women who had progressive disease (20.7 vs 41.3 ng/ml, p=0.045), and were significantly associated with worse prognosis.

"Upon multivariate analysis an increase of serum HER2-neu =20% after 2 months of therapy resulted in an independent prognostic factors for PFS," Maria Teresa Sandri and colleagues report.

Indeed, they found that women with an increase in serum HER2-neu of 20% or more and with levels higher than 15 ng/ml at 2 months had a PFS of 2.9 months, whereas those with elevations under this cut-off point had a PFS of 14.9 months.

Serum EGFR levels did not change significantly from baseline to the 2 month assessment, and did not alter much over the course of chemotherapy. However, low EGFR levels (<45 ng/ml) at baseline were predictive of lower response rates at 2 months and at 24 weeks (p=0.22). "Moreover they were significantly associated with reduced PFS and OS," says the team.

Sandri et al conclude: "The results of this study indicate that serum HER2-neu and serum EGFR are useful for predicting the response to the treatment and the long-term clinical outcome in metastatic breast cancer patients treated with metronomic chemotherapy."

They add: "The values of these markers should be further explored in prospective and possibly multicenter trials involving new agents with anti-angiogenic activity such as bevacizumab, administered either alone or on combination with chemotherapy."

Hidden HER-2/neu-positive breast cancer: How to maximize detection.

From: **Rich Reilly** (richreilly@hotmail.com)
Sent: Sun 10/25/09 9:05 PM
To: Rich Reilly (richreilly@hotmail.com)

1: IDrugs. 2009 Apr;12(4):238-42.Links

Hidden HER-2/neu-positive breast cancer: How to maximize detection.

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The HER-2/neu oncoprotein is an important cellular target for the development of a variety of ted therapies for HER-2/neu-positive breast cancer. Methods for tumor analysis such as ınohistochemistry (IHC) or fluorescence in situ hybridization (FISH) are routinely used to determine lER-2/neu status of patients with breast cancer and their eligibility for HER-2/neu-targeted therapies, as trastuzumab (Herceptin) and lapatnib (Tykerb). In a January 2008 article in the Wall Street ıal, it was reported that breast cancer patients may be receiving the wrong treatments or no treatment ıse of errors in the laboratory tests (IHC/FISH) that are widely used to determine the HER-2/neu s of breast cancers. Numerous reports have demonstrated that 20 to 30% of patients with primary st cancer have HER-2/neu positive tumors. However, several studies have also shown that **up to 40% tients who are designated HER-2/neu negative with primary tumor analysis by IHC/FISH are ally HER-2/neu positive when the corresponding metastatic tumor is also evaluated by FISH. Studies have also demonstrated that up to 40% of patients with breast cancer who have R-2/neu-negative primary tumor as determined by IHC/FISH can develop elevated levels (> g/ml) of the circulating HER-2/neu oncoprotein during metastasis. Therefore, elevated serum -2/neu levels can be used to alert physicians of the possible presence of HER-2/neu-positive st cancer in patients who have been previously classified as HER-2/neu negativ**e. Collectively, studies identify a population of women designated HER-2/neu negative that could have HER-2/neu-ive breast cancer, but have not been eligible for targeted therapies such as trastuzumab and lapatinib. ıen who are incorrectly classified as HER-2/neu negative, but are also ineligible for approved -2/neu-targeted therapies, may also not be considered for clinical trials of additional HER-2/neu pies in development. Several studies have also demonstrated that serum HER-2/neu can be elevated in ıts with early breast cancer, and up to 90% of patients with HER-2/neu-positive metastatic breast er can have elevated serum HER-2/neu levels. These studies have also revealed that the frequency of ıts who have HER-2/neu-positive breast cancer is greater than indicated previously by IHC/FISH. , the number of patients classified incorrectly as HER-2/neu negative could be substantially greater recognized previously. This feature review presents a HER-2/neu testing algorithm that combines the n HER-2/neu test result with IHC/FISH test results to maximize the identification of patients who are -2/neu positive and could be potential candidates for HER-2/neu-targeted therapies. **The HER-2/neu tion also exemplifies that multiple diagnostic tools are required to correctly and accurately tify patients for targeted therapies** - an important lesson as many new biomarkers are identified for ıultitude of new targeted therapies in development for various forms of cancers.

HER1-4 protein concentrations in normal breast tissue from breast cancer

patients are expressed by the same profile as in the malignant tissue.

From: **Rich Reilly** (richreilly@hotmail.com)
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1: Clin Chem Lab Med. 2009;47(8):977-84.  Links

HER1-4 protein concentrations in normal breast tissue from breast cancer patients are expressed by the same profile as in the malignant tissue.

Olsen DA, **Ostergaard B**, **Bokmand S**, **Wamberg PA**, **Jakobsen EH**, **Jakobsen A**, **Brandslund I**.
Department of Clinical Biochemistry, Vejle County Hospital, Vejle, Denmark.
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BACKGROUND: The epidermal growth factor receptor HER2 is overexpressed or amplified in 25%-30% of patients with breast cancer. The mechanism behind HER2 amplification is unknown, but may be a patho-physiological phenomenon caused by continuous stimulation and activation of the HER1-4 system. We have mapped the protein concentrations of HER1-4 in breast cancer tissue, autologous reference tissue, normal breast tissue and serum samples, to see whether non-cancer cells from these patients express a protein profile indicating general activation. METHODS: Tissue samples from malignant and adjacent normal breast tissue (autologous reference tissue) were collected from 118 women consecutively admitted for surgical treatment of breast cancer. In addition, 26 samples of normal breast tissue were collected from healthy women having breast reduction surgery. The tissue samples were homogenized and the proteins extracted. The **tissue and serum concentrations of HER1-4 were determined quantitatively using a commercially available enzyme linked immunosorbent assay (ELISA) method. RESULTS: HER1 was down regulated in cancer tissue when compared to autologous reference tissue (p=8 x 10(-6)), while HER2 (p<10(-7)) and HER3 (p=3 x 10(-5)) were up regulated. Comparing autologous reference tissue with normal tissue showed down regulation of HER1 (p=0.122) and up regulation of HER2 (p=10(-6)), HER3 (p<10(-7)) and HER4 (p<10(-7))**. Furthermore, we observed that correlations between the receptor combinations HER1-2, HER1-3 and HER1-4 were maintained from normal breast tissue to autologous reference breast tissue, but were lost in cancer tissue. CONCLUSIONS: We suggest that these findings indicate that breast cancer is a systemic disease where the HER1-4 system in autologous reference tissue is continuously activated, thus favoring the subsequent development of cancer.

PMID: 19548848

Circulating tumor cells in blood of primary breast cancer patients assessed by a novel RT-PCR test kit and comparison with status of bone marrow-disseminated tumor cells/AdnaTest TumorStemCell and AdnaTest EMT

From: **Rich Reilly** (richreilly@hotmail.com)
Sent: Sat 10/24/09 12:13 AM
To: Rich Reilly (richreilly@hotmail.com)
Attachments:
AdnaTest and TumorStemCell.pdf (196.7 KB)

1: Breast Cancer Res. 2009 Oct 9;11(5):109. [Epub ahead of print] Links

Circulating tumor cells in blood of primary breast cancer patients assessed by a novel RT-PCR test kit and comparison with status of bone marrow-disseminated tumor cells.

Schmitt M, **Foekens JA**.
Clinical Research Unit of the Department of Obstetrics and Gynecology, Technische Universitaet Muenchen, Klinikum rechts der Isar, Ismaninger Strasse 22, D-81675 Munich, Germany. manfred.schmitt@lrz.tum.de.

ABSTRACT: In breast cancer, circulating tumor cells (CTCs)/disseminated tumor cells (DTCs) may serve as independent adverse prognostic variables, to monitor the course of the disease and to predict response or failure to cancer therapy. Most of the techniques to enumerate DTCs in the bone marrow or CTCs in the bloodstream of breast cancer patients rely on a combination of an enrichment step and a detection step. **A novel RT-PCR method, the AdnaTest BreastCancer kit, was developed for the enrichment of CTCs from peripheral blood of breast cancer patients followed by identification of CTC-associated marker transcripts by reverse transcription and PCR.** Although this test has been demonstrated to identify breast cancer patients at risk, standardization of this technique and direct comparison with other established breast cancer CTC enrichment and detection techniques is still lacking, but highly needed. This is done best within prospective clinical trials, such as in the ongoing DETECT, SUCCESS, and BR-01-2004 trials.

PMID: 19833005 [PubMed - as supplied by publisher]

From: richreilly@hotmail.com
To: richreilly@hotmail.com
Subject: AdnaTest TumorStemCell and AdnaTest EMT
Date: Sat, 24 Oct 2009 00:09:46 -0500

AdnaTest TumorStemCell and AdnaTest EMT

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Due to the fact, that metastazation requires a dissemination of tumor stem cells or tumor cells showing EMT, it seems likely that such cells should be detectable amongst the CTC found in the circulation of cancer patients. The detection and characterisation of CTC that show an EMT or stem cell like metabolism could be a powerful diagnostic tool for the early determination of therapy failure or the potential risk of resistance to a given therapeutic intervention. To address this AdnaGen developed 2 research kits for the detection of EMT markers PI3Kα, Akt2 and Twist and for the analysis of the tumor stem cell marker ALDH1, respectively.

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When CTC from metastatic breast cancer patients were analysed by RT-PCR for ALDH1 an over-expression was detected in a substantial amount of samples (Fig. 2). This indicates that CTC might often display tumor stem cell characteristics highlighting their role in metastasis formation. The ALDH1 over-expression allows to analyse the impact of this phenotype changes with regards to prognosis, therapy failure and metastasis formation.

Evaluation of circulating tumor cells in patients with breast cancer: multi-institutional clinical trial in Japan.

From: **Rich Reilly** (richreilly@hotmail.com)
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1: Int J Clin Oncol. 2008 Jun;13(3):252-6. Epub 2008 Jun 14. SpringerLink FULL-TEXT ARTICLE Links

Evaluation of circulating tumor cells in patients with breast cancer: multi-institutional clinical trial in Japan.

Yagata H, **Nakamura S**, **Toi M**, **Bando H**, **Ohno S**, **Kataoka A**.
Department of Breast Surgical Oncology, St Luke's International Hospital, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan. yagata@mvh.biglobe.ne.jp

BACKGROUND: With the development of the CellSearch System, it has become possible to measure circulating tumor cell (CTC) levels with high reproducibility, and the CTC test is currently being used clinically for patients with metastatic breast cancer in the United States. It is imperative that the clinical significance of the CTC test also be examined in Japan. METHODS: Using the CellSearch System, CTC levels were evaluated in 57 healthy individuals and patients with benign breast disease; 30 patients with primary breast cancer (stages 1-3); and 38 patients with metastatic breast cancer. First, the relationship between CTC levels and the presence of metastasis was examined using a cutoff score of 2 CTCs per 7.5 ml whole blood. Then, the patients with metastatic breast cancer were divided into two groups, using a cutoff score of 5 CTCs per 7.5 ml blood, and progression-free survival (PFS) and overall survival (OS) were compared in the two groups. RESULTS: When the clinical cutoff score was set at 2 CTCs per 7.5 ml blood, 0% of the healthy individuals and patients with benign breast disease (0/57), 3.3% of the patients with primary breast cancer (1/30), and 50% of the patients with metastatic breast cancer (19/38) were identified as as having 2 CTCs per 7.5 ml blood. Additionally, with a cutoff score of 5 CTCs, 11 patients were reported to have 5 or more CTCs and both PFS (P = 0.0036) and OS (P = 0.04) were worse for this patient population than for the population with fewer than 5 CTCs. CONCLUSION: **As concluded in a similar clinical trial in the United States, for patients with breast cancer, measuring CTC levels can be both an accurate indicator of metastases and an important measure of patient prognosis.**

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Circulating tumor cells in HER-2 positive metastatic breast cancer patients treated with trastuzumab and chemotherapy.

From: **Rich Reilly** (richreilly@hotmail.com)
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1: Int J Biol Markers. 2009 Jan-Mar;24(1):1-10.Links

Circulating tumor cells in HER-2 positive metastatic breast cancer patients treated with trastuzumab and chemotherapy.

Nunes RA, **Li X**, **Kang SP**, **Burstein H**, **Roberts L**, **Carney W**, **Blackwell K**, **Ryan P**, **Borges V**, **Iglehart JD**, **Friedman P**, **Harris LN**.

Department of Cancer Biology/Adult Oncology, Dana-Farber Cancer Institute, Boston, MA, USA.

The detection of circulating tumor cells (CTCs) in peripheral blood may have important prognostic and predictive implications in breast cancer treatment. A limitation in this field has been the lack of a validated method of accurately measuring CTCs. While sensitivity has improved using RT-PCR, specificity remains a major challenge. The goal of this paper is to present a sensitive and specific methodology of detecting CTCs in women with HER-2 positive metastatic breast cancer, and to examine its role as a marker that tracks disease response during treatment with trastuzumab-containing regimens. The study included patients with HER-2-positive metastatic breast cancer enrolled on two different clinical protocols using a trastuzumab-containing regimen. Serial CTCs were measured at planned time points and clinical correlations were made. **Immunomagnetic selection of circulating epithelial cells was used to address the specificity of tumor cell detection using cytokeratin 19 (CK19). In addition, the extracellular domain of the HER-2 protein (HER-2/ECD) was measured to determine if CTCs detected by CK19 accurately reflect tumor burden. The presence of CTCs at first restaging was associated with disease progression.** We observed an association between CK19 and HER-2/ECD. **The association of HER-2/ECD with clinical response followed a similar pattern** to that seen with CK19. **Finally, the absence of HER-2/ECD at best overall response and a change of HER-2/ECD from positive at baseline to negative at best overall response was associated with favorable treatment response.** Our study **supports the prognostic and predictive role of the detection of CTCs in treatment of HER-2-positive metastatic breast cancer patients.** The association between CK19 and markers of disease burden is in line with the concept that CTCs may be a reliable measure of tumor cells in the peripheral blood of patients with metastatic breast cancer. The association of CTCs at first restaging with treatment failure indicates that CTCs may have a role as surrogate markers to monitor treatment response.

PMID: 19404916

Chemosensitivity profile assay of circulating cancer cells (CTCs): Prognostic and predictive value in epithelial tumors.

From: **Rich Reilly** (richreilly@hotmail.com)
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1: Int J Cancer. 2009 Oct 9. [Epub ahead of print] 

Links

Chemosensitivity profile assay of circulating cancer cells (CTCs): Prognostic and predictive value in epithelial tumors.

Gazzaniga P, **Naso G**, **Gradilone A**, **Cortesi E**, **Gandini O**, **Gianni W**, **Fabbri MA**, **Vincenzi B**, **di Silverio F**, **Frati L**, **Aglianò AM**, **Cristofanilli M**.
Dipartimento Medicina Sperimentale, Sapienza Università di Roma, Viale Regina Elena 324, 00161, Roma, Italy.

The prognostic value associated with the detection of circulating tumour cells (CTCs) in metastatic breast cancer by the Cell Search technology raise additional issues regarding the biological value of

this information. We postulated that a drug resistance profile of CTCs may predict response to chemotherapy in cancer patients and therefore could be being used for patient selection.One hundred five patients with diagnosis of carcinoma were enrolled in a prospective trial. **CTCs were isolated from peripheral blood and positive samples were evaluated for the expression of a panel of genes involved in anticancer drugs resistance. The drug resistance profile was correlated to disease free survival (patients in adjuvant setting) and time to progression (metastatic patients**) in a 24 months follow up. Objective response correlation was a secondary endpoint. Fifty-one percent of patients were found positive for CTCs, while all blood samples from healthy donors were negative. **The drug resistance profile correlates with disease free survival and time to progression (p<0.001 in both). Sensitivity of the test: able to predict treatment response in 98% of patients. Specificity of the test: 100%; no sample from healthy subject was positive for CTCs presence. Positive predictive value and negative predictive value were found to be 96.5% and 100% respectively. We identified a drug resistance profile of CTCs, which is predictive of response to chemotherapy, independent of tumour type and stage of disease. This approach may represent a first step toward the individualization of chemotherapy in cancer patients.** (c) 2009 UICC.

PMID: 19821489

Circulating Tumor Cells: A Useful Predictor of Treatment Efficacy in Metastatic Breast Cancer.

From: **Rich Reilly** (richreilly@hotmail.com)
Sent: Fri 10/23/09 7:29 PM
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1: J Clin Oncol. 2009 Sep 14. [Epub ahead of print] Full Text J Clin Oncol Links

Circulating Tumor Cells: A Useful Predictor of Treatment Efficacy in Metastatic Breast Cancer.

Liu MC, **Shields PG**, **Warren RD**, **Cohen P**, **Wilkinson M**, **Ottaviano YL**, **Rao SB**, **Eng-Wong J**, **Seillier-Moiseiwitsch F**, **Noone AM**, **Isaacs C**.
Lombardi Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC; Northern Virginia Medical Oncology and Hematology Associates, Fairfax, VA; and Harry and Jeanette Weinberg Cancer Institute, Franklin Square Hospital Center, Baltimore, MD.

PURPOSE: Five or more circulating tumor cells (CTCs) per 7.5 mL of blood predicts for poorer progression-free survival (PFS) in patients with metastatic breast cancer (MBC). We conducted a prospective study to demonstrate that CTC results correlate strongly with radiographic disease progression at the time of and in advance of imaging. PATIENTS AND METHODS: Serial CTC levels were obtained in patients starting a new treatment regimen for progressive, radiographically measurable MBC. **Peripheral blood was collected for CTC enumeration at baseline and at 3- to 4-week intervals. Clinical outcomes were based on radiographic studies performed in 9- to 12-week intervals.** RESULTS: Sixty-eight patients were evaluable for the CTC-imaging correlations, and 74 patients were evaluable for the PFS analysis. Median follow-up was 13.3 months. **A statistically significant correlation was demonstrated between CTC levels and radiographic disease progression in patients receiving chemotherapy or endocrine therapy.** This correlation applied to CTC results obtained at the time of imaging (odds ratio [OR], 6.3), 3 to 5 weeks before imaging (OR, 3.1), and 7 to 9 weeks before imaging (OR, 4.9). Results from analyses stratified by type

of therapy remained statistically significant. Shorter PFS was observed for patients with five or more CTCs at 3 to 5 weeks and at 7 to 9 weeks after the start of treatment. CONCLUSION: We provide, to our knowledge, the first evidence of a **strong correlation between CTC results and radiographic disease progression in patients receiving chemotherapy or endocrine therapy for MBC. These findings support the role of CTC enumeration as an adjunct to standard methods of monitoring disease status in MBC**.

PMID: 19752342

Veridex's Cellsearch® Circulating Tumor Cell Test Wins Prestigious Prix Galien Award for Best Medical Technology

From: **Rich Reilly** (richreilly@hotmail.com)
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Veridex's Cellsearch® Circulating Tumor Cell Test Wins Prestigious Prix Galien Award for Best Medical Technology

Reinforces the Unique Innovation of CellSearch® Technology in Predicting the Prognosis of Patients with Metastatic Breast, Colorectal or Prostate Cancer

1 Oct 2009 , Raritan, N.J. : Veridex, LLC announced today that the CellSearch® Circulating Tumor Cell (CTC) Test was honored with the first-ever Prix Galien USA 2009 Award for Best Medical Technology.

The CellSearch® System is the first diagnostic test used to automate the capture and detection of CTCs, tumor cells that have detached from solid tumors and entered the patient's blood. The CellSearch® System assesses CTCs to determine the prognosis and overall survival of patients with metastatic breast, colorectal or prostate cancer at any time during the course of treatment.

"The CellSearch® System represents an important shift in the management of metastatic breast, colorectal or prostate cancer as an adjunct to standard testing methods that provides a more complete picture of patient prognosis," said Michael Samoszuk, M.D., Chief Medical Officer, Ortho Clinical Diagnostics. "The Prix Galien recognition further supports the important role CellSearch® technology plays in providing oncologists with an additional tool to help them provide optimum care for their patients."

Prix Galien USA Award candidates are evaluated on the basis of the innovative nature of the development and applicability of the technology and whether the discovery can be applied to future biomedical science. The Prix Galien USA Awards committee – which includes seven Nobel Laureates – recognizes the technical, scientific and clinical research skills essential for developing innovative medicines and technologies that make positive contributions to human health. The Prix Galien USA Award is considered the industry's

highest accolade for research and development.

About CellSearch® Technology
The CellSearch® CTC Test works by using antibodies that are joined to microscopic iron particles, called ferrofluid. These antibody/ferrofluid combinations attach very specifically to CTCs. Powerful magnets then draw the CTCs out of the blood sample and they are then stained with additional bio-molecules and chemicals so that they can be positively identified as CTCs.

CellSearch® results should be used in conjunction with all clinical information derived from diagnostic tests (e.g., imaging, laboratory tests), physical examination and complete medical history in accordance with appropriate patient management procedures. The CellSearch® test has not been approved to demonstrate that any line of therapy is any more/less effective than any other or no therapy. CellSearch® results and imaging results are not equivalent in assessing the transition of patients between non-progressive disease and progressive disease.

For further information on intended use, warnings and limitations, please refer to the CellSearch® CTC Test Instructions for Use, or visit www.veridex.com.

Circulating Breast Cancer Cells Validated as Index of Metastases

From: **Rich Reilly** (richreilly@hotmail.com)
Sent: Thu 10/15/09 12:56 PM
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Messages from
Dorothy J. Schirf, MD
Medical Writer, MDLinx Oncology

MDLinx

Circulating Breast Cancer Cells Validated as Index of Metastases 10/2/2009

Results of a prospective study, emanating from the Lombardi Comprehensive Cancer Center at Georgetown, have apparently provided solid support for the use of circulating tumor cell (CTC) counts in assessing the progression of metastatic breast cancer. Using commercially available CellSearch® technology, the trial was aimed at monitoring the therapeutic course of patients embarking on various new regimens for their metastatic disease. CTC analyses at baseline and each three to four weeks were compared with standard, but less frequent, radiographic determinations of treatment efficacy.
The researchers ultimately confirmed that a value of five or more CTCs per 7.5 ml of blood (as noted in prior investigations) is a significant marker of disease progression. Furthermore, they found evidence of treatment failure via CTC count in advance of the scheduled imaging tests. Ramifications of these findings for the nature/timing of patient therapy and monitoring are considerable, translating into both quality-of-life and cost benefits.

Clinical implementation of soluble EGFR (sEGFR) as a theragnostic serum

biomarker of breast, lung and ovarian cancer.

From: **Rich Reilly** (richreilly@hotmail.com)
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1: IDrugs. 2009 May;12(5):302-8. Links

Clinical implementation of soluble EGFR (sEGFR) as a theragnostic serum biomarker of breast, lung and ovarian cancer.

Baron AT, **Wilken JA**, **Haggstrom DE**, **Goodrich ST**, **Maihle NJ**.
University of Kentucky, Department of Internal Medicine, Lucille P Markey Cancer Center, 800 Rose Street, Lexington, KY 40536, USA. abaro2@uky.edu

Signal transduction pathways regulated by the EGFR/ERBB/HER proto-oncogene family and receptor tyrosine kinases encoded by these genes are known to become dysregulated during cellular transformation and carcinogenesis. Consequently, biologically targeted antibodies and tyrosine kinase inhibitors directed toward EGFR/ErbB1/HER1 (eg, cetuximab, erlotinib and gefitinib) and ErbB2/HER2 (eg, trastuzumab), and more recently toward ErbB3/HER3 and ErbB4/HER4, are being investigated as therapeutic agents for treating patients with EGFR/ERBB/HER proto-oncogene-driven malignancies. The accurate selection of patients who will respond efficaciously to these agents a priori is a medical challenge. Understanding the clinical utility of soluble EGFR/ErbB/HER (ie, sEGFR/sErbB/sHER) isoforms, which are present in circulatory fluids, as theragnostic cancer biomarkers is an emerging area of contemporary biomedical investigation. This feature article reviews the literature regarding the clinical utility of serum sEGFR/sErbB1/sHER1 in breast, lung and ovarian cancer, and discusses the potential role of sEGFR in predicting and monitoring therapeutic responsiveness, as well as disease recurrence, and/or predicting disease outcome in patients treated with specific small-molecule, hormonal or biotherapeutic drug regimens. Well-designed translational research studies are needed to validate sEGFR as a theragnostic biomarker further and to achieve routine clinical implementation.

PMID: 19431095 [PubMed - in process]