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**NEW Caris Target Now™ Breast Cancer Profiles**  
Individualizing Breast Cancer Treatment

See how the Caris Target Now™ Breast Cancer Profiles may help your patients.

SAN ANTONIO BREAST CANCER SYMPOSIUM • DECEMBER 8TH - 12TH



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Fourth Quarter 2010

## Welcome Colleague

*Caris Target Now News* – a quarterly publication of Caris Life Sciences – keeping you up-to-date about new procedures and advances.

**This is our inaugural issue of the *Caris Target Now News* newsletter and it's an exciting time at Caris Life Sciences.** We continue to advance the science that supports Caris Target Now through the addition of new biomarkers, the development of lineage-specific profiles, adding the most up-to-date clinical research, and in the ways we accept specimens.

We're excited that Caris Life Sciences' laboratories can accept tissue for molecular profiling for almost any specimen type available. That's a big story for us. Caris can accept specimens that are:

1. Fresh-frozen
2. Fresh in an RNA preservative
3. Fresh in Formalin
4. Formaline-fixed paraffin embedded (FFPE)

Caris has validated an RNA expression microarray that measures the expression levels of 24,000 genes in FFPE, fresh frozen and RNA preserved tissues.

We're making it as easy as possible for the oncologist to order Caris Target Now. If a patient has already undergone a prior procedure, we can do the entire profile on FFPE materials. If it's a new procedure, depending on the physician preferences and capabilities, we accept fresh frozen, fresh (in a preservative), or embedded in a block – whatever makes sense for the physician, the hospital laboratory and the patient.



We're introducing some lineage-specific biomarkers that will help physicians choose therapeutic options for patients with therapeutic ambiguities.

It's truly an exciting time at Caris. We hope you'll enjoy this newsletter detailing what we're doing to serve our customers and their patients. ●



“Oncologists commonly expect a one in twenty chance of patient response in 3rd- and 4th-line therapies.”  
– Dr. Jeff Edenfield

## Bisgrove Study Suggests Therapy Options Based on Caris Target Now™ Molecular Tumor Profiling Prolong Progression-Free Survival in Some Cancer Patients

A multi-center, prospective, pilot study published in *The Journal of Clinical Oncology* demonstrates that personalized cancer treatment tailored to a tumor's unique genetic make-up identified therapies that did increase progression-free survival (PFS) over previous therapies in 27% of patients with advanced disease. The study by Von Hoff et al was published online (October 2010) ahead of print (scheduled for December 2010) in *The Journal of Clinical Oncology* with an accompanying editorial.

The purpose of the study was to compare PFS using a treatment regimen based on the molecular profiling (MP) of a patient's tumor with the PFS for the most recent regimen on which the patient had experienced progression after taking that regimen for 6 weeks (i.e., the patient as his own control). Tissue samples from patients with refractory metastatic cancer were submitted for MP in two formats including:

- formalin-fixed tissue for immunohistochemistry and fluorescent in situ hybridization assays
- immediately frozen tissue for oligonucleotide microarray (MA) gene expression assays

The MP approach was found to have clinical benefit for the individual patient who had a PFS ratio (PFS on MP-selected therapy/PFS on prior therapy) of  $\geq 1.3$ .

### Among the 86 patients tumors that were profiled with Caris Target Now:

- 84 (98%) had a detected molecular target
- 66 of the 84 patients were treated with therapies that were linked to their MP results
- 18 (27%) of 66 patients had a PFS ratio of  $\geq 1.3$  (95% CI, 17% to 38%; one-sided, one-sample  $P = .007$ ).

The study concluded that it is possible to identify molecular targets in patients' tumors. In 27% of patients, the MP approach resulted in a longer PFS on a MP based regimen than on the regimen that was based on physicians choice. Limitations of the study included limited prior experience with patients as their own controls and overall patient attrition.

The study involved patients with various tumor types including breast, colorectal, ovarian and rare types of cancer. The investigators in the study utilized Caris Target Now molecular profiling, which is currently available to oncologists and their patients from Caris Life Sciences. “Oncologists commonly expect a one in twenty chance of patient response in 3rd- and 4th-line therapies,” said Dr. Jeff Edenfield, a practicing oncologist with US Oncology, and routine user of Caris Target Now. “This recent study suggests those odds can be improved to one in four when using therapeutic guidance provided by Caris Target Now.”

Since 2008, more than 10,000 cancer patients have received a Caris Target Now molecular profile. Caris Target Now has been designed to provide treating physicians with therapeutic options, often identifying anti-tumor agents that may not have been considered before. The Caris Target Now report is based on the genetic make-up of an individual patient's tumor cross-referenced with a vast and growing proprietary database of clinical literature, correlating genetic tumor information to therapeutic response. Using biomarker-based therapies has been linked to the likelihood of a positive patient response.

In the accompanying editorial, James H. Doroshow, MD, FACP, Director of Division of Cancer Treatment and Diagnosis, National Cancer Institute, commented that despite limitations, lessons can be learned from the study by Von Hoff et al. “First and foremost, this study vividly reminds us that the need for therapeutic intervention arises one patient at a time... Future investigators of new cancer therapies should learn from this initial effort and focus on how these rapidly evolving molecular tools can be used in the development of an entirely new investigative model for the systemic treatment of cancer.”

Caris Life Sciences is currently conducting and initiating additional studies of Caris Target Now molecular tumor profiling through collaboration with leading institutions and cancer centers. ●

1. Von Hoff DD, Stephenson JJ Jr, Rosen P, Loesch DM, Borad MJ, Anthony S, Jameson G, Brown S, Cantafio N, Richards DA, Fitch TR, Wasserman E, Fernandez C, Green S, Sutherland W, Bittner M, Alarcon A, Mallery D, Penny R. Pilot Study Using Molecular Profiling of Patients' Tumors to Find Potential Targets and Select Treatments for Their Refractory Cancers. *J Clin Oncol*. 2010 Oct 4. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed>
2. Doroshow JH. Selecting Systemic Cancer Therapy One Patient at a Time: Is There a Role for Molecular Profiling of Individual Patients with Advanced Solid Tumors? *J Clin Oncol*. 2010 Oct 4. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed>

## Significant Expansion to Panel of Breast Cancer Biomarkers Analyzed by Caris Target Now™ Includes 14 New Biomarkers

A significant expansion to the panel of breast cancer biomarkers analyzed by Caris Target Now includes 14 new biomarkers and aims to identify more relevant therapies for the major subtypes of breast cancer patients.

The recent biomarker updates are appropriate for patients with breast cancer molecular subtypes: hormone receptor positive/HER-2 negative; HER-2 positive; and triple-negative disease. Notable biomarker additions to the panel include TLE3, Ki67 and TOP2A by FISH; which have been associated with therapeutic response for commonly administered chemotherapies.

The Caris Target Now Evidence Team continues to accumulate and aggregate scientific literature at the pace of discovery as evidenced by the expansion of the biomarker panel. The ongoing process ensures that only the most relevant and appropriate information is included in the profile.

In addition to the anticipated benefit to breast cancer patients, the expanded panel will be of assistance to oncologists confronted by standard therapeutic ambiguities when treating their patients. These include patients that have exhausted the standard of care therapies, young patients with aggressive disease for whom time and treatment options may be limited, and patients with comorbidities that exclude certain therapies, such as diabetes and heart disease. ●

### Hot Biomarker - TLE3

#### The Clinical Problem:

Patients presenting with immunohistochemically defined triple-negative breast cancers (TNBCs) do not derive benefit from molecular-targeted treatments (endocrine therapy or anti-HER2 therapy) because they lack those molecular targets. However, TNBCs have been shown to respond to neoadjuvant chemotherapy with mixed sensitivity to anthracyclines and taxanes. As a result, taxanes such as paclitaxel and docetaxel have become the standard of care for first-line treatment of metastatic breast cancer and are frequently incorporated into both adjuvant and neoadjuvant anthracycline containing regimens. Unfortunately, the addition of taxanes to cytotoxic regimens is not always associated with improvement in patient outcomes – highlighting the need for a molecular target to help identify patients who may benefit from taxane therapy.

#### The Hot Biomarker:

TLE3 is emerging as a promising candidate “hot” biomarker for taxane response. TLE3 protein expression is associated with a lower risk of recurrence in patients treated with cytotoxic chemotherapy. In a 2009 study of TNBC patients receiving adjuvant chemotherapy at two independent institutions, TLE3 was associated with improved disease-free survival in patients receiving a taxane-containing regimen as opposed to anthracycline without taxane.

TLE3 is a biomarker to watch, and is now part of the Caris Target Now Breast Profile. ●

1. Kulkarni SA, Hicks DG, Watroba NL, Murekeyisoni C, Hwang H, Khoury T, Beck RA, Ring BZ, Estopinal NC, Schreeder MT, Seitz RS, Ross DT. TLE3 as a candidate biomarker of response to taxane therapy. *Breast Cancer Res*. 2009;11(2):R17. Epub 2009 Mar 23.
2. Masuda H, Masuda N, Kodama Y, Ogawa M, Karita M, Yamamura J, Tsukuda K, Doihara H, Miyoshi S, Mano M, Nakamori S, Tsujinaka T. Predictive factors for the effectiveness of neoadjuvant chemotherapy and prognosis in triple-negative breast cancer patients. *Cancer Chemother Pharmacol*. 2010 Jul 1. [Epub ahead of print]

The Caris Target Now Breast Profile is available today from Caris Life Sciences.