CARIS Dx™

TARGET NOW Accelerating the Delivery of Personalized Medicine

Target Now™ Frequently Asked Questions (FAQs) for Physicians

What is Target Now? Target Now utilizes advanced molecular profiling analysis to provide a more detailed molecular 'blueprint' of a patient's tumor as an aid to the treating oncologist. The comprehensive report provides information on unique molecular targets present and also describes potential associated treatment options from literature.

Through advanced DNA, RNA and protein analysis, Target Now typically identifies multiple unique genes, gene expressions and proteins in each patient's tumor. These targets are listed in order of expression within the tumor. Additionally, Target Now provides information on associated drugs, including non-standard-of care associations, that may potentially have greater efficacy or be resistant if these targets are present based on research publications and clinical studies.

Given the rapid pace of discoveries of biomarkers and their associations with therapies, Target Now is constantly evolving to incorporate the most current research findings. The physicians who request Target Now are invited to join the Target Now Physician Network, whereby they can offer insights into their experiences with the test as well as request research into new markers and therapeutic associations. Additionally, in certain circumstances, Target Now may be accessed through our ongoing research study.

Which of my patients can be tested with Target Now? It is up to the discretion of physicians to determine when to order Target Now. Suggested uses include:

- Patients refractory to second line standard of care therapy; or
- Patients with rare tumor types having less well-defined or 'research only' treatment protocols; or
- Select patients diagnosed with very aggressive cancers having a very high mortality rate with first line standard of care therapy (e.g., pancreatic cancer); or
- Select patients that have yet to undergo first line therapy but have significant co-morbidities that could preclude standard treatment options.

On what type of malignancies can Target Now provide information? Target Now can be run on patients with either solid or non-solid tumors. Because of the robustness and flexibility of the testing platforms, either formalin fixed paraffin-embedded (FFPE) and/or fresh frozen samples can be accepted.

Exactly what type of testing is performed with Target Now? Target Now looks at a 44,000 genes via DNA microarray analysis if fresh frozen samples are available and reports on what we consider the eighty (80) most potentially responsive or resistant gene targets. For FFPE samples, Target Now applies what we consider around twenty (20) of the most current immunohistochemistry (IHC) tests available to determine proteomic expression of either potentially responsive or resistant pathways. For the most robust target information, we ask that both FFPE and fresh frozen samples are provided, but this is not a requirement for Target Now testing. If we receive only FFPE, we will be able to provide you and your patient with information from our comprehensive proteomic IHC analysis and in some cases, depending on the results, this may also include FISH and sequencing.

What are the studies supporting Target Now? Positive individual outcome information from Target Now testing served as the catalyst for a 140 patient clinical study that was first presented at the 2006 American Society of Clinical Oncology (ASCO) Meeting.[1] Additionally, a growing body of research and literature continues to provide support for the link between the expression of molecular targets and the clinical efficacy of their associated therapeutic agents in various cancers. Literature and levels of evidence are available upon request. Moreover, we encourage physician feedback on the latest targeted therapeutics and literature, as it is essential to leveraging the synergy between our laboratory and your practice.

Is there a prospective research study on Target Now? Yes, the SCRI-CA-001 clinical trial for Target Now is currently enrolling patients. More information is available at www.clinicaltrials.gov.

What are the specimen requirements for Target Now? Target Now can be performed on two specimen types: FFPE tissue and/or fresh frozen.

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- For **DNA microarray analysis**, 0.25 grams of **fresh frozen tissue** or **two to three (2-3) 18-gauge frozen needle core biopsies** are required. Samples must contain at least 20% tumor.
- For **IHC analysis, one paraffin block or 30 unstained slides** are required. Core biopsies must have some tumor present in the deeper sections of the paraffin block used for IHC analysis. Blocks will always be returned in a timely fashion, as requested.
- **All samples must be submitted with a recent pathology report and are confirmed via light microscopy, touch prep or cytology that tumor is present. Additionally, it is helpful to receive clinical and prior therapy history for each patient.**

For more detailed specimen information, please see Target Now Optimal Specimen Requirements.

How do I order Target Now? Please contact us at 800.901.5177 and inquire about Target Now ordering information. Client Services will provide a Target Now fresh frozen tissue shipper or assist you in using your own shipping materials in urgent patient circumstances if fresh frozen tissue is being provided.

- Please be aware that shipping fresh frozen samples for DNA microarray analysis requires at least five (5) pounds of dry ice to ensure that sample integrity is not compromised during transport.
- Caris Dx will provide all associated shipping materials (Styrofoam cooler, specimen tube, biohazard bag, pre-printed and pre-paid FedEx air bill, dry ice label, and tissue collection and shipping instructions) but cannot typically provide dry ice.
- Frozen samples should be stored at or below 70°C if they cannot be transported immediately. Paraffin blocks or slides can be stored at room temperature.

For timely results, please only ship specimens Monday-Thursday. Do not ship on Friday or the business day prior to a major holiday as noted on our '2008 Holidays'.

What type of report will I receive? Target Now results are integrated in an easy to interpret informational report. Each report provides a unique and detailed molecular snapshot of a patient's tumor characterization based on the over and under-expression of potentially relevant markers identified. The report also includes information about potential associated therapeutic agents from the scientific literature, however the decision about how to treat any patient is the responsibility of their physician.

Results are summarized in separate sections (microarray and immunohistochemistry) with a quantitative interpretation of each potential molecular target. Information on potential therapeutic associations or resistances are also indicated for each finding. In most cases, one or more potential targets are identified.

What is the turnaround time for Target Now testing? Once we receive the tissue specimens, required forms, and medical information, analysis takes an average of seven (7) to ten (10) business days. If only a paraffin block or slides are submitted, the average turnaround time is typically three (3) to five (5) business days.

Is Target Now reimbursed? The Target Now test is reimbursed by Medicare and other third party payors. Caris Dx will bill third party payors for Target Now testing and there are no out-of-pocket costs for the patient, except for co-pays or deductibles as required by law or the patient's insurance plan.

Will my office need to obtain prior authorization from the patient's insurance company prior to Target Now testing? If required, prior authorization should be obtained before submitting a specimen. Caris Dx can help you obtain this information.

Who do I call for additional information or with questions on Target Now? Please call us at 800.901.5177.

1 Von Hoff DD, Penny R, et al. Frequency of potential therapeutic targets identified by immunohistochemistry (IHC) and DNA microarray (DMA) in tumors from patients who have progressed on multiple therapeutic agents. JCO, 2006 ASCO Annual Meeting Proceedings Part I. Vol. 24, No. 18S (June 20 Supplement), 2006: 3071.