Circulating Tumor Cells Predict Drug Response

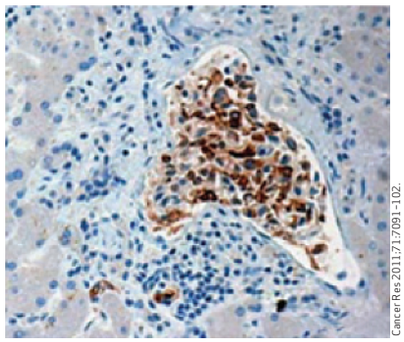
Gene expression profiling of circulating tumor cells (CTC) may predict whether patients with pancreatic cancer will respond to a particular drug regimen, according to preliminary results of a prospective study presented at the 2013 Gastrointestinal Cancers Symposium of the American Society for Clinical Oncology in San Francisco, CA, in January. The study also identified molecular pathways that warn of emerging drug resistance, suggesting that oncologists could tailor treatment to individual patients, monitor their response, and alter therapy if needed.

People with pancreatic cancer face a grim prognosis: Less than 5% will survive 5 years. Many patients are not candidates for surgery and rely on various chemotherapy regimens to slow disease progression. However, physicians lack a validated biomarker to guide therapy selection, says Kenneth Yu, MD, a medical oncologist at Memorial Sloan-Kettering Cancer Center in New York, NY, and the study's senior author. "If we had a model that could give us some guidance in the right direction, I think it would be valuable," he adds.

The study included 50 patients with pancreatic adenocarcinoma who were not eligible for surgery and who received one of 12 treatment regimens recommended by their oncologist, such as FOLFIRINOX, a combination of 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; gemcitabine (Gemzar; Eli Lilly); and docetaxel (Taxotere; Sanofi).

The researchers performed gene expression profiling on CTCs in participants' blood samples collected prior to chemotherapy and after disease progression. They applied a pharmacogenomic model developed by CellPath Therapeutics (Baltimore, MD) to the gene expression profiles to predict sensitivity to various chemotherapy regimens.

Although the profiling results did not guide treatment, the researchers found that patients who received a chemotherapy regimen that the model indicated would be effective for them did better than those who followed a regimen that the model predicted would be ineffective—with average times to disease progression of 7.3 months and 3.7 months, respectively.



Cancer Res 2011;71:7091–102.

Gene expression profiling of circulating pancreatic tumor cells (above) and a pharmacogenomic model predicting sensitivity to various drugs may indicate the most effective treatment for a patient.

Among the 20 patients whose disease progressed, chemotherapy sensitivity profiles had changed, suggesting that different drugs might be needed.

The researchers also analyzed pathways that might predict treatment response. They found that among patients with stage IV cancers that progressed, disruption of the E2F1 pathway, which regulates cell division, forecast a longer treatment response, whereas disruption of the NF-κB pathway, which has been implicated in cell division and cell survival, predicted a shorter treatment response. Additionally, the researchers discovered disruptions in the Rb1 and phospholipase C pathways at the time of disease progression.

Yu's team will continue to follow these patients and launch additional studies to further validate the approach. "Much work still needs to be done to prove that it will be effective in guiding treatment," he says. ■

Cancer Drug Approvals Rise in 2012

The year 2012 continued the upward trend in oncology drug approvals issued by the U.S. Food and Drug Administration (FDA). The Office of Hematology and Oncology Products (OHOP), in the FDA's Center for Drug Evaluation and Research, gave the green light to 13 new agents—up from 11 in 2011 and just 2 in 2010.

NOTED

- **The U.S. Food and Drug Administration (FDA) approved the use of Gleevec (imatinib; Novartis) in combination with chemotherapy to treat children newly diagnosed with Philadelphia chromosome–positive (Ph^+) acute lymphoblastic leukemia.** The tyrosine kinase inhibitor was approved in 2011 to treat children newly diagnosed with Ph^+ chronic myeloid leukemia.
- **A phase III clinical trial has shown that Abraxane (nab-paclitaxel; Celgene) plus gemcitabine can extend survival of late-stage, treatment-naïve pancreatic cancer patients.** The MPACT (Metastatic Pancreatic Adenocarcinoma Clinical Trial) investigation among 861 patients revealed that patients treated with the drug combination had a median overall survival of 8.5 months, versus 6.7 months for patients receiving gemcitabine alone. Results were presented in January at the American Society of Clinical Oncology 2013 Gastrointestinal Cancers meeting.
- **Stemline Therapeutics of New York, NY, raised about $38 million in the first U.S. biotech initial public offering of 2013.** The company develops therapeutics that target cancer stem cells and tumor bulk.
- **The time required for regulatory approval for starting clinical research varied widely across geographic regions in the Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization (ALTTO) international phase III study** (Oncologist 2013 Jan 28 [epub ahead of print]). The median time to regulatory approval was 236 days in South America, 62 days in the Asia-Pacific, 52 days in Europe, and 26 days in North America, the study reported.
- **The European Medicines Agency finalized its updated guidelines for evaluating cancer therapies.**
- **In the fourth quarter of 2012, $1.3 billion was invested in 135 U.S. biotechnology firms,** according to the MoneyTree Report by PricewaterhouseCoopers and the National Venture Capital Association (NVCA) based on data from Thomson Reuters. "Life sciences investment was suppressed for much of the year, particularly with first-time fundings, due in part to the impact of the regulatory and reimbursement environments," comments NVCA president Mark Heesen.