Genomic profiling for cancer of unknown primary site

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Genomic profiling of cancer of an unknown primary site (CUP) found at least one clinically relevant genomic alteration in most of the samples tested, an indication of potential to influence and personalize therapy for this type of cancer, which responds poorly to nontargeted chemotherapy treatments, according to a study published online by *JAMA Oncology*.

Between 2 percent and 9 percent of all cancer diagnoses present as a metastatic CUP, and about two-thirds of CUP tumors are adenocarcinomas (which tend to develop in glandular tissue). No drugs are specifically approved to treat CUP and because the response to nontargeted chemotherapy treatments is poor, five-year survival is currently about 11 percent and median overall survival ranges from 11 weeks to 11 months, according to the study background.

Jeffrey S. Ross, M.D., of Foundation Medicine, Inc., Cambridge, Mass., and Albany Medical College, Albany, N.Y., and coauthors performed genomic profiling on 200 CUP samples to look for targetable genomic alterations that might identify opportunities to target therapies for patients with CUP. Of the 200 samples, 125 were adenocarcinomas of unknown primary site (ACUPs) and 75 other CUPs without the features of adenocarcinomas.

The authors identified at least one genomic alteration in 192 (96 percent) of CUP specimens. Within the 200 samples, a total of 841 alterations were identified in 121 genes, for an average of 4.2 genomic alterations per tumor. One or more potentially targetable genomic alterations also

was identified in 169 of 200 (85 percent) CUP specimens.

The authors highlight a number of important limitations to this work and note that prospective randomized clinical trials are needed to confirm the observations described in the present study.

"Given the poor prognosis of CUP treated by nontargeted conventional therapies, comprehensive genomic profiling shows promise to identify targeted therapeutic approaches to improve outcomes for this disease while potentially reducing the often costly and time-consuming search for the tumor's anatomic site of origin," the study concludes.

In a related editorial, Gauri Varadhachary, M.D., of the University of Texas MD Anderson Cancer Center, Houston, writes: "From a development perspective, it is especially encouraging that several molecular targets may be independent of the tumor site, making it possible to include patients with CUP in new studies of targeted therapies and allowing us to piggyback on the broader advances in personalized cancer therapy. We will require creative approaches to clinical studies and learning from the current trends. These trends can then perhaps help in establishment of an international CUP mutation consortium that groups CUP subtypes (e.g., liver, osseous, nodal, carcinomatosis dominant presentations) and mutations to plan innovative smaller trials. Just as we need to be selective in our diagnostic approach using an effective algorithm that leverages the proteomics and genomics techniques, we need to be selective in our research efforts to deliver validated new approaches to our patients with CUP."

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