KRAS and BRAF mutation screening in metastatic colorectal cancer costly in relation to benefits

November 28 2012

Researchers report that screening for KRAS and BRAF mutations can reduce the cost of anti-EGFR treatment for metastatic colorectal cancer but with a very small reduction in overall survival according to a new study published on November 28 in the *Journal of the National Cancer Institute*.

Metastatic colorectal cancer patients whose tumors harbor mutations in KRAS (and to a lesser extent, in BRAF) are unlikely to respond to costly anti-EGFR therapies. Screening of patients who are candidates for these therapies for mutations in one of these genes (KRAS) has been recommended, with the goal of providing treatment to those who are likely to benefit from it while avoiding unnecessary costs and harm to those who are not likely to benefit. However, the real-world impact of mutation screening for both KRAS and BRAF is unclear.

To better understand the impact of mutation screening with regard to health outcomes, costs, and value, Ajay S. Behl, Ph.D., M.B.A., of the HealthPartners Research Foundation in Bloomington, Minnesota, and colleagues, performed a cost-effectiveness analysis that took into account the treatments, resection of metastases, and survival for the different types of metastases. They conducted patient-level decision analytic simulation modeling comparing four strategies involving KRAS and BRAF mutation testing to select treatments for metastatic colorectal cancer patients: no anti-EGFR therapy (best supportive care); anti-EGFR

therapy without screening; screening for KRAS mutations only (before providing anti-EGFR therapy); and screening for KRAS and BRAF mutations (before providing anti-EGFR therapy).

The researchers found that compared with no anti-EGFR therapy, screening for both KRAS and BRAF mutations showed a very high (ie, unfavorable) incremental cost-effectiveness ratio, meaning it was very costly in relation to its benefits. Compared with anti-EGFR therapy without screening, screening for KRAS mutations saved approximately $7,500 per patient; adding BRAF mutation screening saved another $1023, with little reduction in expected survival.

The authors write, "In general, our results are less supportive of the use of anti-EGFR therapy than previous analyses, and they indicate lower cost savings from KRAS testing than previously reported. Although we cannot confirm that anti-EGFR therapy is a cost-effective use of health care resources, we can affirm that KRAS testing is cost-saving. BRAF testing may offer additional savings."

In an accompanying editorial, Josh J. Carlson, M.P.H., Ph.D., of the Department of Pharmacy, University of Washington, and Scott D. Ramsey, MD, PhD, of the Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, both in Seattle, note two practical points highlighted by the study: that molecular testing is as much about generating cost savings by identifying nonresponders as it is about improving survival by identifying responders, and that good modeling must account for the fact that community practice (as opposed to clinical trials) "is messy." They write, "most importantly, this study of an unusually accurate test raises important issues that should be considered for other molecular tests in other settings."

Provided by Journal of the National Cancer Institute