



## Fact Sheet

### Lewin Case Study III

## Diagnostic Testing for KRAS Genetic Mutation in Patients with Metastatic Colorectal Cancer

Genetic testing for the KRAS gene mutation enables physicians to target front-line cancer drugs on those patients with metastatic colorectal cancer who are able to benefit from such drugs, while avoiding those patients who would suffer serious side-effects. Better targeting of therapy in this way can dramatically improve outcomes for patients, reduce damaging side-effects, and potentially save some \$740 million annually.

### Background

In 2009, an estimated 50,000 people will die from colorectal cancer in the US. Costs of the disease are \$7.5 - \$9.5 billion annually.

Among the primary front-line therapies for colon cancer are drugs that inhibit what are known as epidermal growth factor receptors (EGFR)—proteins that can cause uncontrolled cancer cell growth. But some 40 percent of cancer patients carry a genetic variation—a mutated form of a gene called KRAS—that prevents them from benefitting from such drugs. Instead, they can suffer serious side-effects from them, as well as the resulting delays in the start of effective therapy. KRAS testing identifies the genetic make-up of a patient's tumor, which allows physicians to avoid use of the drug in those patients who would suffer such side-effects. Genetic mutation testing of this kind is one example of a new clinical field called pharmacogenetics, which examines how variations in an individual's genes can dictate how he or she responds to a drug.

### Highlights

- Recent analyses of randomized controlled clinical trials shows that the patient response to front-line cancer drugs (EGFR inhibitors) for metastatic colon cancer is strongly influenced by their KRAS mutation status.
- Strong evidence supports the clinical validity and utility of KRAS mutation testing to guide therapy selection for patients with metastatic colorectal cancer. KRAS test results can have a direct influence on clinical decisions that lead to improved patient health outcomes for patients.
- Among the benefits of identifying KRAS genetic variation mutation are avoiding prescription of ineffective drugs and expediting the use of the best alternative drug ther-

apy, as well as avoiding unnecessary patient exposure to drug toxicities and side-effects. These can include rash, fatigue, stomach pain, breathing difficulties, gastrointestinal problems, infection, and fever.

- The National Comprehensive Cancer Network updated in 2008 its clinical guidelines to recommend that KRAS testing be part of the pre-treatment work-up for all patients with metastatic colorectal cancer.
- The American Society of Clinical Oncology in 2009 issued a “provisional clinical opinion” calling for KRAS testing for patients with metastatic colorectal cancer who are candidates for the front-line drug therapy. The group said that patients who have the KRAS mutation should not receive the drug.
- The FDA in July 2009 announced revisions to the prescribing information of targeted front-line drugs for metastatic colorectal cancer, requiring inclusion of information on variations in the KRAS gene and its effect on patient response to those therapies. The FDA also updated the clinical studies section of the label to include results from recent analyses of randomized controlled trial data that support KRAS testing.
- The economic value of KRAS testing includes reduced costs attributed to avoidance of ineffective treatment, reduced costs of managing adverse effects from ineffective therapy, and reduced overall costs of metastatic colorectal cancer.
- Testing patients with metastatic colorectal cancer for the KRAS gene mutation prior to prescribing one of the front-line cancer drugs (EGFR inhibitor) could save the US health care system \$740 million annually, according to one study—although this estimate may be high.