

## *BRAF* Testing in Metastatic Colorectal Cancer

### Description

Patients with metastatic colorectal cancer (mCRC) who fail 1<sup>st</sup>-line chemotherapy may be considered for 2nd (or 3rd) line therapy using one of the anti-EGFR monoclonal antibodies cetuximab (Erbix<sup>®</sup>) or Panitumumab (Vectibix<sup>®</sup>). It has been determined, and ASCO guidelines recommend, testing patient tumor tissue for K-ras (*KRAS*) mutations and only administering these drugs to patients whose tumor is negative for the K-ras mutation (i.e., wild type). However, even in K-ras negative mCRC patients, approximately 30-40 % of patients treated with these drugs will not respond. Thus, it has been suggested that the K-ras negative mCRC patient population can be further stratified additional biomarkers. The *BRAF* V600E mutation is one of these markers for which early evidence suggested improvement in stratification of K-ras negative mCRC patients. However, current best evidence suggests that while *BRAF* mutation testing may help predict survival independent of treatment this testing does not predict which K-ras negative mCRC patients will or will not respond to the anti-EGFR monoclonal antibodies (MoAbs).

Tissue tested: Tumor specimen

Testing available: ARUP

**Action: Evidence does not support *BRAF* mutation analysis on tumor tissue to help choose between anti-EGFR monoclonal antibodies and other anti-neoplastic drugs. *BRAF* mutation analysis for the purpose of making treatment decisions about the use of anti-EGFR monoclonal antibodies is NOT covered by SelectHealth.**

- A 2010 ASCO Provisional Clinical Opinion states that there is “insufficient data to justify an opinion at present” concerning the utility of *BRAF* testing for the use of anti-EGFR MoAbs.<sup>1</sup>
- A 2010 National Comprehensive Cancer Network guideline Update for colon cancer states that testing patients with metastatic CRC for the *BRAF* gene mutation is now "optional" for mCRC prognosis and therapy evaluation. However, its use continues to be controversial and evidence inconsistent.<sup>2</sup>

**Alert: *BRAF* testing of tumor tissue is also performed, and recommended by Intermountain guidelines, for testing of CRC patients when performed as part of screening for Lynch syndrome. This test (*BRAF*) result is applicable to the indications discussed above. The test DOES NOT need to be repeated.**

### Resources:

1. ASCO Provisional Clinical Opinion: Testing for *KRAS* Gene Mutations in Patients with Metastatic Colorectal Carcinoma to Predict Response to Anti-Epidermal Growth Factor Receptor Monoclonal Antibody Therapy. <http://jco.ascopubs.org/cgi/reprint/JCO.2009.21.9170v1>
2. NCCN Colon Cancer Guideline Update Includes *BRAF* Testing, Adjuvant Chemotherapy. <http://www.nccn.org/about/news/newsinfo.asp?NewsID=240>
3. Tol J, Dijkstra JR, Klomp M, Teerenstra S, Dommerholt M, Vink-Börger ME, van Cleef PH, van Krieken JH, Punt CJ, Nagtegaal ID. Markers for EGFR pathway activation as predictor of outcome in metastatic colorectal cancer patients treated with or without cetuximab. *Eur J Cancer*. 2010 Apr 20.
4. Lièvre A, Blons H, Laurent-Puig P. Oncogenic mutations as predictive factors in colorectal cancer. *Oncogene*. 2010 Apr 12.