Uncovering Treatment Options for Patients with Colorectal Cancer

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Recommend Molecular Testing in Colorectal Cancer (CRC)\(^1,2\)

1 **RAS Mutations– KRAS and NRAS:**
   RAS mutations often confer resistance to EGFR therapies\(^3\)

2 **BRAF Mutations:**
   BRAF is a strong prognostic marker\(^4\) and may help inform the use of BRAF-targeted therapy

3 Anti-HER2 therapy is only indicated in HER2-amplified tumors that are also RAS and BRAF wild type

4 **MSI Status:**
   Testing MSI may help inform the use of immunotherapy in patients with metastatic CRC

Our portfolio of tests analyzes all guideline recommended genes and biomarkers for relevant alterations in patients with CRC including KRAS, NRAS, BRAF, HER2 and MSI.\(^*\)

The Value of Comprehensive Genomic Profiling with Foundation Medicine:

**88%**

Of the 6.4% of patients that harbor potentially resistant KRAS mutations outside of codons 12 and 13, **88% may not be identified by focused PCR-based testing methods** as having such a KRAS mutation.

**3%**

TMB can potentially identify an additional **3% of CRC patients**\(^1\) who are MSS (microsatellite stable) but **who may benefit from cancer immunotherapy**.\(^6\)

- Based on a TMB-high cut-off of 12 mutations per megabase. Research is ongoing to determine appropriate cut-offs for colorectal and other cancer types, which could impact the number of MSS patients who are determined to have a high TMB in that disease.

**Patients with rare alterations in genes such as ALK, ROS1 and NTRK have a poorer prognosis and may have exceptional benefit from new targeted therapies and clinical trials.**\(^7\)

**Additional clinically relevant genes for CRC patients:** PIK3CA, PTEN, CTNNB1, APC, RET, ERBB2, and others.

FDA-approved portfolio of tests to help identify more treatment options:

**TISSUE BIOPSY**

FoundationOne CDx is FDA-approved and covered by Medicare for qualifying patients.\(^8\)
- Analyzes 324 genes
- Reports TMB and MSI

**LIQUID BIOPSY**

FoundationOne Liquid CDx is FDA-approved and covered by Medicare for qualifying patients.\(^8\)
- Analyzes 324 genes
- bTMB, MSI-High, and tumor fraction

\(^*\) FoundationOne Liquid CDx only reports MSI when determined to be high.

\(^8\) FoundationOne Liquid CDx is FDA-approved to report substitutions and indels in 311 genes, including rearrangements and copy number losses only in BRCA1/2. Comprehensive results across all 324 genes, including bTMB, MSI-H status, and tumor fraction are reported in the professional services section of the report.
## NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®)
### Version 4.2020 Colon Cancer

### CLINICAL PRESENTATION

- Suspected or proven metastatic synchronous adenocarcinoma (Any T, any N, M1)

### WORKUP*

- Colonoscopy
- Chest/abdominal/pelvic CT
- CBC, chemistry profile
- CEA
- Determination of tumor gene status for RAS and BRAF mutations and HER2 amplifications (individually or as part of next-generation sequencing [NGS panel])
  - Determination of tumor MMR or MSI status (if not previously done)
  - Biopsy, if clinically indicated
  - Consider PET/CT scan (skull base to mid-thigh) if potentially surgically curable M1 disease in selected cases
  - Consider MRI of liver for liver metastases that are potentially resectable
  - Multidisciplinary team evaluation, including a surgeon experienced in the resection of hepatobiliary and lung metastases

### FINDINGS

- Synchronous liver only and/or lung only metastases
- Resectable
- Synchronous abdominal/peritoneal metastases
- Unresectable (potentially convertible or unconvertible)
- Synchronous unresectable metastases of other sites

*See Principles of Imaging (COL-A).
†See Principles of Pathologic Review (COL-B 4 of 8) - KRAS, NRAS, and BRAF Mutation Testing and Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing. If known RAS/RAF mutation, HER2 testing is not indicated. NGS panels have the ability to pick up rare and actionable mutations and fusions.
‡See Principles of Surgery (COL-C 2 of 3).
§Consider colon resection only if imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms.

### TO LEARN MORE:

Visit [www.foundationmedicine.com](http://www.foundationmedicine.com)

### TO SIGN UP OR ORDER A TEST:

Visit [www.foundationmedicine.com/signup](http://www.foundationmedicine.com/signup)

FoundationOne®CDx and FoundationOne®Liquid CDx are qualitative next-generation sequencing based in vitro diagnostic tests for advanced cancer patients with solid tumors and are for prescription use only. FoundationOne CDx utilizes FFPE tissue and analyzes 324 genes as well as genomic signatures. FoundationOne Liquid CDx analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 37 genes. The tests are companion diagnostics to identify patients who may benefit from treatment with specific therapies in accordance with the therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the tests does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy for testing with FoundationOne CDx when archival tissue is not available which may pose a risk. Patients who are tested with FoundationOne Liquid CDx and are negative for companion diagnostic mutations should be reflexed to tumor tissue testing and mutation status confirmed using an FDA-approved tumor tissue test, if available. For the complete label, including companion diagnostic indications and important risk information, please visit [www.F1CDxLabel.com](http://www.F1CDxLabel.com) and [www.F1LCDxLabel.com](http://www.F1LCDxLabel.com).

### References:

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8. The Centers for Medicare & Medicaid Services (CMS) Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R) see Appendix B.