Uncovering Treatment Options for Patients with Colorectal Cancer

FOUNDATION MEDICINE®

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

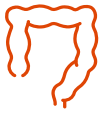
1 | ***RAS* Mutations– *KRAS* and *NRAS:*** *RAS* mutations often confer resistance to *EGFR* therapies[3]

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.

Rankin et al.,
Broad Detection of Alterations...,
The Oncologist

3% TMB can potentially identify an additional **3% of CRC patients**† 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.

Fabrizio et al.,
Beyond microsatellite testing...,
Journal of GI Oncology

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:

FOUNDATION**ONE®CDx**

TISSUE BIOPSY

FoundationOne CDx is FDA-approved and covered by Medicare for qualifying patients.[8]

- Analyzes 324 genes
- Reports TMB and MSI

FOUNDATION**ONE®LIQUID CDx**

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.
† 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‡
  - Unresectable (potentially convertible‡ or unconvertible)
- Synchronous abdominal/peritoneal metastases
- 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*

TO SIGN UP OR ORDER A TEST:

Visit *www.foundationmedicine.com/signup*

References:

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer V.4.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed July 1, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer V.6.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed July 1, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
3. Luo et al. World J Gastroenterol 2014 April 14; 2014: 3858-3874.
4. Lo Nigro C, Ricci V, Vivenza D, et al. World J Gastroenterol. 2016;22(30):6944-54.
5. Rankin A, Klempner SJ, Erlich R, et al. Broad Detection of Alterations Predicted to Confer Lack of Benefit From EGFR Antibodies or Sensitivity to Targeted Therapy in Advanced Colorectal Cancer. The Oncologist. 2016.
6. Fabrizio D, George T, et al. Beyond microsatellite testing: assessment of tumor mutational burden identifies subsets of colorectal cancer who may respond to immune checkpoint inhibition. Journal of Gastrointestinal Oncology. 2018.
7. Pietrantonio F, et al. JNCI J Natl Cancer Inst, 2017, Vol. 109, No. 12.
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.

FOUNDATION MEDICINE®

www.foundationmedicine.com | Tel 888.988.3639 | Fax 617.418.2290 | US-PF-2000023