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}

RAS Mutations- KRAS and NRAS: RAS mutations often confer resistance to EGFR therapies³

BRAF Mutations: BRAF is a strong prognostic marker⁴ and may help inform the use of BRAF-targeted therapy

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

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:



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



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



FOUNDATIONONE®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 **WORKUP* FINDINGS PRESENTATION** Suspected or Colonoscopy Synchronous liver Resectable[‡] proven metastatic only and/or lung Chest/abdominal/pelvic CT only metastases synchronous Unresectable CBC, chemistry profile adenocarcinoma (potentially CEA (Any T, any N, M1) convertible[‡] or **Determination of tumor** unconvertible) gene status for RAS and **BRAF** mutations and HER2 Synchronous amplifications (individually abdominal/ or as part of next-generation peritoneal sequencing [NGS panel]) metastases · Determination of tumor MMR or MSI status (if not previously done) · Biopsy, if clinically indicated **Synchronous** unresectable Consider PET/CT scan (skull base to mid-thigh) if potentially metastases surgically curable M1 disease in of other sites§ 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 See Principles of Surgery (COL-C 2 of 3). 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 Consider colon resection only if imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms. RAS/RAF mutation, HER2 testing is not indicated. NGS panels have the ability to pick up rare and actionable mutations and fusions.

Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines*) for Colon Cancer V.4.2020. ©2020 National Comprehensive Cancer Network, Inc All rights reserved. The NCCN Guidelines* and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available.

TO LEARN MORE:

Visit www.foundationmedicine.com

TO SIGN UP OR ORDER A TEST:

Visit 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 311 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 and www.F1LCDxLabel.com.

References:

- 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
- what acceler regarding then content, use of application and disclaims any responsibility for their application or use in any way.

 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.
- Luo et al. World J Gastroenterol 2014 April 14; 2014: 3858-3874
- Lo Nigro C, Ricci V, Vivenza D, et al. World J Gastroenterol. 2016;22(30):6944-54.
 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 Fabrizio D, George I, et al. Beyoni microsactinic testinia, assessment of unior midation burden identifies subsets of colorectal cancer who may respond to immune checkpoint inhibition. Journal of Gastrointestinal Oncology. 2018.
 Pietrantonio F, et al. JNCI J Natl Cancer Inst, 2017, Vol. 109, No. 12.
 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.

