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 therapies³

2. **BRAF Mutations:**
   - BRAF is a strong prognostic marker⁴ 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.⁶

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.

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

- Patients with rare alterations in genes such as ALK, ROS1 and NTRK⁷ 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.

A portfolio of tests to help identify more treatment options:

- **FOUNDATION ONE® CDx**
  - **TISSUE BIOPSY**
  - FoundationOne CDx is FDA-approved with Medicare coverage for qualifying Medicare patients.⁸
  - Analyses 324 genes
  - Reports TMB and MSI

- **FOUNDATION ONE® LIQUID**
  - **LIQUID BIOPSY**
  - FoundationOne Liquid is a laboratory developed test that delivers high-quality answers from a simple blood draw.
  - Analyses 70 genes
  - Reports MSI-H status

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¹ 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.

² Fabrizio et al., Beyond microsatellite testing..., Journal of GI Oncology

³ Rankin et al., Broad Detection of Alterations..., The Oncologist

⁴ TMB can potentially identify an additional 3% of CRC patients who are MSS (microsatellite stable) but who may benefit from cancer immunotherapy.

⁵ NTRK not currently tested on FoundationOne Liquid

⁶ Fabrizio et al., Beyond microsatellite testing..., Journal of GI Oncology

⁷ 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.

⁸ FoundationOne Liquid only reports MSI when determined to be high.
## NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®)
### Version 1.2020 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
- Synchronous unresectable metastases of other sites§

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* 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).

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**References:**

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8. Medicare and Medicare Advantage members have coverage of FoundationOne CDx in accordance with the Centers for Medicare and Medicaid Services (CMS) national coverage determination (NCD) criteria.

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