mCRC Biomarker Testing Quick Reference Guide

Purpose: A Standalone Guide to Initiate the Conversation Around Standardizing Testing, Speeding Time to Treatment, and Supporting Shared Decision-Making

Who this is for: Oncology nurses, PAs, nurse navigators, pathologists, and tumor board members committed to delivering biomarker-informed care to all CRC patients—efficiently and equitably.

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1. Getting Started – The Biomarker Implementation Roadmap

A. Build Tissue-First Protocols

- Co-develop biopsy standards with proceduralists (gastroenterologists, surgeons, IR) and pathology.
- Aim for ≥20% tumor content and 10 unstained slides at 4µm each for initial biopsy.
- Add tissue adequacy checklist to procedure request forms.
- Trigger liquid biopsy within 24 hours if tissue is inadequate or delayed.

B. Pre-Build CRC Biomarker Panels in the EHR

- Standard panel (reflex or manual order):
  MMR/MSI, KRAS/NRAS, BRAF, HER2, PIK3CA (optional: NTRK, DPYD, ctDNA).
- Align with NCCN 2025 and local pathway guidelines.
- Embed test panel orders into biopsy result and diagnosis templates.
- Include test reflex triggers (e.g., CRC diagnosis triggers biomarker panel).

C. Enable Reflex Testing via Pathology

- Pathologist initiates biomarker testing automatically at diagnosis.
- Add a standing order protocol for reflex testing in the EHR.
- Monitor reflex rates monthly with lab/path admin support.

D. Assign a Biomarker Testing Navigator (BTN)

- This is the single most important success factor. Role includes:
  - Checking sample adequacy
  - Following through on test order completion
  - Tracking turnaround time
  - Closing the loop with oncologist and patient
- Empower this person with EMR access and escalation pathways.

E. Secure Insurance Authorization Early

- Create a payer cheat sheet for common CPT codes and pre-approval steps.
- Establish testing coverage workflows with billing staff.
- Provide “justification scripts” to support appeals or peer-to-peer reviews.

F. Set and Monitor a Target

🎯 Goal: ≥90% of CRC patients tested according to NCCN within 14 days of diagnosis.
Track monthly. Share results with MDT. Refine workflows. Celebrate wins.

2. CRC Biomarkers: Quick Reference Table

Biomarker	When to Test	Implication	Line of Therapy
MSI-H/MMR	At diagnosis	ICI eligibility	1st-line (if dMMR)
KRAS/NRAS	At diagnosis	Anti-EGFR use	1st/2nd-line
BRAF V600E	At diagnosis	Targeted therapy	2nd-line or later
HER2	At progression (RAS WT)	HER2 therapy	≥2nd-line
NTRK	Rare	TRK inhibitors	Any line
DPYD	Before 5-FU	Reduce toxicity	Prior to treatment
ctDNA	At recurrence/progression	MRD/prognosis	Surveillance/post-adjuvant

Notes:

1. Confirm labs do not drop low-frequency biomarkers due to tissue volume limits. Equivocal HER2 (IHC 2+) requires FISH confirmation.
2. Verify test is an FDA-approved companion diagnostic when possible, especially for HER2 and BRAF-directed therapies, to support reimbursement.

3. Step-by-Step Reflex Testing Workflow

1. CRC diagnosis confirmed by pathologist.
2. Pathologist checks for:
    - ≥20% tumor content
    - 10 unstained slides at 4µm
3. If tissue is inadequate:
    - Liquid biopsy ordered within 24–48 hours.
4. Reflex biomarker panel auto-ordered in EHR:
    - MSI/MMR, KRAS/NRAS, BRAF, HER2, PIK3CA
5. BTN confirms test sent and received by lab.
6. BTN follows up in 5 business days; alerts on delays.
7. Results shared with oncologist; therapy options reviewed in tumor board.

Target: Achieve testing completion and results availability within **14 days of diagnosis**.

Note: Repeat testing at progression (especially HER2, ctDNA, NTRK) may require **updated pathology reports** or peer-to-peer justifications. Pre-cert teams should be looped in early.

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4. Checklist for Biomarker testing Navigator

☐ CRC diagnosis confirmed and documented by pathologist

☐ Check sample adequacy per NCCN standards

— ≥20% tumor content

— 10 unstained slides (4µm each)

☐ If tissue is insufficient, initiate liquid biopsy order

☐ Verify that reflex biomarker panel was auto-ordered in EHR

— MSI/MMR, KRAS/NRAS, BRAF, HER2, PIK3CA

☐ Confirm sample (tissue or blood) sent and received by testing lab

☐ Monitor test turnaround and follow up on delays
☐ Notify oncologist promptly once results are available
☐ Document testing completion and patient communication in EMR

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5. Patient Conversation Quick Script to Support Shared Decision Making

"Your doctor has ordered biomarker testing to better understand the genetic makeup of your cancer. This helps us select treatments that are more likely to work for you. It's a simple process—either from your tumor sample or blood—and results are typically ready in 7–14 days. Most insurance covers this, but we'll help you check to avoid surprises. Our goal is to match you with the best possible treatment, as quickly as we can."

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6. Insurance and Cost Considerations

Test Type	Medicare Coverage	Commercial Insurance
Tissue-based NGS	Covered (Medicare NCD 90.2, LCD L38203)	Prior auth required; widely covered (FoundationOne®, Caris® preferred)
Liquid biopsy	Guardant360® covered	FoundationOne® Liquid often covered, confirm plan specific
Specific Biomarkers (DPYD, HER2 IHC/FISH)	Part B (case-by-case)	Varies; prior authorization needed

Tip: Work with your billing or administrative team to set up pre-approval processes with insurance companies for commonly used biomarker tests. This helps reduce delays caused by prior authorization requirements and ensures patients know what's covered - making the testing process smoother and more predictable for everyone.

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7. Tumor Board Planning Page

For each new CRC patient:

- ☐ Biomarker results complete and reviewed
- ☐ Patient eligible for targeted or ICI therapy?
- ☐ Tumor sidedness factored into anti-EGFR decisions?
- ☐ Clinical trial options reviewed based on biomarker profile?
- ☐ Treatment recommendation documented and communicated?
- ☐ ctDNA considered at progression or recurrence?
- ☐ Repeat biopsy/testing considered if initial markers inconclusive?

✅ **Don't Miss These!**

- RAS/BRAF results not yet back but treatment started
- MSI/MMR not ordered on metastatic patient
- Right-sided tumor being considered for anti-EGFR
- HER2 testing missing in RAS WT disease post-progression

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8. Physician's Notes and Recommendations