Personalized Medicine testing recommendations for:

Colorectal Cancer

Newly Diagnosed Stage I-III (somatic)

When and what should be tested?

- Treatment eligible
- Stage I-III
- Newly diagnosed to make determination on adjuvant therapy as well as choice of regimen
- Tissue sample preferred
- Liquid biopsy if tissue sample inadequate for further testing

FDA/NCCN approved

- MLH1
- MSH2
- MSH6 or PMS2 for loss of protein expression via IHC
- MSI via PCR
- MRD
- MMR
- POLE/POLD1 with hypermutated phenotype (e.g., TMB>50)
- Testing for somatic PI3K pathway alterations for stage II-III*
- Consider MRD assessment for stage II-III

Emerging

Assume CEA testing at initial diagnosis and ongoing monitoring will be conducted as standard of care. Initial evaluation of CEA will be an important monitoring consideration

*Somatic PI3K pathway alterations include mutations in PI3KCA exon 9 and 20, other PIK3CA, PI3K3R1, and PTEN mutations; and deep deletions of PTEN

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Personalized Medicine testing recommendations for:

Colorectal Cancer

Newly Diagnosed Advanced Disease or Progression on Treatment (somatic)

When and what should be tested?

- Treatment eligible
- Stage IV (newly diagnosed, advanced, or progressed on treatment
- Tissue sample preferred
- Liquid biopsy if tissue sample inadequate for further testing

FDA/NCCN approved

- Biomarker testing ordered as rapidly as possible following diagnosis, including:
  - KRAS
  - NRAS
  - BRAF V600E
  - HER2 overexpression /amplifications
  - MMR or MSI
- Testing should be conducted as part of a multigene panel testing (MGPT), which would identify rare and actional mutations and fusions such as:
  - NTRK 1/2/3
  - RET
  - POLE/POLD1 mutation

Emerging

Complete appropriate diagnostic testing for all patients as outlined in this recommendation

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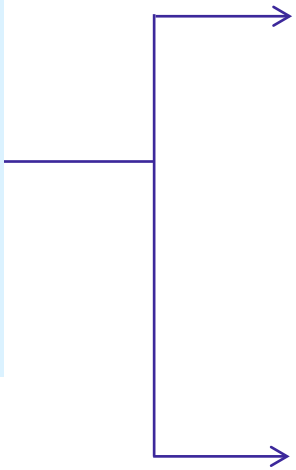
Personalized Medicine testing recommendations for:

Colorectal Cancer

Prior to Second Line Therapy with I/O Agent (somatic)

When and what should be tested?

- Treatment eligible
- All patients prior to second line therapy with I/O agent
- Tissue sample preferred
- Liquid biopsy if tissue sample inadequate for further testing



FDA/NCCN approved

- Test individually or as part of tissue-or blood-based MGPT"
  - KRAS
  - NRAS
  - BRAF
  - HER2 overexpression/amplification
  - NTRK
- If not previously done:
  - MSI (for each metastatic lesion)
  - dMMR
  - TMB
  - POLE/POLD1

Emerging

Complete appropriate diagnostic testing for all patients as outlined in this recommendation

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Personalized Medicine testing recommendations for:

Colorectal Cancer

Genetic High-Risk Patients

When and what should be tested?

- Histologically verified colorectal cancer in 3 relatives, at least one first degree relative
- Colorectal cancer in two successive generations
- At least one member being younger than 50 years
- Upon treatment by a medical oncologist
- Peripheral blood for germline mutation
- Tissue analysis

FDA/NCCN approved

- Testing for Lynch Syndrome*
- MLH1, MSH2, MSH6 or PMS2 via IHC test
- MLH1, MSH2, MSH6, PMS2 mutation or EPCAM (TACSTD1) mutation, MSI via PCR test
- If abnormal IHC or MSI, then MLH1 promoter methylation, EPCAM mutation or BRAF V600E should be tested

Emerging

- n/a

* MSI may be indicative of Lynch Syndrome, yet not diagnostic

If previously seen by a gastroenterologist, then testing of Lynch Syndrome should already have been conducted. If not, follow the recommendations above

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