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
- MMR
- POLE/POLD1 with hypermutated phenotype (e.g., TMB>50)
- Testing for somatic PI3K pathway alterations for stage II-III*
- Consider MRD for risk assessment and assessing the need for adjuvant treatment

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

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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

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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