

# Gastric Cancer

## GI Hereditary Risk Assessment

### When and what should be tested?

- Treatment eligible
- Newly diagnosed
- Recurrent disease
- At time of initial diagnosis
- Tumor sample or blood

### FDA/NCCN approved

- CDH1: cadherin-1, CTNNA-1: alpha-1 catenin (Hereditary Diffuse Gastric Cancer/HDGC)
- EPCAM, MLH1, MSH2, MSH6, PMS2 (Lynch Syndrome)
- SMAD4, BMPR1A (Juvenile Polyposis Syndrome)
- STK11 (Peutz-Jeghers Syndrome)
- APC (Familial Adenomatous Polyposis)
- If high suspicion, consider screening for rarer syndromes

### Emerging

- n/a

### Informational Considerations

- CDH1 for HGC should be considered if the patient has a personal or family history of diffuse gastric cancer (DGC) or lobular breast cancer (LBC) or both. More specifically, consider the following:
  - Two gastric cancer cases in a family with one confirmed diffuse gastric cancer (DGC) diagnosed at any age
  - Three confirmed cases of DGC in first- or second-degree relatives independent of age
  - DGC diagnosed before age 50 w/o a family history
  - Personal or family history of DGC and lobular breast cancer, one diagnosed before age 70
  - Two cases of lobular breast cancer in family members < 50 years of age
  - Cleft lip or palate and DGC: high risk for CDH1
  - Persons of Maori ethnicity and DGC: high risk for CDH1
  - Personal history of bilateral LBC before age 70
  - Family history of  $\geq 2$  first-degree or second-degree relatives with gastric cancer with at least one diagnosed at age  $\leq 50$  y or at least one confirmed to be DGC at any age

# Gastric Cancer

## Locally Advanced/Recurrent, Metastatic Disease (somatic)

### When and what should be tested?

- Treatment eligible
- Newly diagnosed locally advanced or recurrent disease
- At time of initial diagnosis
- Tumor sample or blood – NGS testing should be considered

### FDA/NCCN approved

- Test in ALL patients:
  - MLH1
  - MSH2
  - MSH6
  - PMS2
  - dMMR
  - MSI
- Test in locally advanced/recurrent, metastatic disease:
  - HER2
  - PD-L1
  - TMB
  - NTRK
  - RET gene rearrangement
  - BRAF V600E
  - CLDN18.2

### Emerging

- MUC17
- MRD

### Informational Considerations

- EBV Testing of tumor(subset of MSS gastric cancers do respond to immunotherapy)
- Liquid biopsy(ct DNA tests to be considered in patients who cannot undergo biopsy or on disease progression)