Gastric Cancer

FDA/NCCN approved **GI Hereditary Risk Assessment** • 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) When and what should be tested? APC (Familial Adenomatous Polyposis) Treatment eligible • If high suspicion, consider screening for rarer syndromes · Newly diagnosed Recurrent disease **Emerging** n/a · At time of initial diagnosis Tumor sample or blood 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 ≥2 first-degree or second-degree relatives with gastric cancer with at least one diagnosed at age ≤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

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

