GI SPECIMEN ANCILLARY TESTING
Updated by Hanlin Wang, MD, PhD 8/12/2018

Routinely testing all metastatic GI malignancies (including pancreaticobiliary malignancies) for MMR deficiency by IHC given the approval of PD1 inhibitors in all GI cancers that are MSI-H

GASTROINTESTINAL STROMAL TUMORS (GIST), ALL SITES
BIOPSIES AND EXCISIONS
- C-KIT/PDGFR Molecular testing – ordered on ALL initial diagnoses of GIST at all sites. If molecular was ordered on the biopsy, it does not have to be repeated on the resection following the biopsy. If the patient has recurrent/metastatic disease, contact clinician to see if repeat molecular testing is indicated.

Ordered through Oregon Health Sciences University (Lab of Dr. Chris Corless), The lab does sequential testing, first C-KIT and only if negative PDGFR is evaluated. Choose representative block and order pull block ("PULB") and write in the instructions "Please send to Oregon Health Sciences for c-kit mutation analysis". Can also send email to AP Sendout Bench - SurgicalPathologySendouts@mednet.ucla.edu after order is placed. When the OHSU results are received, Transcription will add the results into an addendum and email the attending pathologist when it is ready for review and signout. The outside report will be scanned into the case in Beaker and into the patient’s chart in Care Connect under the Pathology tab.

NEUROENDOCRINE TUMORS, ALL SITES
BIOPSIES AND EXCISIONS
- KI67 %

Choose representative block for immunohistochemistry (PowerPath code “KI67”). It has been recommended that a minimum of 500 tumor cells be counted to determine the Ki67 index; however, this practice may not be practical for routine clinical purposes, and it is acceptable to estimate the labeling index by eyeballing at hot spots. A notation should be made if less cells are available.

ESOPHAGUS
ADENOCARCINOMA
BIOPSIES AND EXCISIONS
Nothing ordered routinely but some oncologists will request HER2neu (as in gastric cancer)

STOMACH AND GE JUNCTION
ADENOCARCINOMA
BIOPSIES AND EXCISIONS
- HER2neu by immunohistochemistry FIRST
Choose representative block and order Her2 immunohistochemistry. If IHC result is 2+ (equivocal), then order FISH. Negative (0 or 1+) or Positive (3+) HER2 IHC results do NOT require further HER2 FISH. Immunohistochemistry results are reported using CAP criteria. Please note the different criteria used for biopsy and resection specimens.

- HER2neu by FISH
  Choose representative block and order FISH with H & E. When H & E slide arrives, fill out cytogenetics requisition for Her2 FISH and send to cytogenetics lab.

SMALL BOWEL
ADENOCARCINOMA
  BIOPSIES AND EXCISIONS
  Nothing ordered routinely but may order tests by request.

COLON
ADENOCARCINOMA
  BIOPSIES:
  1. Order DNA mismatch repair proteins by immunohistochemistry on ALL cases (if there is adequate tissue)
  - DNA mismatch repair proteins by immunohistochemistry
    [immuno codes: PMS2; hMLH-1, hMSH-2, hMSH-6]

    If loss of MLH1 is present, order BRAF testing for mutation analysis to determine if the loss is due to germline mutation (Lynch syndrome) or MLH1 promoter hypermethylation (sporadic). Use template below for reporting.

RESECTIONS:
  1. Order MSI by PCR using the following criteria
  2. Order DNA mismatch repair proteins by immunohistochemistry as above if not already performed on the biopsy (eg, bx performed at OSH)

- MSI by PCR
  If IHC has already been done on a biopsy and a normal expression pattern is observed, MSI PCR will not be performed on the resection specimen from the same patient UNLESS:
  1) Patient age under 50
  2) Personal hx of Lynch-related tumor(s) – may need to be informed by clinicians
  3) Family hx of CRC or Lynch syndrome – may also need to be informed by clinicians
  4) Histologic features suggestive of MSI on resection specimens (mucinous, poorly differentiated, medullary, tumor infiltrating lymphocytes, Crohn-like peritumoral lymphoid response)
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Choose one representative block of tumor and order in PowerPath (code: “MSIT”). Also choose one representative block of normal colon (usually a margin) and order control (code “MSIN”).

- **KRAS mutational analysis on all stage IV cases** (based on pathology or clinical history)
  Choose one representative block of tumor and order in PowerPath (code: “KRAS”)

  If KRAS result is wildtype, order reflex CRC Panel Sequencing analysis (BRAF, KRAS, NRAS, PIK3CA, and AKT1) [Order code: Colorec]

  If KRAS result is wildtype, also order reflex HER2 IHC. Order HER2 FISH if IHC score is 2+.

- **BRAF mutational analysis (using the CRC panel)**
  Should be performed if if loss of MLH-1 by IHC is present

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**PANCREAS**
**DUCTAL ADENOCARCINOMA** (all resection cases)
- Immunohistochemistry for **SMAD4** (aka DPC4)

**AMPULLA**
**ADENOCARCINOMA** (all resection cases)
- Immunohistochemistry for CK7, CK20, CDX2, MUC1 and MUC2

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**TABLE 2. IHC Schema for Subtyping Ampullary Adenocarcinoma**

| IHC-IN | 1. Positive for CK20 or CDX2 or MUC2 AND negative for MUC1  
|        | 2. Positive for CK20, CDX2, and MUC2, irrespective of MUC1 staining pattern |
| IHC-PB | Positive for MUC1 AND negative for CDX2 and MUC2, irrespective of CK20 staining pattern |
| IHC-ambiguous | Other combinations of phenotypes, including negative for all stains |

IN, intestinal type; PB, pancreaticobiliary type.

Ang DC, et al. AJSP 2014; 38:1371-9