Oncology Clinical Pathways
Gastric Cancer

April 2025 – V1.2025

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Gastric Cancer – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans – Exposure to Ionizing Radiation

- Cancer of the stomach

Gulf War and Post 9/11 Veterans

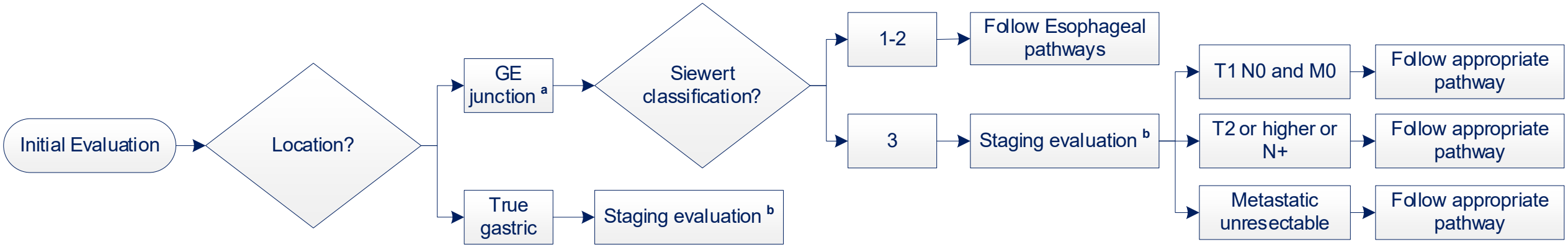
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if you served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Gastrointestinal cancer of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

Gastric Cancer – Initial Evaluation

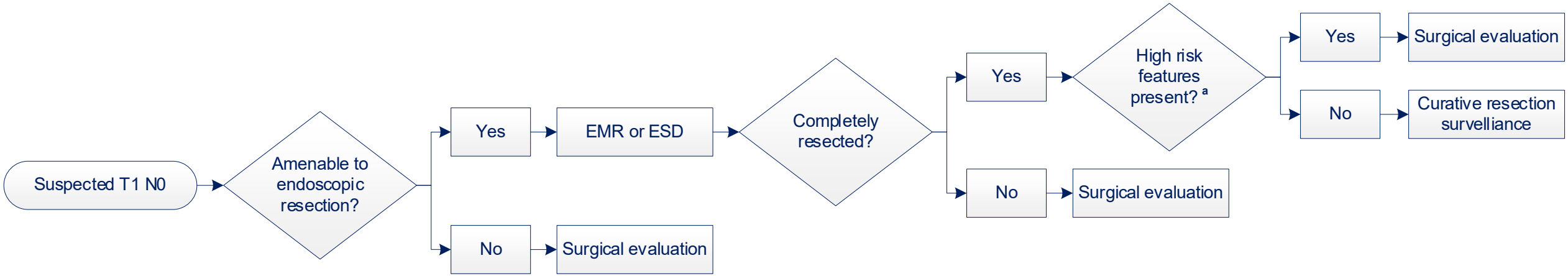


Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **GE junction** is considered GE junction if any portion of the tumor involves the GE junction

[b] **Staging evaluation** CT chest, abdomen, and pelvis with oral and IV contrast and/or PET/CT as indicated; endoscopic ultrasound in the absence of metastatic disease; staging laparoscopy with peritoneal lavage for T3 or N+ and M0

Gastric Cancer – Suspected T1 N0



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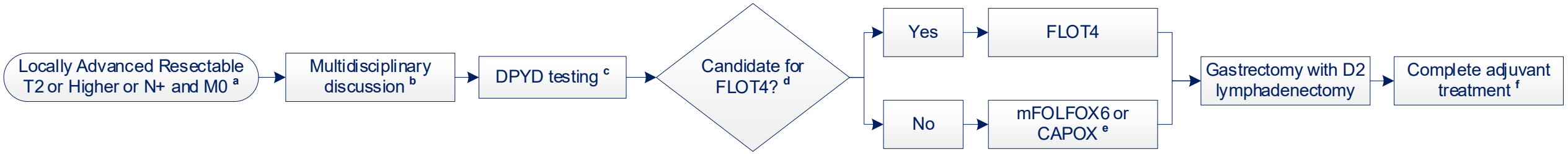
[a] **High risk features** endoscopic resection can be considered curative if the specimen has clear lateral and deep margins; histopathology well or moderately differentiated; does not penetrate the superficial submucosa; no LVI

EMR endoscopic mucosal resection
ESD endoscopic submucosal dissection

Gastric Cancer – Locally Advanced Resectable T2 or Higher or N+ and M0



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[a] **Treatment for locally advanced resectable T2 or higher or N+ and M0** MSI-H/dMMR gastric cancer is evolving; currently, the team does not have a separate pathway for MSI-H/dMMR subgroup of patients; but the pathway as outlined above or an alternative treatment with checkpoint inhibitors can be utilized

[b] **Multidisciplinary discussion** to include at a minimum surgical oncology and medical oncology

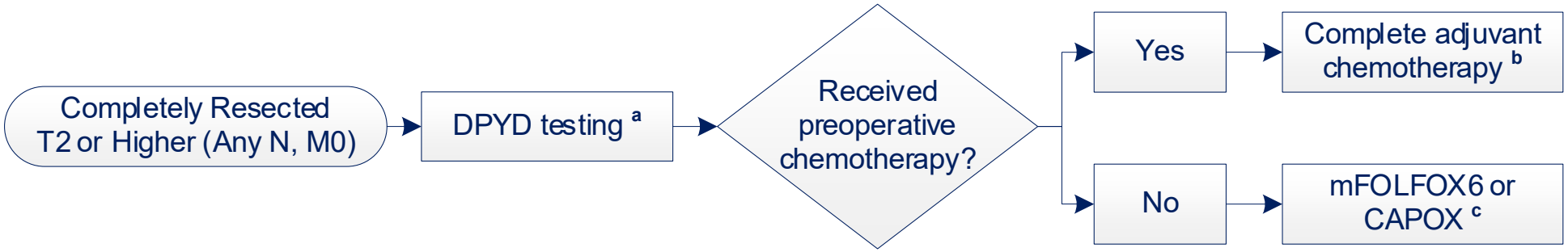
[c] **Perform DPYD testing if not already performed** if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD results if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

[d] **Candidate for FLOT4** defined as fit patient with ECOG PS 0-1

[e] **Capecitabine** avoid capecitabine if adherence issues, unable to self-report toxicity, or severe renal impairment (CrCl < 30ml/min)

[f] **Complete adjuvant treatment** continue same treatment regardless of response; consider chemoradiation if positive margin or inadequate nodal dissection; total duration of chemotherapy (pre and post surgery) is 6 months without RT and 4 months with RT

Gastric Cancer – Completely Resected T2 or Higher (Any N, M0)



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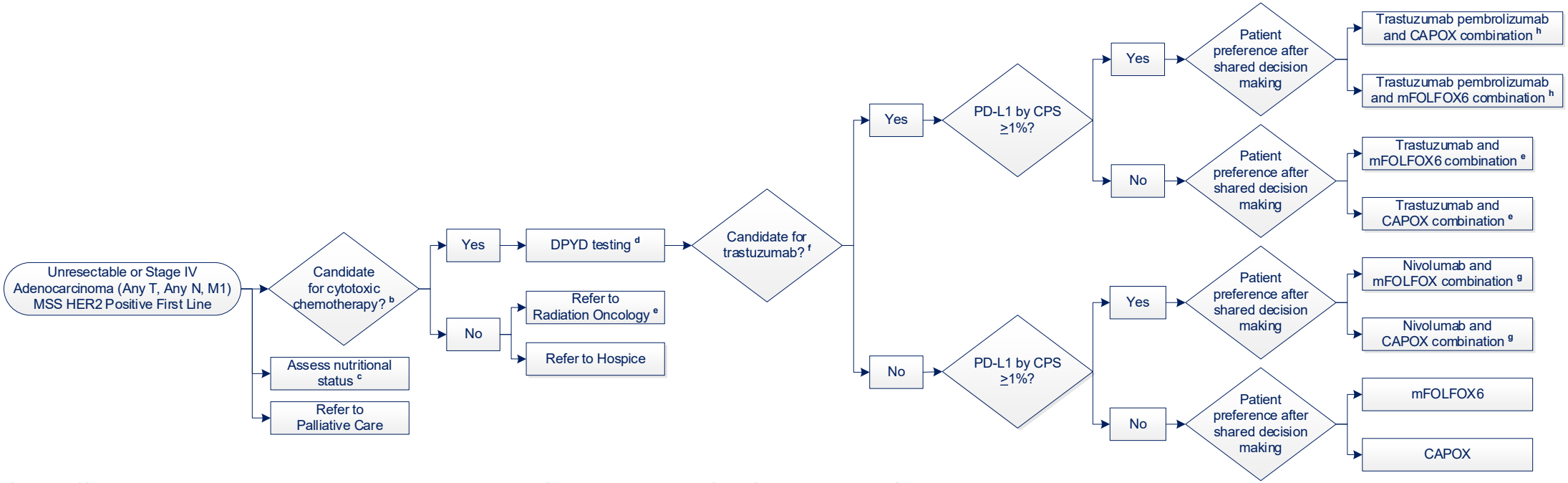
[a] **Perform DPYD testing if not already performed** if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD results if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

[b] **Complete adjuvant treatment** continue same treatment regardless of response; consider chemoradiation if positive margin or inadequate nodal dissection; total duration of adjuvant therapy (pre and post surgery combined) recommended to be 6 months

[c] **Capecitabine** avoid capecitabine if adherence issues, unable to self-report toxicity, or severe renal impairment (CrCl < 30ml/min)

Gastric Cancer – Unresectable or Stage IV Adenocarcinoma (Any T, Any N, M1) MSS HER2 Positive First Line



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[a] **HER2 positive** considered IHC score +3 or an IHC score of +2 and FISH/ISH positive

[b] **Candidate for cytotoxic chemotherapy** consider if patient can tolerate a platinum- and fluoropyrimidine-based doublet

[c] **Assess nutritional status** and consider palliative stent or other nutritional support modalities when clinically appropriate

[d] **Perform DPYD testing if not already performed** if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD results if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

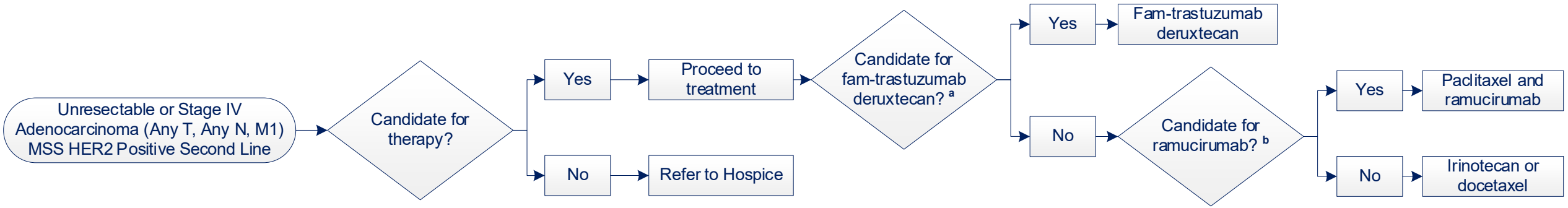
[e] **Radiation Oncology** consider palliative radiation when clinically appropriate

[f] **Candidate for trastuzumab or biosimilar** patient with HER2-positive disease and no clinically significant CV disease (defined as LVEF< 50%, MI within prior 6 months, symptomatic CHF (NYHA class II to IV), unstable angina or cardiac arrhythmia requiring therapy)

[g] **Candidate for immune checkpoint inhibitor** patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

[h] **Pembrolizumab** for two years

Gastric Cancer – Unresectable or Stage IV Adenocarcinoma (Any T, Any N, M1) MSS HER2 Positive Second Line



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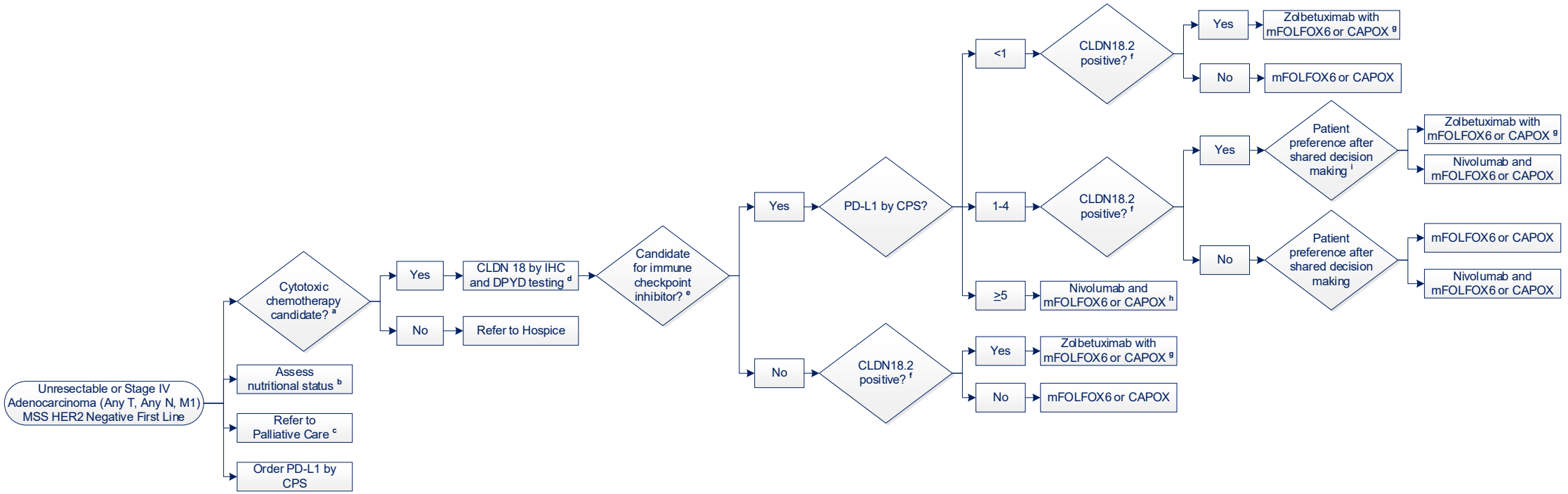
[a] **Candidate for fam-trastuzumab deruxtecan** received trastuzumab in the first-line setting; baseline LVEF ≥ 50% and/or no clinically significant cardiac disease (defined as LVEF< 50%, MI within prior 6 months, symptomatic CHF (NYHA class II to IV), unstable angina or cardiac arrhythmia requiring therapy); no ILD or pneumonitis; ANC ≥ 1500/mm^3

[b] **Candidate for ramucirumab** received fluoropyrimidine and platinum agent in the first-line setting; ECOG PS 0-2; ANC ≥ 1500/mm^3. Note: Due to anti-VEGF effects patients with the following should not receive ramucirumab: non-healing wound/fracture, major surgery in prior 4 weeks, bleeding disorder or coagulopathy, recent history of GI perforation, unstable cardiac condition (uncontrolled HTN, arterial thromboembolism, symptomatic CHF (NYHA II-IV) or arrhythmia), or active cocaine use

Gastric Cancer – Unresectable or Stage IV Adenocarcinoma (Any T, Any N, M1) MSS HER2 Negative First Line



Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Candidate for cytotoxic chemotherapy** consider if patient can tolerate a platinum- and fluoropyrimidine-based doublet

[b] **Assess nutritional status** consider palliative stent or other nutritional support modalities when clinically appropriate

[c] **Assess palliative care** consider palliative radiation when clinically appropriate

[d] **Perform DPYD testing if not already performed** if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD results if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

[e] **Qualify for immune checkpoint inhibitor** no active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

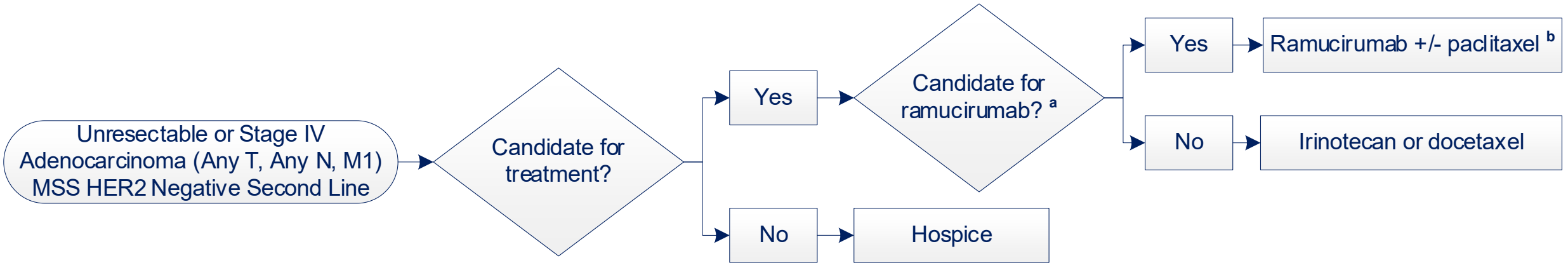
[f] **CLDN18.2 positivity** defined as ≥ 75% of tumor cells demonstrating moderate to strong membranous CLDN18 IHC

[g] **Zolbetuximab** acute nausea and/or vomiting may occur within 1 hour of zolbetuximab infusion; management includes a slower infusion rate and combination antiemetics (i.e. 5-HT3 receptor antagonist, NK-1 receptor blockers, dexamethasone, etc.)

[h] **CPS ≥5** there is longer follow up data with nivolumab and chemotherapy in the metastatic first line setting of esophageal cancer; the largest benefit of adding immune therapy to chemotherapy is in the CPS ≥5 patient population

[i] **CPS 1-4 and CLDN18.2 positive** there is no head to head comparison between zolbetuximab and chemotherapy or immunotherapy and chemotherapy; toxicity profiles are different, therefore discussion with patients that quality for either regimens is recommended

Gastric Cancer – Unresectable or Stage IV Adenocarcinoma (Any T, Any N, M1) MSS HER2 Negative Second Line

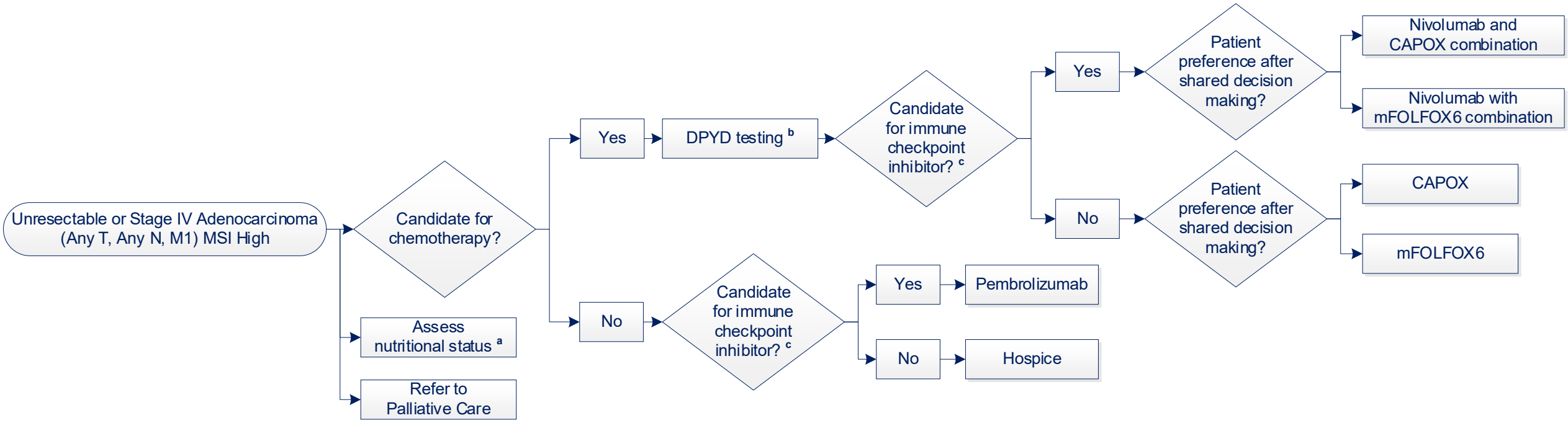


Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Candidate for ramucirumab** received fluoropyrimidine and platinum agent in the first-line setting; ECOG PS 0-2; ANC ≥ 1500/mm^3; due to anti-VEGF effects patients with the following should not receive ramucirumab: non-healing wound/fracture, major surgery in prior 4 weeks, bleeding disorder or coagulopathy, recent history of GI perforation, unstable cardiac condition (uncontrolled HTN, arterial thromboembolism, symptomatic CHF [NYHA II-IV] or arrhythmia), or active cocaine use

[b] **Ramucirumab** for patients that qualify for ramucirumab with paclitaxel, this combination is preferred based on the RAINBOW trial; ramucirumab alone is FDA approved based on REGARD trial, but should only be used in patients who do not qualify for the combination regimen; the majority of patients who have relapsed esophageal cancer are symptomatic, however, ramucirumab alone does not demonstrate partial or complete responses and only shows an increase to stable disease compared to placebo

Gastric Cancer – Unresectable or Stage IV Adenocarcinoma (Any T, Any N, M1) MSI High



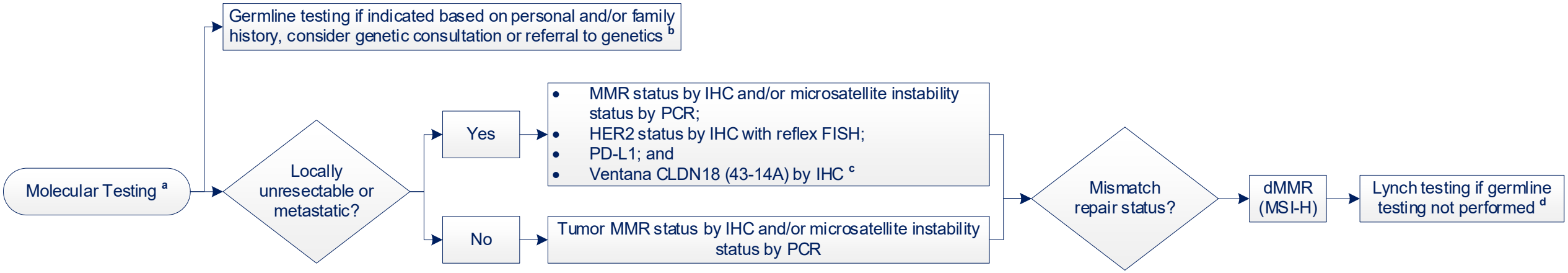
Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Assess nutritional status** consider palliative stent or other nutritional support modalities when clinically appropriate

[b] **Perform DPYD testing if not already performed** if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD results if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

[c] **Qualify for immune checkpoint inhibitor** patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

Gastric Cancer – Molecular Testing



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[a] **Molecular Testing** perform for pathologically confirmed cancer

[b] **Germline testing** consider germline testing if any of the following apply: 1) personal history of early-onset gastric cancer (age 50 or younger); or 2) significant personal and/or family history of multiple polyps or other hereditary cancer syndrome-associated cancers (e.g., colorectal, endometrial, gastric, ovarian, pancreas, urothelial, brain (usually glioblastoma), biliary tract, and small intestine, as well as sebaceous adenomas, sebaceous carcinomas, and keratoacanthomas as seen in Muir-Torre syndrome); or 3) pathogenic or likely pathogenic variant in a gene associated with known hereditary cancer syndrome is present in the patient's tumor or a family member; an appropriate germline testing panel should include at minimum the following genes: APC, ATM, BRCA1, BRCA2, BMPR1A, CDH1, CTNNA1, EPCAM, MLH1, MSH2, MSH6, MUTYH, PALB2, PMS2, POLD1, SMAD4, STK11, and TP53

[c] **Ventana CLDN18 (43-14A)** positivity is defined as ≥ 75% of tumor cells demonstrating moderate to strong membranous CLDN18 IHC

[d] **Lynch testing** the diagnostic Lynch genetic testing algorithm may be used if germline testing is not already performed and other criteria for germline testing have not been met (see above); it largely depends on the pattern of MLH1, MSH2, MSH6, and PMS2 expression by IHC; diagnostic Lynch genetic testing should be performed if 1) there is loss of MSH2, MSH6, MSH2/MSH6, or PMS2 expression by IHC; or 2) there is loss of MLH1 expression by IHC AND MLH1 promoter is UNmethylated; or 3) the tumor is MSI-H by PCR or NGS AND IHC is equivocal or cannot be performed AND MLH1 promoter is Unmethylated; adiagnostic Lynch genetic testing panel should include at minimum the following genes: EPCAM, MLH1, MSH2, MSH6, and PMS2

CGP comprehensive genomic profiling
dMMR deficient mismatch repair
IHC immunohistochemistry

Gastric Cancer – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Gastric Cancer All Stages	IHC*	Mismatch repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2).	Local VA or locally contracted vendor	No	Tumor Tissue
	PCR*	Microsatellite instability (MSI) status by PCR.	Regional Testing Center (GLA)	Yes	Tumor Tissue and Normal Tissue or Blood
	PGx	DPYD Testing**	Fulgent	Yes	Saliva, Blood
Metastatic or Unresectable Gastric Cancer	IHC	HER2 IHC with reflex to FISH if 2+ on IHC	Local VA or locally contracted vendor	No	Tumor Tissue
	FISH	Reflex to HER2 FISH if 2+ on IHC	Local VA or locally contracted vendor	No	Tumor Tissue
	IHC	PD-L1 IHC (clone 22C3 with CPS score)	Local VA or locally contracted vendor	No	Tumor Tissue
	IHC	Claudin 18.2	Local VA or locally contracted vendor or FMI	Yes when ordered with CGP through FMI	Tumor Tissue
Age <50	Germline NGS***	Full Germline NGS panel	Fulgent Prevention Genetics	Yes Yes	Saliva, Blood
Personal or Family History of Multiple Polyps or Other Cancers Associated with Hereditary Cancer Syndromes	Germline NGS***	Full Germline NGS panel	Fulgent Prevention Genetics	Yes Yes	Saliva, Blood
Deficient MMR or MSI-H tumor	Germline NGS****	If full germline testing not performed, perform Germline Lynch testing if: 1) MSH2 or MSH6 loss by IHC; 2) MLH1 or PMS2 loss by IHC and MLH1 unmethylated; or 3) MSI-H without IHC testing and MLH1 unmethylated	Fulgent Prevention Genetics	Yes Yes	Saliva, Blood

* For higher stage disease, perform both MMR and MSI.

** Perform DPYD Testing If not already Performed; if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD testing if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

*** VA Common Hereditary POC panel or Equivalent Germline Test; Full Germline NGS should include at a minimum APC, ATM, BRCA1, BRCA2, BMPR1A, CDH1, CTNNA1, EPCAM, MLH1, MSH2, MSH6, MUTYH, PALB2, PMS2, POLD1, SMAD4, STK11, and TP53; For genetic online ordering, refer to CCGS page for further details

**** Germline Lynch testing should include at minimum the following genes: EPCAM (deletion), MLH1, MSH2, MSH6, PMS2, POLE, and POLD1