Oncology Clinical Pathways
Biliary Tract Cancer

December 2023 – V2.2023

Table of Contents

Biliary Tract 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.

Vietnam Veterans – Agent Orange Exposure or Specified Locations

- Cancer of the bile duct

Gulf War and Post 9/11 Veterans

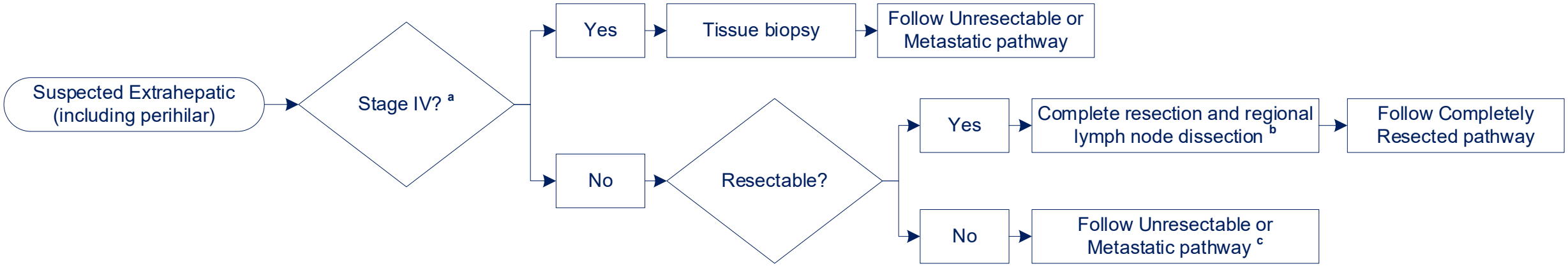
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if you served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- 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)

Biliary Tract Cancer – Suspected Extrahepatic



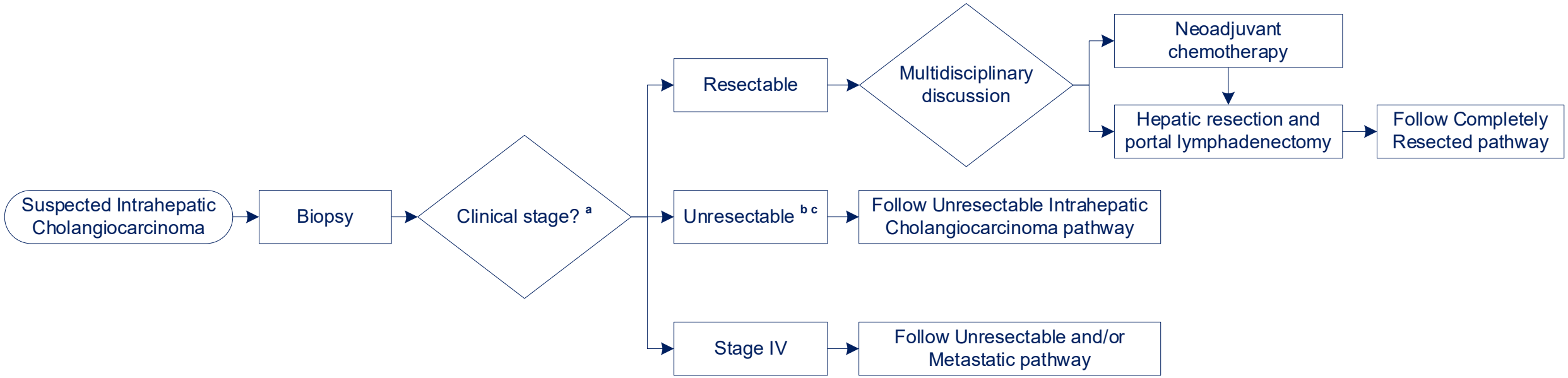
Clinical trial(s) always considered on pathway.

[a] **Stage** multiphase CT or MRI + contrast, CT chest, labs (CEA, CA 19-9, AFP, LFTs, viral hepatitis serologies); contrast MRI with MRCP preferred for evaluating gallbladder masses and tumors with bile duct involvement; delayed phase imaging preferred for intrahepatic bile duct cancer

[b] **Resectable** pancreaticoduodenectomy required for distal bile duct tumors and major hepatic resection for proximal perihilar tumors

[c] **Transplant Candidate** if patient is a potential transplant candidate, place referral to transplant center; avoid fine needle biopsy; unresectable perihilar or hilar cholangiocarcinomas (CCAs) ≤3 cm without metastases and nodal disease may be considered for liver transplantation

Biliary Tract Cancer – Suspected Intrahepatic



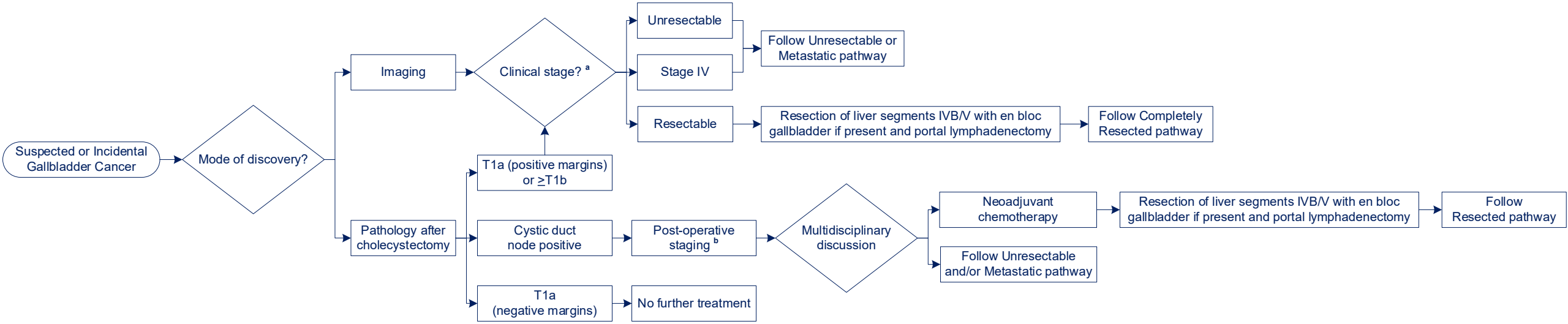
Clinical trial(s) always considered on pathway.

[a] **Clinical Stage** multiphase CT or MRI + contrast, CT chest, labs (CEA, CA 19-9, AFP, LFTs, viral hepatitis serologies); contrast MRI with MRCP preferred for evaluating gallbladder masses and tumors with bile duct involvement; delayed phase imaging preferred for intrahepatic bile duct cancer

[b] **Unresectable** includes both anatomically unresectable or patient is not a candidate for resection

[c] **Transplant Candidate** in highly selective patients if transplant is considered, place referral to transplant center prior to biopsy

Biliary Tract Cancer – Suspected or Incidental Gallbladder Cancer

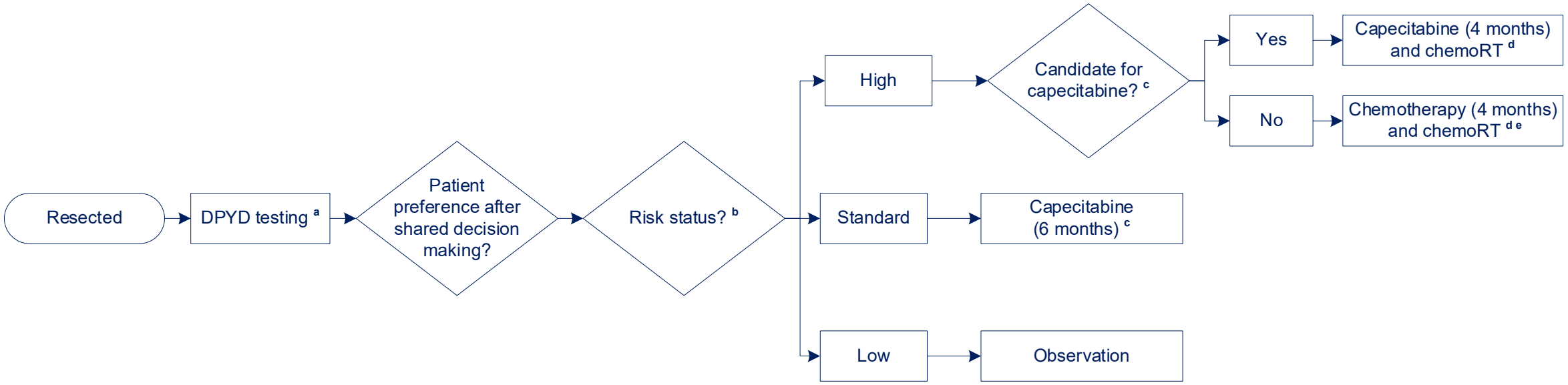


Clinical trial(s) always considered on pathway.

[a] **Clinical Stage** multiphase CT or MRI + contrast, CT chest, labs (CEA, CA 19-9, AFP, LFTs, viral hepatitis serologies), fine needle aspiration/core biopsy; contrast MRI with MRCP preferred for evaluating gallbladder masses and tumors with bile duct involvement; delayed phase imaging preferred for intrahepatic bile duct cancer

[b] **Post-Op Staging** includes multiphasic CT abdomen/pelvis, contrast MRI, chest CT, CEA, CA 19-9

Biliary Tract Cancer – Resected



Clinical trial(s) always considered on pathway.

[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.

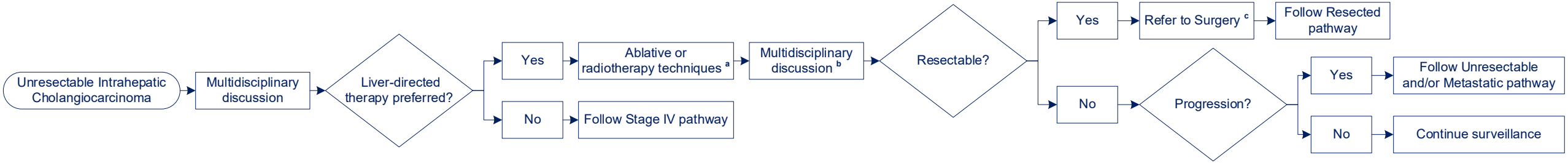
[b] **Risk Status** patients with R1 (positive margins); lymph node disease will be considered high risk; T1NO gallbladder cancers will be considered low risk; all other patients will be considered standard risk

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

[d] **ChemoRT** if R1 resection, consider capecitabine and RT or protracted infusion 5-fluorouracil and RT before systemic capecitabine; should consider protracted infusion 5-fluorouracil and RT

[e] **Chemotherapy** consider gemcitabine-based chemotherapy regimen

Biliary Tract Cancer – Unresectable Intrahepatic



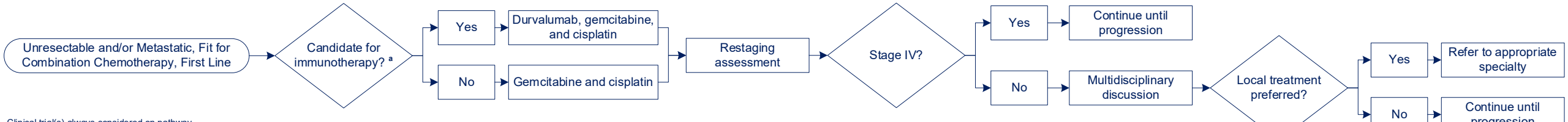
Clinical trial(s) always considered on pathway.

[a] **Ablative or Radiotherapy Techniques** include external beam radiation, thermal ablation with microwave or RFA, radiation segmentectomy (y90), irreversible electroporation, transarterial chemoembolization, or histotripsy based on multidisciplinary discussion and availability

[b] **Multidisciplinary Discussion** perform at time of restaging

[c] **Surgery** referral to hepato-biliary surgery if available

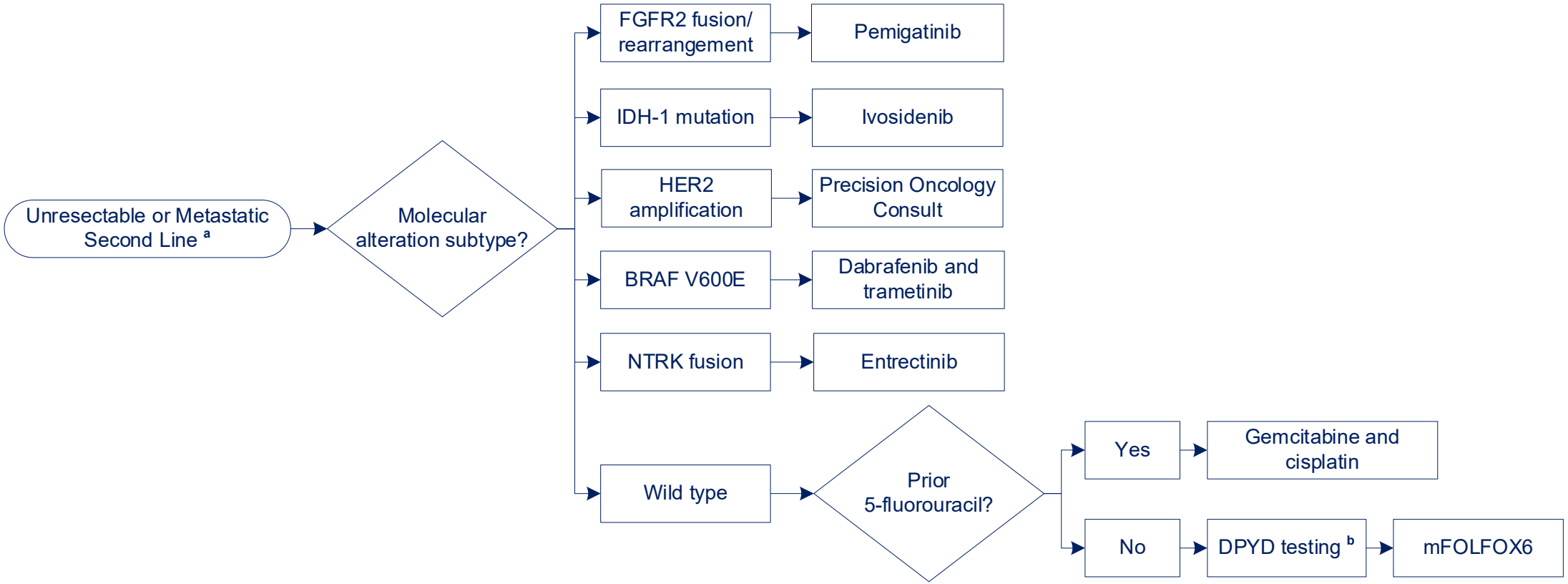
Biliary Tract Cancer – Unresectable or Metastatic First Line



Clinical trial(s) always considered on pathway.

[a] **Candidate for Immunotherapy** prior recipients of solid organ transplant or those with uncontrolled autoimmune/inflammatory condition should not be offered immunotherapy

Biliary Tract Cancer – Unresectable or Metastatic Second Line

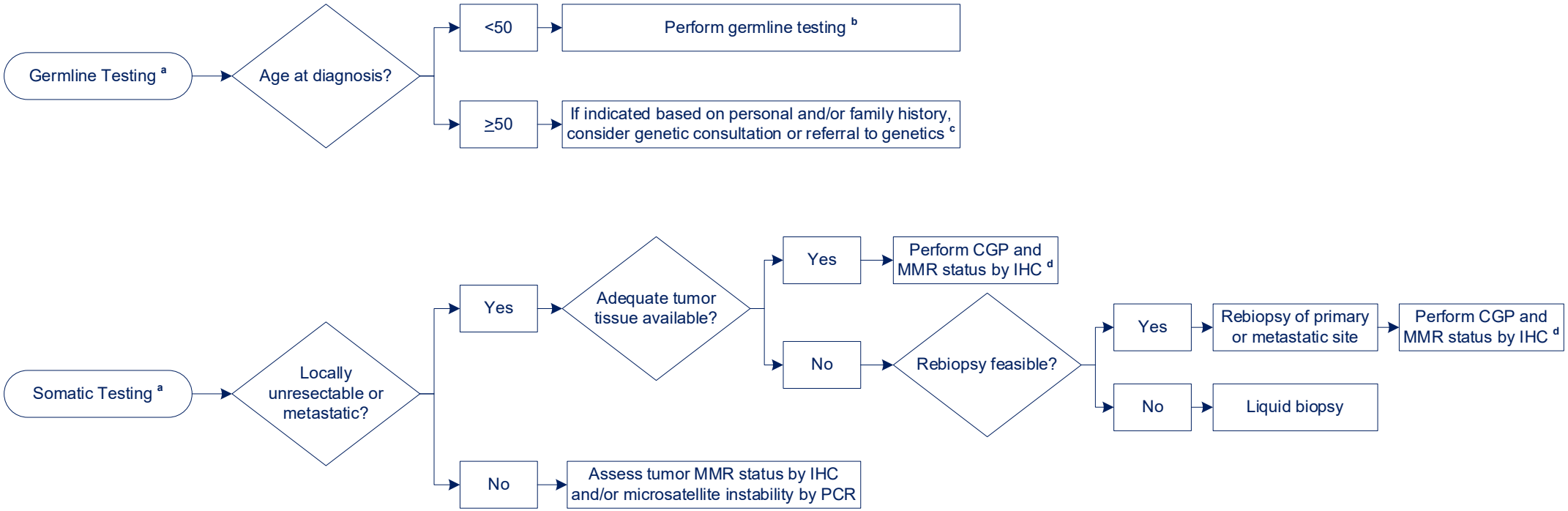


Clinical trial(s) always considered on pathway.

[a] **Second Line** prior progression on first line chemotherapy or relapse within 6 versus 12 months of completion of adjuvant treatment

[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.

Biliary Tract Cancer – Molecular Testing



Clinical trial(s) always considered on pathway.

[a] **Molecular Testing** perform for all pathologically confirmed biliary tract cancers

[b] **Germline Testing** for bile duct cancer should include at minimum the following genes: BRCA1, BRCA2, BAP1, PALB2, EPCAM (deletion), MLH1, MSH2, MSH6, PMS2

[c] **Personal and Family History** consider germline testing if there is a personal history of other cancers (e.g., breast, ovarian, pancreas, colorectal, gastric, endometrial) or family history of a close relative with bile duct cancer or multiple relatives with other cancers

[d] **CGP** with platform that uses DNA and RNA based testing or DNA and RNA based CGP

CGP Comprehensive Genomic Profiling

Biliary Tract Cancer – Molecular Testing Table

Indication	Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Biliary Tract	Localized, Resectable Disease	IHC*	MLH1, MSH2, MSH6, PMS2	Local VA or Locally contracted vendor	No	Tumor Tissue
		PCR*	Microsatellite instability (MSI) status by PCR	Regional Testing Center (GLA)	Yes	Tumor Tissue, Blood
	Metastatic or Unresectable Cholangiocarcinoma	Somatic NGS**	DNA and RNA-based Comprehensive genomic profiling (CGP)	Tempus	Yes	Tumor Tissue, Blood
		IHC**	MLH1, MSH2, MSH6, and PMS2	Tempus	Yes	Tumor Tissue
	Age <50	Germline NGS***	Germline NGS panel	Fulgent Genetics	Yes	Blood, Saliva
	Personal or Family History of Other Bile Duct Cancers, Multiple Cancers, or Other Lynch-Associated Cancers	Germline NGS***	Germline NGS panel	Fulgent Genetics	Yes	Blood, Saliva
	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 or 2) MLH1 or PMS2 loss by IHC and *MLH1* unmethylated or 3) MSI-H without IHC testing and *MLH1* unmethylated	Fulgent Genetics	Yes	Blood, Saliva

* Localized, resectable disease needs either IHC or PCR to assess MMR status

** Metastatic or unresectable disease should perform BOTH IHC and NGS for MMR status

*** Germline testing should include at a minimum BRCA1, BRCA2, BAP1, PALB2, EPCAM (deletion), MLH1, MSH2, MSH6, and PMS2.

Questions?

Contact VHAOncologyPathways@va.gov