Oncology Clinical Pathways
Ovarian & Fallopian Cancer

April 2025 – V1.2025

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Ovarian & Fallopian 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 Exposed to Ionizing Radiation

- Cancer of the ovary

Gulf War and Post 9/11 Veterans

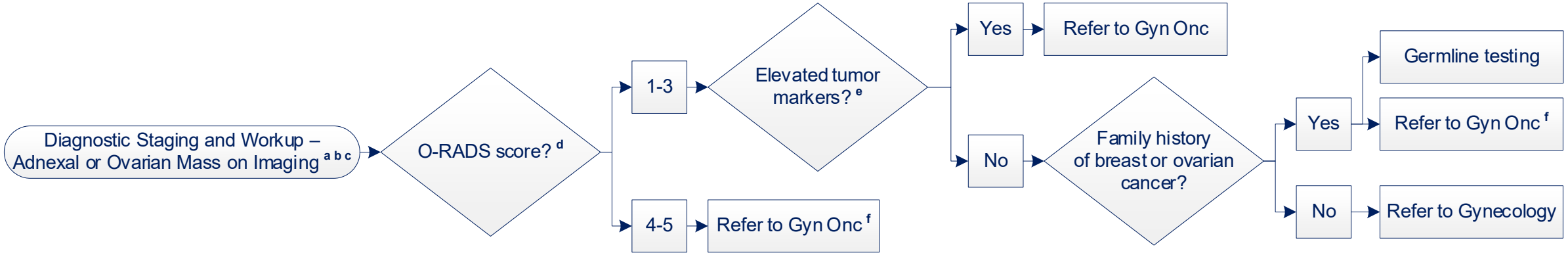
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Reproductive 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)

Ovarian & Fallopian Cancer – Diagnostic Workup and Staging – Adnexal or Ovarian Mass



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

[a] **Diagnostic Staging and Workup** indications for imaging include
1. unexplained symptoms such as but not limited to bloating, pelvic-abdominal pain, urinary urgency or frequency, changes in bowel habit, early satiety;
2. clinically-suspicious lesions upon abdominal and pelvic exam

[b] **All Adnexal Masses** should be referred to Gyn or Gyn Onc per pathway

[c] **Imaging** transabdominal-transvaginal pelvic ultrasound and/or abdominal-pelvic CT or MRI

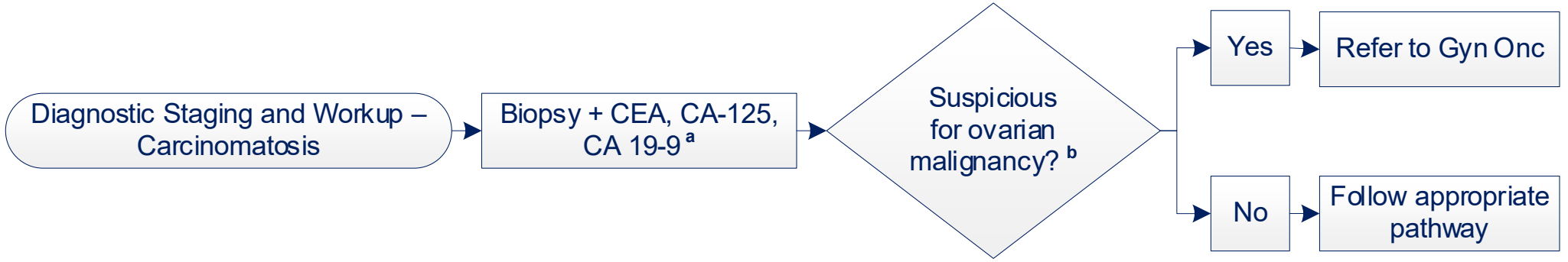
[d] **O-RADS score** currently only available on transvaginal or transabdominal ultrasound or MRI; for CT, complex masses, i.e., septations, mural nodules, papillary projections, ascites, increased Doppler flow, should be referred to Gyn Oncology

[e] **CA125 and CEA** for premenopausal patients with complex masses highly suspicious for malignancy and for all postmenopausal patients; additional tumor markers such as inhibin A/B, LDH, AFP, HCG, HE4, CA19-9 may be ordered per clinician decision-making; germ cell tumors may be more common in Veterans than non-Veterans

[f] **Refer to NTO** if local gyn oncologist not available via IFC Durham order (select BGSOE)

ORADS Ovarian-Adnexal Reporting and Data System

Ovarian & Fallopian Cancer – Diagnostic Workup and Staging – Carcinomatosis



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[a] **Obtain CT chest** if chest imaging not previously obtained

[b] **Suspicious for ovarian malignancy** examples include high-grade or low-grade serous histology and/or PAX8 positive

Ovarian & Fallopian Cancer – Histology

Epithelial Borderline	Epithelial Malignant
Serous borderline tumor	Low-grade serous carcinoma
Borderline Brenner tumor	High-grade serous carcinoma
Mucinous borderline tumor	Mesonephric-like adenocarcinoma
Endometrioid borderline tumor	Undifferentiated and dedifferentiated carcinoma
Seromucinous borderline tumor	Carcinosarcoma
Clear cell borderline tumor	Mixed carcinoma
	Endometrioid stromal sarcoma
	Adenosarcoma
	Malignant Brenner tumor
	Endometrioid carcinoma
	Mucinous carcinoma
	Clear cell carcinoma
	Seromucinous carcinoma

Sex Cord-Stromal Tumors	Germ Cell Tumors
Ovarian fibroma	Immature teratoma
Thecoma	Dysgerminoma
Luetinized thecoma associated with sclerosing peritonitis	Yolk sac tumor
Sclerosing stromal tumor	Embryonal carcinoma
Signet-ring stromal tumor	Nongestational choriocarcinoma
Leydig cell tumor	Mixed germ cell tumor
Steroid cell tumor	Monodermal teratoma and somatic-type tumors arising from a dermoid cyst
Ovarian fibrosarcoma	Struma ovarii
Adult granulosa cell tumor	Carcinoid
Juvenile granulosa cell tumor	Neuroectodermal-type tumors
Sertoli cell tumor	Monodermal cystic teratomas
Sex cord tumor with annular tubules	Somatic neoplasms arising from teratomas
Sertoli-Leydig cell tumor	Germ cell-sex cord-stromal tumors
Sex cord-stromal tumors NOS	Gonadoblastoma
Gynandroblastoma	Mixed germ cell-sex cord-stromal tumor, unclassified
	Rete adenocarcinoma

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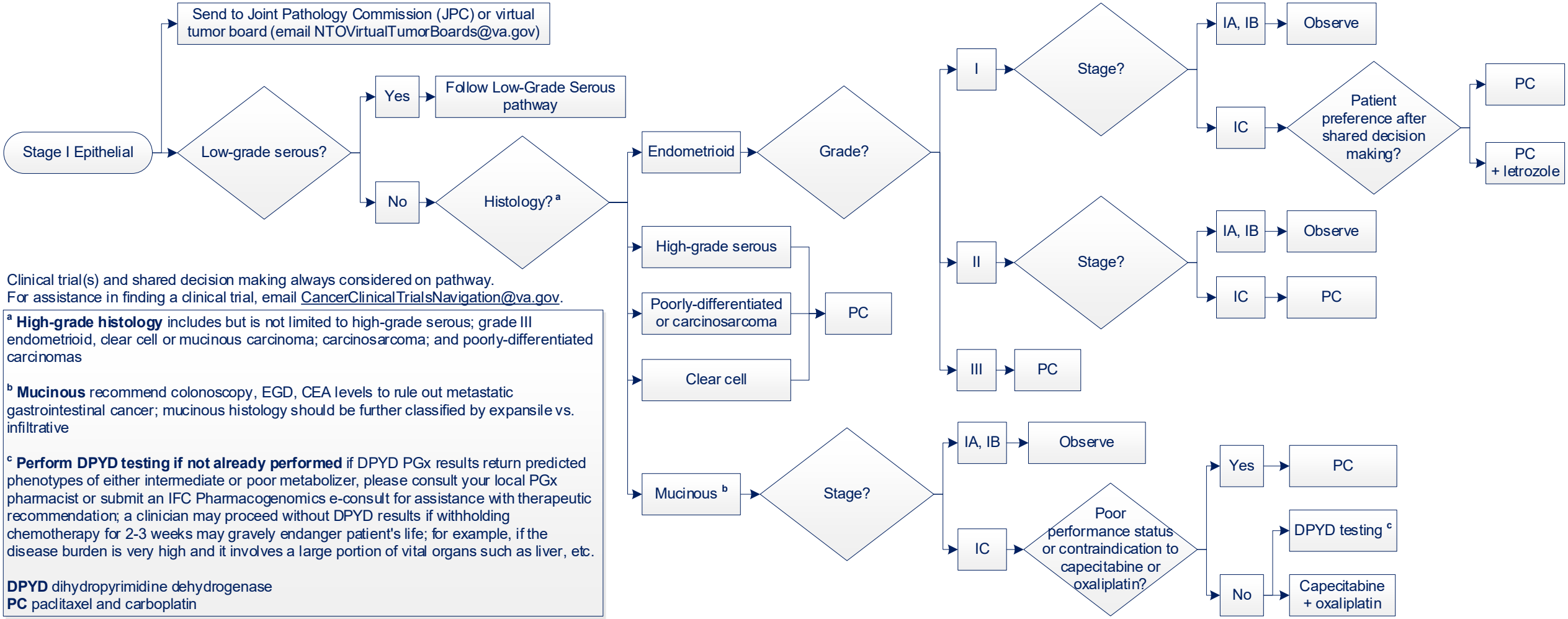
Ovarian & Fallopian Cancer – Stage I Epithelial



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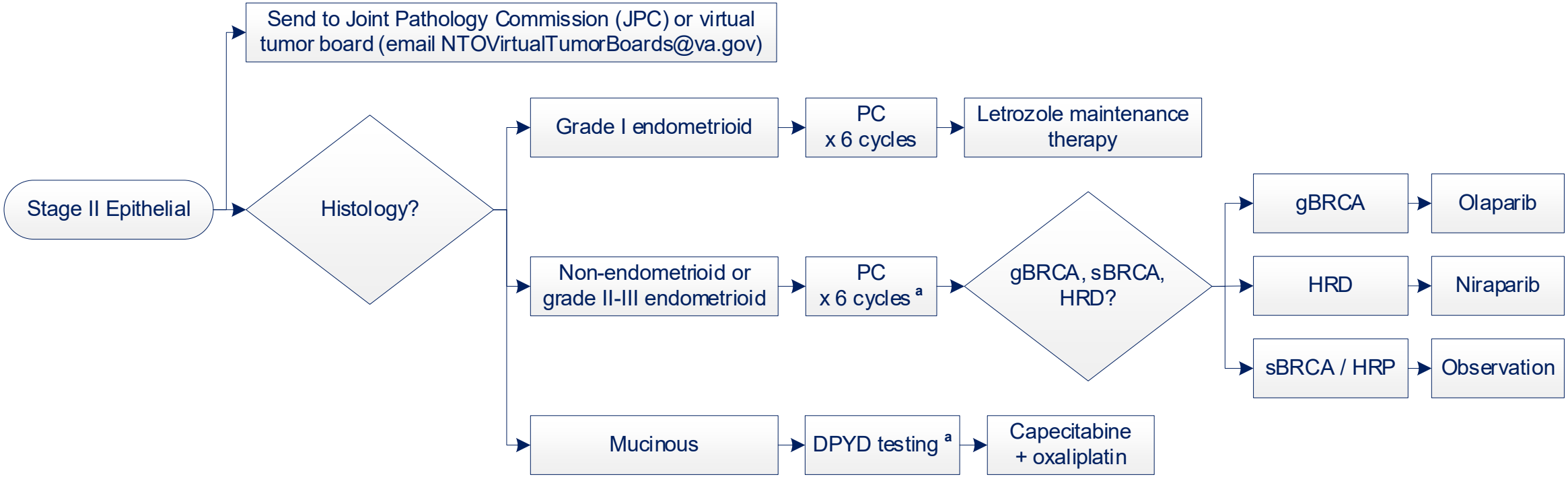
[a] **High-grade histology** includes but is not limited to high-grade serous; grade III endometrioid, clear cell or mucinous carcinoma; carcinosarcoma; and poorly-differentiated carcinomas

[b] **Mucinous** recommend colonoscopy, EGD, CEA levels to rule out metastatic gastrointestinal cancer; mucinous histology should be further classified by expansile vs. infiltrative

[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.

DPYD dihydropyrimidine dehydrogenase
PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Stage II Epithelial



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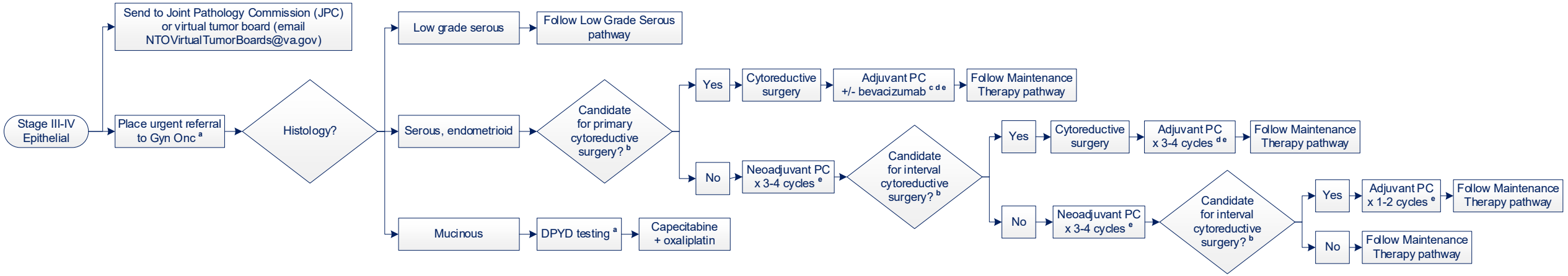
DPYD dihydropyrimidine dehydrogenase
HRD homologous recombination deficiency
HRP homologous recombination proficiency
PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Stage III-IV Epithelial



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[a] **Refer to NTO** if local gyn oncologist not available

[b] **Candidate for cytoreductive surgery** based on imaging, CT chest-abdomen-pelvis, performance status, and medical comorbidities; recommend diagnostic laparoscopy for assessment

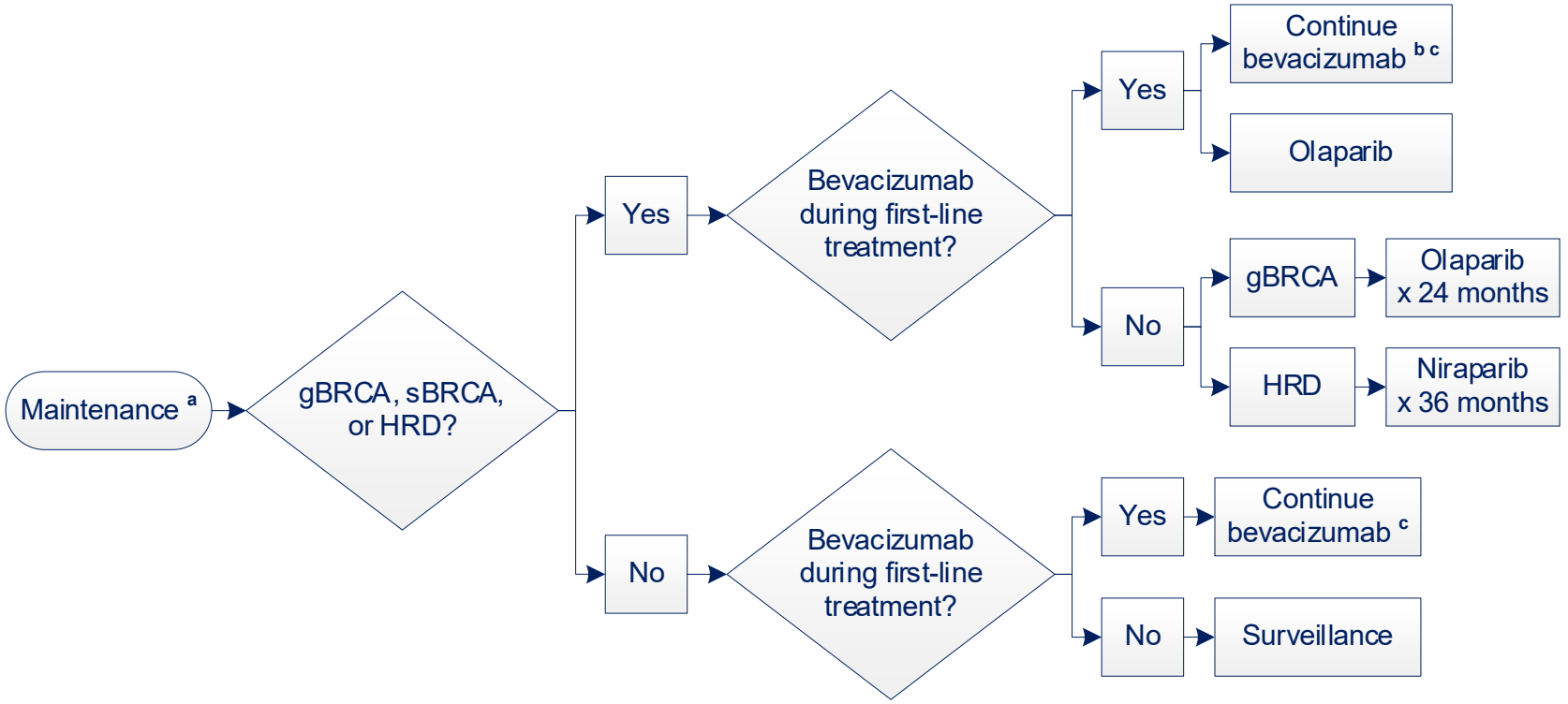
[c] **Candidate for bevacizumab** ECOG PS 0-2; bevacizumab should be held in the following patients: non-healing wound/fracture, major surgery in prior 4 weeks, recent history of GI perforation or small bowel obstruction, or unstable cardiac condition (uncontrolled HTN, arterial thromboembolism)

[d] **Bevacizumab** consider bevacizumab if suboptimal cytoreductive surgery > 1cm residual disease or significant burden of ascites or pleural infusions

[e] **PC** first-line chemotherapy for ovarian cancer consists of 6-9 cycles

PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Maintenance



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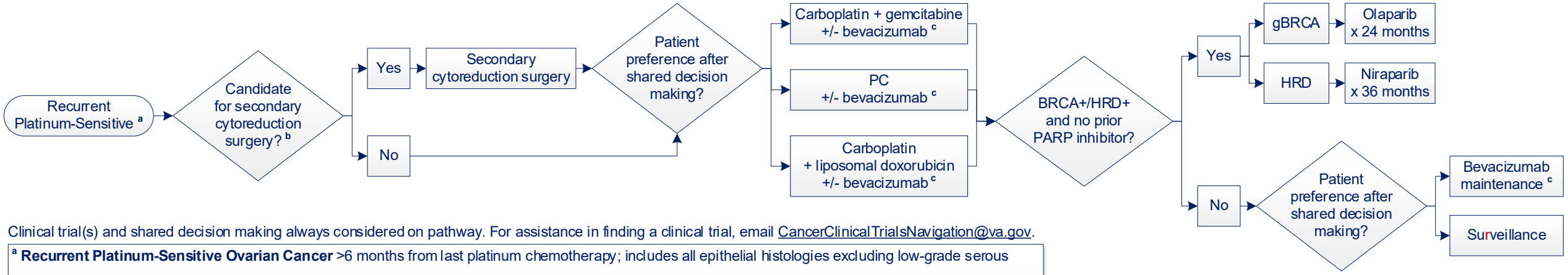
[a] **Maintenance therapy** after first-line chemotherapy for high-grade serous, endometrioid or clear cell histology with partial or complete response to chemotherapy

[b] **Bevacizumab** if bevacizumab with olaparib, up to 15 months, including those given during chemotherapy or until disease progression

[c] **Bevacizumab** if bevacizumab alone, up to 22 cycles total including those given during chemotherapy or until disease progression

HRD homologous recombination deficiency

Ovarian & Fallopian Cancer – Recurrent Platinum-Sensitive



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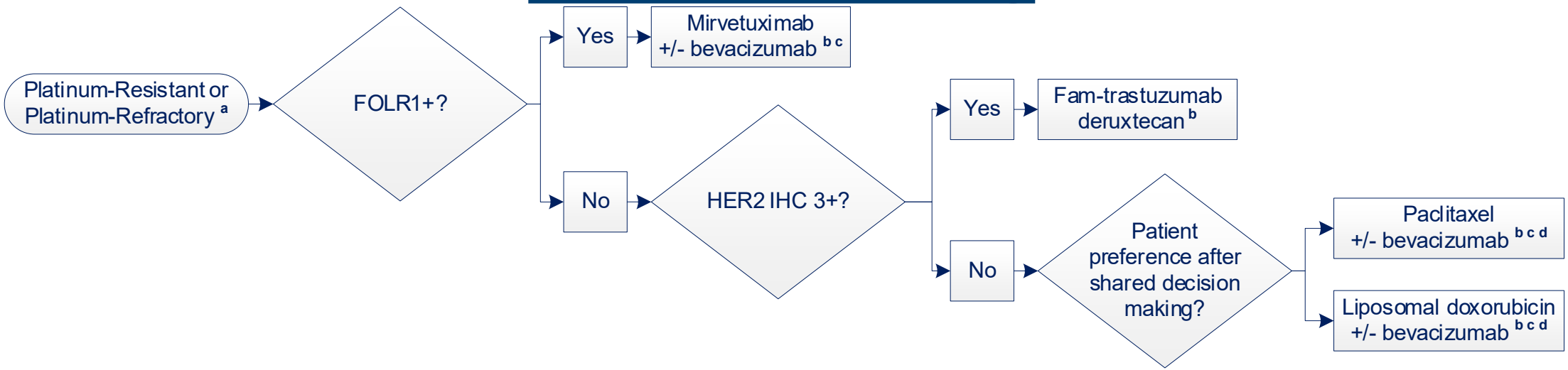
[a] **Recurrent Platinum-Sensitive Ovarian Cancer** >6 months from last platinum chemotherapy; includes all epithelial histologies excluding low-grade serous

[b] **Candidate for secondary cytoreduction surgery** consider if oligometastatic disease, ECOG 0-1, low-to-minimal ascites; complete optimal primary cytoreduction or early stage disease at initial surgery; CT chest-abdomen-pelvis is recommended prior to surgery

[c] **Bevacizumab** there is evidence to repeat bevacizumab therapy and maintenance in individuals who have previously received bevacizumab, including those who have progressed on bevacizumab; standard criteria for bevacizumab include ECOG PS 0-2; bevacizumab should be held in the following patients: non-healing wound/fracture, major surgery in prior 4 weeks, recent history of GI perforation or small bowel obstruction, or unstable cardiac condition (uncontrolled HTN, arterial thromboembolism)

HRD homologous recombination deficiency
PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Platinum-Resistant or Platinum-Refractory



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[a] **Platinum-Resistant or Platinum Refractory** platinum-resistant is disease recurrence within six months of prior platinum therapy; platinum-refractory is progression during platinum-based chemotherapy; platinum-refractory patients should be strongly considered for clinical trial

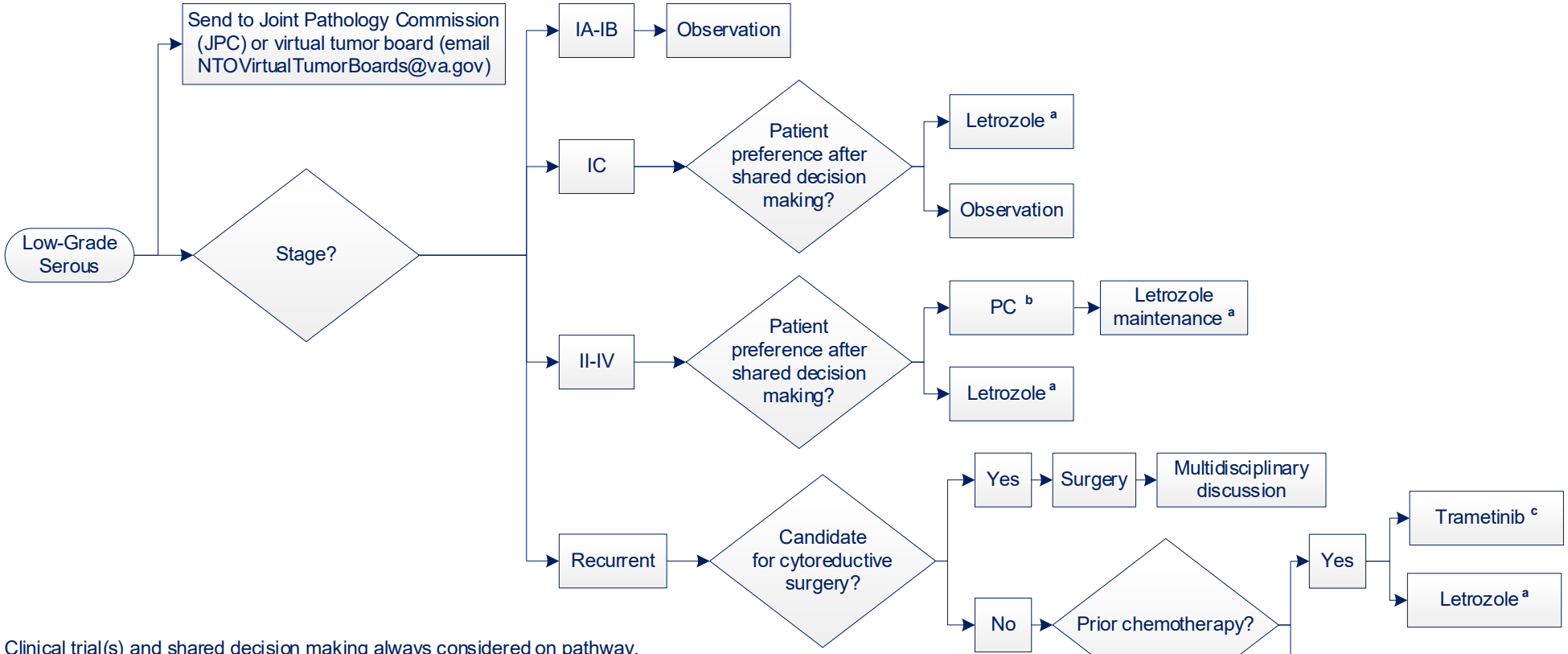
[b] **Multidisciplinary discussion** at time of disease progression, discuss at virtual tumor board (email NTOVirtualTumorBoards@va.gov)

[c] **Bevacizumab** there is evidence to repeat bevacizumab therapy and maintenance in individuals who have previously received bevacizumab, including those who have progressed on bevacizumab; standard criteria for bevacizumab include ECOG PS 0-2; bevacizumab should be held in the following patients: non-healing wound/fracture, major surgery in prior 4 weeks, recent history of GI perforation or small bowel obstruction, or unstable cardiac condition (uncontrolled HTN, arterial thromboembolism)

[d] **Other single agent regimens** include gemcitabine, pemetrexed, cyclophosphamide, topotecan

FOLR1 folate receptor alpha

Ovarian & Fallopian Cancer – Low-Grade Serous



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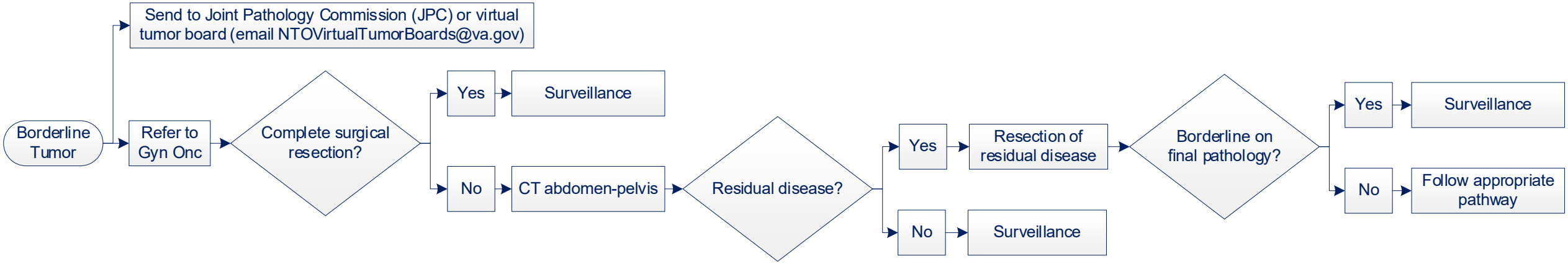
[a] **Letrozole** is preferred agent; other options include other aromatase inhibitors (i.e., anastrozole, exemestane), leuprolide acetate, or goserelin acetate

[b] **Bevacizumab** should be considered for stage IV disease, significant ascites, or pleural effusions; bevacizumab should be held in the following patients: non-healing wound/fracture, major surgery in prior 4 weeks, recent history of GI perforation or small bowel obstruction, or unstable cardiac condition (uncontrolled HTN, arterial thromboembolism)

[c] **Chemotherapy** can be considered for select platinum-sensitive low-grade serous recurrences

PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Borderline Tumor



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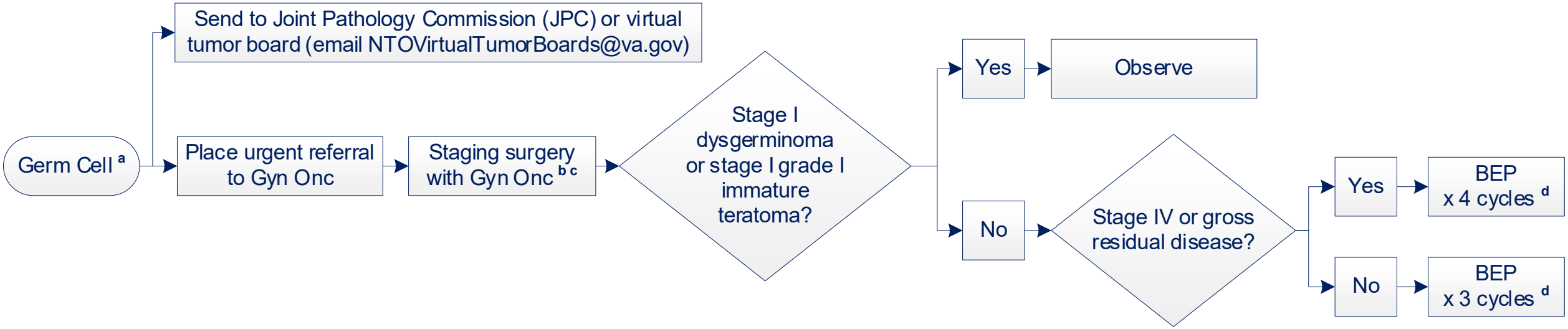
Ovarian & Fallopian Cancer – Germ Cell



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[a] **Germ Cell** suspected by appearance on imaging or tumor markers (e.g., inhibin, DHEA, AMH, testosterone) or incidental diagnosis; refer to Histology slide

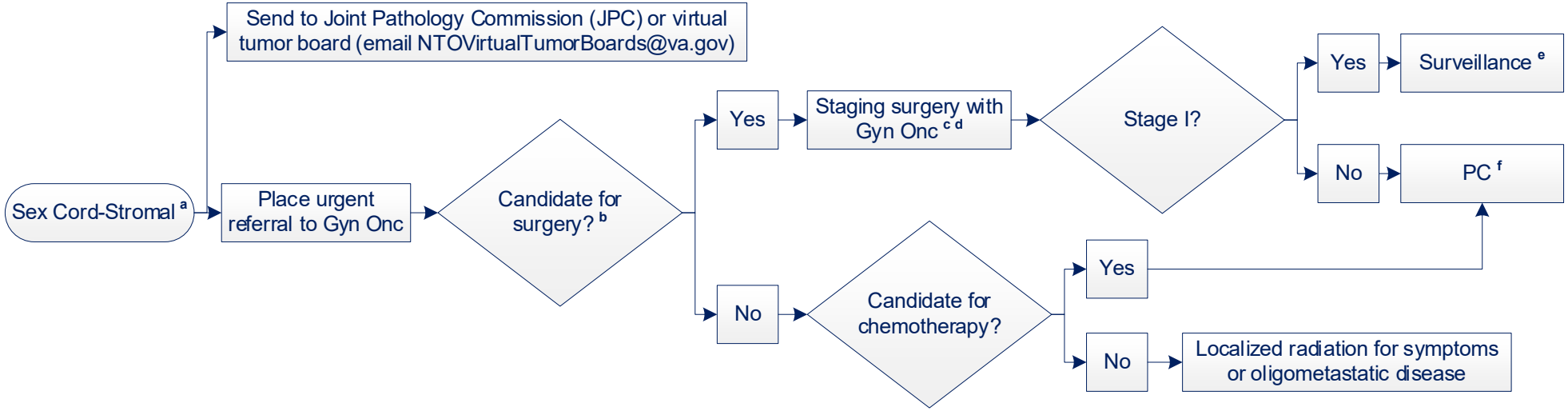
[b] **Staging surgery** fertility-sparing surgery with staging can be considered for premenopausal patients with disease confined to one ovary and desired fertility

[c] **Staging for germ cell** includes pelvic washings, peritoneal biopsies, omental biopsy, and lymphadenectomy

[d] **BEP** consider 4 cycles of BEP if high-risk tumor markers: AFP > 10,000 mcg/L, serum beta hCG > 50,000 unit/L, LDH > 10 x normal range

BEP bleomycin, etoposide, cisplatin

Ovarian & Fallopian Cancer – Sex Cord-Stromal



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

[a] **Sex Cord-Stromal** suspected by appearance on imaging or tumor markers (e.g., inhibin, DHEA, AMH, testosterone) or incidental diagnosis

[b] **Cytoreductive surgery** should be considered at recurrence

[c] **Staging surgery** fertility-sparing surgery with staging can be considered for premenopausal patients with disease confined to one ovary and desired fertility; endometrial sampling required for patients with fertility-sparing surgery

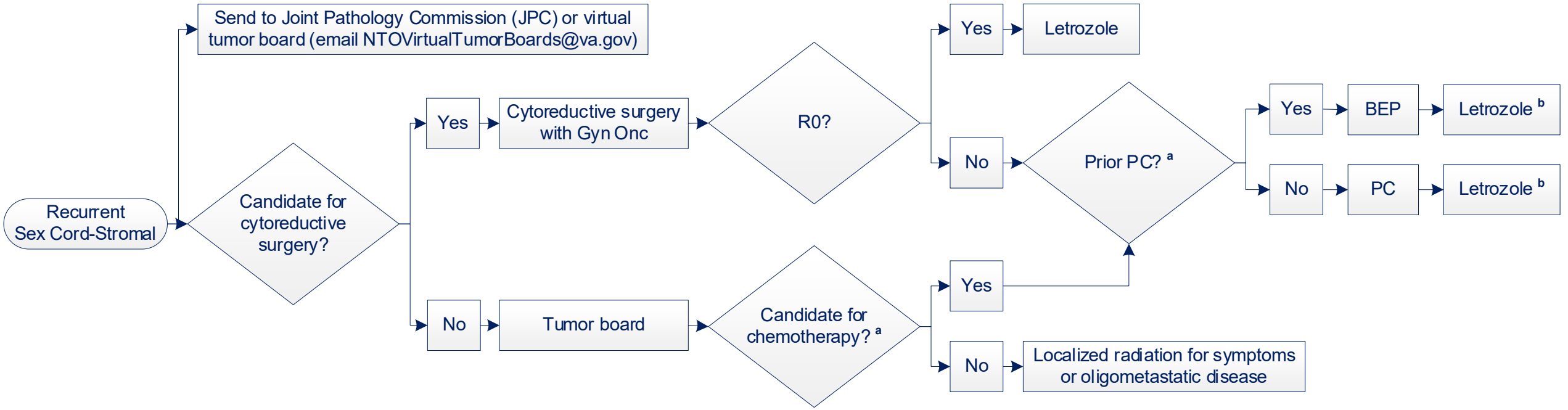
[d] **Staging for sex cord-stromal tumors** includes pelvic washings and peritoneal biopsies and omental biopsy; lymphadenectomy may be omitted; repeat surgery can be omitted for patients with incidental diagnosis of sex cord-stromal tumor, oophorectomy, and negative imaging

[e] **Surveillance** platinum-based chemotherapy can be considered for high-risk Stage I sex cord-stromal tumors, e.g., ruptured Stage IC or poorly-differentiated; inhibin levels should be followed for granulosa cell tumors

[f] **PC** is preferred; other options include EP or BEP

BEP bleomycin, etoposide, cisplatin
EP etoposide and cisplatin
PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Recurrent Sex Cord-Stromal



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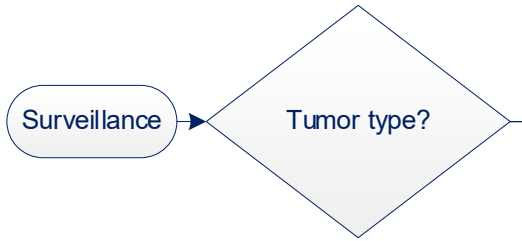
[a] **PC** x 6-9 cycles preferred; EP or BEP can be used if not already given; bevacizumab can also be considered as a single-agent in later recurrences

[b] **Letrozole** hormonal maintenance therapy should be considered for patients without prior progression on hormonal maintenance therapy, aromatase inhibitors are preferred with leuprolide as alternative option for granulosa cell tumors

BEP bleomycin, etoposide, cisplatin
EP etoposide and cisplatin
PC paclitaxel and carboplatin

Ovarian & Fallopian Cancer – Surveillance



Epithelial borderline

	Year 1	Year 2	Year 3-5	After Year 5
Physical exam, pelvic exam, symptom review, tumor markers if initially elevated	Every 3-6 months	Every 6 months		Annually
Pelvic ultrasound for patients with fertility-sparing surgery	Every 6 months			

Epithelial malignant / Sex cord-stromal

	Year 1	Year 2	Year 3-5	After Year 5
Physical exam, pelvic exam, symptom review, tumor markers if initially elevated	Every 3 months	Every 4 months	Every 6 months	Annually
Imaging (CT/MRI first-line) as clinically indicated				

Germ cell: dysgerminoma

	Year 1	Year 2	Year 3-5	After Year 5
Physical exam, pelvic exam, symptom review, tumor markers if initially elevated	Every 3 months		Every 6 months	Annually
CT abdomen-pelvis	Every 3 months	Every 6 months	Annually	As clinically indicated

Germ cell: non-dysgerminoma

	Year 1	Year 2	Year 3-5	After Year 5
Physical exam, pelvic exam, symptom review, tumor markers if initially elevated	Every 3 months		Every 6 months	Annually
CT abdomen-pelvis-chest	Every 3 months	Every 6 months		
CT abdomen-pelvis			Annually	As clinically indicated

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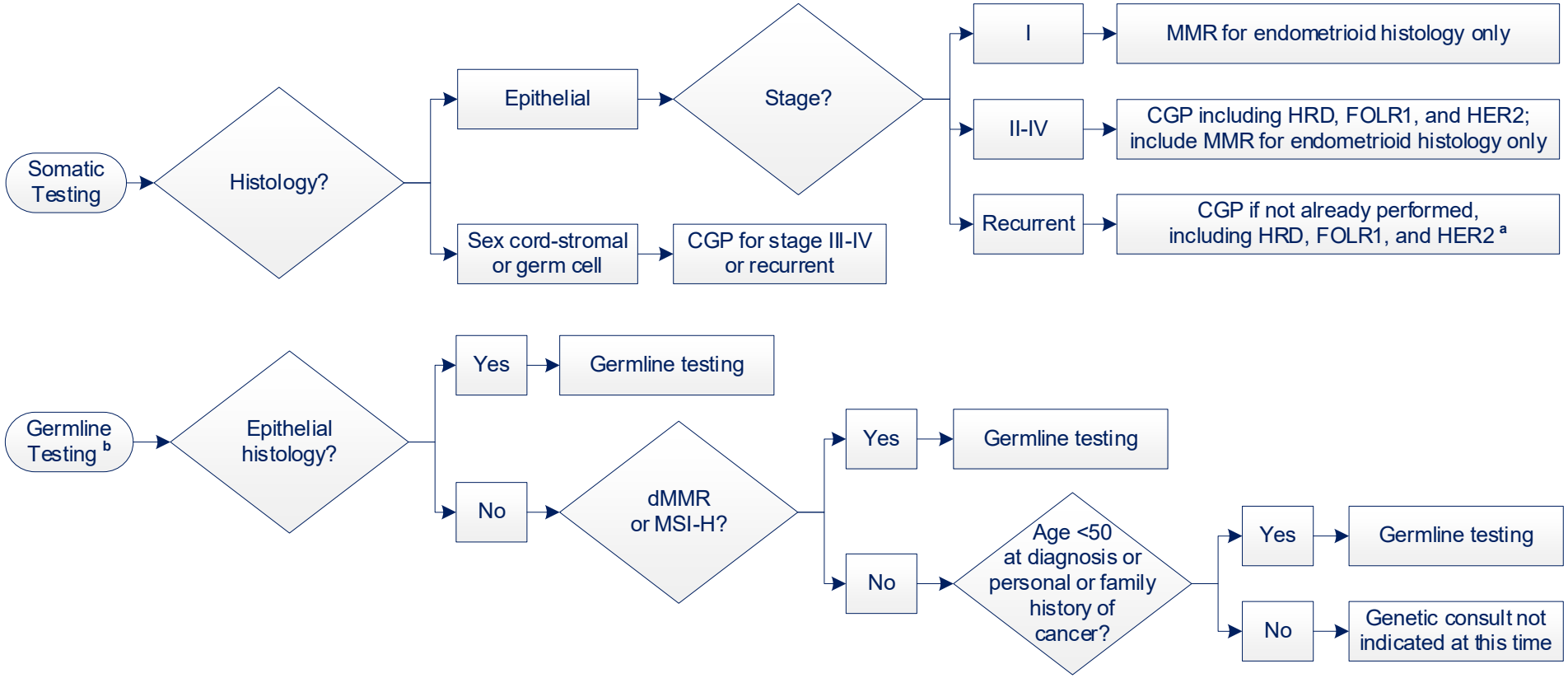
Ovarian & Fallopian Cancer – Molecular Testing



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[a] **CGP** other reasons to repeat include prior targeted therapy (including PARP inhibitors), variant histology in metastatic disease

[b] **Germline Testing** recommend panel genetic testing for genes associated with ovarian cancer including ATM, BRCA1, BRCA2, BRIP1, Lynch syndrome genes [MLH1, MSH2, MSH6, EPCAM], PALB2, RAD51C, and RAD51D

CGP comprehensive genomic profiling
FOLR1 folate receptor alpha
HRD homologous recombination deficiency

Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Epithelial Tumor, Endometrioid Histology, Stage I	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, Normal Tissue, Blood
Epithelial Tumor, All Histologies, Stage II-IV	IHC	MLH1, MSH2, MSH6, PMS2	Tempus	Yes	Tumor Tissue
	IHC	Folate Receptor alpha (FOLR1)	Foundation Medicine when ordered with NGS	Yes	Tumor Tissue
	IHC	HER2	Foundation Medicine when ordered with NGS	Yes	Tumor Tissue
	Somatic NGS	CGP using both DNA and RNA based methodology	Tempus Foundation Medicine	Yes Yes	Tumor Tissue, Blood
Epithelial Tumor, Mucinous Histologies, All Stages	PGx	DPYD*	Fulgent	Yes	Blood, Saliva
Epithelial Tumor, All Histologies, All Stages	Germline NGS	Germline NGS panel (VA POC recommended)	Fulgent	Yes	Blood, Saliva

* 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.