Oncology Clinical Pathways
Cervical Cancer

April 2025 – V1.2025

Table of Contents

Cervical 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.

Gulf War and Post 9/11 Veterans

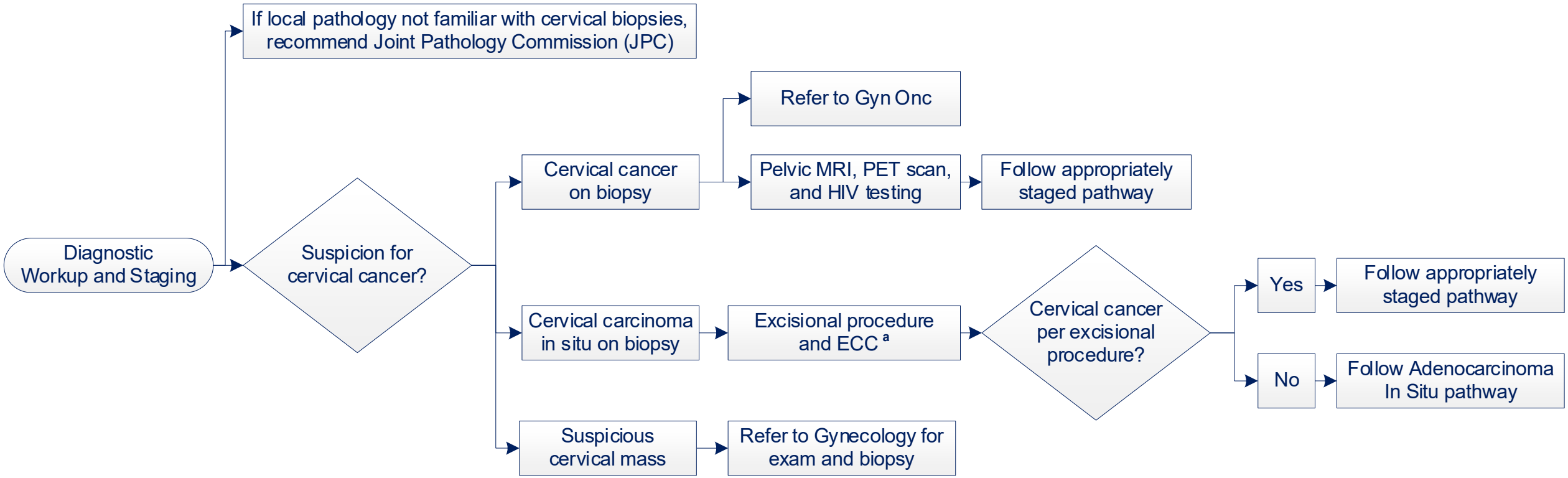
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- 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)

Cervical Cancer – Diagnostic Workup and Staging

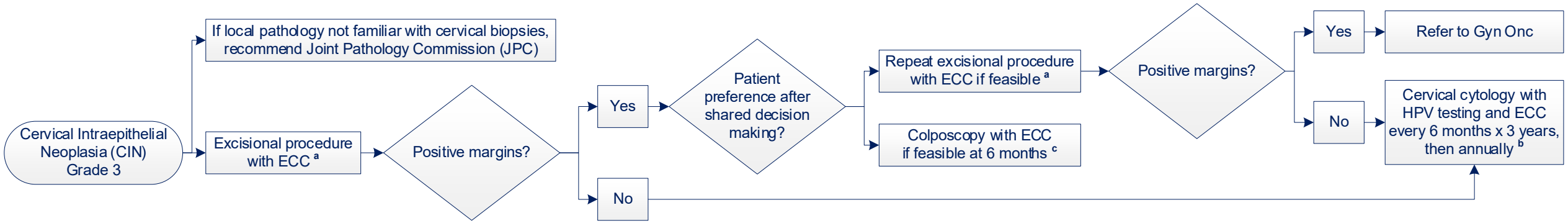


Clinical trial(s) and shared decision making always considered on pathway. For assistance in finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Excisional procedure** LEEP or cold knife cone; consider cold knife cone in these situations

ECC endocervical curettage
LEEP loop electrosurgical excision procedure

Cervical Cancer – Cervical Intraepithelial Neoplasia (CIN) Grade 3



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

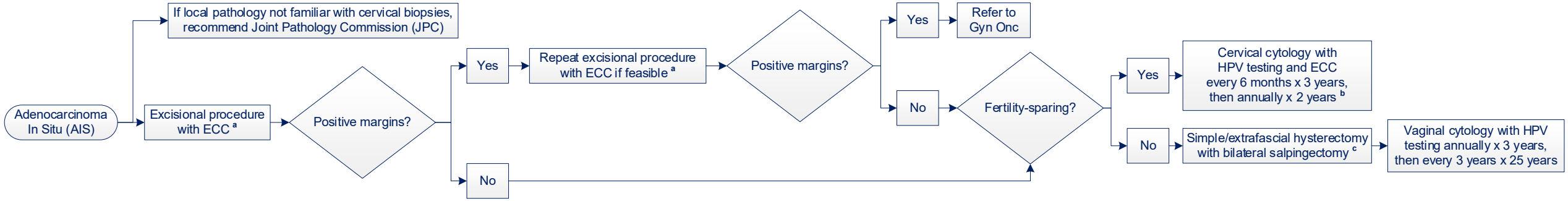
[a] **Excisional procedure** LEEP or cold knife cone; consider cold knife cone in these situations

[b] **Cervical cytology** If adenocarcinoma in situ, recommend endocervical sampling with cervical cytology; hysterectomy with bilateral salpingectomy is recommended at completion of childbearing (hysterectomy for cervical cancer should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer)

[c] **Colposcopy** recommended it patient concerned about future fertility

ECC endocervical curettage
LEEP loop electrosurgical excision procedure

Cervical Cancer – Adenocarcinoma In Situ (AIS)



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

[a] **Excisional procedure** LEEP or cold knife cone; consider cold knife cone in these situations

[b] **Cervical cytology** If adenocarcinoma in situ, recommend endocervical sampling with cervical cytology; hysterectomy with bilateral salpingectomy is recommended at childbearing

[c] **Hysterectomy for cervical cancer** should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer

ECC endocervical curettage
LEEP loop electrosurgical excision procedure

Cervical Cancer – Sedlis and Peters Criteria

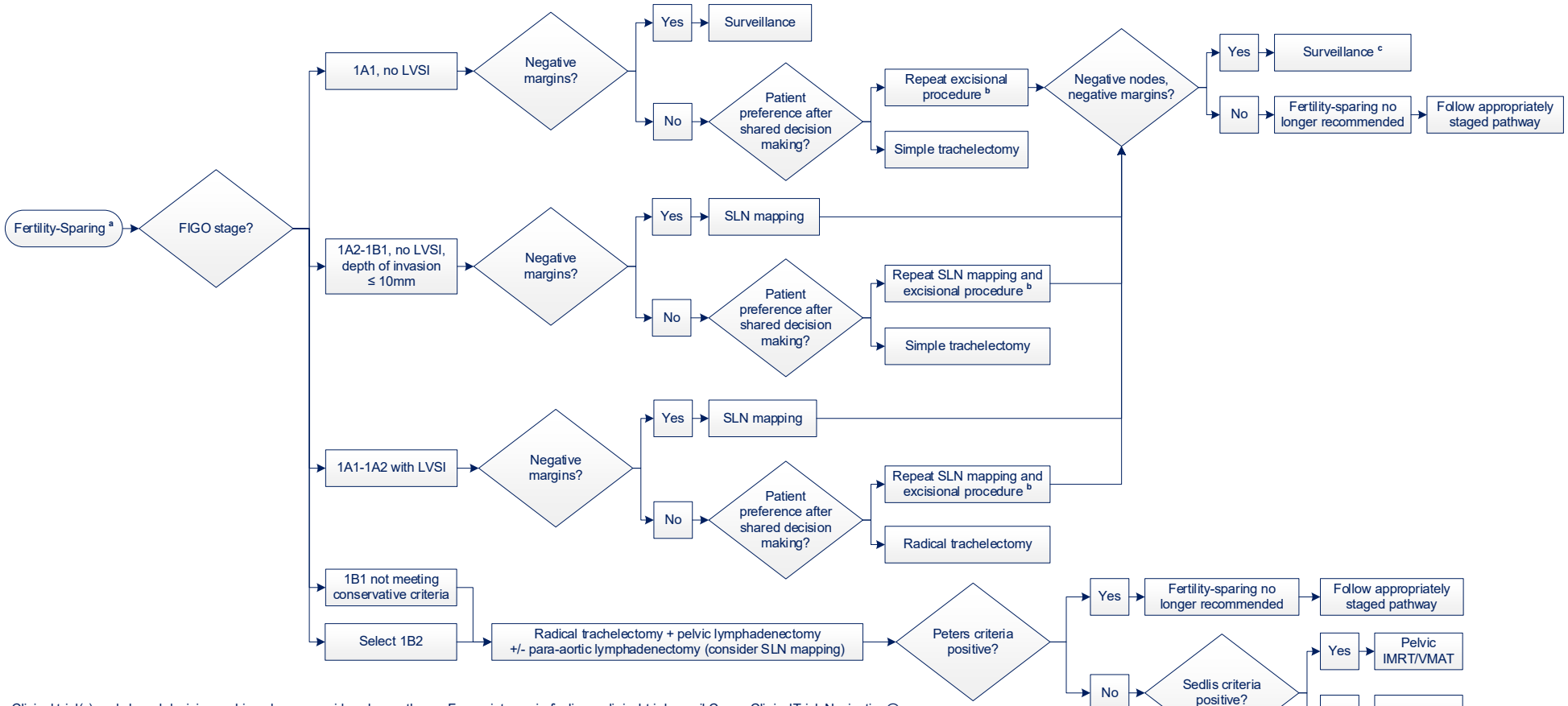
Sedlis Criteria		
LVSI	**Stromal Invasion**	**Tumor Size** by clinical palpitation
+	Deep 1/3	Any
+	Middle 1/3	≥ 2 cm
+	Superficial 1/3	≥ 5 cm
-	Middle or deep 1/3	≥ 4 cm

Peters Criteria
Positive margins
Positive pelvic lymph nodes
Parametrial invasion

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

LVSI lymphovascular space involvement

Cervical Cancer – Fertility-Sparing



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

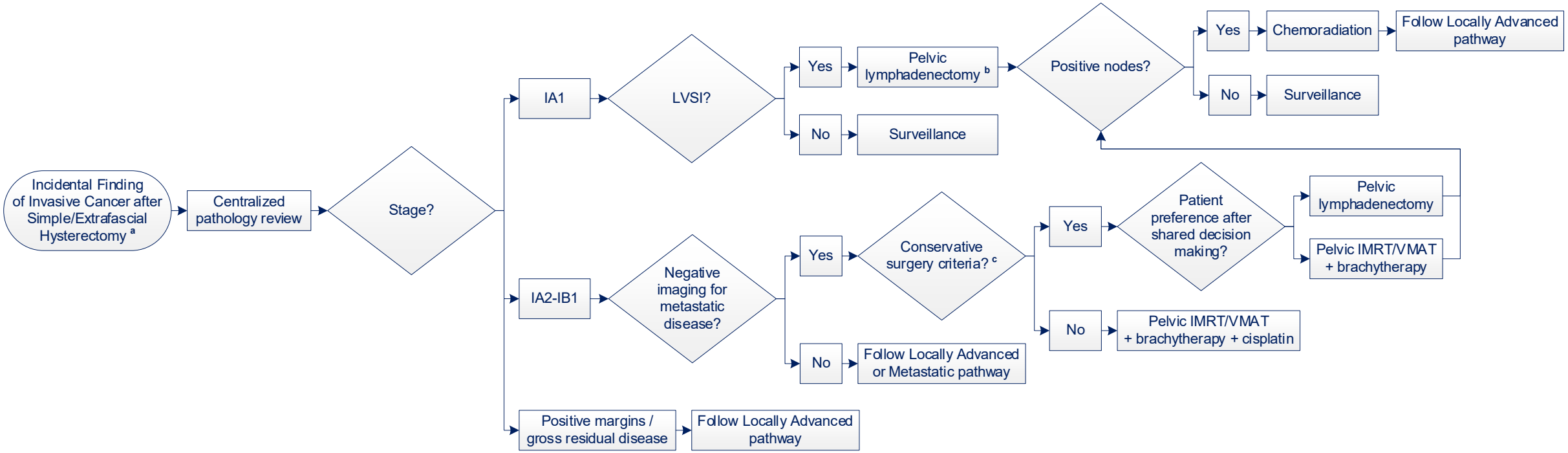
[a] **Fertility-Sparing** surgery is not recommended in individuals with small cell neuroendocrine histology and gastric type adenocarcinoma or those who have other medical contraindications to pregnancy; fertility-sparing surgery is most validated in tumors ≤ 2 cm

[b] **Excisional procedure** LEEP or cold knife cone; consider cold knife cone in these situations

[c] **Hysterectomy bilateral salpingectomy** recommended at completion of childbearing (hysterectomy for cervical cancer should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer)

IMRT intensity-modulated radiation therapy
LEEP loop electrosurgical excision procedure
LVSI lymphovascular space involvement
SLN sentinel lymph node
VMAT volumetric-modulated arc therapy

Cervical Cancer – Incidental Finding of Invasive Cancer after Simple/Extrafascial Hysterectomy



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

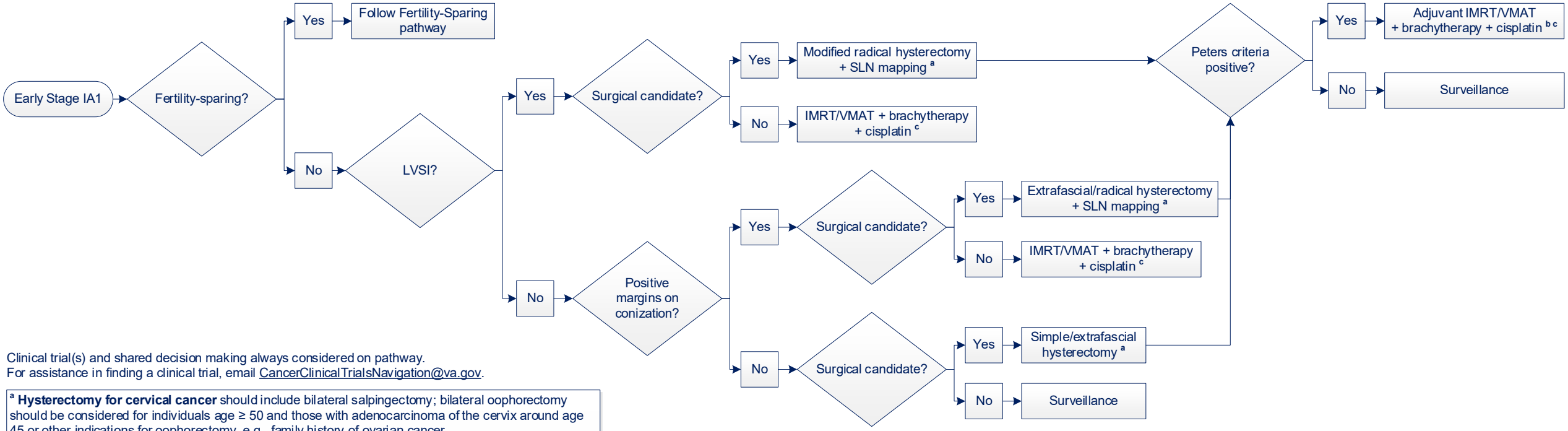
[a] **Simple/Extrafascial Hysterectomy** this is a standard hysterectomy not performed by a Gyn Oncologist (hysterectomy for cervical cancer should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer)

[b] **Pelvic lymphadenectomy** or pelvic IMRT/VMAT as an alternative

[c] **Conservative surgery criteria** No LVSI, negative margins, grade 1-2 adenocarcinoma or SCC, depth of invasion ≤10mm, tumor size ≤2cm

IMRT intensity-modulated radiation therapy
LVSI lymphovascular space involvement
SCC squamous cell carcinoma
VMAT volumetric-modulated arc therapy

Cervical Cancer – Early Stage IA1



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

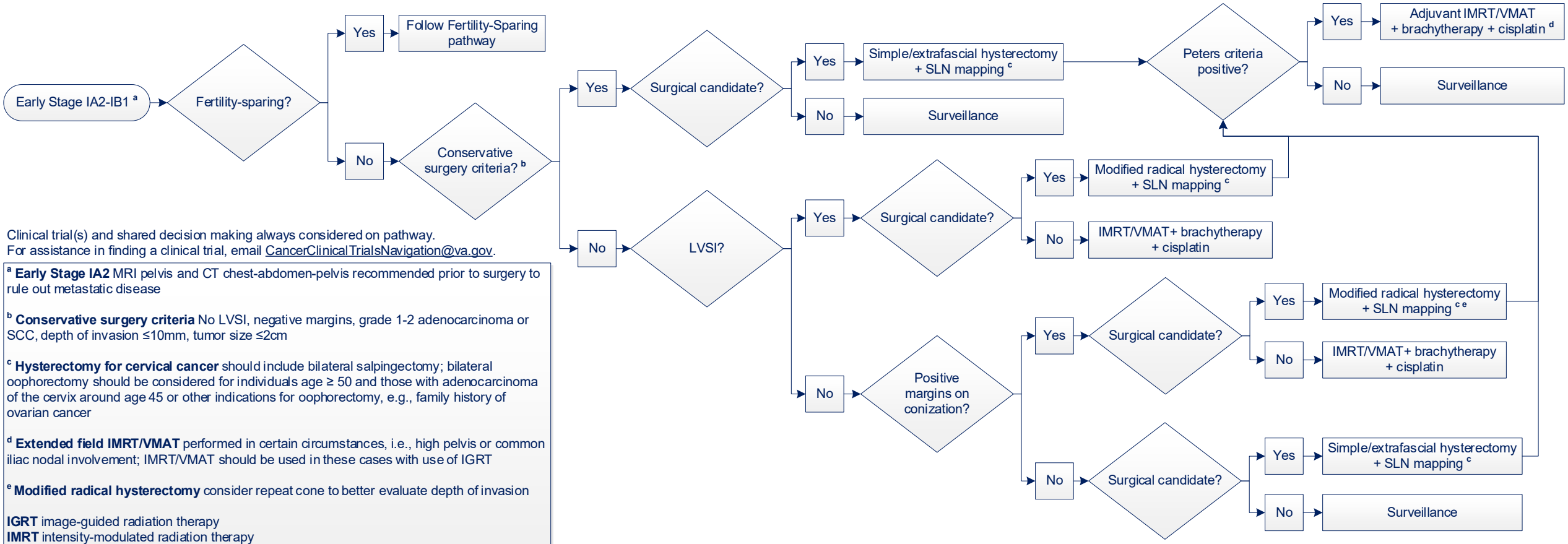
[a] **Hysterectomy for cervical cancer** should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer

[b] **Extended field IMRT/VMAT** performed in certain circumstances, i.e., high pelvis or common iliac nodal involvement; IMRT/VMAT should be used in these cases with use of IGRT

[c] **Cisplatin** carboplatin if ineligible for cisplatin (i.e., renal insufficiency, history of thrombocytopenia, etc.)

IGRT image-guided radiation therapy
IMRT intensity-modulated radiation therapy
LVSI lymphovascular space involvement
SLN sentinel lymph node
VMAT volumetric-modulated arc therapy

Cervical Cancer – Early Stage IA2-IB1



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

[a] **Early Stage IA2** MRI pelvis and CT chest-abdomen-pelvis recommended prior to surgery to rule out metastatic disease

[b] **Conservative surgery criteria** No LVSI, negative margins, grade 1-2 adenocarcinoma or SCC, depth of invasion ≤10mm, tumor size ≤2cm

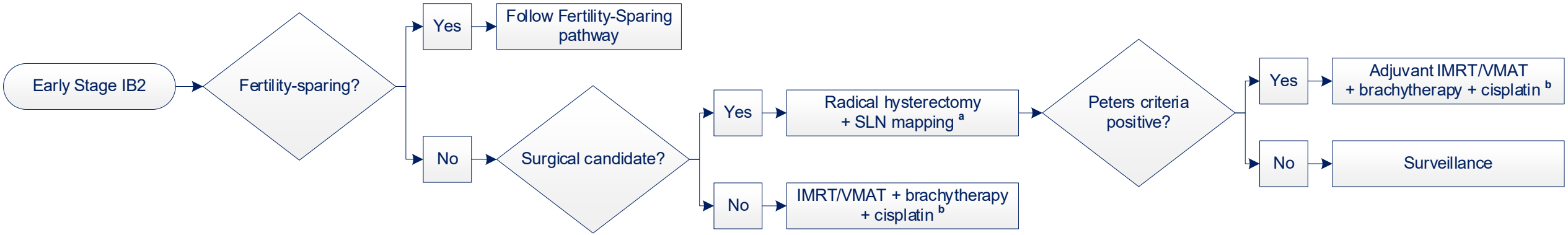
[c] **Hysterectomy for cervical cancer** should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer

[d] **Extended field IMRT/VMAT** performed in certain circumstances, i.e., high pelvis or common iliac nodal involvement; IMRT/VMAT should be used in these cases with use of IGRT

[e] **Modified radical hysterectomy** consider repeat cone to better evaluate depth of invasion

IGRT image-guided radiation therapy
IMRT intensity-modulated radiation therapy
LVSI lymphovascular space involvement
SLN sentinel lymph node
VMAT volumetric-modulated arc therapy

Cervical Cancer – Early Stage IB2



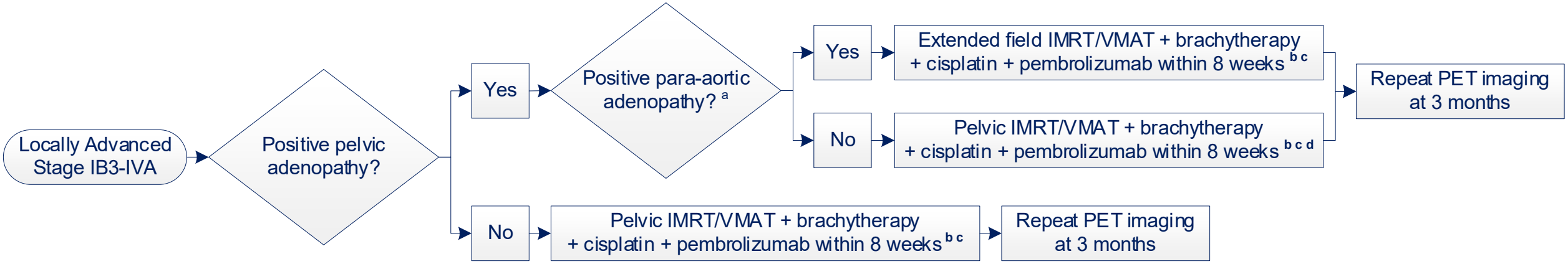
Clinical trial(s) and shared decision making always considered on pathway. For assistance in finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Hysterectomy for cervical cancer** should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer

[b] **Extended field IMRT/VMAT** performed in certain circumstances, i.e., high pelvis or common iliac nodal involvement; IMRT/VMAT should be used in these cases with use of IGRT

IGRT image-guided radiation therapy
IMRT intensity-modulated radiation therapy
LVSI lymphovascular space involvement
SLN sentinel lymph node
VMAT volumetric-modulated arc therapy

Cervical Cancer – Locally Advanced Stage IB3-IVA



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

[a] **Positive adenopathy** upon PET imaging or surgical staging/biopsy

[b] **IMRT/VMAT** volumes should include gross disease, cervix, entire uterus (for intact patients), margin on gross disease into vagina, parametria, uterosacral ligaments; lymph node volumes should include obturator, internal, external iliac, common iliac (as appropriate), presacral, para-aortic (as appropriate); ensure appropriate PTV expansions

- Radiation: pelvic field 4500- 5040 cGy with consideration SIB for positive LN; consideration for parametrial boost up to 5-10 Gy in select cases
- Brachytherapy boost is recommended for all patients undergoing definitive radiation for cervical cancer; brachytherapy should only be completed at a facility with routine experience in cervical cancer

[c] **Pembrolizumab** candidate for immunotherapy if patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent > 10mg/day), or prior allogeneic HSCT/solid organ transplant; continue single agent pembrolizumab for up to 24 months per ENGOT-cx11/GOG-3047/Keynote A18

[d] **Extended field IMRT/VMAT** performed in certain circumstances, i.e., high pelvis or common iliac nodal involvement; IMRT/VMAT should be used in these cases with use of IGRT

IGRT image-guided radiation therapy
IMRT intensity-modulated radiation therapy
SIB simulated integrated boost
VMAT volumetric-modulated arc therapy

Cervical Cancer – Metastatic Stage IVB

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

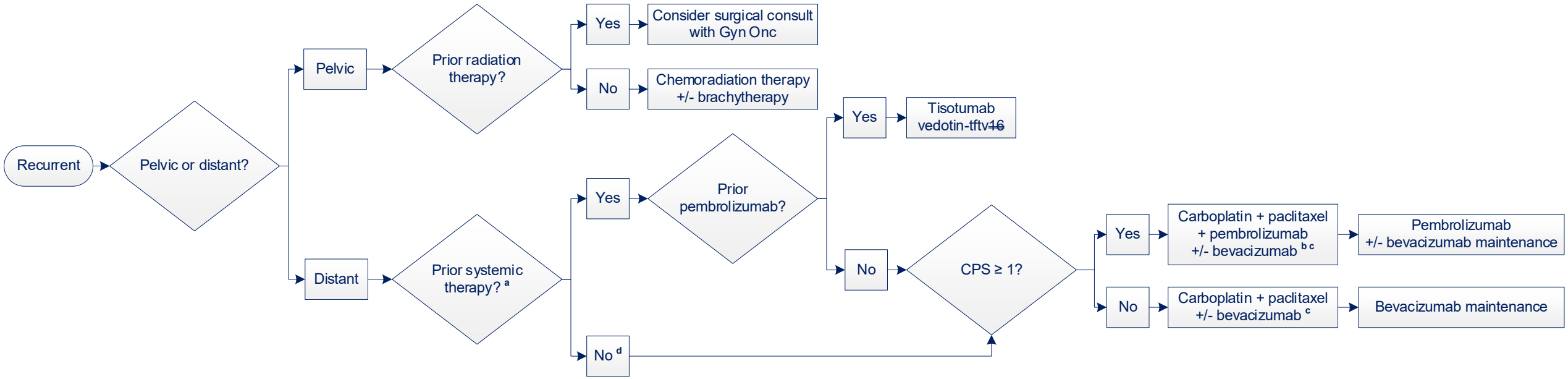
[a] **Cisplatin** if no prior cisplatin exposure and adequate kidney function; carboplatin can be used as an alternative; pembrolizumab for PDL1 positive tumors should be used as treatment and maintenance

[b] **Palliative radiation** may be considered for persistent life-threatening vaginal bleeding or consistent bulky disease

[c] **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] **Pembrolizumab** candidate for immunotherapy if patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent > 10mg/day), or prior allogeneic HSCT/solid organ transplant; continue single agent pembrolizumab for up to 24 months per ENGOT-cx11/GOG-3047/Keynote A18

Cervical Cancer – Recurrent



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

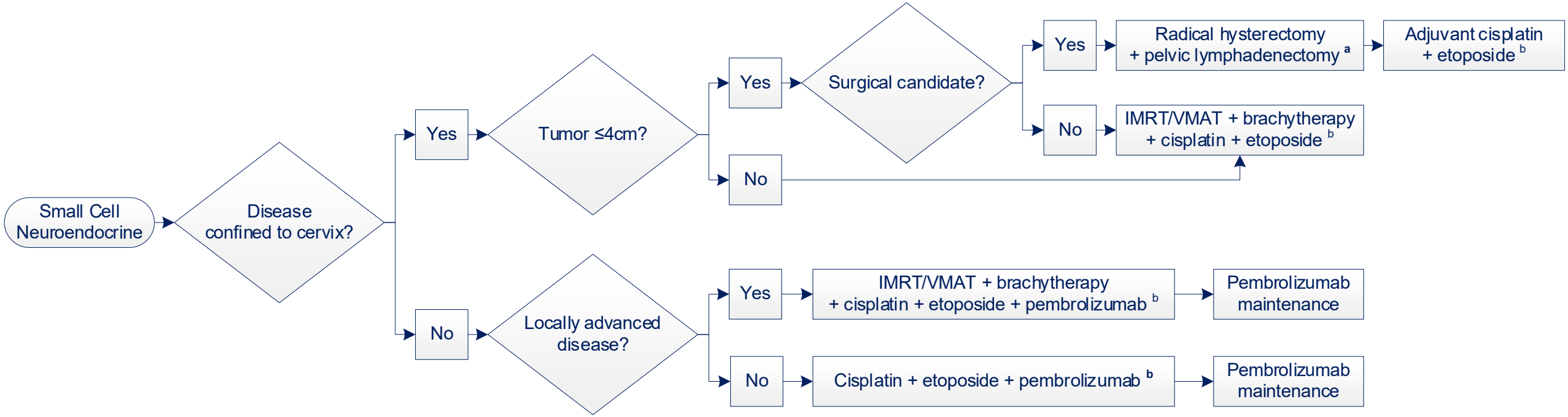
[a] **Systemic therapy** Radiation sensitizing chemotherapy is not considered systemic therapy

[b] **Pembrolizumab** for PDL1 positive tumors should be used as treatment and maintenance; candidate for immunotherapy if patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent > 10mg/day), or prior allogeneic HSCT/solid organ transplant; continue single agent pembrolizumab for up to 24 months per ENGOT-cx11/GOG-3047/Keynote A18

[c] **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] **Palliative radiation** may be considered for persistent life-threatening vaginal bleeding or consistent bulky disease

Cervical Cancer – Small Cell Neuroendocrine



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

[a] **Hysterectomy for cervical cancer** should include bilateral salpingectomy; bilateral oophorectomy should be considered for individuals age ≥ 50 and those with adenocarcinoma of the cervix around age 45 or other indications for oophorectomy, e.g., family history of ovarian cancer

[b] **Cisplatin + etoposide** dosing per Salvo G, Gonzalez Martin A, Gonzales NR, Frumovitz M. Updates and management algorithm for neuroendocrine tumors of the uterine cervix. *Int J Gynecol Cancer*. 2019 Jul;29(6):986-995. doi: 10.1136/ijgc-2019-000504.

IMRT intensity-modulated radiation therapy
VMAT volumetric-modulated arc therapy

Cervical Cancer – Surveillance

Surveillance Stage I

	Year 1-2	Year 3-5	After Year 5
Exam including pelvic and symptom review	Every 3-6 months	Every 6-12 months	Annually if no recurrence
CT chest, abdomen, pelvis	As clinically indicated		
Pelvic MRI for fertility-sparing	6 months after surgery then annually x 2-3 years		
Cervical/vaginal cytology screening [b]	Annually		

Surveillance Stage II-III

	Year 1-2	Year 3-5	After Year 5
Exam including pelvic and symptom review	Every 3 months	Every 6 months	Annually if no recurrence
CT chest, abdomen, pelvis	As clinically indicated		
Cervical/vaginal cytology screening [b]	Annually		

Surveillance Stage IV

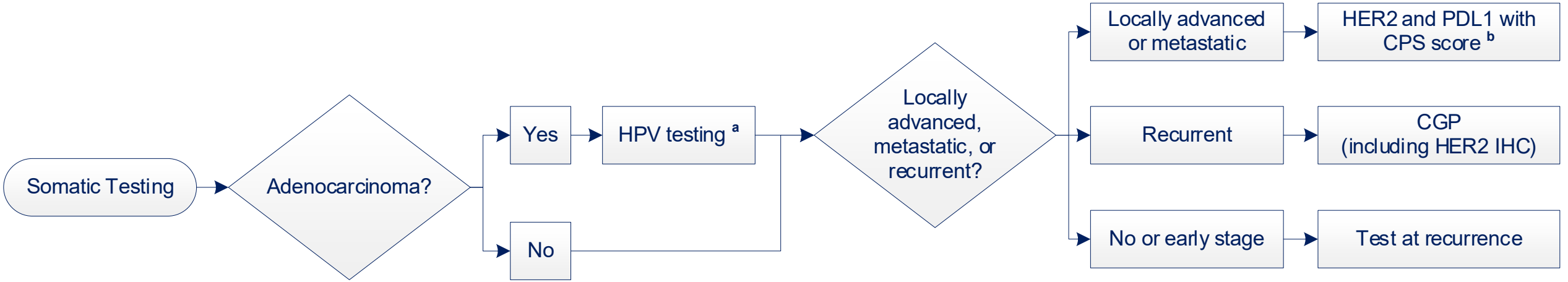
	Year 1-2	Year 3-5	After Year 5
Exam including pelvic and symptom review	Every 3 months	Every 6 months	Annually if no recurrence
Imaging	CT, MRI, or PET every 6-12 months [a]		As clinically indicated
Cervical/vaginal cytology screening [b]	Annually		

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

[a] **Stage IV Imaging** If first surveillance PET CT is indeterminate, recommend repeating in 3 months

[b] **Cytology** If patient with history of radiation for cervical cancer and ASCUS or LSIL cytology, no further intervention required

Cervical Cancer – Molecular Testing



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

[a] **HPV** in situ hybridization (ISH) or molecular testing is preferred, but p16 may be acceptable if HPV testing is not available; if HPV negative, consider pathology review to rule out endometrial etiology

[b] **HER2** for IHC 2 or 3+

CGP comprehensive genomic profiling
CPS combined positive score

Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Adenocarcinoma	ISH	HPV	Local VA	No	Tumor Tissue
Persistent, Recurrent, or Metastatic Disease	IHC	PD-L1 clone 22C3 with CPS	Local VA or locally contracted vendor	No	Tumor Tissue
	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
	Methylation Testing	MLH1 promoter hypermethylation testing (in the setting of loss of MLH1 or PMS2 expression by IHC). Hypermethylation suggests somatic mutation. Unmethylated calls for Germline Lynch testing.	Local VA or locally contracted vendor	No	Tumor Tissue
	Germline	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 Genetics	Yes	Blood, Saliva