

Oncology Clinical Pathways

Soft Tissue Sarcoma

May 2025 – V1.2025



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Soft Tissue Sarcoma – 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

- Soft tissue sarcoma (not including osteosarcoma, chondrosarcoma, Kaposi's sarcoma or mesothelioma)

Atomic Veterans Exposed to Ionizing Radiation

- Cancer of the thyroid, breast, pharynx, esophagus, stomach, small intestine, pancreas, bile ducts, gall bladder, salivary gland, urinary tract, brain, bone, lung, colon or ovary

Gulf War and Post 9/11 Veterans

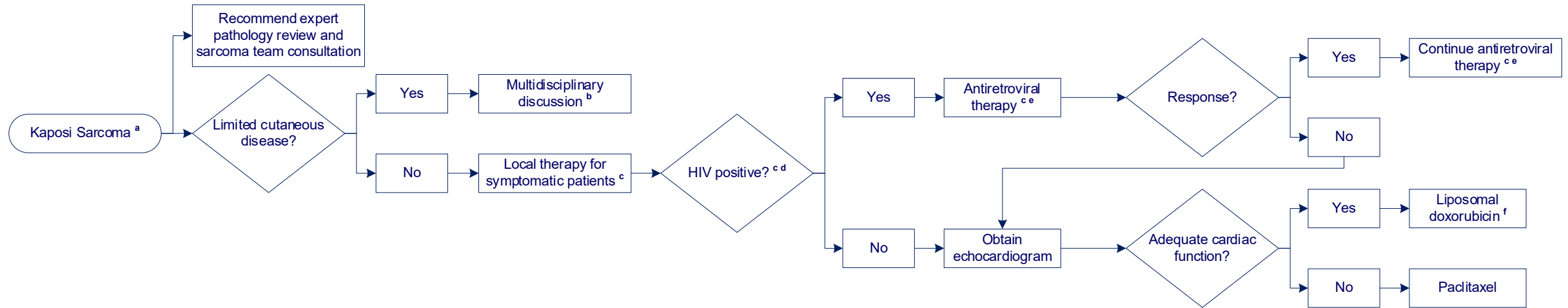
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if you served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Head cancer of any type
- Neck cancer of any type
- 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 \(va.gov\)](https://www.va.gov/presumptive-disability-benefits/)

Soft Tissue Sarcoma – Kaposi Sarcoma



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

^a **Diagnosis** includes imaging CT or MRI and biopsy of affected organ

^b **Multidisciplinary Discussion** to determine appropriateness of referral to Radiation Oncology, Interventional Radiology, Surgery, and/or topical/intralesional therapies

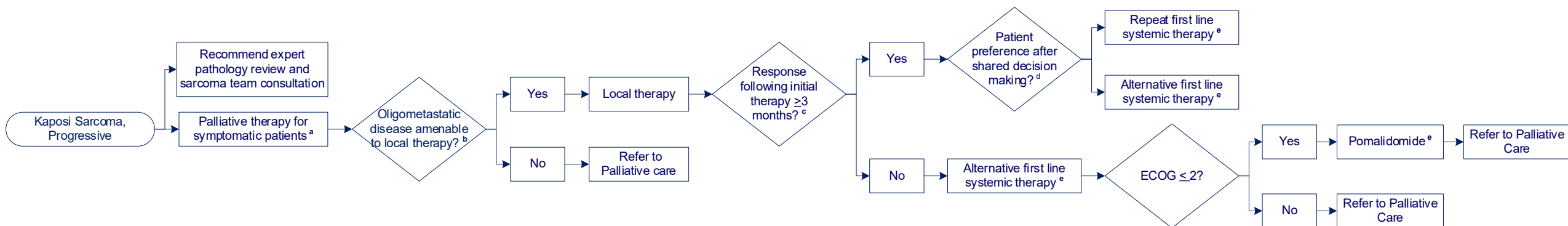
^c **Referral** to Radiation Oncology for palliative radiation for patients with symptomatic lesions

^d **Kaposi Sarcoma** related to transplant requires treatment with sirolimus

^e **Imaging** every 3 months to assess for progression

^f **Imaging** every 3 months to assess for progression, continue to monitor cardiac function with echocardiogram every 3 months

Soft Tissue Sarcoma – Kaposi Sarcoma, Progressive



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

^a **Referral** to radiation oncology for palliative local radiation or palliative total skin electron beam therapy for patients with symptomatic lesions

^b **Local Therapy** with palliative intent

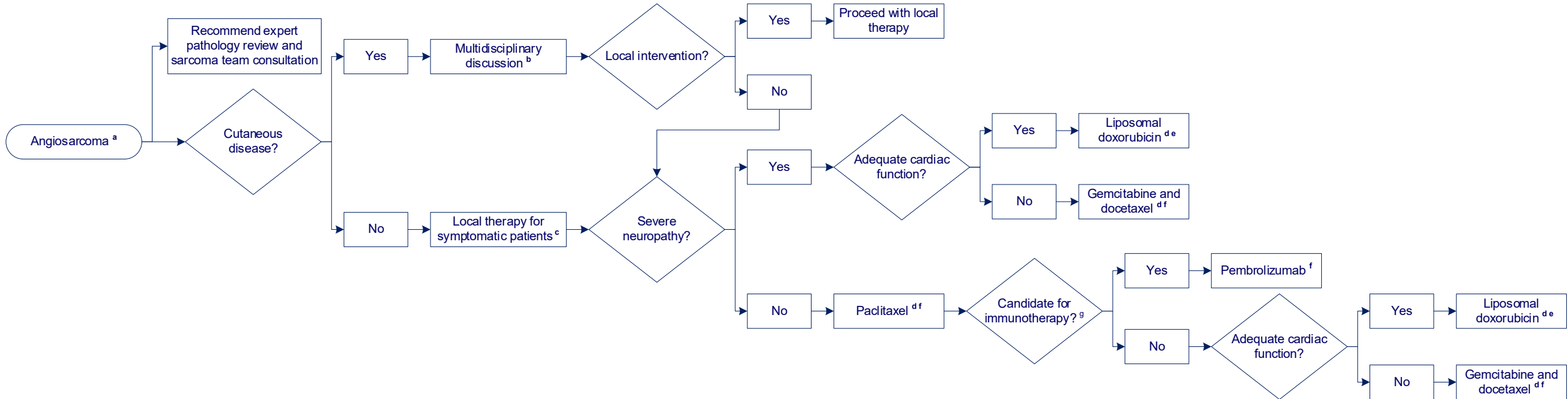
^c **Therapy** for patients who progress is based on shared decision making with patient

^d **Shared Decision Making** is critical for consideration of repeat of chemotherapy versus proceeding with first line chemotherapy based on patient's tolerance, response, preference and comorbidities

^e **Imaging** every 3 months to assess for progression

ECOG Eastern Cooperative Oncology Group performance status

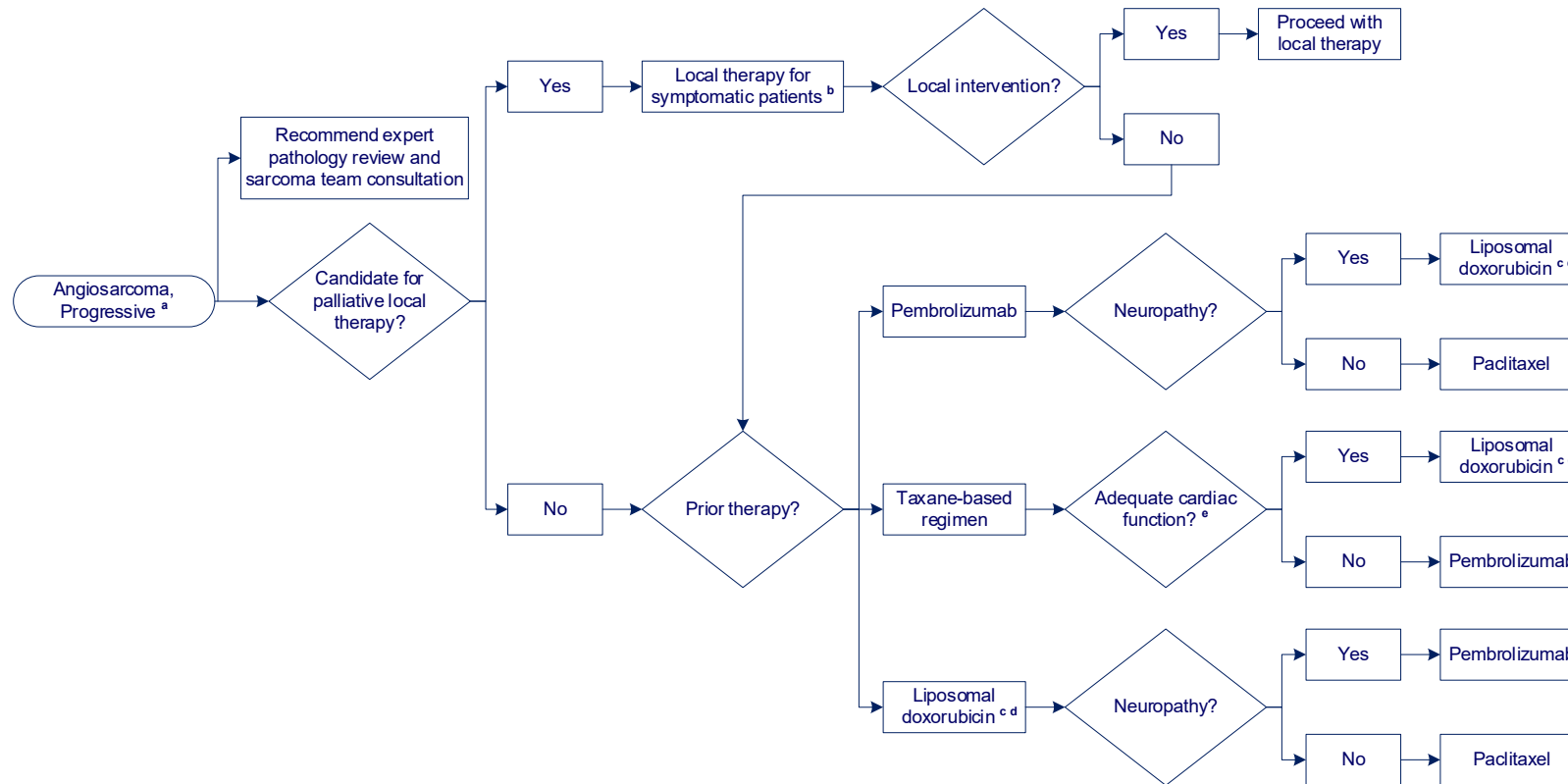
Soft Tissue Sarcoma – Angiosarcoma



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

- ^a **Diagnosis** includes imaging CT or MRI and biopsy of affected organ
- ^b **Multidisciplinary Discussion** to determine appropriateness of referral to Radiation Oncology, Interventional Radiology, Surgery, and/or topical/intralesional therapies
- ^c **Referral** to Radiation Oncology for palliative radiation for patients with symptomatic lesions
- ^d **Therapy** for patients who progress is based on shared decision making with patient
- ^e **Imaging** every 3 months to assess for progression; obtain echocardiogram for baseline cardiac status when starting doxorubicin and continue to monitor cardiac function with echocardiogram every 3 months
- ^f **Imaging** every 3 months to assess for progression
- ^g **Candidate for Immunotherapy** patients with no active autoimmune disease, primary immune deficiency, concurrent immunosuppression (prednisone equivalent > 10mg/day) or prior allogeneic HSCT/solid organ transplant

Soft Tissue Sarcoma – Angiosarcoma, Progressive



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

^a **Diagnosis** includes imaging CT or MRI and biopsy of affected organ

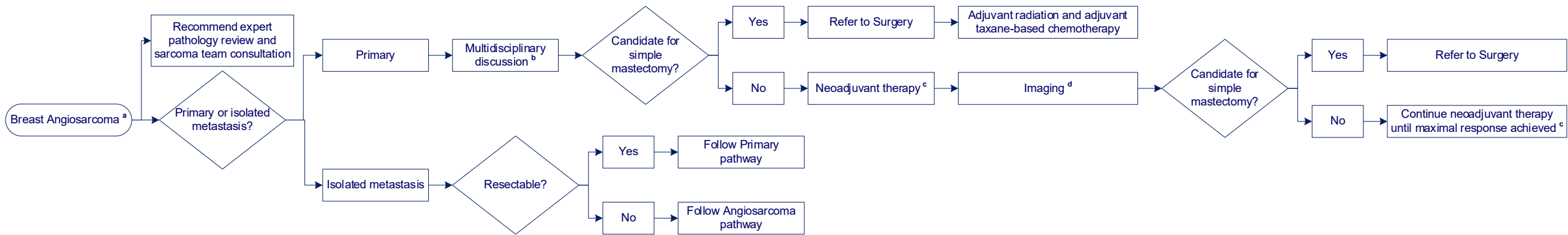
^b **Referral** to radiation oncology for palliative radiation for patients with symptomatic lesions

^c **Therapy** for patients who progress is based on shared decision making with patient

^d **Imaging** every 3 months to assess for progression; obtain echocardiogram for baseline cardiac status when starting doxorubicin and continue to monitor cardiac function with echocardiogram every 3 months

^e **Cardiac Function** adequate ejection fraction >55% or <10% drop from prior echocardiogram

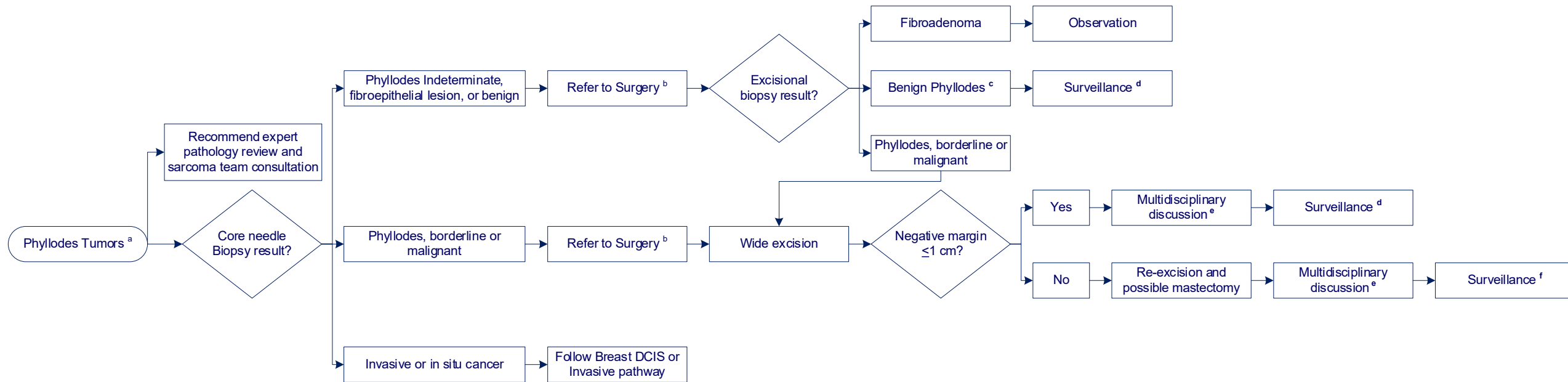
Soft Tissue Sarcoma – Breast Angiosarcoma



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

- ^a **Imaging** MRI to determine baseline status
- ^b **Multidisciplinary Discussion** for systemic or local therapies
- ^c **Neoadjuvant Therapy** including taxane-based therapy or preoperative radiation for large or inoperable tumors
- ^d **Imaging** MRI after 3 months

Soft Tissue Sarcoma – Phyllodes Tumors



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

^a **Clinical Suspicion** based on palpable mass, rapid growth, size >3 cm, imaging with ultrasound suggestive of fibroadenoma; obtain mammogram for patients > 30 years

^b **Excision** does not require axillary resection

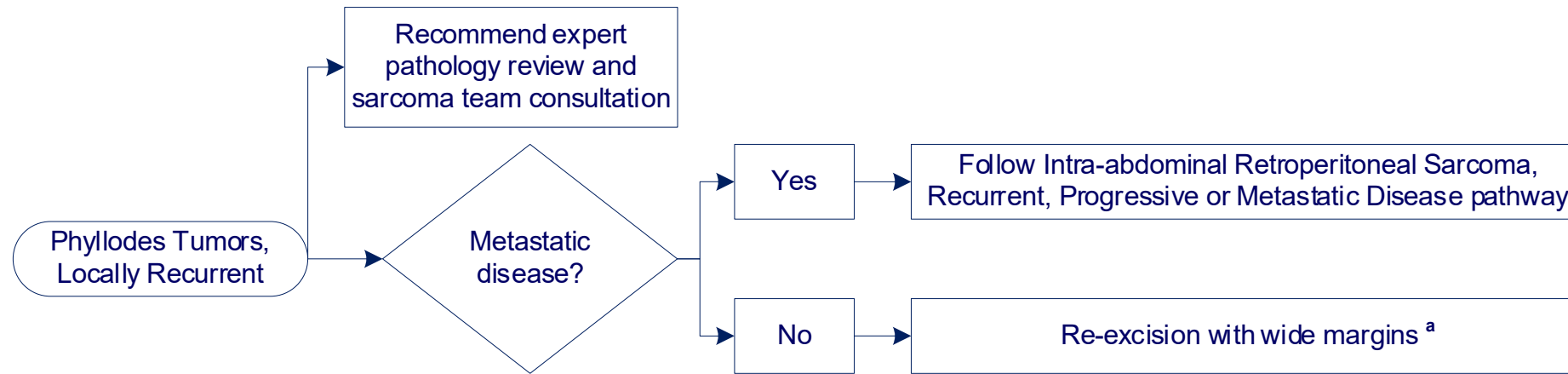
^c **Margin** should be no more than 1 mm; negative margin not required

^d **Surveillance** if ≥30 years old ultrasound alternating with mammogram every 6 months for 3 years and then annually for 5 years; if <30 years old ultrasound every 6 months for 2 years then annually for 3 years

^e **Adjuvant Radiation** should be administered if recurrence would lead to morbidity; adjuvant chemotherapy should be doxorubicin-based

^f **Surveillance** including clinical exam every 6 months for mastectomy patients

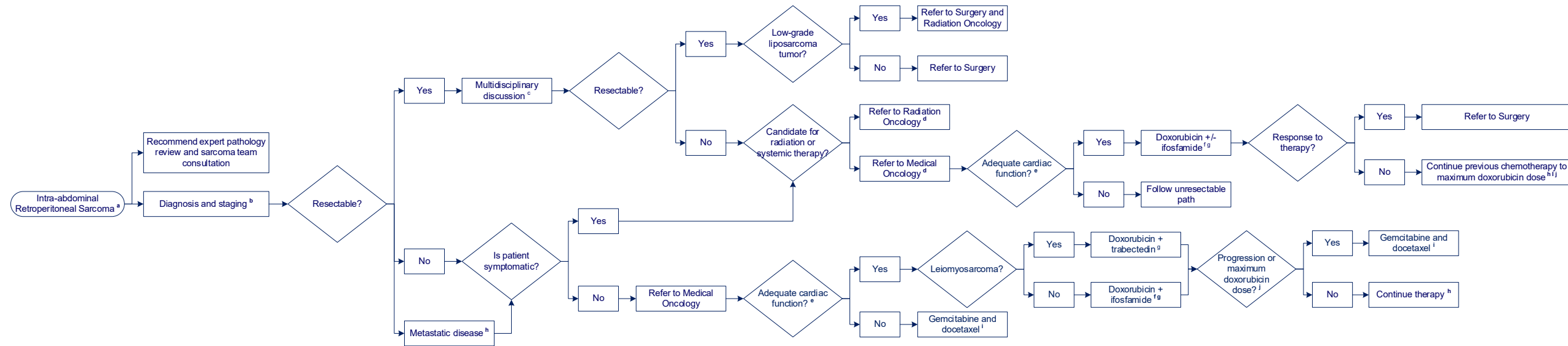
Soft Tissue Sarcoma – Phyllodes Tumors, Locally Recurrent



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

^a **Adjuvant Radiation** should be administered to patients if recurrence would lead to morbidity; adjuvant chemotherapy should be doxorubicin-based

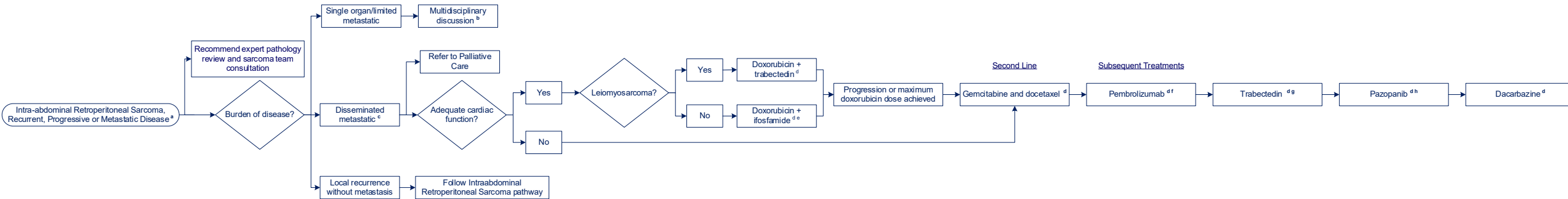
Soft Tissue Sarcoma – Intra-abdominal Retroperitoneal Sarcoma



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

- ^a **Diseases** excluding gastrointestinal stromal tumors, endometrial sarcoma, and desmoid tumors
- ^b **Diagnosis and Staging** includes imaging CT with contrast of chest, abdomen, pelvis and percutaneous biopsy
- ^c **Assess** for surgical resection or neoadjuvant therapy; chemotherapy is recommended for tumors if high risk for metastatic disease or if downstaging is required prior to surgery
- ^d **Re-evaluate** role of other therapies or surgery at completion of therapy
- ^e **Cardiac Function** adequate ejection fraction >55% or <10% drop from prior echocardiogram
- ^f **Ifosfamide** assess patient for age, co-morbidities, tolerability, and risk for developing neurotoxicity and/or hemorrhagic cystitis
- ^g **Imaging** every 3 months to assess for progression, obtain baseline echocardiogram and continue to monitor cardiac function with echocardiogram every 3 months
- ^h **Oligometastatic Patients** can be referred to surgery or radiation for metastatic directed therapy; polymetastatic patients can be referred to radiation for local palliation of symptomatic disease
- ⁱ **Imaging** every 3 months to assess for progression
- ^j **Continue** until maximal cardiac dose of doxorubicin (450 mg) is achieved, maximum tolerated dose is indicated, or disease progression

Soft Tissue Sarcoma – Intra-abdominal Retroperitoneal Sarcoma, Recurrent, Progressive, or Metastatic Disease

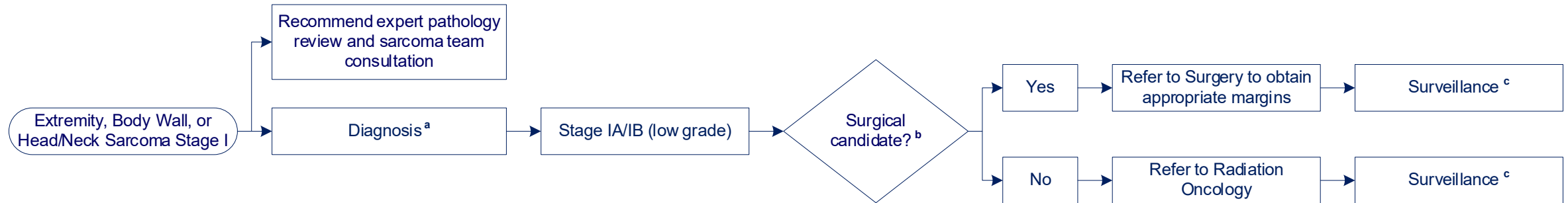


Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

^a Diseases excluding gastrointestinal stromal tumors, endometrial sarcoma, and desmoid tumors
^b Multidisciplinary Discussion should include metastasectomy, radiation, ablation, embolization, and systemic therapy
^c Radiation Therapy should be considered for palliation of localized symptomatic sites of disease
^d Surveillance CT scan of chest, abdomen, pelvis every 3 months for restaging
^e Continue until maximal cardiac dose of doxorubicin is achieved, maximum tolerated dose is indicated, or disease progression
^f Pembrolizumab for use when TMB ≥ 10 or dMMR/MSI-H, atezolizumab is approved for alveolar soft-part sarcoma
^g Trabectedin if not previously given is preferred in myxoid liposarcomas; for patients unable to tolerate trabectedin, eribulin may be given as an alternative
^h Pazopanib is FDA-approved in advanced non-lipogenic soft tissue sarcoma; for patients unable to tolerate pazopanib, cabozantinib may be an alternative that is supported by phase 2 data
MSI Microsatellite Instability TMB Tumor Mutational Burden

Soft Tissue Sarcoma – Extremity, Body Wall, or Head/Neck

Sarcoma Stage I



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

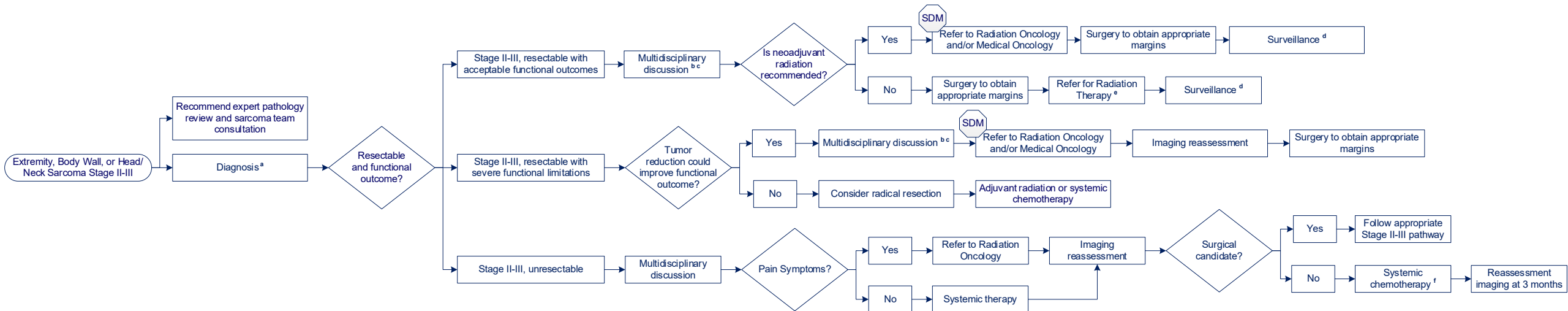
^a **Diagnosis** includes adequate imaging of primary tumor, core needle biopsy with **carefully planned needle track**; place biopsy along future resection axis with minimal dissection and careful attention to hemostasis

^b **Candidacy** based on tumor location and tolerance for surgery

^c **Surveillance** history, physical, and CT chest and imaging of primary tumor location every 3-6 months for 3 years and then annually

Soft Tissue Sarcoma – Extremity, Body Wall, or Head/Neck

Sarcoma Stage II-III



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

^a **Diagnosis** includes adequate imaging of primary tumor, core needle biopsy with **carefully planned needle track**; biopsy along future resection access with minimal dissection and attention to hemostasis

^b **Multidisciplinary Discussion** to determine role and timing of radiation (preoperative is preferred over postoperative), consideration including tumor size, location, and operative outcome

^c **Stage III** peri-operative anthracycline-based chemotherapy x3 months should be considered in patients with high-grade tumor, histology (Osteosarcoma, Ewing sarcoma, Rhabdomyosarcoma, Synovial Sarcoma), and tumor size >10 cm

^d **Surveillance** history, physical, and CT chest and imaging of primary tumor location every 3-6 months for 3 years and then annually

^e **Adjuvant Radiation** for high-grade tumors should be considered following R1 and R2 resection status and based on location

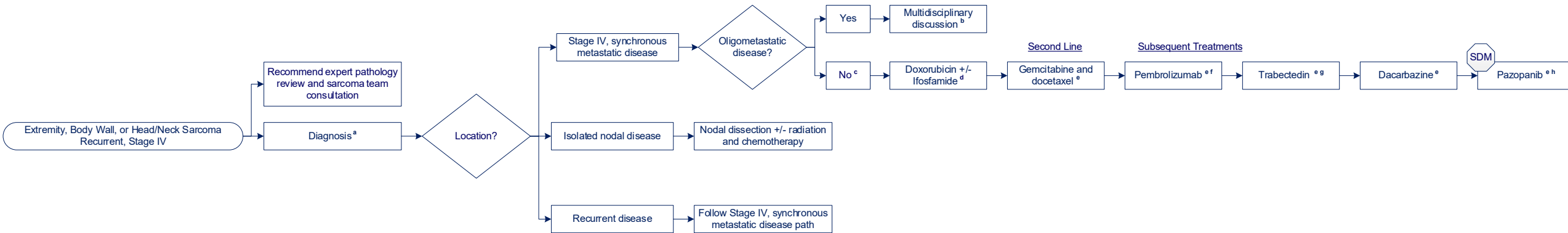
^f **Multidisciplinary Discussion** to determine the role of systemic chemotherapy, metastasectomy, radiation, ablation, embolization, and/or observation if patient is asymptomatic

SDM Pembrolizumab shared decision making is critical at the time of consideration for neoadjuvant radiation with pembrolizumab for the histologic subtype of undifferentiated pleomorphic sarcoma or dedifferentiated pleomorphic liposarcoma or myxofibrosarcoma

SDM Shared Decision Making

Soft Tissue Sarcoma – Extremity, Body Wall, or Head/Neck

Sarcoma Recurrent, Stage IV



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

^a **Diagnosis** includes adequate imaging of primary tumor, core needle biopsy with **carefully planned needle track**; place biopsy along future resection axis with minimal dissection and careful attention to hemostasis

^b **Multidisciplinary Discussion** to determine the role of systemic chemotherapy, metastasectomy, radiation, ablation, embolization, and/or observation if patient is asymptomatic

^c **Synovial Sarcoma** special consideration for use of afamitresgene autoleucel (afami-cel), also known as Tecelra, is a T-cell receptor (TCR) therapy, to treat metastatic synovial sarcoma

^d **Doxorubicin +/- Ifosfamide** based on comorbidity, age, and functional status; if doxorubicin not received in the previous ≤ 6 months and cardio toxicity limit has not been met from anthracycline use

^e **Surveillance** CT scan of chest, abdomen, pelvis every 3 months for restaging

^f **Pembrolizumab** for use when TMB ≥ 10 or dMMR/MSI-H, atezolizumab is approved for alveolar soft-part sarcoma

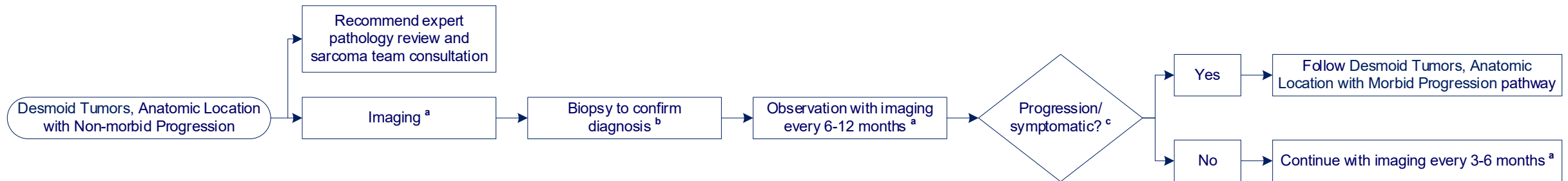
^g **Trabectedin** if not previously given is preferred in myxoid liposarcomas; for patients unable to tolerate trabectedin, eribulin may be given as an alternative

^h **Pazopanib** is FDA-approved in advanced non-lipogenic soft tissue sarcoma; for patients unable to tolerate pazopanib, cabozantinib may be an alternative that is supported by phase 2 data

SDM Pazopanib shared decision making is critical at the time of consideration based on symptoms from prior chemotherapy and histologic subtypes including alveolar soft-part sarcoma, undifferentiated pleomorphic sarcoma, extraskeletal myxoid chondrosarcoma, and leiomyosarcoma; imitations of the study include phase 2B study with multiple soft tissue histologies, small population number and short follow-up

SDM Shared Decision Making

Soft Tissue Sarcoma – Desmoid Tumors, Anatomic Location with Non-morbid Progression



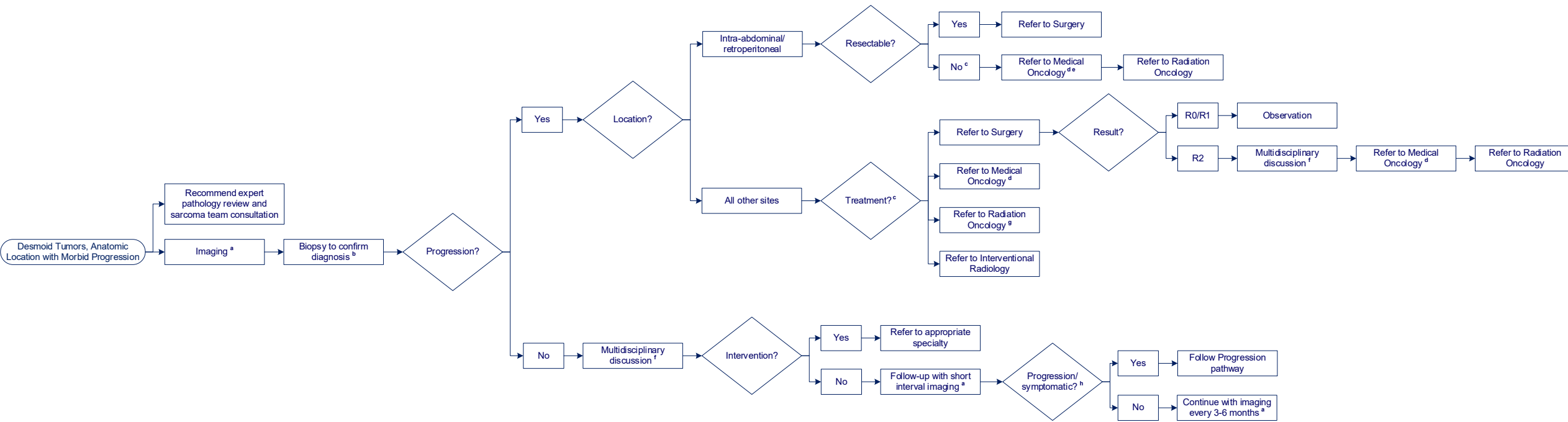
Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

^a **Imaging** primary CT appropriate for intra-thoracic or intra-abdominal, MRI is preferred for extremity

^b **Desmoid Tumor** located in intra-abdominal or abdominal wall confirmed, refer to Germline Testing pathway for evaluation of Gardner Syndrome/Familial Adenomatous Polyposis (FAP)

^c **Symptomatic Management** of pain may include sulindac or celecoxib

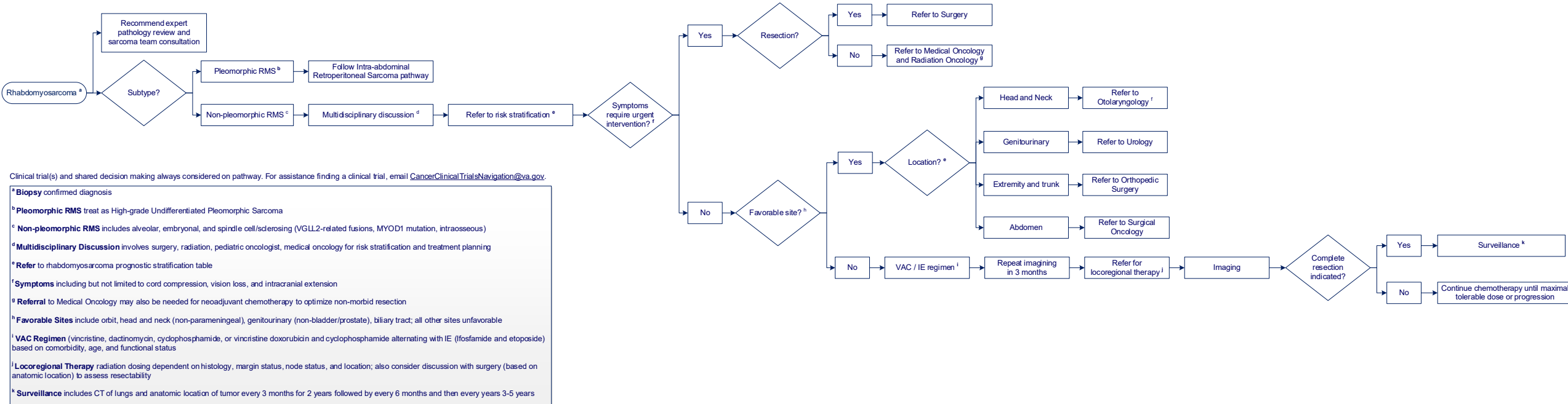
Soft Tissue Sarcoma – Desmoid Tumors, Anatomic Location with Morbid Progression



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

- ^a **Imaging** primary CT appropriate for intra-thoracic or intra-abdominal, MRI is preferred for extremity
- ^b **Desmoid Tumor** located in intra-abdominal or abdominal wall confirmed, refer to Germline Testing pathway for evaluation of Gardner Syndrome/Familial Adenomatous Polyposis (FAP)
- ^c **Multidisciplinary Discussion** to evaluate the role of surgery versus systemic therapy
- ^d **Sorafenib or Nirogacestat** administration is dependent on patient symptoms and co-morbidities; consult sarcoma expert prior to use of cyto-toxic chemotherapy
- ^e **Radiation Therapy** for lack of response in systemic therapy or progression
- ^f **Multidisciplinary Discussion** to determine role of adjuvant radiation, local regional therapies, systemic therapy, or radical re-resection
- ^g **Radiation** is recommended if surgery is technically challenging and would lead to significant morbidity
- ^h **Symptomatic Management** of pain may include sulindac or celecoxib

Soft Tissue Sarcoma – Rhabdomyosarcoma



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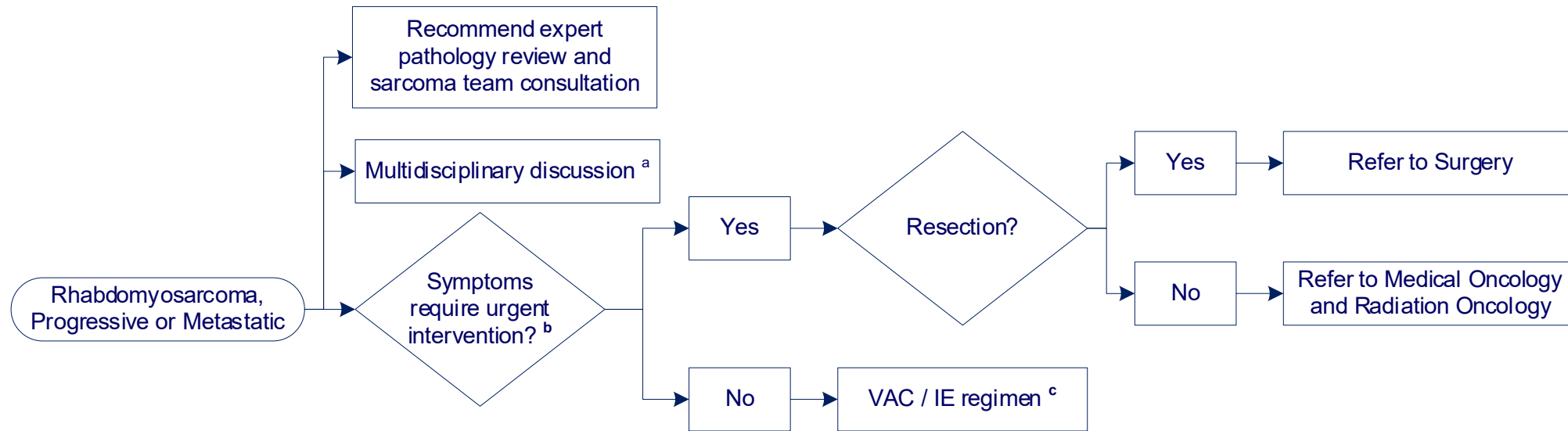
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Soft Tissue Sarcoma – Rhabdomyosarcoma, Progressive or Metastatic



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

^a **Multidisciplinary Discussion** to determine role of radiation, ablation, systemic therapy, or radical resection

^b **Symptoms** including but not limited to cord compression, vision loss, and intracranial extension

^c **VAC Regimen** (vincristine, dactinomycin, cyclophosphamide, or vincristine doxorubicin and cyclophosphamide alternating with Ifosfamide and etoposide (IE) based on comorbidity, age, and functional status; if VAC not received in the previous ≤ 6 months and cardio toxicity limit has not been met from anthracycline use

Soft Tissue Sarcoma – Rhabdomyosarcoma

Prognostic Stratification Table

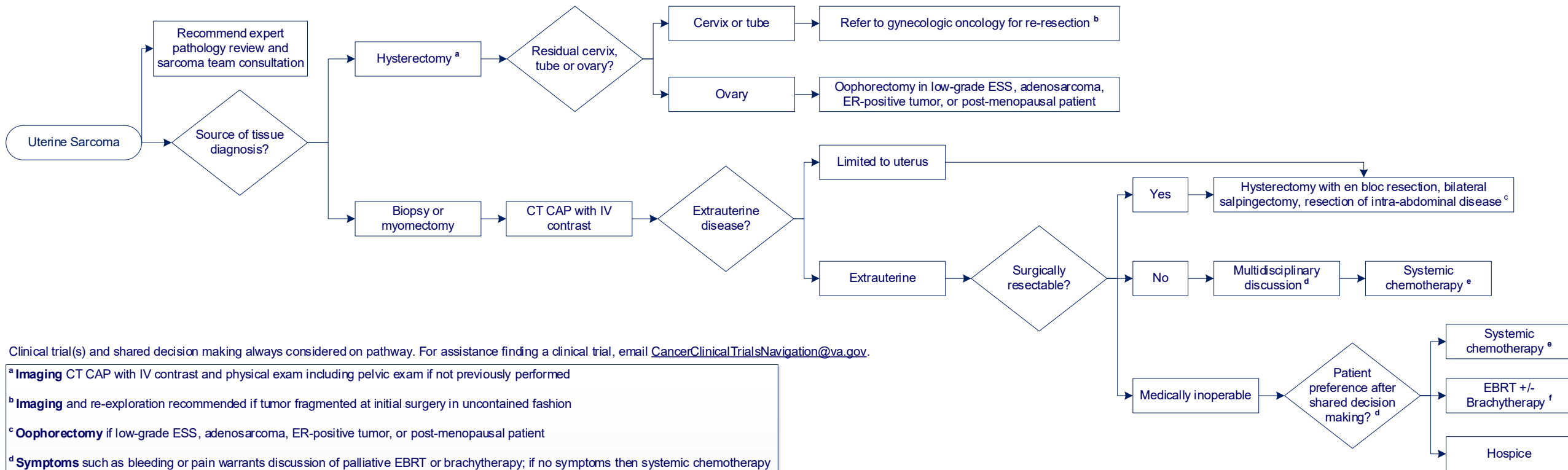
Rhabdomyosarcoma Prognostic Stratification Table								
Prognosis (EFS)	Stage	Clinical Group	Site	Size	Age	FOXO1 Fusion Status*	Mets	Nodes
Excellent (>85%) Low risk subset A	1	I	Favorable	a or b	<21	Negative	M0	N0
	1	II	Favorable	a or b	<21	Negative	M0	N0
	1	III	Orbit only	a or b	<21	Negative	M0	N0
	2	I	Unfavorable	a	<21	Negative	M0	N0 or NX
	1	II	Favorable	a or b	<21	Negative	M0	N1
Very good (70 to 85%) Low risk subset B	1	III	Orbit only	a or b	<21	Negative	M0	N1
	1	III	Favorable, excluding orbit	a or b	<21	Negative	M0	N0 or N1 or NX
	2	II	Unfavorable	a	<21	Negative	M0	N0 or NX
	3	I or II	Unfavorable	a	<21	Negative	M0	N1
	3	I or II	Unfavorable	b	<21	Negative	M0	N0 or N1 or NX
Good (50 to 70%) Intermediate Risk	2	III	Unfavorable	a	<21	Negative	M0	N0 or NX
	3	III	Unfavorable	a	<21	Negative	M0	N1
	3	III	Unfavorable	b	<21	Negative	M0	N0 or N1 or NX
	1, 2, 3	I, II, III	Favorable or unfavorable	a or b	<21	Positive	M0	N0 or N1 or NX
	4	IV	Favorable or unfavorable	a or b	<10	Negative	M1	N0 or N1 or NX
Poor (<30%) High Risk	4	IV	Favorable or unfavorable	a or b	≥10	Negative	M1	N0 or N1 or NX
	4	IV	Favorable or unfavorable	a or b	<21	Positive	M1	N0 or N1 or NX

The risk group descriptions in this table are based upon the results of historically completed trials using the EFS estimates of the individual patient groups. Current Children's Oncology Group (COG) protocols can deviate from these definitions for protocol purposes (refer to text).

Event-Free Survival (EFS); favorable site: orbit/eyelid, head and neck (excluding parameningeal), genitourinary (not bladder or prostate), and biliary tract; unfavorable site: bladder, prostate, extremity, parameningeal, trunk, retroperitoneal, pelvis, other; a: tumor size 5 cm in diameter; b: tumor size >5 cm in diameter; N0: regional nodes clinically not involved; N2: regional nodes clinically involved; NX: node status unknown; M0: no distant metastases; M1: distant metastases present.

* For the management of tumors with alveolar histology and negative for FOXO1 fusion, refer to up-to-date content on treatment of rhabdomyosarcoma.

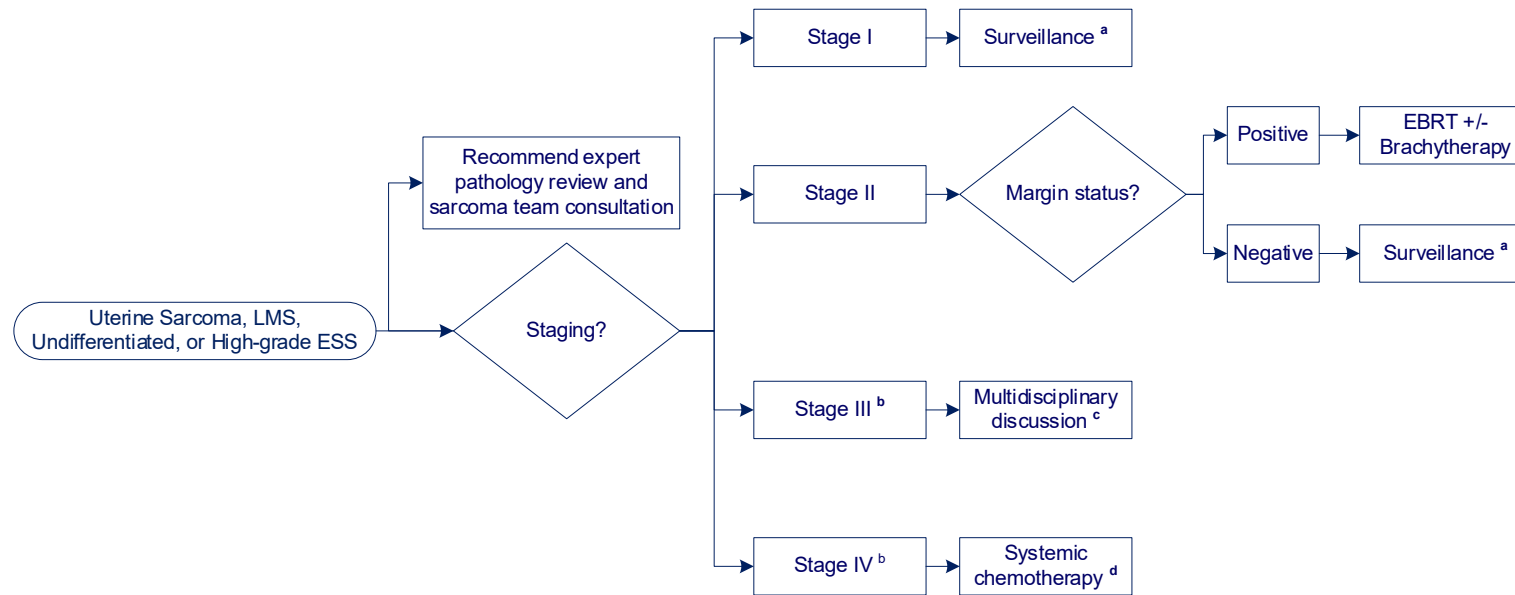
Soft Tissue Sarcoma – Uterine Sarcoma



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

- ^a **Imaging** CT CAP with IV contrast and physical exam including pelvic exam if not previously performed
 - ^b **Imaging** and re-exploration recommended if tumor fragmented at initial surgery in uncontained fashion
 - ^c **Oophorectomy** if low-grade ESS, adenosarcoma, ER-positive tumor, or post-menopausal patient
 - ^d **Symptoms** such as bleeding or pain warrants discussion of palliative EBRT or brachytherapy; if no symptoms then systemic chemotherapy
 - ^e **Imaging** CT CAP with IV contrast and physical exam including pelvic exam
 - ^f **EBRT/IMRT/VMAT** are preferred techniques when expertise is available
- ESS** Endometrial Stromal Sarcoma
EBRT External Beam Radiation Therapy
IMRT Intensity Modulated Radiation Therapy
VMAT Volumetric Modulated Arc Therapy

Soft Tissue Sarcoma – Uterine Sarcoma, LMS, Undifferentiated, or High-grade ESS



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

^a **Surveillance** imaging CT CAP with IV contrast and physical exam including pelvic exam

^b **Stage III and IV** molecular testing recommended

^c **Multidisciplinary Discussion** for systemic chemotherapy and/or EBRT (IMRT/VMAT are preferred techniques when expertise is available) or surveillance if no residual disease

^d **Palliative Radiation** for pain or bleeding may be considered

LMS Leiomyoma Sarcoma

ESS Endometrial Stromal Sarcoma

EBRT External Beam Radiation Therapy

IMRT Intensity Modulated Radiation Therapy

VMAT Volumetric Modulated Arc Therapy



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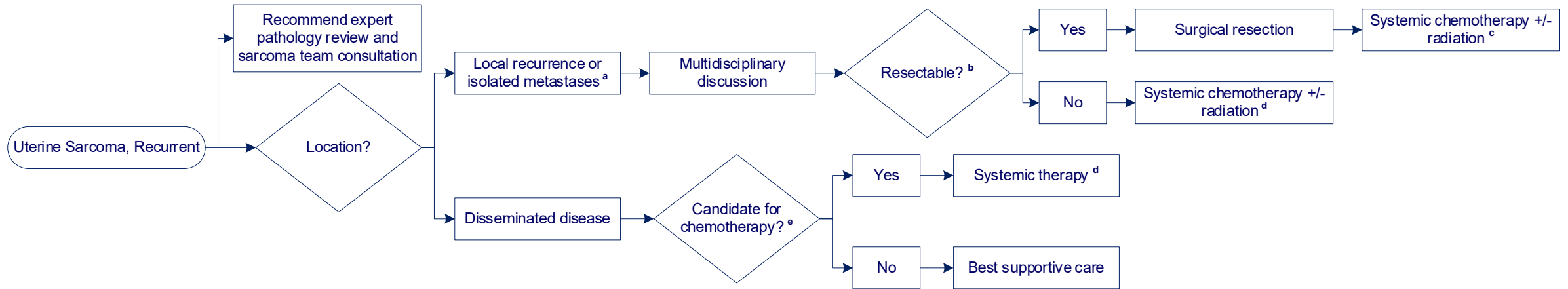
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Soft Tissue Sarcoma – Uterine Sarcoma, Recurrent



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^a **Local Recurrence** defined as vaginal or pelvis, imaging negative for distant disease

^b **Resectability** take into account date of last treatment, prior radiation, and medical co-morbidities

^c **Adjuvant Therapy** take into account radiation therapy for positive margin status, prior radiation, and previous systemic therapy

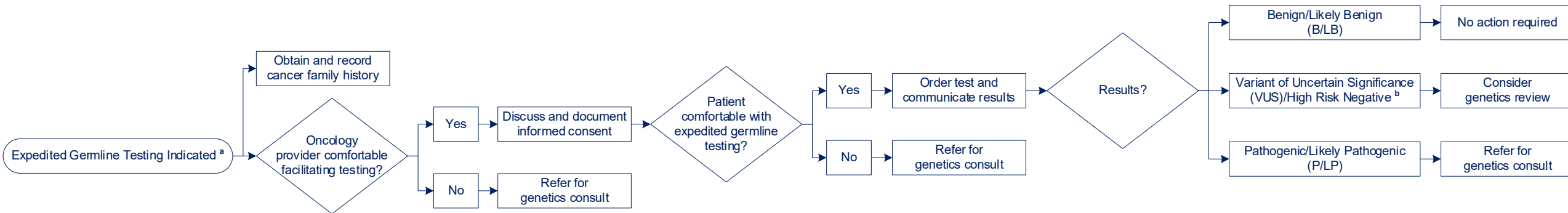
^d **Palliative Radiation** for controlled bleeding and/or pain, or radiation not previously given

^e **Refer** to table for recurrent uterine sarcoma disseminated disease histology

Soft Tissue Sarcoma – Uterine Sarcoma Chemotherapy

Uterine Sarcoma Chemotherapy		
		Chemotherapy
Histology	Uterine Leiomyosarcoma - First Line Therapy	Doxorubicin + Trabectedin
	Uterine Leiomyosarcoma - Second Line Therapy	Gemcitabine + Docetaxel
	Low-grade Endometrial Stromal Sarcoma (ESS)	Aromatase inhibitor
	PEComa First Line Therapy	Albumin-bound sirolimus
	PEComa Second Line Therapy	Everolimus
Molecular Testing	BRCA-altered Leiomyosarcoma (LMS)	Olaparib
	Neurotrophic Tyrosine Receptor Kinase (NTRK) Gene Fusion	Larotrectinib
	Anaplastic Lymphoma Kinase (ALK) Translocation	Crizotinib
	Microsatellite Instability (MSI)	Pembrolizumab

Soft Tissue Sarcoma – Expedited Germline Testing Indicated



^a **Expedited Germline Testing Indications** include results that may impact treatment and/or specific tumor types: gynecologic (ovarian, tubal, serous uterine), breast, pancreatic and ampullary, prostate (high grade/metastatic), medullary thyroid, pheochromocytoma, paraganglioma, or colon under age 50; specific indications may be found on their respective tumor-specific clinical pathways

^b **VUS/High Risk Negative** patients with personal and/or family history suggestive of hereditary cancer syndrome may benefit from formal genetics consult

Soft Tissue Sarcoma – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Soft Tissue Sarcoma Other Than GIST	Somatic NGS	DNA and RNA-based Comprehensive genomic profiling (CGP)	Tempus Foundation Medicine (F1CDx+F1RNA)	Yes Yes	Tumor Tissue
Age <50 or Personal or Family History of Other Cancers	Germline NGS	Germline NGS panel for Uterine cancers*	Fulgent Genetics	Yes	Blood, Saliva
*Germline Lynch NGS panel should include at minimum the following genes: <i>EPCAM(deletion)</i> , <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , and <i>PMS2</i>					

