Oncology Clinical Pathways
Lung Cancer

November 2024 – V5.2024

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Lung 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

- Respiratory cancers

Atomic Veterans Exposed to Ionizing Radiation

- Lung cancer
- Bronchioloalveolar carcinoma

Gulf War and Post 9/11 Veterans

If the patient served any amount of time in Afghanistan, Djibouti, Syria, or Uzbekistan during the Persian Gulf War, from Sept. 19, 2001, to the present or the Southwest Asia theater of operations from Aug. 2, 1990, to the present, specific conditions include:

- Adenosquamous carcinoma of the lung
- Large cell carcinoma of the lung
- Salivary gland-type tumors of the lung
- Sarcomatoid carcinoma of the lung
- Typical and atypical carcinoid of the lung

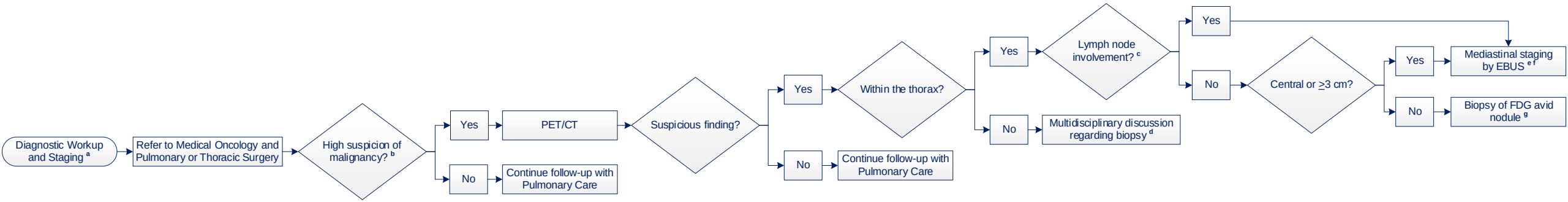
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Respiratory 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)

Lung Cancer – Diagnostic Workup and Staging



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

[a] **Diagnostic Workup and Staging** for pulmonary nodule evaluation, nodule with a high probability of cancer, nodule already diagnosed with lung cancer, or abnormal thoracic findings with concerns of cancer

[b] **High Suspicion of Malignancy** includes but is not limited to growth, radiographic properties, or large size

[c] **Lymph Node Involvement** includes any thoracic lymph node pathologic enlargement or FDG avidity

[d] **Molecular Testing** adequacy of tumor tissue should be considered in selection of the biopsy site and the amount of tissue; pursue the least invasive/risk biopsy when appropriate

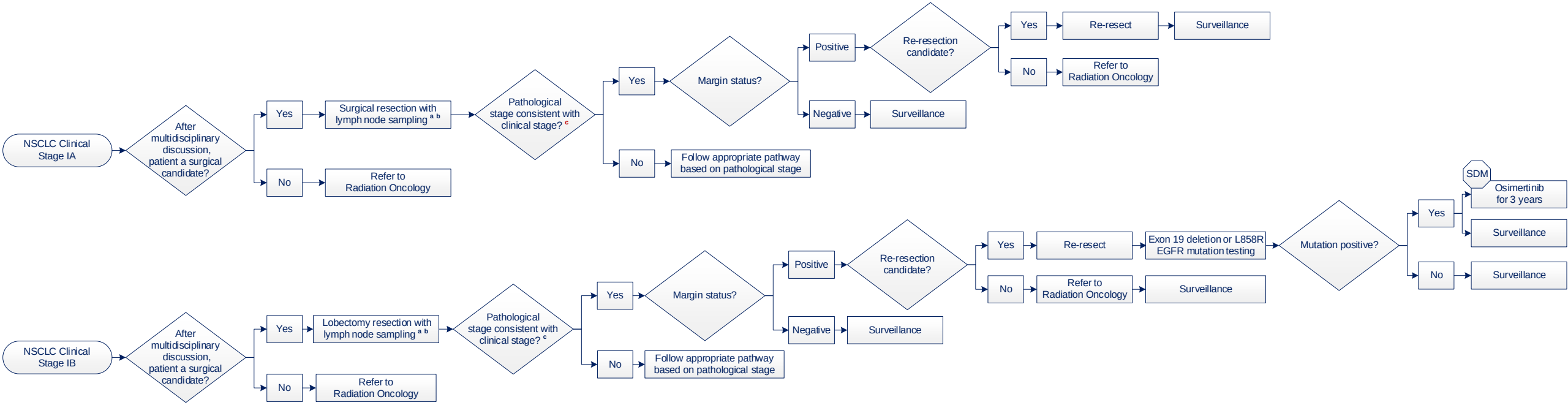
[e] **Mediastinal Staging** includes EBUS examination of all paratracheal and hilar stations with sampling of any nodes > 0.5 cm; EUS or mediastinoscopy may be an alternative staging modality based upon the location of the concerning lymph node(s)

[f] **Imaging** brain MRIs are indicated for Stage II and above

[g] **FDG Avid Nodules** can be evaluated by percutaneous biopsy, surgical biopsy, or navigational bronchoscopy; multidisciplinary discussion can assist in the care plan

EBUS Endobronchial Ultrasound
EUS Endoscopic Ultrasound
FDG Fluorodeoxyglucose

Lung Cancer – NSCLC Clinical Stage IA and IB



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[a] **Surgical Resection** includes lobectomy as preferred resection but sublobar can be considered as clinically indicated; consider sublobar resection for <2cm, peripheral, confirmed negative 10, 4, 7 nodes

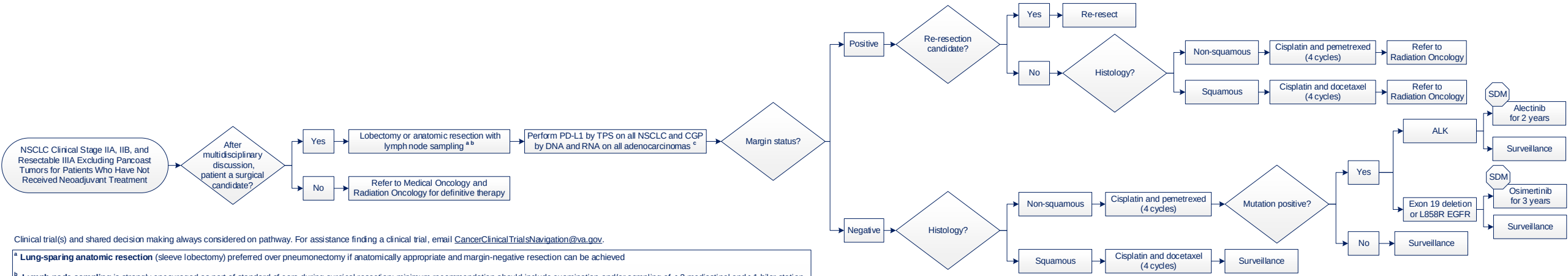
[b] **Lymph node sampling** is strongly encouraged as part of standard of care during surgical resection; minimum recommendation should include examination and/or sampling of ≥3 mediastinal and ≥1 hilar station

[c] **Pathology Review** includes a comprehensive pathology review for high risk features such as poorly differentiated tumors, vascular invasion, wedge resection, visceral pleural involvement, or lymph known status unknown; if ≥1 of these features are present, consider assessment by Medical Oncology post-operatively

SDM Osimertinib shared decision making is critical at the time of consideration of adjuvant Osimertinib for 3 years; adjuvant Osimertinib was shown to improve DFS and OS in EGFR exon 19 or exon 21 mutant NSCLC patients with stage I-III; the study had limitations including the majority of patients not receiving Osimertinib at the time of disease recurrence and inadequate staging; adjuvant Osimertinib is FDA approved in Stage IB but OS benefit is smaller in this subset and HR crosses 1 stressing the importance of discussing both adjuvant Osimertinib and surveillance with the patient

SDM Shared Decision Making

Lung Cancer – NSCLC Clinical Stage IIA, IIB, and Resectable IIIA Excluding Pancoast Tumors for Patients Who Have Not Received Neoadjuvant Treatment



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[a] **Lung-sparing anatomic resection** (sleeve lobectomy) preferred over pneumonectomy if anatomically appropriate and margin-negative resection can be achieved

[b] **Lymph node sampling** is strongly encouraged as part of standard of care during surgical resection; minimum recommendation should include examination and/or sampling of ≥3 mediastinal and ≥1 hilar station

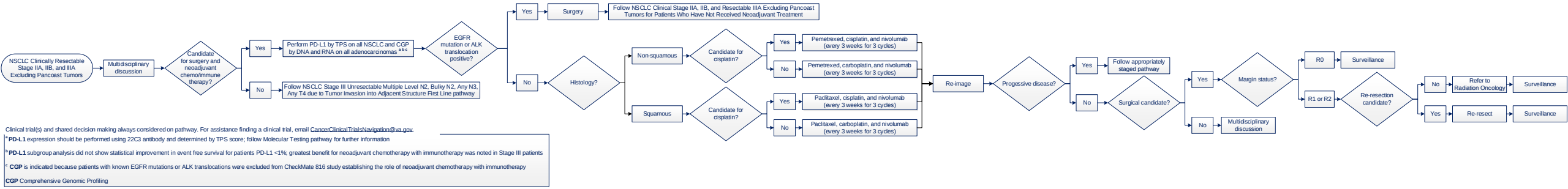
[c] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

SDM Alectinib shared decision making is critical at the time of consideration of adjuvant alectinib for 2 years; adjuvant alectinib was shown to improve DFS in ALK rearranged NSCLC patients with Stage II-III; the study had limitations including inadequate staging and randomization of patients to either adjuvant chemotherapy or alectinib; OS are not available yet and will likely not be available for years

SDM Osimertinib shared decision making is critical at the time of consideration of adjuvant Osimertinib for 3 years; adjuvant Osimertinib was shown to improve DFS and OS in EGFR exon 19 or exon 21 mutant NSCLC patients with Stage II-III; the study had limitations including the majority of patients not receiving Osimertinib at the time of disease recurrence and inadequate staging

CGP Comprehensive Genomic Profiling
SDM Shared Decision Making

Lung Cancer – NSCLC Clinically Resectable Stage IIA, IIB, and IIIA Excluding Pancoast Tumors



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

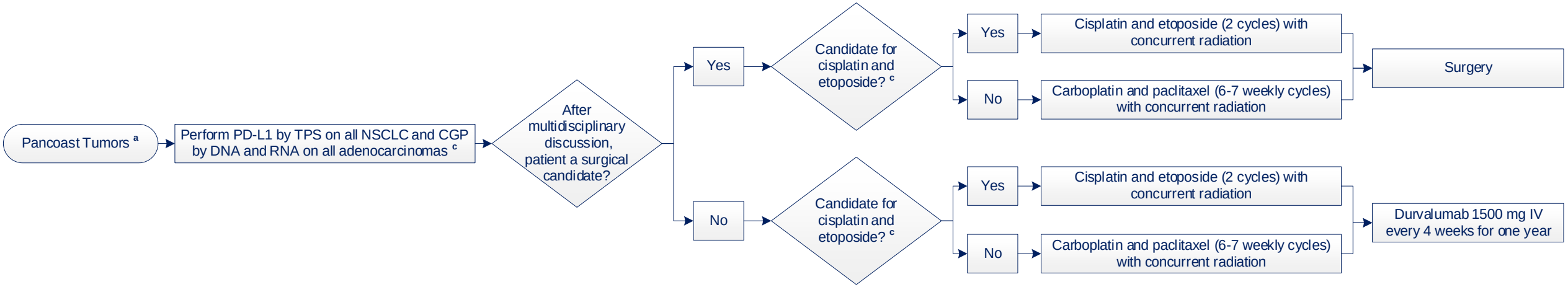
[a] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

[b] **PD-L1** subgroup analysis did not show statistical improvement in event free survival for patients PD-L1 <1%; greatest benefit for neoadjuvant chemotherapy with immunotherapy was noted in Stage III patients

[c] **CGP** is indicated because patients with known EGFR mutations or ALK translocations were excluded from CheckMate 816 study establishing the role of neoadjuvant chemotherapy with immunotherapy

CGP Comprehensive Genomic Profiling

Lung Cancer – Pancoast Tumors



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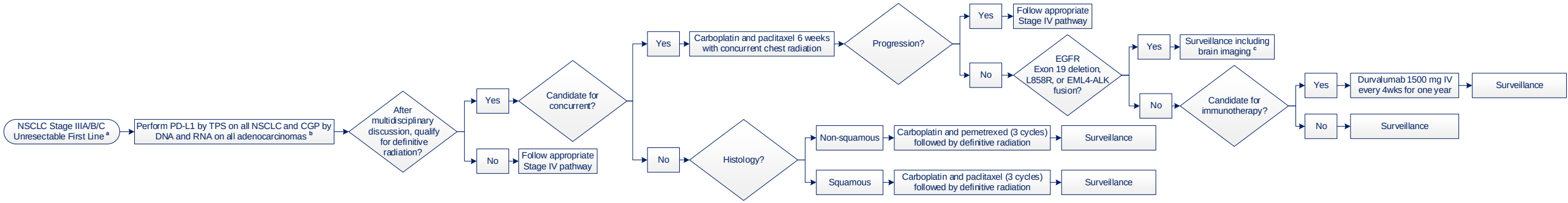
[a] **Pancoast Tumors** clinical diagnosis that includes any of these stages: T3N0, T4N0, and T4N1 are generally considered resectable and T4N2 is considered unresectable

[b] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

[c] **Candidate for Cisplatin and Etoposide** contraindications include abnormal renal function, ECOG 2, or abnormal heart function

Lung Cancer – NSCLC Stage IIIA/B/C Unresectable First Line



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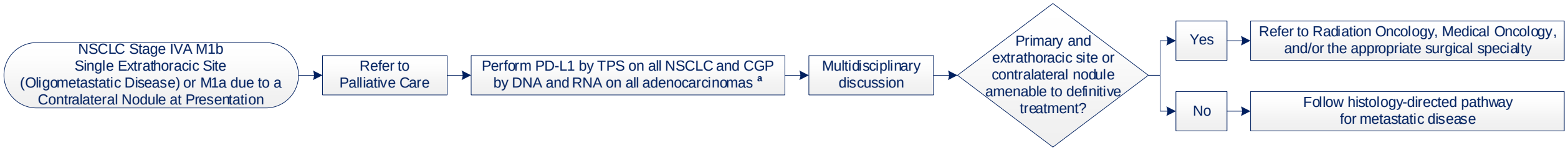
[a] **NSCLC Stage IIIA/B/C Unresectable** includes multiple level N2, bulky N2, any N3, any T4 due to tumor invasion into adjacent structure or poor surgical candidates due to prohibitive risk

[b] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information; CGP is indicated because the role of consolidation durvalumab is unclear in EGFR mutant or ALK translocation positive patients

[c] **Surveillance Including Brain Imaging** includes brain MRI and CT scan of the chest to the adrenals every 3-4 months for 2 years with reduced frequency of imaging as clinically appropriate after 2 years

CGP Comprehensive Genomic Profiling

Lung Cancer – NSCLC Stage IVA M1b Single Extrathoracic Site or M1a Due To A Contralateral Nodule at Presentation

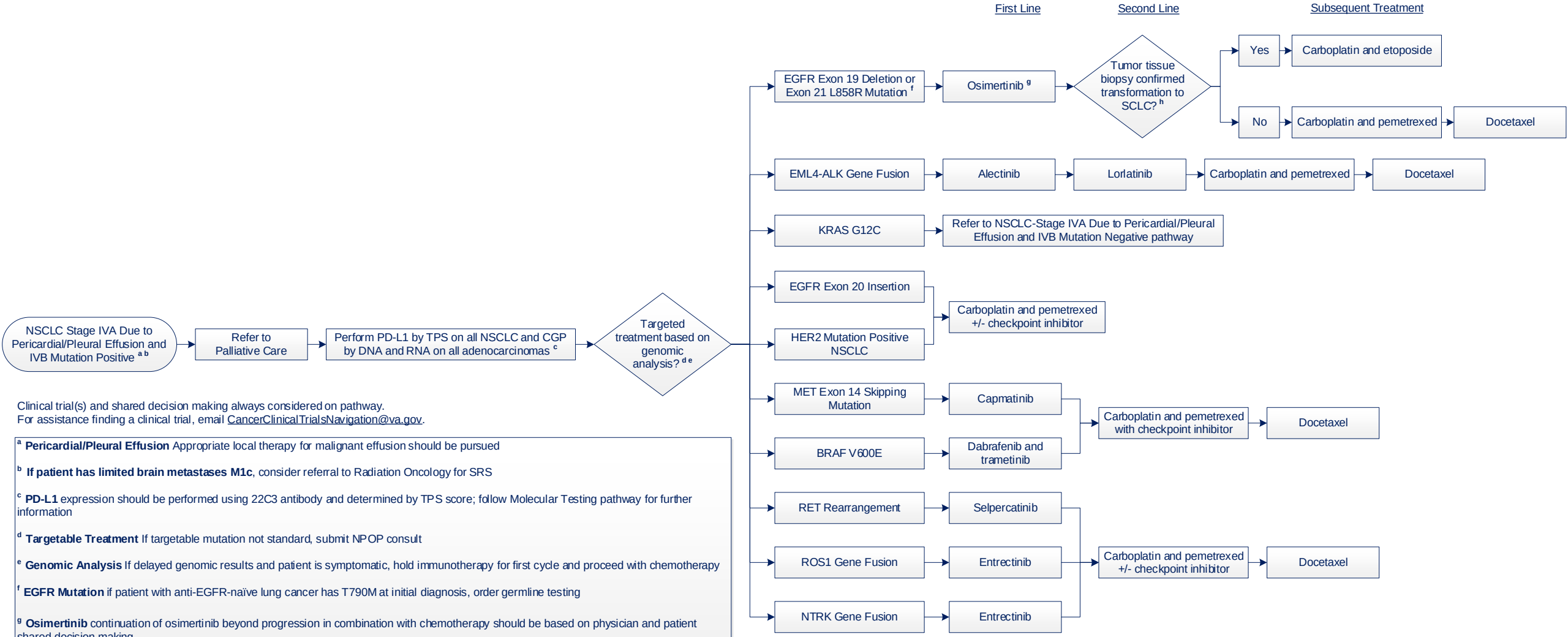


Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

CGP Comprehensive Genomic Profiling

Lung Cancer – NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Positive



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

[a] **Pericardial/Pleural Effusion** Appropriate local therapy for malignant effusion should be pursued

[b] **If patient has limited brain metastases M1c**, consider referral to Radiation Oncology for SRS

[c] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

[d] **Targetable Treatment** If targetable mutation not standard, submit NPOP consult

[e] **Genomic Analysis** If delayed genomic results and patient is symptomatic, hold immunotherapy for first cycle and proceed with chemotherapy

[f] **EGFR Mutation** if patient with anti-EGFR-naïve lung cancer has T790M at initial diagnosis, order germline testing

[g] **Osimertinib** continuation of osimertinib beyond progression in combination with chemotherapy should be based on physician and patient shared decision making

[h] **Driver Mutation Repeat Testing** recommendations on NGS testing for patients with driver mutations can be found on the NPOP SharePoint

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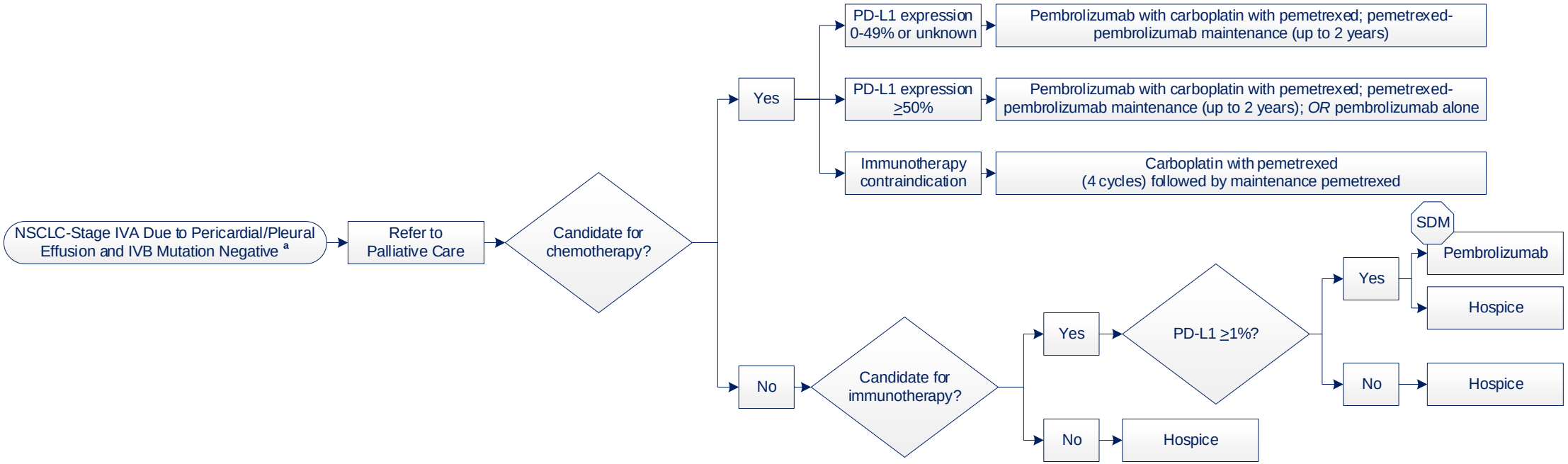
Lung Cancer – NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative



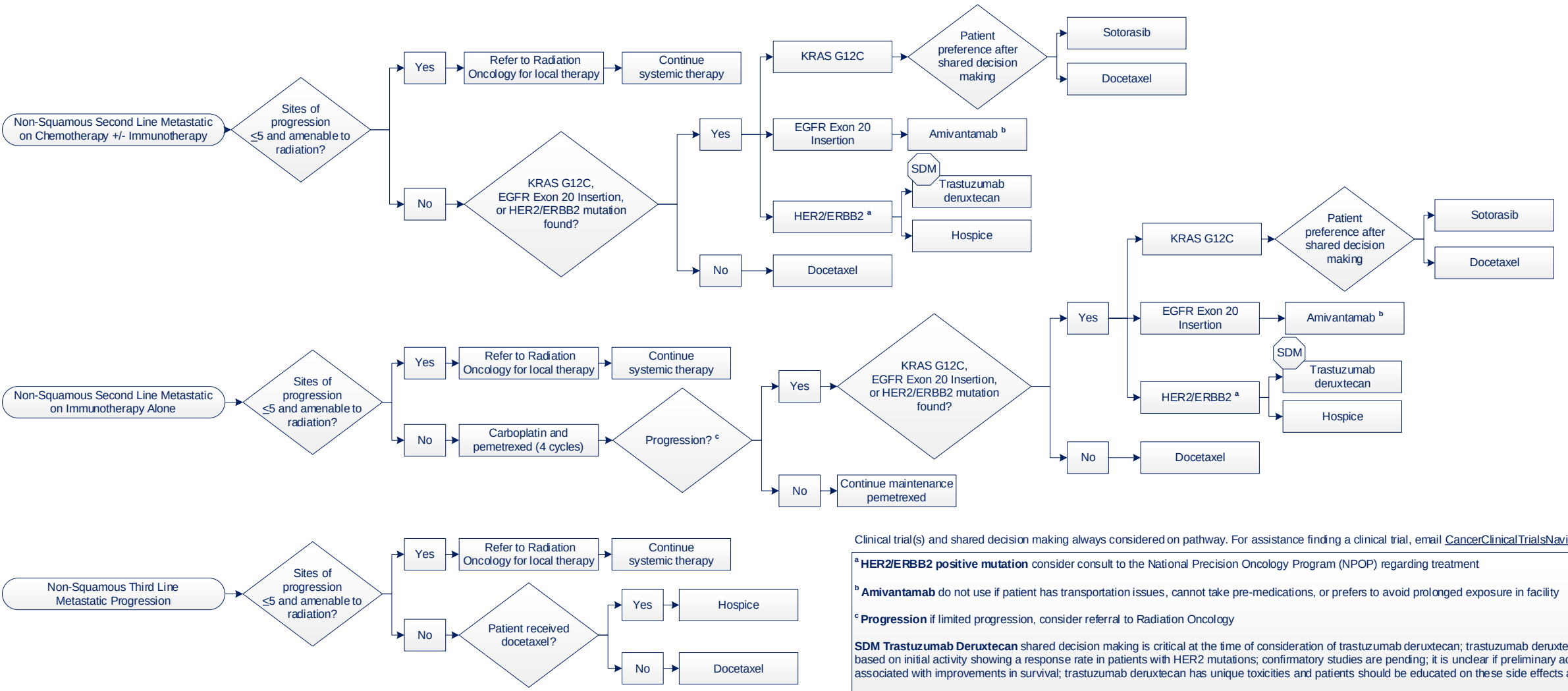
Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Pericardial/Pleural Effusion** appropriate local therapy for malignant effusion should be pursued; pathway also applicable for first line treatment of KRAS G12C, EGFR Exon 20 insertion, and HER2 mutation positive NSCLC

SDM Pembrolizumab shared decision making is critical at the time of consideration of pembrolizumab if PD-L1 >1%; pembrolizumab was approved as single agent in PD-L1 ≥1% based on KEYNOTE-042; the inclusion of PD-L1 >50% patients in the study limits the interpretation of the benefit of single agent pembrolizumab in the 1-50% group; therefore while this is an FDA approved indication, shared decision making in patients that do not qualify for chemotherapy and that have a PD-L11-50% should include a thorough discussion of the limited activity of single agent immunotherapy noted in this subset in other trials

SDM Shared Decision Making

Lung Cancer – Non-Squamous Second and Third Lines Metastatic



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

[a] **HER2/ERBB2 positive mutation** consider consult to the National Precision Oncology Program (NPOP) regarding treatment

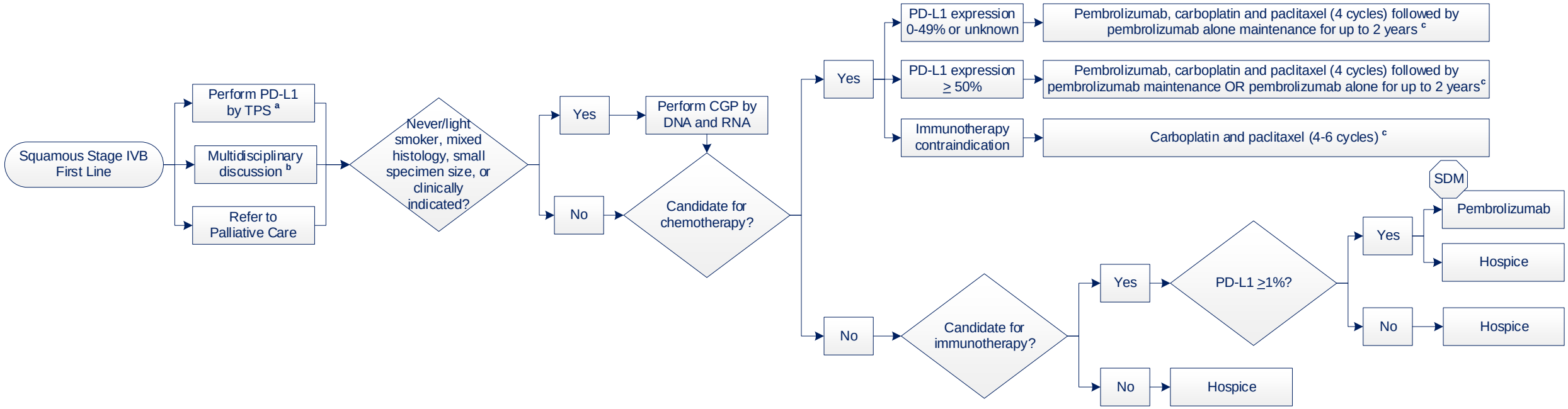
[b] **Amivantamab** do not use if patient has transportation issues, cannot take pre-medications, or prefers to avoid prolonged exposure in facility

[c] **Progression** if limited progression, consider referral to Radiation Oncology

SDM Trastuzumab Deruxtecan shared decision making is critical at the time of consideration of trastuzumab deruxtecan; trastuzumab deruxtecan was approved based on initial activity showing a response rate in patients with HER2 mutations; confirmatory studies are pending; it is unclear if preliminary activity will be associated with improvements in survival; trastuzumab deruxtecan has unique toxicities and patients should be educated on these side effects and monitored closely

SDM Shared Decision Making

Lung Cancer – Squamous Stage IVB First Line



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

[a] **PD-L1** expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

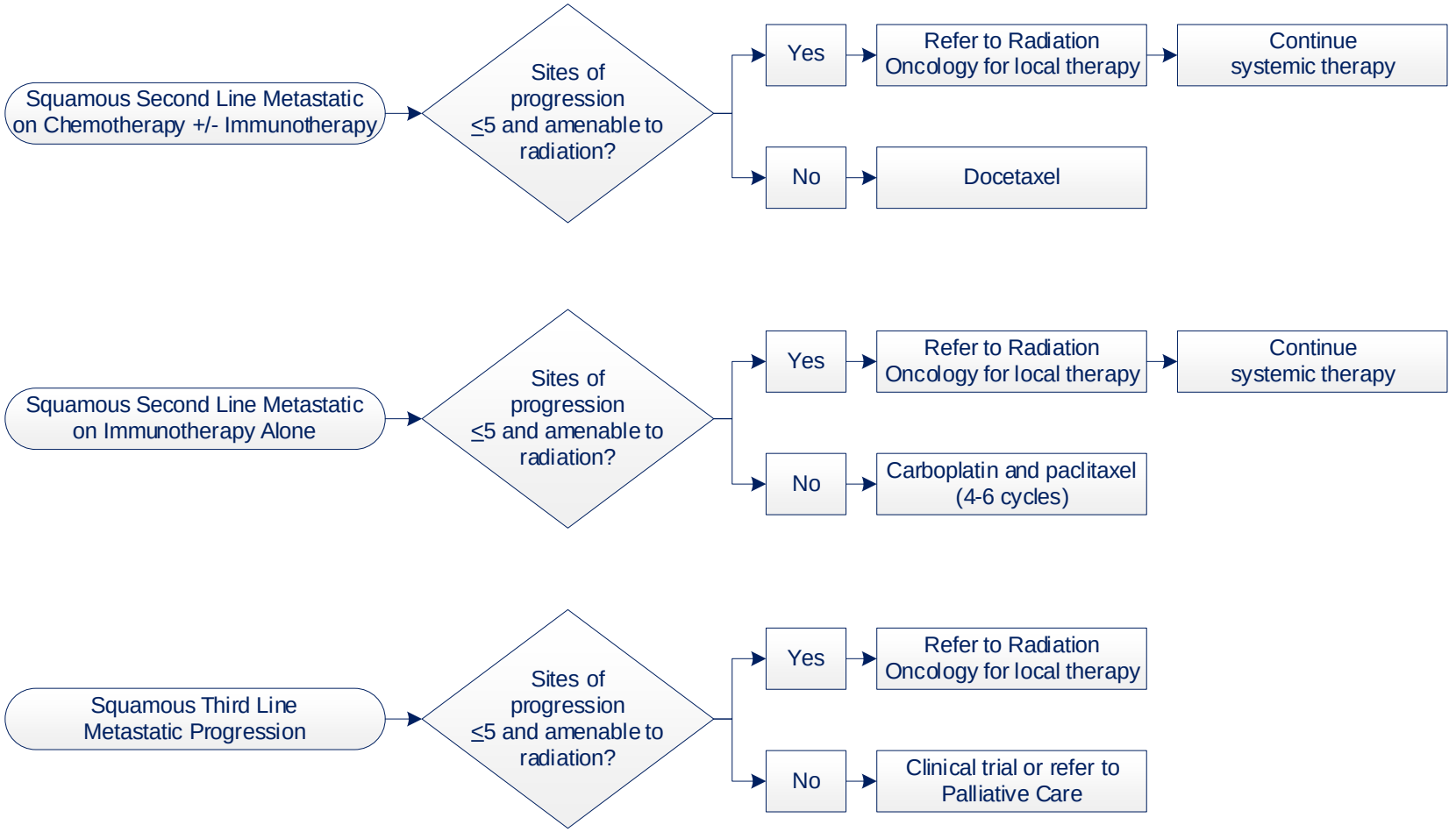
[b] **If patient is symptomatic** refer to Radiation Oncology

[c] **If limited progression**, consider referral to Radiation Oncology and continuation of first-line systemic therapy

SDM Pembrolizumab shared decision making is critical at the time of consideration of pembrolizumab if PD-L1 >1%; pembrolizumab was approved as single agent in PD-L1 ≥1% based on KEYNOTE-042; the inclusion of PD-L1 >50% patients in the study limits the interpretation of the benefit of single agent pembrolizumab in the 1-50% group; therefore while this is an FDA approved indication, shared decision making in patients that do not qualify for chemotherapy and that have a PD-L11-50% should include a thorough discussion of the limited activity of single agent immunotherapy noted in this subset in othertrials

SDM Shared Decision Making

Lung Cancer – Squamous Second and Third Lines Metastatic



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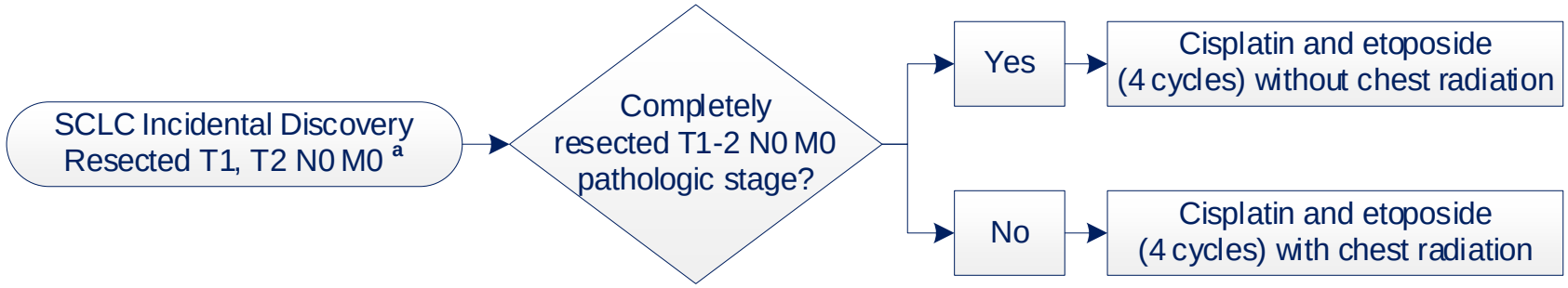
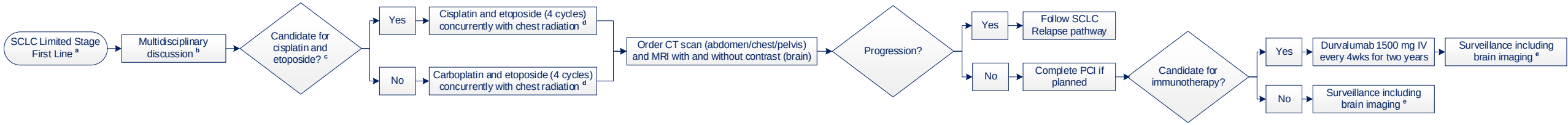
Lung Cancer – SCLC Incidental Discovery Resected T1, T2 N0 M0



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

[a] **Large Cell Neuroendocrine Tumors** can be treated like SCLCs

Lung Cancer – SCLC Limited Stage First Line



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

[a] **Large Cell Neuroendocrine Tumors** can be treated like SCLCs

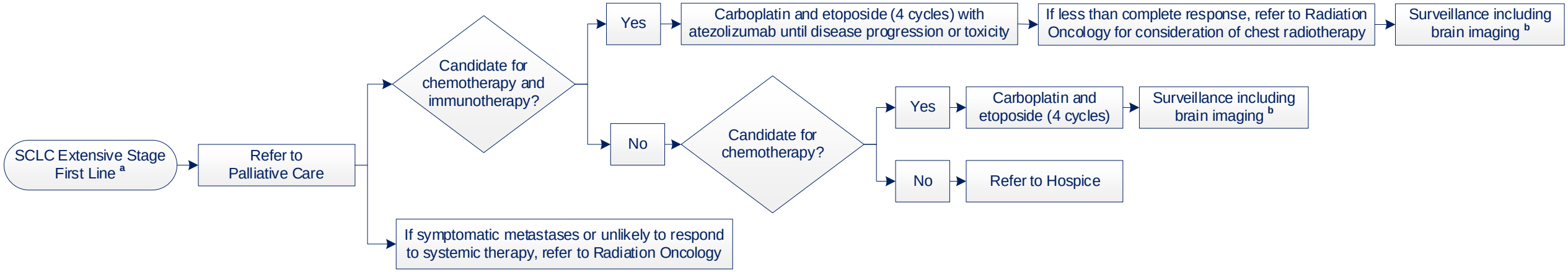
[b] **In the rare case of T1-2 N0 M0**, surgery can be considered followed by adjuvant chemotherapy

[c] **Candidate for cisplatin and etoposide** contraindications include abnormal renal function, ECOG 2, or abnormal heart function

[d] **Initiate radiation** as early as possible, within the first or second cycle of chemotherapy

[e] **Surveillance Including Brain Imaging** includes brain MRI and CT scan of the chest to the adrenals every 3-4 months for 2 years with reduced frequency of imaging as clinically appropriate after 2 years

Lung Cancer – SCLC Extensive Stage First Line

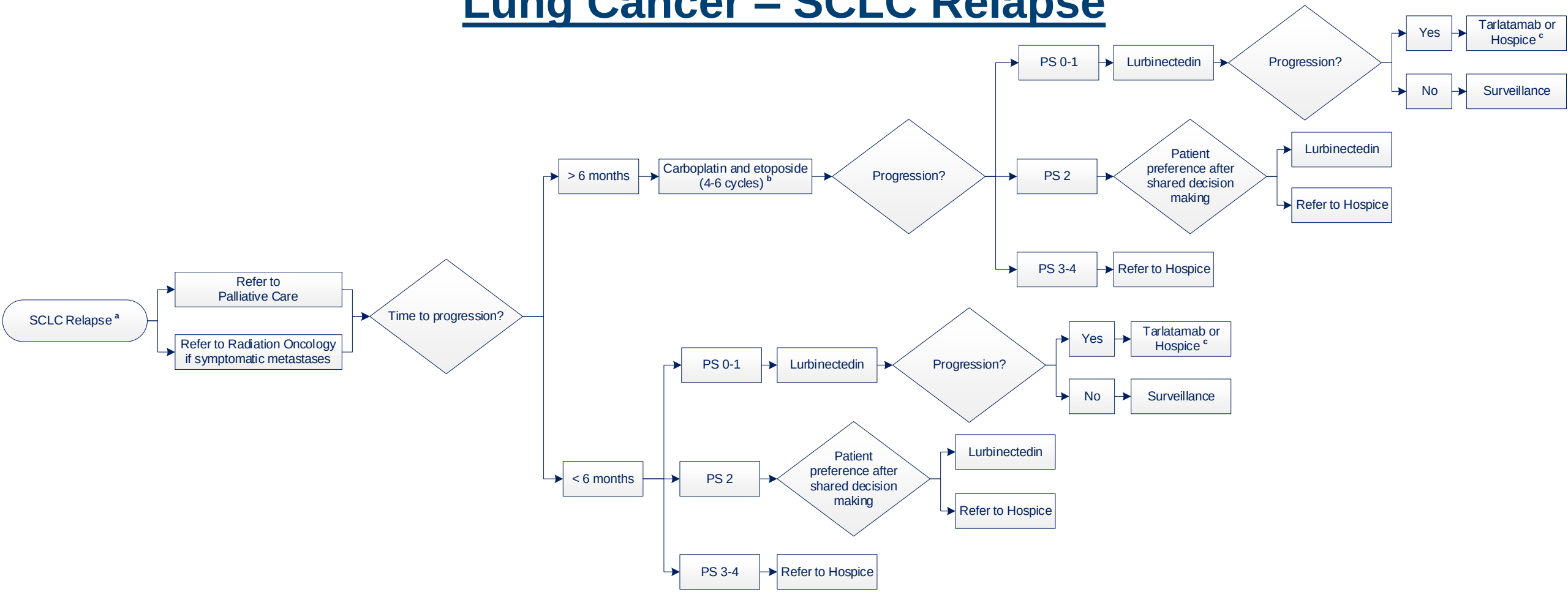


Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Large Cell Neuroendocrine Tumors** can be treated like SCLCs

[b] **Surveillance Including Brain Imaging** includes brain MRI and CT scan of the chest to the adrenals every 3-4 months for 2 years with reduced frequency of imaging as clinically appropriate after 2 years

Lung Cancer – SCLC Relapse



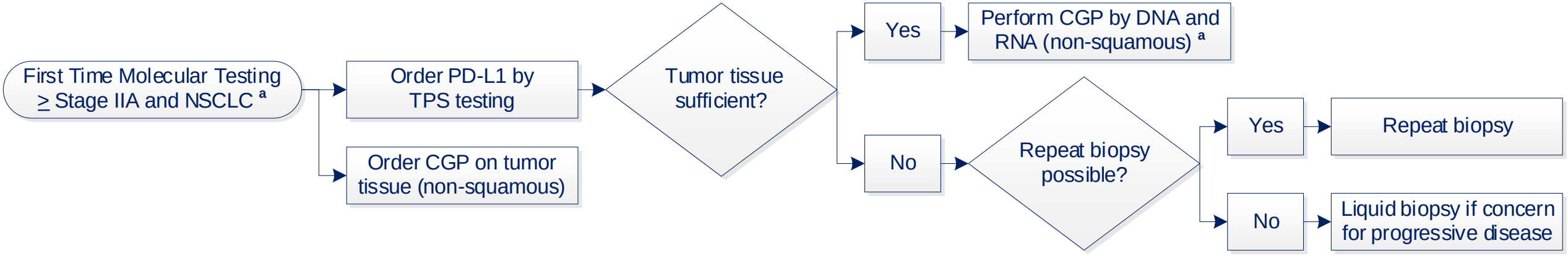
Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Large Cell Neuroendocrine Tumors** can be treated like SCLCs

[b] **If patient is progressing** and did not receive immunotherapy upfront, patient can receive carboplatin, etoposide, and atezolizumab

[c] **Tarlatamab** this therapy is highly toxic and administration requires significant facility support and comprehensive protocols with experienced personnel capable of identifying, monitoring and managing CRS and Neurotoxicity (ICANS); in addition, patient requirements: PS 0-1, cardiac ejection fraction ≥50%, no evidence or ILD, estimated GFR ≥30 mL/min/1.73m2, adequate blood counts and liver function, and the absence of known or suspected infectious diseases

Lung Cancer – Molecular Testing



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

[a] **Molecular Testing** is not routinely recommended for SCLC or large cell neuroendocrine tumors; molecular testing may be ordered for mixed histology or squamous cell carcinoma as clinically appropriate

CGP Comprehensive Genomic Profiling

Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Stage IIA and Higher NSCLC	IHC	PD-L1 expression by IHC using 22C3 antibody	Tempus Foundation Medicine Local Vendor	Yes (when ordered with CGP) Yes (when ordered with CGP) No	Tumor Tissue
Stage IIA and Higher NSCLC Non-Squamous	Somatic NGS*	DNA and RNA-based comprehensive genomic profiling (CGP)	Tempus Foundation Medicine	Yes Yes	Tumor Tissue, Blood
Stage IV Squamous Never/Light Smoker, Mixed Histology, or Small Specimen Size	Somatic NGS*	DNA and RNA-based comprehensive genomic profiling (CGP)	Tempus Foundation Medicine	Yes Yes	Tumor Tissue, Blood
* Somatic NGS testing should adequately cover point mutations, small insertion/deletion mutations, amplifications, and fusion oncogenes; at minimum testing should include coverage of EGFR, ALK, ROS1, RET, MET, BRAF, KRAS, NTRK1, NTRK2, NTRK3, and HER2					
** Tissue testing strongly preferred because it is the only method for RNA based testing. Liquid testing is suboptimal but acceptable only if adequate tissue cannot be obtained.					

Lung Cancer – Surveillance for Surgically Treated NSCLC Stage IA/IB, IIA/IIB, or IIIA

Surveillance for Surgically Treated NSCLC Stage IA/IB, IIA/IIB, or IIIA [a]

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 5+
H&P [b]	Every 6 months			Annually		
CT Chest [c]	Every 6 months			Annually		Annual low dose CT [d]

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

[a] **Surveillance** once treatment is completed; routine brain imaging is not recommended unless otherwise specified on pathway

[b] **H&P** to include smoking cessation

[c] **CT of Chest** initial baseline scan within 3 months of definitive treatment; more frequent scanning may be required

[d] **Annual Low Dose CT** more frequent scanning intervals may be appropriate in some patients, to include SBRT patients; for years 3-5+, low-dose CT scans may be used to screen for a second primary malignancy

Lung Cancer – Surveillance for NSCLC Stage III Curative Intent with Definitive Chemoradiation

Surveillance for NSCLC Stage III Curative Intent with Definitive Chemoradiation [a]

	Year 1 [d]	Year 2	Year 3	Year 4	Year 5	Year 5+
H&P [b]	Every 3 months	Every 4 months	Every 6 months			
CT Chest [c]	Every 3 months	Every 4 months	Every 6 months			Annual low dose CT [e]

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

[a] **Surveillance** once treatment is completed; routine brain imaging is not recommended unless otherwise specified on pathway

[b] **H&P** to include smoking cessation

[c] **CT of Chest** initial baseline scan within 3 months of definitive treatment; more frequent scanning may be required

[d] **Year 1** not intended to provide guidance for imaging consolidation immunotherapy

[e] **Annual Low Dose CT** more frequent scanning intervals may be appropriate in some patients, to include SBRT patients; for years 3-5+, low-dose CT scans may be used to screen for a second primary malignancy