台北榮總胸腺癌診療共識

V.2.0 2025

台北榮總肺癌團隊

Revised on 2025/11/24

TNM classification

AJCC 9th edition

T (Tumor) Categories

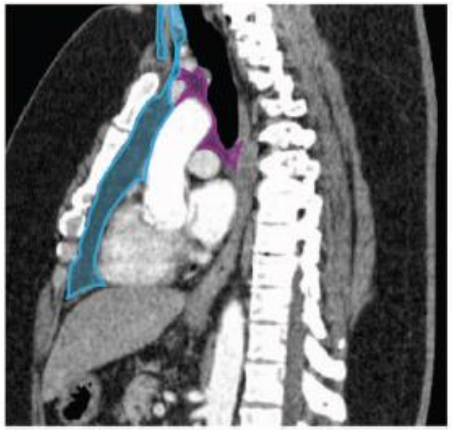
- **T1:** Tumor is limited to the thymus or mediastinum only
  - **T1a:** Tumor ≤5 cm in greatest dimension
  - **T1b:** Tumor >5 cm in greatest dimension
- **T2:** Tumor directly invades the pericardium (partial or full thickness), lung, or phrenic nerve
- **T3:** Tumor directly invades one or more of the following:
  - Brachiocephalic vein
  - Superior vena cava
  - Chest wall
  - Extrapericardial pulmonary arteries or veins
- **T4:** Tumor directly invades one or more of the following:
  - Aorta (ascending, arch, or descending)
  - Arch vessels
  - Intrapericardial pulmonary arteries or veins
  - Myocardium
  - Trachea
  - Esophagus

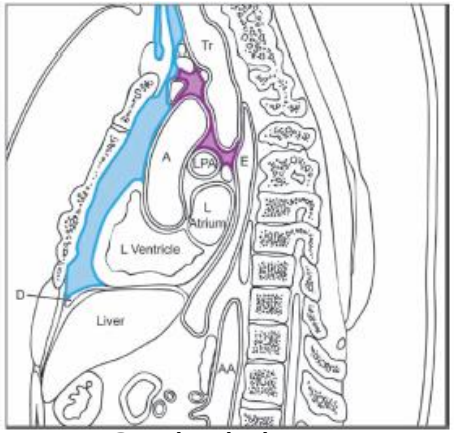
TNM classification

AJCC 9th edition

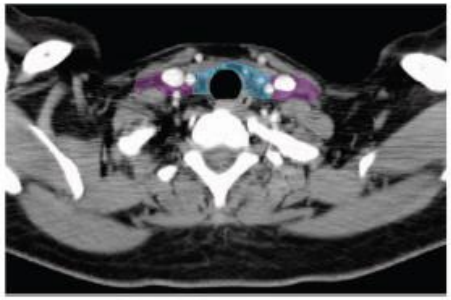
N (Lymph Node) Categories
• **N0**: No regional lymph node metastasis • **N1**: Metastasis in anterior (perithymic) lymph nodes • **N2**: Metastasis in deep intrathoracic or cervical lymph nodes (e.g., paratracheal, subcarinal, aortopulmonary window, hilar, jugular, or supraclavicular nodes)
Definition of distant metastasis (M)
• **M0:** No distant metastasis • **M1a:** Presence of separate pleural or pericardial nodule(s) (droplet metastases) • **M1b:** Presence of pulmonary intraparenchymal nodules or distant organ metastasis

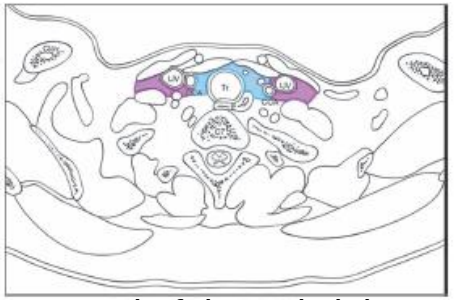
ITMIG/IASLC node compartments for thymic malignancies. Graphic depiction of N1 (anterior region, blue) and N2 (deep region, purple) node compartments



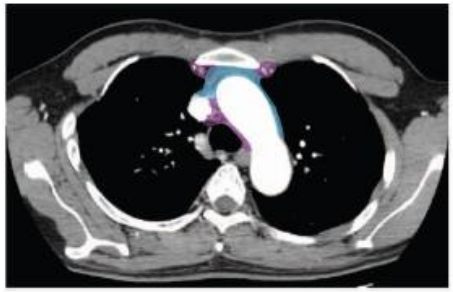


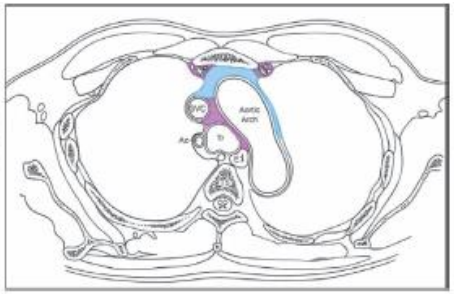
Sagittal view

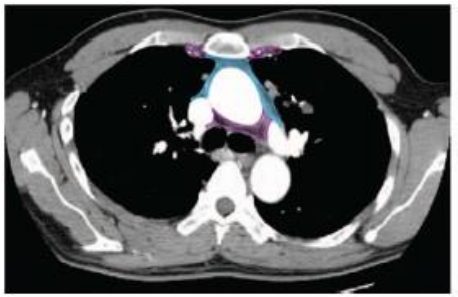


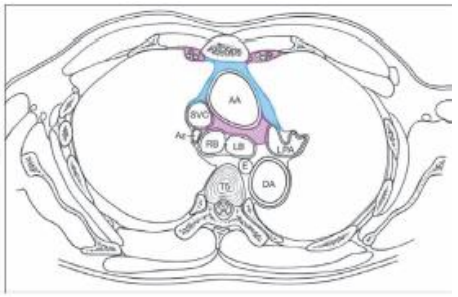


Level of thoracic inlet

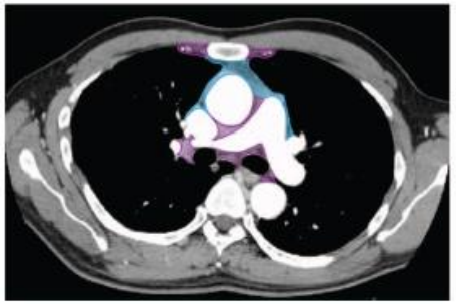


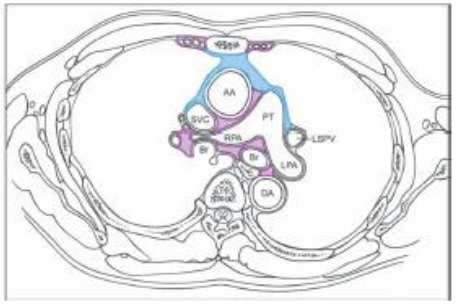


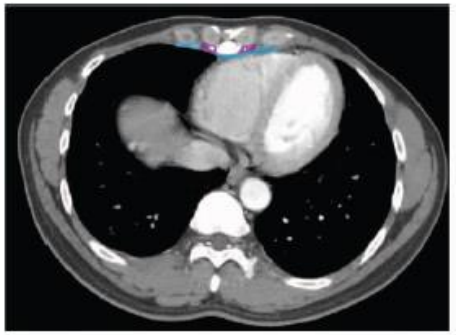


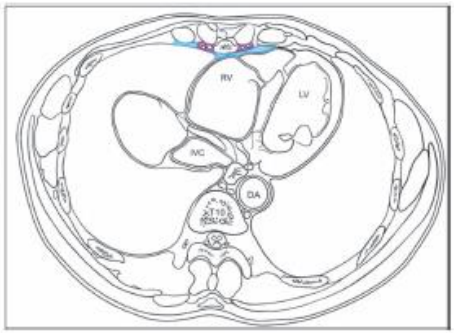


Level of aortopulmonary window









J Thorac Oncol. 2014 Sep;9(9 Suppl 2):S81-7

Table 35.1 Lymph node regions for thymic malignancies

	Region Boundaries	Node Groups*
N1: Anterior Region	*Superior:* hyoid bone *Lateral (neck):* medial border of carotid sheaths *Lateral (chest):* mediastinal pleura *Anterior:* Sternum *Posterior (medially):* great vessels, pericardium *Posterior (laterally):* phrenic nerve *Inferior:* Xiphoid, diaphragm	Low anterior cervical: pretracheal, paratracheal, peri-thyroid, precricoid/delphian Peri-Thymic Prevascular Para-aortic, Ascending Aorta, Superior Phrenics Supradiaphragmatic / Inferior Phrenics / Pericardial
N2: Deep Region	*Superior:* Level of lower border of cricoid cartilage *Anteromedial (neck):* lateral border of sternohyoid, medial border of carotid sheath *Posterolateral (neck):* anterior border of trapezius *Anterior (chest): Right* – Anterior Border of SVC; *Left* – aortic arch, aortopulmonary window *Posterior (Chest):* Esophagus *Lateral (chest):* pulmonary hila *Inferior:* Diaphragm	Lower Jugular Supraclavicular/venous angle: confluence of internal jugular & subclavian vein Internal Mammary nodes Upper Paratracheal Lower Paratracheal Subaortic / Aortopulmonary Window Subcarinal Hilar

*Region and node group boundaries match those established by the American Academy of Otolaryngology - Head and Neck Surgery, American Society for Head and Neck Surgery, and the International Association for the Study of Lung Cancer where applicable.
SVC, superior vena cava

TNM classification

AJCC 9th edition

- **Stage grouping**

Stage	T	N	M
I	**T1**	N0	M0
II	**T2**	N0	M0
IIIa	**T3**	N0	M0
IIIb	**T4**	N0	M0
IVa	T any	**N1**	M0
	T any	N0, 1	**M1a**
IVb	T any	**N2**	M0, 1a
	T any	N any	**M1b**

Modified Masaoka Staging

Staging

Table 1. Modified Masaoka clinical staging of thymoma[1-3]

Masaoka Stage	Diagnostic Criteria
Stage I	Macroscopically and microscopically completely encapsulated
Stage II	(A) Microscopic transcapsular invasion (B) Macroscopic invasion into surrounding fatty tissue or grossly adherent to but not through mediastinal pleura or pericardium
Stage III	Macroscopic invasion into neighboring organs (ie, pericardium, great vessels, lung) (A) Without invasion of great vessels (B) With invasion of great vessels
Stage IV	(A) Pleural or pericardial dissemination (B) Lymphogenous or hematogenous metastasis

[1] Reprinted from Wright CD. Management of thymomas. Crit Rev Oncol Hematol 2008;65:109-120, with permission from Elsevier.
[2] Note that the Masaoka staging system is also used to stage thymic carcinomas.
[3] Detterbeck FC, Nicholson AG, Kondo K, et al. The Masaoka-Koga stage classification for thymic malignancies: clarification and definition of terms. J Thorac Oncol 2011;6:S1710-S1716.

WHO Histologic Classification

WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION[1]

Thymomas	Essential criteria	Desirable criteria
Type A	• A thymic epithelial tumour with bland spindle and oval, and rarely polygonal, epithelial cells with a fascicular, storiform, or pericytomatous growth pattern • Most cases lack areas of necrosis and have a low mitotic count and a low Ki-67 index • Atypical type A thymomas may have higher mitotic count and focal necrosis	• Strong expression of epithelial markers • Paucity or absence of immature TdT-positive T cells throughout the tumour
Type AB	• A thymic tumour with a lobulated growth pattern • Admixed spindle cell–predominant lymphocyte-poor component (type A) and lymphocyte-rich component (type B) • Bland spindle, oval, and focally polygonal thymic epithelial cells and focal or diffuse abundance of immature T cells • In type A tumours with focal lymphocytic stroma in which lymphocytes are difficult to count, ≥10% area showing infiltrate of TdT-positive T cells should be classified as type AB thymoma	TdT immunostaining to assess TdT-positive cell density for differential diagnosis with type A thymoma
Type B1	• A thymic epithelial tumour with organoid (corticomedullary) architecture with cortical predominance • Dispersed, non-clustered thymic epithelial cells among densely packed lymphocytes • Medullary islands are obligatory	• Cytokeratin and/or p40/p63 stains to highlight dispersed epithelial cells • Sheets of TdT-positive immature T cells interspersed with TdT-negative nodular (medullary) areas
Type B2	• Lobulated architecture • Abundance of lymphocytes • Polygonal/oval neoplastic epithelial cells that are more numerous than in the normal thymic cortex and often present in clusters	Keratin and/or p40/p63 stains to highlight the increased density of dispersed and/or clustered epithelial cells compared with the normal thymic cortex
Type B3	• Lobulated tumour • Sheets of mildly/moderately atypical, polygonal tumour cells • Interspersed perivascular spaces • Paucity of lymphocytes	TdT immunostain to highlight the small population of immature T cells

[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

WHO Histologic Classification

WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION[1]

Thymomas	Essential criteria	Desirable criteria
Micronodular thymoma with lymphoid stroma	• Multiple small discrete nodules composed of bland spindle or oval epithelial cells • Abundant epithelial cell–free lymphoid stroma	Predominant CD20-positive B cells in stroma
Metaplastic thymoma	• Biphasic thymic tumour • Anastomosing islands of polygonal epithelial cells, which may show variable nuclear atypia • Background of bland-looking spindly cells	
Lipofibroadenoma	A benign thymic tumour resembling fibroadenoma of the breast with a predominance of fibrous tissue over adipocytes and delicate strands of epithelial cells	
Squamous carcinomas	**Essential criteria**	**Desirable criteria**
Squamous cell carcinoma, NOS	• Invasive SCC of the thymus, often accompanied by desmoplastic to sclerohyaline stroma • Exclusion of invasion from adjacent pulmonary carcinoma or metastasis	• Positive immunostaining for p63/p40, CD5, KIT (CD117), FOXN1, and/or CD205 • Assay of *KIT* mutation may be helpful to identify a potential therapeutic target
Basaloid carcinoma	A basaloid carcinoma of the thymus with nests or cystic spaces lined by basaloid neoplastic cells with peripheral palisading	Immunostaining positive for p63/p40 and/or KIT (CD117) and negative for TTF1, neuroendocrine markers, and NUT
Lymphoepithelial carcinoma	• Primary thymic carcinoma • Sheets, nests, and cords of carcinoma cells with syncytial appearance, vesicular chromatin, and prominent nucleoli • Many admixed lymphocytes and plasma cells	• Immunohistochemistry (IHC) for pancytokeratins, p63/p40 • In situ hybridization for EBER – the result does not affect diagnosis of cases with typical lymphoepithelial carcinoma morphology, but EBER positivity supports diagnosis in lymphocyte-poor cases

[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

WHO Histologic Classification

WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION[1]

Adenocarcinomas	Essential criteria	Desirable criteria
Adenocarcinoma NOS	Adenocarcinoma of thymus after exclusion of mediastinal metastasis from other sites and defined types of thymic adenocarcinoma (low-grade papillary, enteric-type)	Immunophenotyping to rule out mediastinal metastasis or defined types of thymic adenocarcinoma
Low-grade papillary adenocarcinoma	• A primary thymic low-grade adenocarcinoma with tubulopapillary growth • Tubulopapillary structures lined by cuboidal or polygonal cells	Immunostains to exclude papillary neoplasms of the thyroid, pleura, lung, and extrathoracic sites
Thymic carcinoma with adenoid cystic carcinoma-like features	• Thymic carcinoma morphologically similar to adenoid cystic carcinoma, but generally lacking true glands within the cribriform-basaloid islands • Exclusion of metastasis from salivary gland, lung, or breast	• IHC positive for pancytokeratins, CK5/6, p63/p40 • Negative staining for SMA, KIT (CD117)
Adenocarcinoma, enteric-type	• A primary thymic tumour mimicking colorectal adenocarcinoma • Exclusion of metastasis from an enteric primary	Expression of at least one marker of enteric differentiation (CK20, CDX2, MUC2)
Adenosquamous carcinomas	**Essential criteria**	**Desirable criteria**
Adenosquamous carcinoma	• A primary thymic carcinoma with both squamous and glandular differentiation in which each component constitutes ≥10% of the tumour within a resection specimen • Exclusion of mucoepidermoid carcinoma	The squamous component should be positive for p63/40 and/or CK5/6
NUT carcinomas	**Essential criteria**	**Desirable criteria**
NUT carcinoma	Demonstration of *NUTM1* rearrangement by molecular methods or NUT-positive IHC in a poorly differentiated squamous cell carcinoma or other poorly differentiated carcinoma	

[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

WHO Histologic Classification

WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION[1]

Salivary gland-like carcinomas	Essential criteria	Desirable criteria
Mucoepidermoid carcinoma	• A primary thymic carcinoma characterized by a combination of mucus-producing, intermediate, and squamoid cells growing in nests and cystic structures • In high-grade MEC, the diagnosis requires the presence of at least focal intracellular mucin	• IHC positive for pancytokeratins, CK5/6, p63/p40 • *MAML2* rearrangement studies might be helpful in difficult cases, in particular high-grade cases, although negative results do not rule out the diagnosis.
Clear cell carcinoma	• Islands and trabeculae of carcinoma cells with clear cytoplasm • Abundant hyalinized stroma in hyalinizing clear cell carcinoma	• Cytokeratin and p40/p63 immunostaining • *EWSR1* translocation for hyalinizing clear cell carcinoma
Undifferentiated carcinomas	**Essential criteria**	**Desirable criteria**
Carcinoma, undifferentiated	• Primary malignant thymic tumour showing only epithelial differentiation and not conforming to any other defined entity • IHC and molecular studies required to exclude other diagnoses to exclude other diagnoses	
Thymic carcinomas	**Essential criteria**	**Desirable criteria**
Thymic carcinoma, NOS	Exclusion of any of the above thymic carcinoma types; currently comprises hepatoid carcinoma, rhabdoid carcinoma, undifferentiated large cell carcinoma with Castleman disease-like reaction, and sebaceous carcinoma	

[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

WHO Histologic Classification

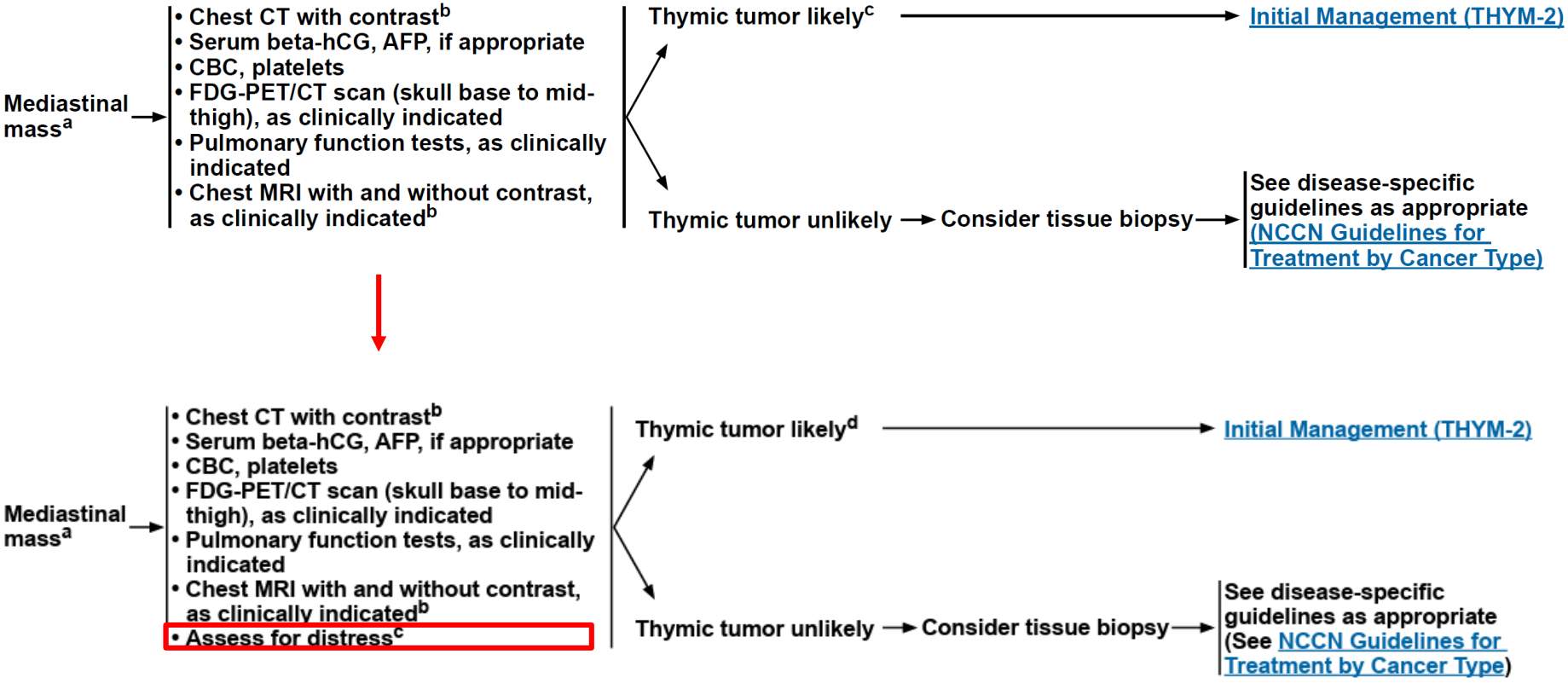
WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION[1]

Thymic Neuroendocrine Neoplasms: Neuroendocrine tumors		
Carcinoid tumour, NOS/ neuroendocrine tumour, NOS	**Essential criteria**	**Desirable criteria**
Typical carcinoid	Primary thymic neuroendocrine tumor (NET) with low-grade nuclear features, neuroendocrine morphology (eg, trabecular or rosetting), absence of any necrosis, and mitotic count of <2 mitoses/2 mm²	• Strong expression of keratins and neuroendocrine markers (eg, synaptophysin and chromogranin), usually negative for TTF1 • Ki-67 can be useful in distinguishing carcinoids from high-grade LCNEC and small cell carcinoma, particularly in small crushed biopsies
Atypical carcinoid	Same as TC, but with comedonecrosis and/or mitotic count of 2–10 mitoses/2 mm²	

Thymic Neuroendocrine Neoplasms: Neuroendocrine carcinomas	Essential criteria	Desirable criteria
Small cell carcinoma	• Radiological evidence of thymic origin • Exclusion of a tumour spreading from the lung or metastatic from another extrapulmonary site to the thymus • A tumour consisting purely of small cells with characteristic morphology similar to lung SmCCs • Combined SmCC: a small carcinoma combined with another histology such as thymoma or other type of thymic carcinoma	Positive IHC for cytokeratins and neuroendocrine markers, as well as elevated Ki-67 (usually >50%)
Large cell neuroendocrine carcinoma of the thymus	• Neuroendocrine morphology • Mitotic count of >10 mitoses/2 mm² • Necrosis, often geographical • Positive neuroendocrine IHC	High Ki-67 index: >30%, generally 40%–80%; negative p40 IHC

[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

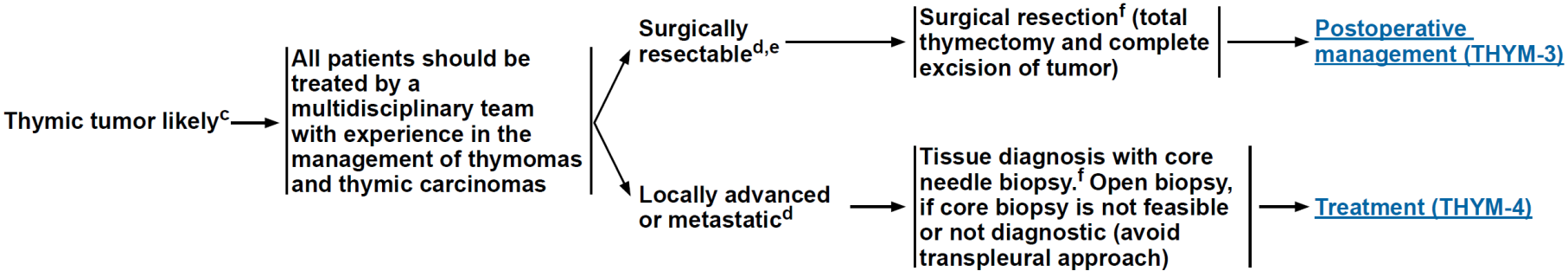
Initial evaluation



[a] Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.
[b] When assessing a mediastinal mass, detection of thymic malignancy versus thymic cyst or thymic hyperplasia can be better discriminated with chest MRI compared to chest CT, potentially avoiding an unnecessary thymectomy.
[c] Refer to the NCCN Distress Thermometer and Problem List, which includes social determinants of health. See NCCN Guidelines for Distress Management (DIS-A).
[d] Well-defined anterior mediastinal mass in the thymic bed, tumor markers negative, absence of other adenopathy, and absence of continuity with the thyroid. Marom EM, et al. J Thorac Oncol 2011;6:S1717-S1723.

Cytotoxic chemotherapeutic agents can cause hair loss, which is distressing for patients

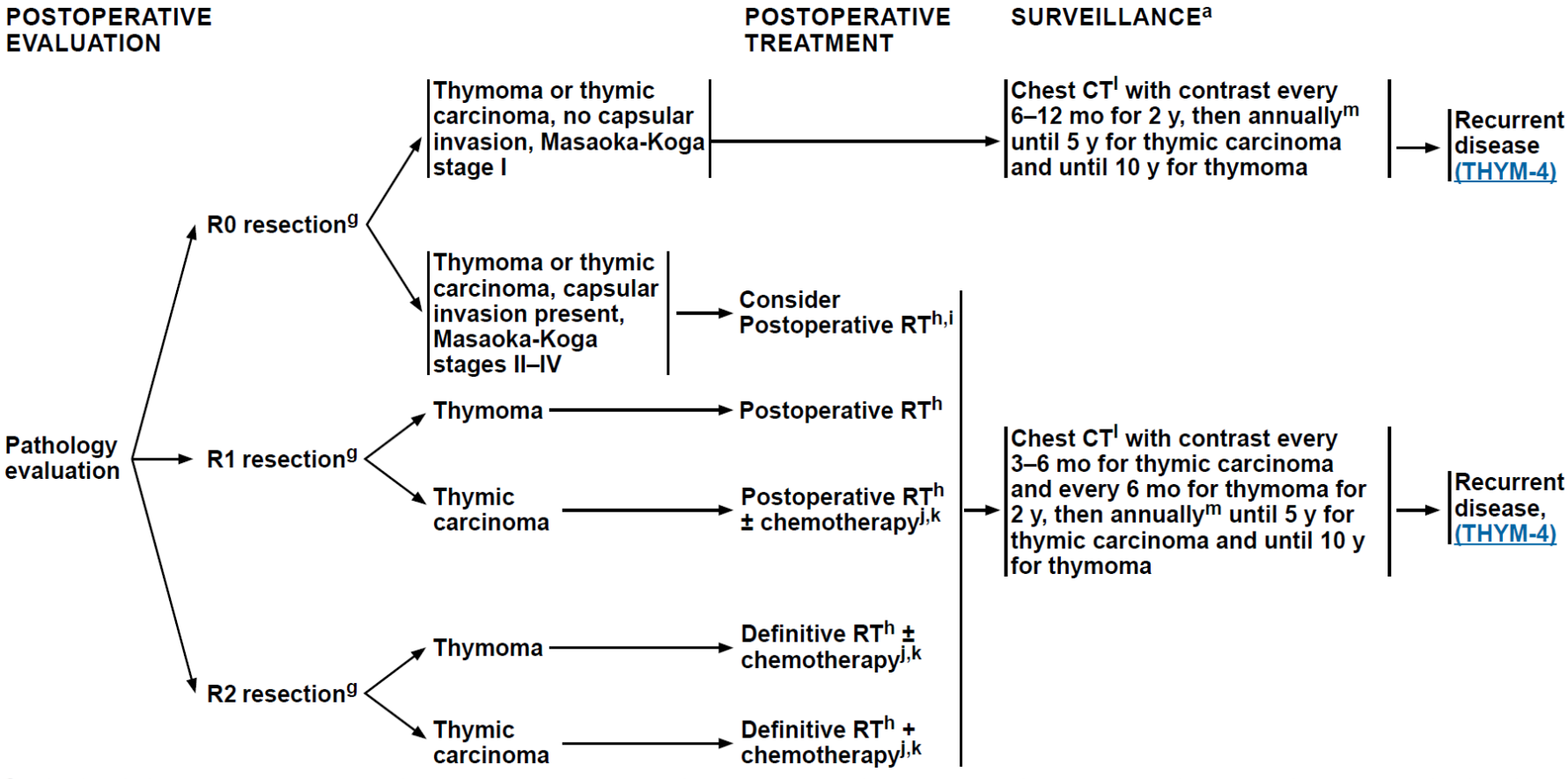
Initial management



[c] Well-defined anterior mediastinal mass in the thymic bed, tumor markers negative, absence of other adenopathy, and absence of continuity with the thyroid. Marom EM, et al. J Thorac Oncol 2011;6:S1717-S1723.

[d] Determination of resectability should be made by a thoracic surgeon, with primary focus on thoracic oncology and in multidisciplinary consultation with medical oncology as needed. Resectability is defined as complete (R0) resection.

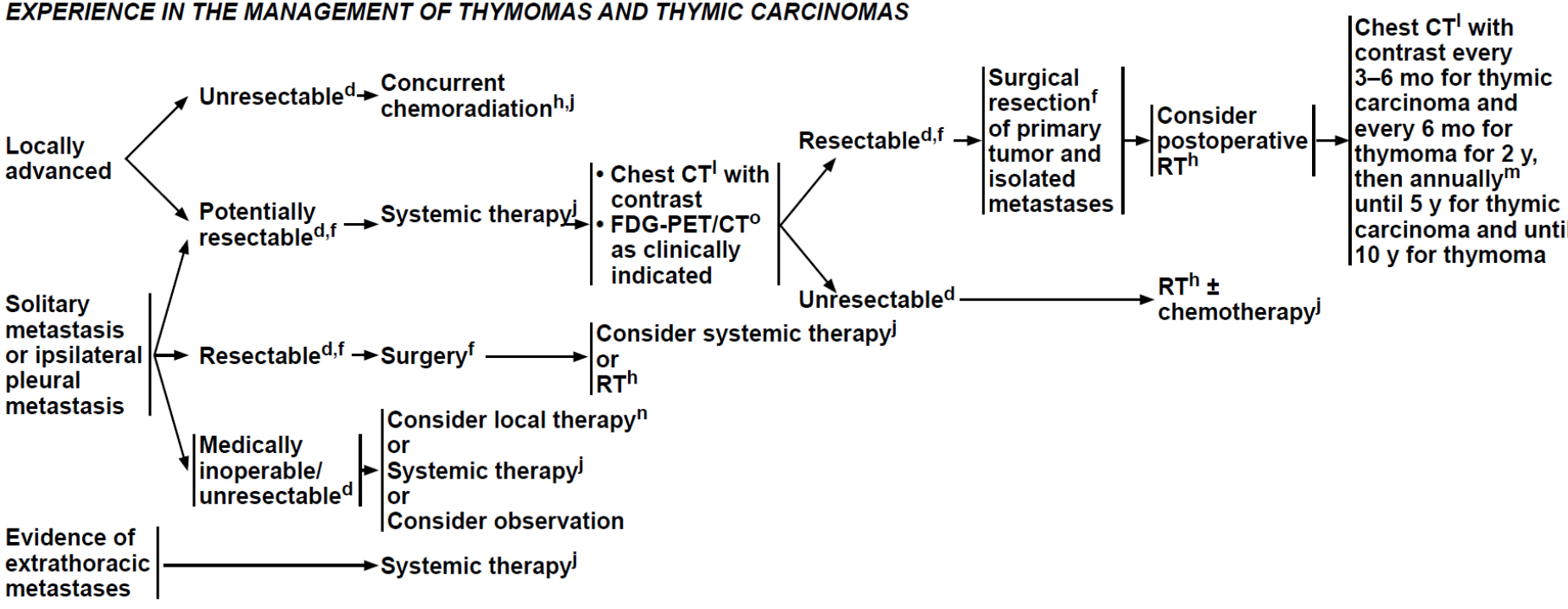
[e] If R0 resection considered uncertain, preoperative systemic therapy should be considered. See Principles of Systemic Therapy (THYM-C).



[a] Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.
[g] R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.
[h] Principles of Radiation Therapy (THYM-B).
[i] Decisions about adjuvant radiation therapy (RT) in this setting should be based on multidisciplinary evaluation.
[j] Principles of Systemic Therapy (THYM-C).
[k] There is a diversity of opinion on treatment approach. Ruffini E, et al. Eur J Cardiothorac Surg 2019;55:601-609.
[l] MRI is an appropriate alternative to CT in certain clinical situations.
[m] The duration for surveillance has not been established.

RECURRENT, ADVANCED, OR METASTATIC DISEASE | **TREATMENT** | **SURVEILLANCE[a]**

ALL PATIENTS SHOULD BE TREATED BY A MULTIDISCIPLINARY TEAM WITH EXPERIENCE IN THE MANAGEMENT OF THYMOMAS AND THYMIC CARCINOMAS



[a] Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.
[d] Determination of resectability should be made by a thoracic surgeon, with primary focus on thoracic oncology and in multidisciplinary consultation with medical oncology as needed. Resectability is defined as complete (R0) resection.
[f] Principles of Surgical Resection (THYM-A).
[h] Principles of Radiation Therapy (THYM-B).
[j] Principles of Systemic Therapy (THYM-C).
[l] MRI is an appropriate alternative to CT in certain clinical situations.
[m] The duration for surveillance has not been established.
[n] Local therapies can include image-guided thermal ablation or RT.
[o] FDG-PET/CT includes skull-base to mid-thigh.

Principles of surgical resection (I)

- Surgical resection should be performed on carefully evaluated patients by thoracic surgeons with experience in managing thymomas and thymic carcinomas. Locally advanced (unresectable) and resectable stage ≥ II cases should be discussed and evaluated by a multidisciplinary team.
- Surgical biopsy should be avoided if a resectable thymoma is strongly suspected based on clinical and radiologic features because of the substantial potential of tumor seeding when the tumor capsule is violated.
- Biopsy of a possible thymoma should avoid a transpleural approach because of the substantial risk of converting a stage I thymomas to a stage IV thymoma by spreading tumor within the pleural space.
- Prior to surgery, patients should be evaluated for signs and symptoms of myasthenia gravis and should be medically controlled prior to undergoing surgical resection.
- If an R0 resection is considered uncertain, patients should be considered for neoadjuvant systemic therapy. Debulking tumors is discouraged.
- Goal of surgery is complete excision of the lesion with total thymectomy and complete resection of contiguous and noncontiguous disease

Principles of surgical resection (II)

- Complete resection may require the resection of adjacent structures, including the pericardium, phrenic nerve, pleura, lung, and even major vascular structures. Bilateral phrenic nerve resection should be avoided due to severe respiratory morbidity.
- Surgical clips should be placed at the time of resection to areas of close margins, residual disease, or tumor adhesion to unresected normal structures to help guide accurate radiation therapy when indicated.
- During thymectomy, the pleural surfaces should be examined for pleural metastases. If feasible, resection of pleural metastases to achieve complete gross resection is appropriate.
- ~~Minimally invasive procedures are not routinely recommended due to the lack of long-term data. However,~~ **Minimally invasive procedures for thymectomy may be considered** ~~for clinical stage I-II~~ **if all oncologic principles** ~~goals~~ **can be met as in standard of care open thymectomy,** ~~procedures,~~ **and if performed in specialized centers by surgeons with experience in these techniques.**

Rationale of Radiotherapy for Invasive thymoma and thymic carcinoma

- Thymoma is the most common tumor of the anterior mediastinum, accounting for approximate 20% of all mediastinal tumors in adults.
- Complete surgical resection is the treatment of choice for all thymomas regardless of invasiveness.
- Radiotherapy is excellent adjuvant therapy for invasive thymomas, which are generally radio-responsive.
- RT should be given for unresectable or incomplete resection patients with invasive thymoma or thymic carcinoma.

Rationale of Radiotherapy for Invasive thymoma and thymic carcinoma

General Principles

- Recommendations regarding RT should be made by radiation oncologists with experience in managing thymomas and thymic carcinomas.
- Definitive RT should be given for patients with unresectable disease (if disease progresses on induction systemic therapy), for patients with incompletely resected invasive thymoma or thymic carcinoma, or as adjuvant therapy after systemic therapy and surgery for patients with locally advanced disease.
- Radiation oncologists need to communicate with the surgeon to review the operative findings and to help determine the target volume at risk. They also need to communicate with the pathologist regarding the detailed pathology on histology, disease extent such as extracapsular extension, and surgical margins.
- The review of preoperative imaging and co-registration of preoperative imaging into the planning system are helpful in defining treatment volumes.

Radiation Dose

- The dose and fractionation schemes of RT depend on the indication of the radiation and the completeness of surgical resection in postoperative cases.
- A dose of 60–66 Gy should be given to patients with unresectable disease.[3]
- For adjuvant treatment, the radiation dose consists of 45–50 Gy for clear/close margins and 54 Gy for microscopically positive resection margins. A total dose of 60–66 Gy should be given to patients with gross residual disease (similar to patients with unresectable disease),[3-6] when conventional fractionation (1.8–2.0 Gy per daily fraction) is applied.
- Depending on the treatment objectives in the palliative setting, typical palliative doses (eg, 8 Gy in a single fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions) up to definitive doses for more durable local control and highly conformal techniques for limited volume metastases may be appropriate, given the relatively long natural history of even metastatic thymoma.

For unresectable disease: 60-66 Gy (with daily fraction between 1.8 to 2 Gy)

For post-operative status: 45-50 Gy for radical surgery

54 Gy for close margin and 60-66 Gy for gross residual lesions.

Radiation dose less than 40 Gy possess higher relapse incidence.

For large, invasive thymoma, neoadjuvant RT has been advocated.

Rationale of Radiotherapy for Invasive thymoma and thymic carcinoma

Radiation Volume

- The gross tumor volume should include any grossly visible tumor. Surgical clips indicative of gross residual tumor should be included for postoperative adjuvant RT.
- The clinical target volume (CTV) for postoperative RT should encompass the entire thymus (for partial resection cases), surgical clips, and any potential sites with residual disease. The CTV should be reviewed with the thoracic surgeon.
- Extensive elective nodal irradiation (entire mediastinum and bilateral supraclavicular nodal regions) is not recommended, as thymomas do not commonly metastasize to regional lymph nodes.[5]
- The planning target volume (PTV) should consider the target motion and daily setup error. The PTV margin should be based on the individual patient's motion, simulation techniques used (with and without inclusion motion), and reproducibility of daily setup of each clinic.

GTV: gross visible tumor volume

CTV: encompassing the entire thymus, surgical clips and potential site with residual disease.

PTV: including target motion and setup error.

Post-operative radiotherapy will be arranged within 4-6 weeks after surgical intervention.

Rationale of Radiotherapy for Invasive thymoma and thymic carcinoma

Radiation Techniques

- Target motion should be managed using the Principles of Radiation Therapy in the NCCN Guidelines for Non-Small Cell Lung Cancer. There can be significant tumor volume motion secondary to breathing and heartbeat, so motion management techniques such as four-dimensional computed tomography (4D-CT) scans are appropriate. Intravenous contrast is often beneficial as well.
- In addition to the normal tissue constraints in the Principles of Radiation Therapy in the NCCN Guidelines for Non-Small Cell Lung Cancer, more conservative limits are recommended to minimize the dose to the heart and its substructures to the maximal extent possible, as portions of the pericardium typically require treatment to control this disease. Since these patients are younger and mostly long-term survivors, the dose to the heart should be as low as reasonably achievable to reduce the possibility of long-term cardiac sequelae from the RT.
- A minimum technological standard for RT is CT-planned 3D conformal RT (3D-CRT). More advanced technologies are appropriate, if available, to further reduce cardiac dose. These technologies include (but are not limited to) intensity-modulated RT (IMRT) and volumetric modulated arc therapy (VMAT). In particular, these are preferred over 3D-CRT to improve target coverage and dose conformity. Reducing the PTV margin also significantly reduces heart dose. To ensure accurate daily treatment setup and delivery, image-guided RT (IGRT) is appropriate. Compared to IMRT, proton therapy has been shown to improve dosimetry, thus allowing for better sparing of normal organs (lungs, heart)[8] with favorable local control and toxicity, and is appropriate as well.[9]
- Stereotactic ablative radiotherapy (SABR) may be appropriate for limited focal metastases, whereas conventional fractionation is appropriate for larger metastases.

Radiotherapy technique: including IMRT, VMAT and Tomotherapy

Carbon ion radiotherapy(CIRT) may be considered after case-specific discussion at MDT and CIRT tumor board.

Modern RT techniques can help to reduce the dose of normal tissues, including heart and lung.

More conservative limits are recommended to minimize the dose volumes to all the normal structures. Since these patients are younger and mostly long-term survivors, the mean total dose to the heart should be as low as reasonably achievable to potentially maximize survival.

Masaoka stage II and III thymoma

- Post-OP RT for Masaoka stage II and III thymoma remains controversial and should be discussed in MDT.

Chemotherapy/others

PRINCIPLES OF SYSTEMIC THERAPY

FIRST-LINE COMBINATION CHEMOTHERAPY REGIMENS[a]

THYMOMA

Preferred

- CAP (Cyclophosphamide/Doxorubicin/Cisplatin)[1]

Other Recommended

- Carboplatin/Paclitaxel[2,3,b]
- CAP (Cyclophosphamide/Doxorubicin/Cisplatin)/Prednisone[4]
- ADOC (Doxorubicin/Cisplatin/Vincristine/Cyclophosphamide)[5]
- PE (Cisplatin/Etoposide)[6,b]
- Cisplatin/Etoposide/Ifosfamide[7]

THYMIC CARCINOMA

Preferred

- Carboplatin/Paclitaxel[2,3,b]
- Carboplatin/Paclitaxel + Ramucirumab[8,c]

Other Recommended

- CAP (Cyclophosphamide/Doxorubicin/Cisplatin)[1]
- CAP (Cyclophosphamide/Doxorubicin/Cisplatin)/Prednisone[4]
- ADOC (Doxorubicin/Cisplatin/Vincristine/Cyclophosphamide)[5]
- PE (Cisplatin/Etoposide)[6,b]
- Cisplatin/Etoposide/Ifosfamide[7]
- Carboplatin/Paclitaxel + Atezolizumab[9,d,e,f]

Subsequent Therapy THYM-2 of 3

References on THYM-C 3 of 3

[a] If patients cannot tolerate first-line combination regimens, consider subsequent systemic therapy options.
[b] Regimens can be used with RT, as definitive concurrent chemoradiation.
[c] There is no published experience using this as a preoperative therapy. Patients with untreated brain metastases or major standard contraindications to antiangiogenics were excluded from the study.
[d] PD-1/PD-L1 inhibitor therapy is not recommended for patients with thymoma. In patients with thymic carcinoma, there is concern for a higher rate of immune-related adverse events (eg, myocarditis) than seen in most other malignancies treated with PD-1/PD-L1 inhibitor therapy. See NCCN Guidelines for the Management of Immunotherapy-Related Toxicities.
[e] PD-1/PD-L1 inhibitor therapy is not recommended in the neoadjuvant setting.
[f] Atezolizumab and hyaluronidase-tqjs subcutaneous injection may be substituted for IV atezolizumab. Atezolizumab and hyaluronidase-tqjs has different dosing and administration instructions compared to IV atezolizumab.

Note: All recommendations are category 2A unless otherwise indicated.

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Chemotherapy/others

SUBSEQUENT SYSTEMIC THERAPY
(regimens noted in alphabetical order)

THYMOMA

Preferred

- Everolimus[10]
- Gemcitabine/Capecitabine[g,h,11,12]
- Octreotide[i] (including LAR) (if octreotide scan or dotatate PET/CT positive)[13]
- Octreotide[i] (including LAR)/Prednisone (if octreotide scan or dotatate PET/CT positive)[13,14]
- Pemetrexed[15]

Other Recommended

- Fluorouracil[g]/Leucovorin[16]
- Paclitaxel[17]

Useful in Certain Circumstances

- Etoposide[6,18]
- Ifosfamide[19]

THYMIC CARCINOMA

Preferred

- Gemcitabine/Capecitabine[g,h,11,12]
- Lenvatinib[j,20]
- Pembrolizumab[d,e,k,21,22]
- Sunitinib[23]

Other Recommended

- Axitinib + Avelumab[d,e,24]
- Everolimus[10]
- Fluorouracil[g]/Leucovorin[16]
- Paclitaxel[17]
- Pemetrexed[15]

Useful in Certain Circumstances

- Etoposide[6,18]
- Ifosfamide[19]

References on THYM-C 3 of 3

[d] PD-1/PD-L1 inhibitor therapy is not recommended for patients with thymoma. In patients with thymic carcinoma, there is concern for a higher rate of immune-related adverse events (eg, myocarditis) than seen in most other malignancies treated with PD-1/PD-L1 inhibitor therapy. See NCCN Guidelines for the Management of Immuotherapy-Related Toxicities.

[e] PD-1/PD-L1 inhibitor therapy is not recommended in the neoadjuvant setting.

[g] For information regarding DPYD testing, see NCCN Guidelines for Colon Cancer.

[h] Gemcitabine or Capecitabine may be given as single agents.

[i] Nuclear medicine scan (octreotide scan or dotatate PET/CT [dotatate PET/CT preferred if available]) to assess for octreotide-avid disease.

[j] There is a high risk for side effects and frequent dose reductions may be needed.

[k] Pembrolizumab and berahyaluronidase alfa-pmph subcutaneous injection may be substituted for IV pembrolizumab. Pembrolizumab and berahyaluronidase alfa-pmph has different dosing and administration instructions compared to IV pembrolizumab.

Note: All recommendations are category 2A unless otherwise indicated.

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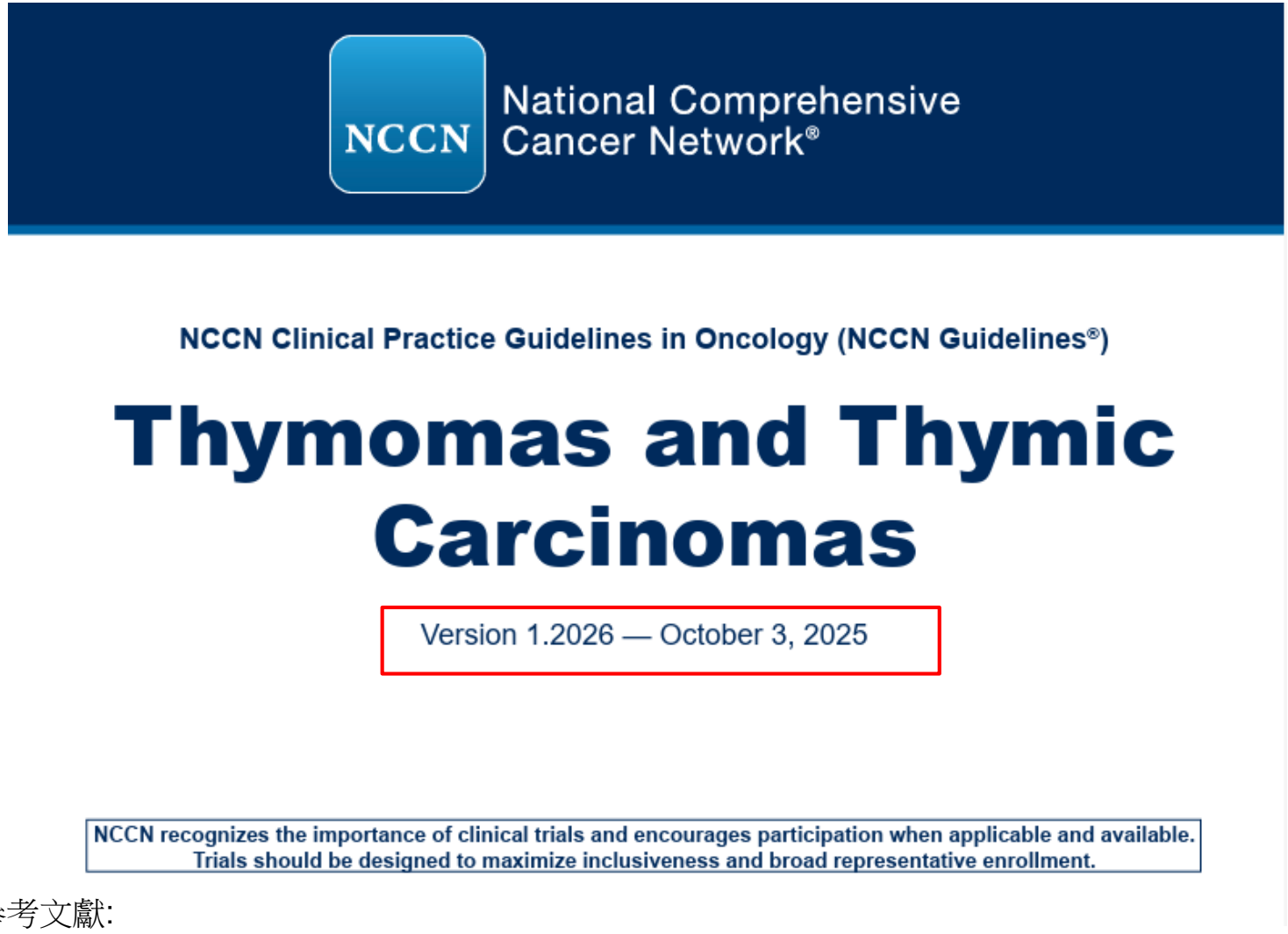
主要依據- NCCN v1. 2026



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