台北榮總胸腺癌診療共識

V.1.0 2023

台北榮總肺癌團隊

Revised on 2023/8/28

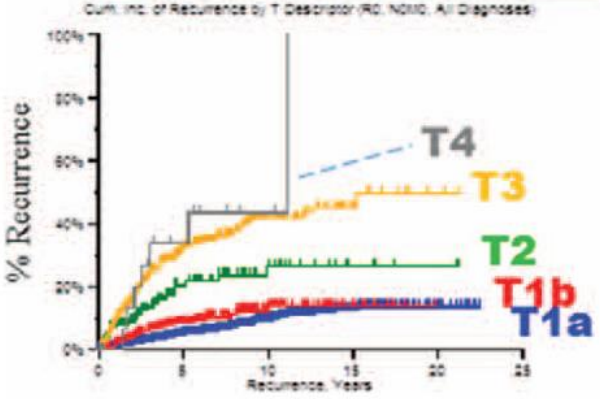
TNM classification

Definition of primary tumor (T)

T category	T description (AJCC 2017)	Previous T description (WHO 2004)
TX	Primary tumor cannot be assessed	Primary tumor cannot be assessed
T0	No evidence of primary tumor	No evidence of primary tumor
T1	Tumor encapsulated or extending into the mediastinal fat; may involve the mediastinal pleura	Tumor completely encapsulated
T1a	Tumor with no mediastinal pleura involvement	-
T1b	Tumor with direct invasion of mediastinal pleura	-
T2	Tumor with direct invasion of the pericardium (either partial or full thickness)	Tumor invades *pericapsular connective tissue*
T3	Tumor with direct invasion into any of the following: Lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, or extrapericardial pulmonary artery or veins	Tumor invades into neighboring structures, such as *pericardium, mediastinal pleura*, thoracic wall, great vessels and lung
T4	Tumor with invasion into any of the following: Aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus	Tumor with *pleural or pericardial dissemination*

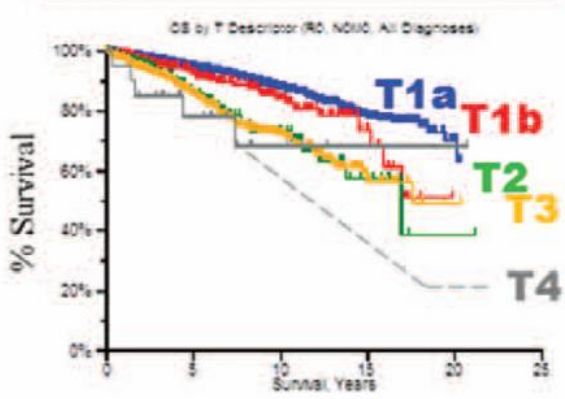
Outcomes of all Patients by T Categories

Recurrence, R0



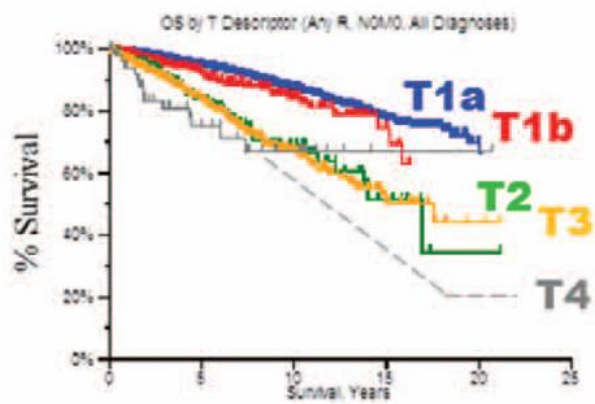
Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T1a	168/3383	4.8% (4.8, 4.9)	9.5% (9.3, 9.7)
T1b	34/276	8.7% (6.3, 9)	12.3% (11.5, 13.1)
T2	22/124	20% (17.6, 22.8)	26.6% (22.1, 31.1)
T3	14/33	33% (25.6, 34.4)	42% (37, 46.9)
T4	7/18	34% (10.6, 57.4)	43.2% (20, 66.9)

Overall Survival, R0



Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T1a	329/4815	95% (93.7, 95.3)	88% (86.4, 89.5)
T1b	34/319	93% (89.6, 96.2)	85% (78.5, 90.5)
T2	30/187	87% (80.3, 93.3)	73% (63.5, 83.1)
T3	16/388	86% (82.6, 89.3)	73% (67.3, 77.7)
T4	5/23	78% (58.7, 97.6)	68% (43.6, 93.1)

Overall Survival, R any



Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T1a	367/5135	94% (93.6, 95.1)	87% (85.6, 88.7)
T1b	38/382	92% (89.4, 95.8)	84% (78.6, 90)
T2	43/239	84% (77.6, 90)	69% (59.7, 78.1)
T3	16/378	83% (80.3, 84.5)	67% (63.4, 72.8)
T4	13/67	75% (61.8, 88.1)	67% (50.8, 82.6)

TABLE 3. Differences between T Categories

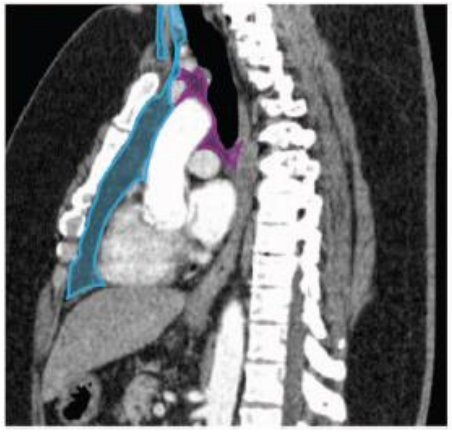
	CIR, R0 (363/4256)[a]		OS, R0 (506/5932)[a]		OS, any R (624/6561)[a]	
Variable	**HR**	***p***	**HR**	***p***	**HR**	***p***
HR vs. adjacent T category						
T2 vs. T1	3.10	<0.0001	2.05	0.0002	2.30	<0.0001
T3 vs. T2	1.67	0.025	1.03	NS	1.00	NS
T4 vs. T3	1.30	NS	1.00	NS	0.94	NS

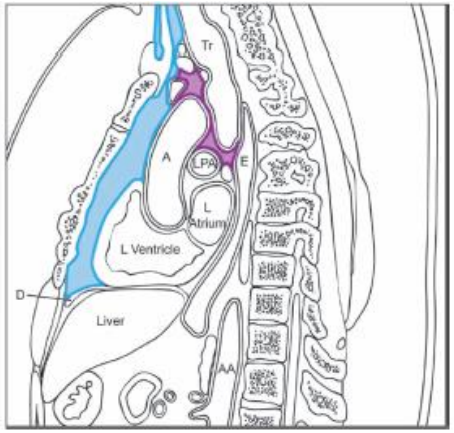
J Thorac Oncol. 2014 Sep;9(9 Suppl 2):S73-80

Definition of Regional lymph nodes (N)

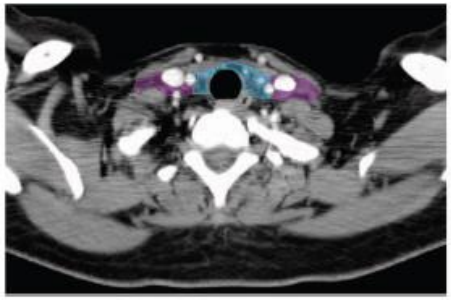
N category	N description (AJCC 2017)	Previous N description (WHO 2004)
NX	Regional LN cannot be assessed	Regional LNs cannot be assessed
N0	No regional LN metastasis	No regional LN metastasis
N1	Metastasis in anterior (perithymic) LNs	Metastasis in anterior mediastinal LNs
N2	Metastasis in deep intrathoracic or cervical LNs	Metastasis in other intrathoracic LNs excluding anterior mediastinal LNs
N3	---	Metastasis in *scalene* and/or *supraclavicular LNs*

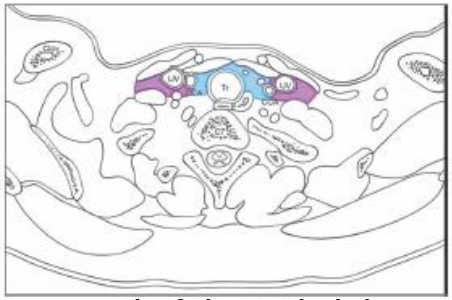
ITMIG/IASLC node compartments for thymic malignancies. Graphic depiction of N1 (anterior region, blue) and N2 (deep region, purple) node compartments



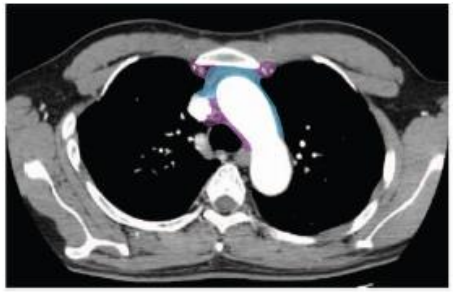


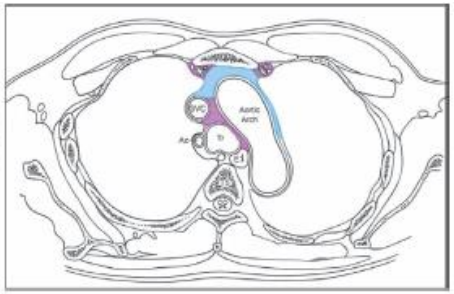
Sagittal view

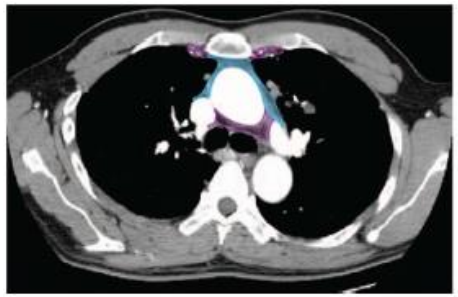


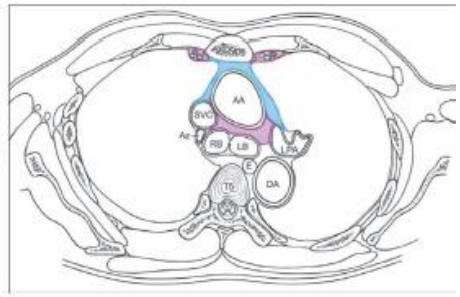


Level of thoracic inlet

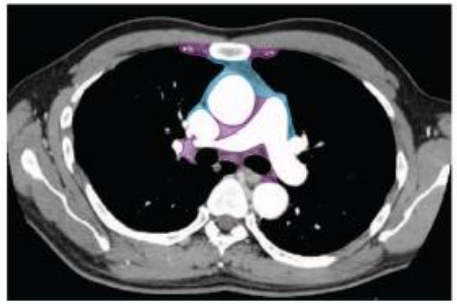


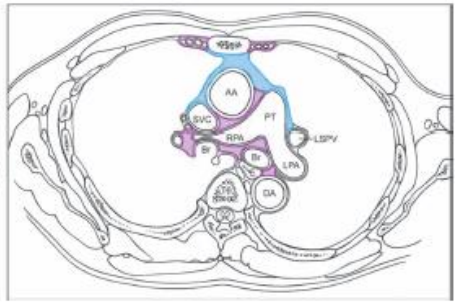


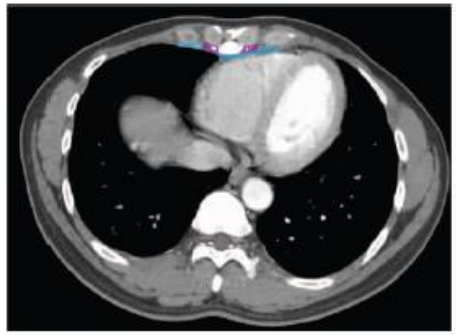


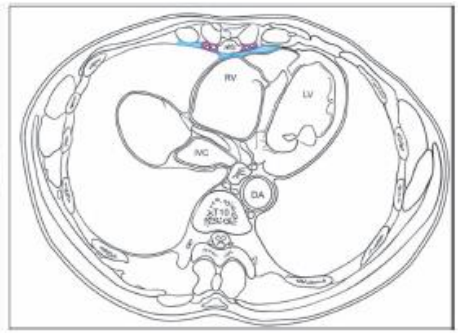


Level of aortopulmonary window









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

Definition of distant metastasis (M)

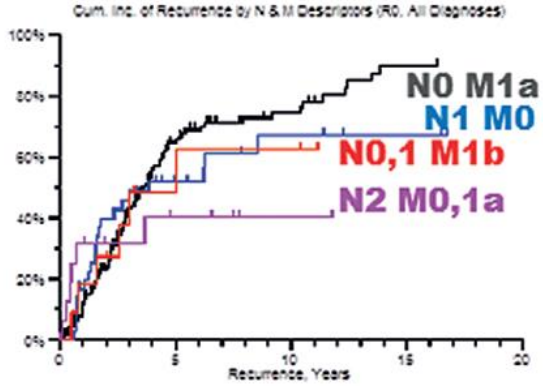
M category	M description (AJCC 2017)	Previous M description (WHO 2004)
M0	No pleural, pericardial, or distant metastasis	No distant metastasis
M1	Pleural, pericardial, or distant metastasis	Distant metastasis
M1a	Separate pleural or pericardial nodule(s)	-
M1b	Pulmonary intraparenchymal nodule or distant organ metastasis	-

Stage grouping

AJCC 2017					WHO 2004		
T1a,b	N0	M0	I	I	T1	N0	M0
T2	N0	M0	II	II	T2	N0	M0
T3	N0	M0	IIIA	III	T1	*N1*	M0
T4	N0	M0	IIIB	III	T2	*N1*	M0
Any T	N1	M0	IVA	III	*T3*	N0,N1	M0
Any T	N0, N1	M1a	IVA	IV	*T4*	Any N	M0
Any T	N2	M0, M1a	IVB	IV	Any T	*N2,N3*	M0
Any T	Any N	M1b	IVB	IV	Any T	Any N	*M1*

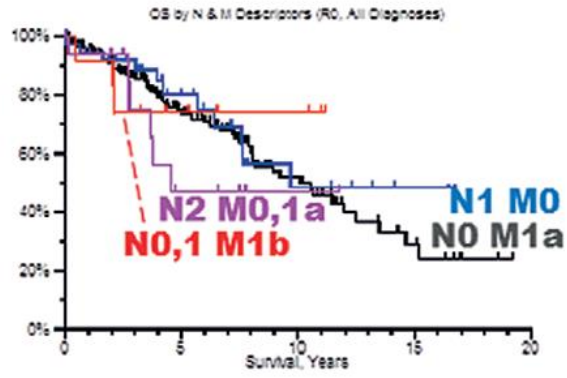
Outcomes of All Patients by Proposed N and M Categories

Recurrence, R0



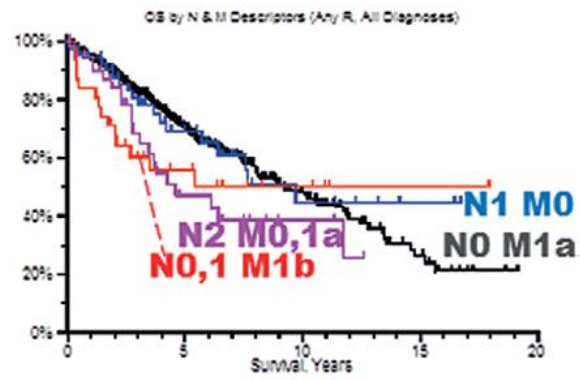
Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T any N0 M1a	94/154	65% (45.3, 84.3)	75% (36.3, 100)
T any N1 M0	21/39	52% (31.8, 72)	67% (13.8, 100)
T any N0,1 M1b	6/11	49% (0, 100)	63% (0, 100)
T any N2 M0,1a	6/17	40% (19.6, 61.1)	40% (19.6, 61.1)

Overall Survival, R0



Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T any N0 M1a	61/203	74% (66.2, 81.4)	52% (40.5, 63.2)
T any N1 M0	11/40	80% (65.7, 94.9)	49% (24.5, 72.5)
T any N0,1 M1b	3/12	74% (48.7, 99.4)	74% (48.7, 99.4)
T any N2 M0,1a	6/17	47% (17.2, 76.5)	47% (17.2, 76.5)

Overall Survival, any R



Stage	Events/N	5-Yr Estimate (CI)	10-Yr Estimate (CI)
T any N0 M1a	179/579	71% (65.9, 75.2)	48% (41.2, 54.6)
T any N1 M0	18/54	69% (54.5, 83.4)	45% (24.4, 64.7)
T any N0,1 M1b	14/31	56% (37.7, 74.2)	50% (30.9, 69.8)
T any N2 M0,1a	20/42	47% (29, 65.2)	39% (20.4, 56.7)

TABLE 2. Total Proportion of Recurrences or Deaths

	Recurrence, R0		Deaths, R0		Deaths, any R	
	%	Events/*n*	%	Events/*n*	%	Events/*n*
Stage IVa	**59**	**119/201**	**30**	**75/251**	**32**	**209/654**
N1 M0	54	21/39	28	11/40	33	18/54
N0 M1a	61	94/154	30	61/203	31	179/579
N1 M1a	50	4/8	38	3/8	57	12/21
Stage IVb	**49**	**17/35**	**33**	**14/43**	**43**	**43/99**
N2 M0,1a	35	6/17	35	6/17	48	20/42
N0,1 M1b	55	6/11	25	3/12	45	14/31
N2 M1b/X + NX M1b	71	5/7	36	5/14	35	9/26

The total number of recurrences or deaths observed at any time out of the total number of evaluable patients in each category.

R, resection status; R0, complete resection.

AJCC 2017			
T1a,b	N0	M0	I
T2	N0	M0	II
T3	N0	M0	IIIA
T4	N0	M0	IIIB
Any T	N1	M0	IVA
Any T	N0, N1	M1a	IVA
Any T	N2	M0, M1a	IVB
Any T	Any N	M1b	IVB

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

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]

Thymoma subtype[a]	Obligatory criteria	Optional criteria
Type A	Occurrence of bland, spindle shaped epithelial cells (at least focally); paucity[b] or absence of immature (TdT+) T cells throughout the tumor	Polygonal epithelial cells CD20+ epithelial cells
Atypical type A variant	Criteria of type A thymoma; in addition: comedo-type tumor necrosis; increased mitotic count (>4/2mm^2); nuclear crowding	Polygonal epithelial cells CD20+ epithelial cells
Type AB	Occurrence of bland, spindle shaped epithelial cells (at least focally); abundance[b] of immature (TdT+) T cells focally or throughout tumor	Polygonal epithelial cells CD20+ epithelial cells
Type B1	Thymus-like architecture and cytology: abundance of immature T cells, areas of medullary differentiation (medullary islands); paucity of polygonal or dendritic epithelia cells without clustering (i.e.<3 contiguous epithelial cells)	Hassall's corpuscles; perivascular spaces
Type B2	Increased numbers of single or clustered polygonal or dendritic epithelial cells intermingled with abundant immature T cells	Medullary islands; Hassall's corpuscles; perivascular spaces
Type B3	Sheets of polygonal slightly to moderately atypical epithelial cells; absent or rare intercellular bridges; paucity or absence of intermingled TdT+ T cells	Hassall's corpuscles; perivascular spaces
MNT[c]	Nodules of bland spindle or oval epithelial cells surrounded by an epithelial cell-free lymphoid stroma	Lymphoid follicles; monoclonal B cells and/or plasma cells (rare)
Metaplastic thymoma	Biphasic tumor composed of solid areas of epithelial cells in a background of bland-looking spindle cells; absence of immature T cells	Pleomorphism of epithelial cells; actin, keratin, or EMA-positive spindle cells
Rare others[d]		

[a] Thymoma composed of two or more types are termed "thymoma," with listing of the components in 10% increments.
[b] Paucity versus abundance: any area of crowded immature T cells or moderate numbers of immature T cells in >10% of the investigated tumor are indicative of "abundance."
[c] MNT, micronodular thymoma with lymphoid stroma.
[d] Microscopic thymoma; sclerosing thymoma, lipofibroadenoma.

[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).

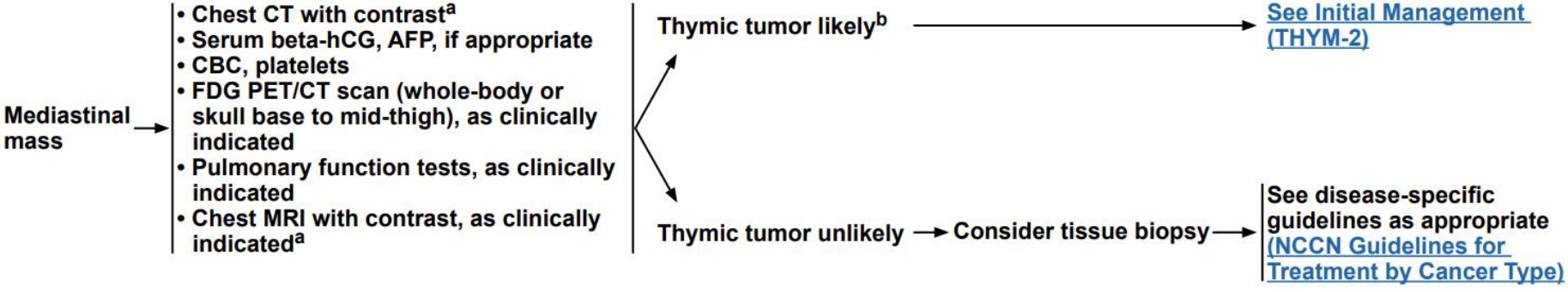
WHO Histologic Classification

Thymic Carcinoma Subtypes

- **Squamous carcinomas**
  - Squamous cell carcinoma, NOS
  - Basaloid carcinoma
  - Lymphoepithelial carcinoma
- **Adenocarcinomas**
  - Adenocarcinoma, NOS
  - Low grade papillary adenocarcinoma
  - Thymic carcinoma with adenoid cystic carcinoma-like features
  - Adenocarcinoma, enteric-type
- **Adenosquamous carcinoma**
- **NUT carcinomas**
- **Salivary gland-like carcinomas**
  - Mucoepidermoid carcinoma
  - Clear cell carcinoma
  - Sarcomatoid carcinoma
  - Carcinosarcoma
- **Carcinoma, undifferentiated, NOS**
- **Thymic Carcinoma, NOS**

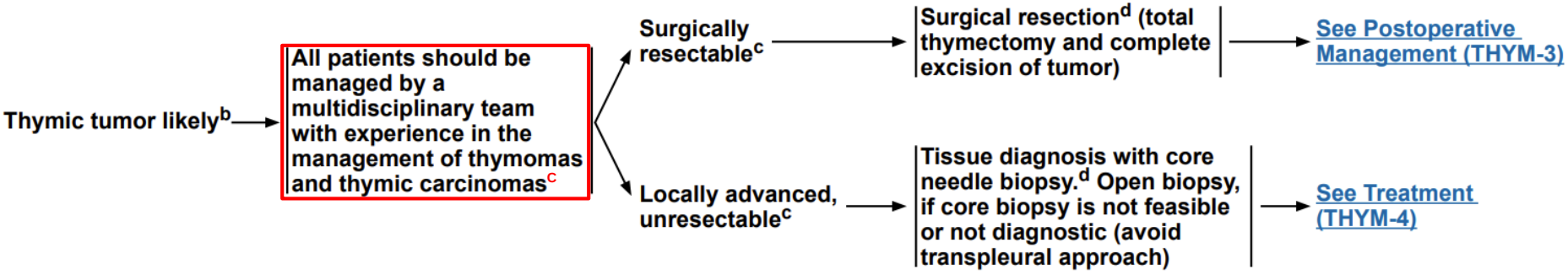
[1] Marx A, Detterback F, Marom EM, et al. Tumours of the thymus. In: WHO Classification of Tumours Editorial Board. Thoracic tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2021 [2021 9 12]. (WHO classification of tumours series, 5th ed.; vol. 5).

Initial evaluation



[a] 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.
[b] 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.

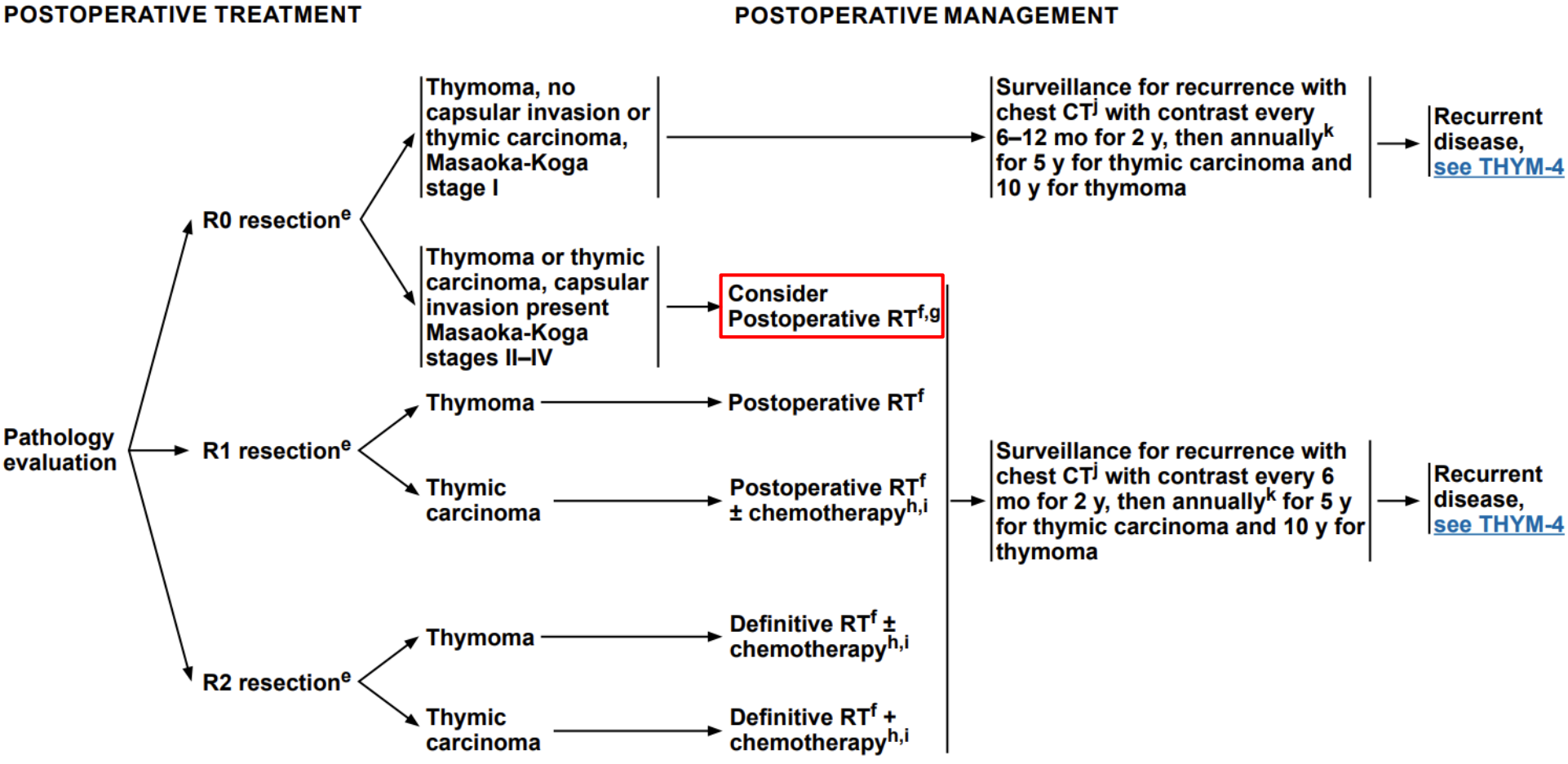
Initial management



[b] 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.

[c] 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. (手術切除主要仍由胸腔外科醫師決定，若有需要則提多專科會議討論。)

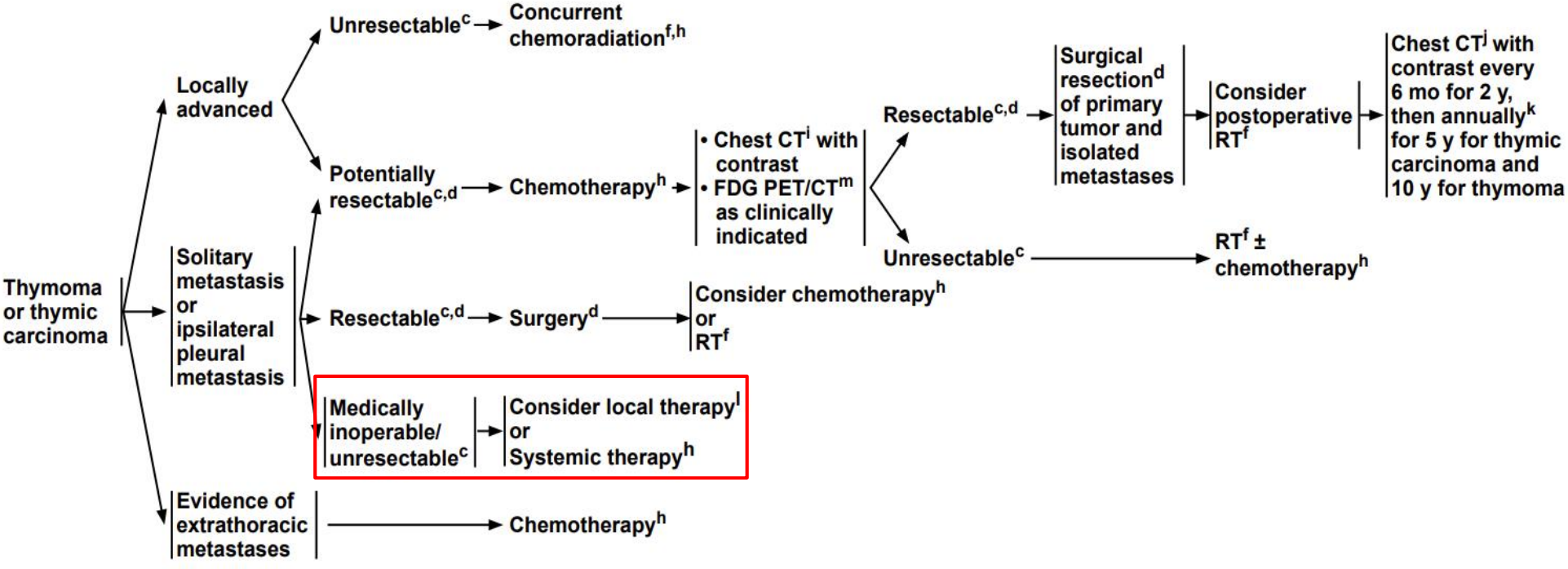
[d] See Principles of Surgical Resection (THYM-A).



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

LOCALLY ADVANCED, ADVANCED, OR RECURRENT DISEASE | **TREATMENT** | **SURVEILLANCE**

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



[c] 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.
[d] See Principles of Surgical Resection (THYM-A).
[f] See Principles of Radiation Therapy (THYM-B).
[h] See Principles of Systemic Therapy for Thymomas and Thymic Carcinomas (THYM-C).
[j] MRI is an appropriate alternative to CT in certain clinical situations.
[k] The duration for surveillance has not been established.
[l] Local therapies can include image-guided thermal ablation or RT.
[m] FDG-PET includes whole-body or 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.
- 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 may be considered for clinical stage I-II if all oncologic goals can be met as in standard 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 a board-certified radiation oncologist.
- RT should be given for patients with unresectable (if disease progresses on induction chemotherapy) or incompletely resected invasive thymoma or thymic carcinoma.
- 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.
- Acronyms and abbreviations for RT are the same as listed in the Principles of RT for non-small cell lung cancer. See NCCN Guidelines for Non-Small Cell Lung Cancer.

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 60-70 Gy should be given to patients with unresectable disease.
- 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 Gy and above should be given to patients with gross residual disease (similar to patients with unresectable disease),[3,4] when conventional fractionation (1.8 to 2.0 Gy per daily fraction) is applied.

For unresectable disease: 60-70 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 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

- CT-based planning is highly recommended. CT scans should be taken in the treatment position with arms raised above the head (treatment position). Simulations of target motion are encouraged whenever possible. CT scans can be performed at the end of natural inhale, exhale, and under free breathing when more sophisticated techniques like 4-D CT, gated CT, or active breathing control are not available. Target motion should be managed using the Principles of RT for non-small cell lung cancer. See NCCN Guidelines for Non-Small Cell Lung Cancer. Intravenous contrast is beneficial in the unresectable setting.
- Radiation beam arrangements should be selected based on the shape of PTV aiming to confine the prescribed high dose to the target and minimize dose to adjacent critical structures. Anterior-posterior and posterior-anterior ports weighing more anteriorly, or wedge pair technique may be considered. These techniques, although commonly used during the traditional 2-D era, can generate an excessive dose to normal tissue. A dose-volume histogram of the lungs, heart, and cord need to be carefully reviewed for each plan.
- RT should be given by 3-D conformal technique to reduce surrounding normal tissue damage (eg, heart, lungs, esophagus, spinal cord). Intensity-modulated RT (IMRT) may further improve the dose distribution and decrease the dose to the normal tissue as indicated. If IMRT is applied, the ASTRO/ACR IMRT guidelines should be strictly followed.[6,7]
- In addition to following the normal tissue constraints recommendation using the Principles of RT for non-small cell lung cancer, 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 dose to the total heart should be limited to ≤30 Gy.

Radiotherapy technique: including IMRT, VMAT and Tomotherapy

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.

Chemotherapy/others

PRINCIPLES OF SYSTEMIC THERAPY

FIRST-LINE COMBINATION CHEMOTHERAPY REGIMENS[a]

THYMOMA

Preferred (Other Recommended for Thymic Carcinoma)

- **CAP**[1]
  Cisplatin 50 mg/m² IV day 1
  Doxorubicin 50 mg/m² IV day 1
  Cyclophosphamide 500 mg/m² IV day 1
  Administered every 3 weeks

Other Recommended for Thymic Carcinoma and Thymoma

- **CAP with prednisone**[2]
  Cyclophosphamide 500 mg/m² IV on day 1;
  Doxorubicin, 20 mg/m²/day IV continuous infusion on days 1–3;
  Cisplatin 30 mg/m² days 1–3;
  Prednisone 100 mg/day days 1–5;
  Administered every 3 weeks

- **ADOC**[3]
  Doxorubicin 40 mg/m² IV day 1;
  Cisplatin 50 mg/m² IV day 1;
  Vincristine 0.6 mg/m² IV day 3;
  Cyclophosphamide 700 mg/m² IV day 4
  Administered every 3 weeks

- **PE**[4]
  Cisplatin 60 mg/m² IV day 1; Etoposide 120 mg/m²/day IV days 1–3;
  Administered every 3 weeks

- **Etoposide/ifosfamide/cisplatin**[5]
  Etoposide 75 mg/m² on days 1–4; Ifosfamide 1.2 g/m² on days 1–4; Cisplatin 20 mg/m² on days 1–4
  Administered every 3 weeks

THYMIC CARCINOMA

Preferred (Other Recommended for Thymoma)

- **Carboplatin/paclitaxel**[6,7]
  Carboplatin AUC 6
  Paclitaxel 200 mg/m²
  Administered every 3 weeks

[a] If patients cannot tolerate first-line combination regimens, consider second-line systemic therapy options.

Chemotherapy/others

SECOND-LINE SYSTEMIC THERAPY
(in alphabetical order)

THYMOMA

Other Recommended

- Etoposide[4,8,9]
- Everolimus[10]
- 5-FU and leucovorin[11]
- Gemcitabine ± capecitabine[12,13]
- Ifosfamide[14]
- Octreotide[b] (including LAR) +/- prednisone[15,16]
- Paclitaxel[17]
- Pemetrexed[18]

THYMIC CARCINOMA

Other Recommended

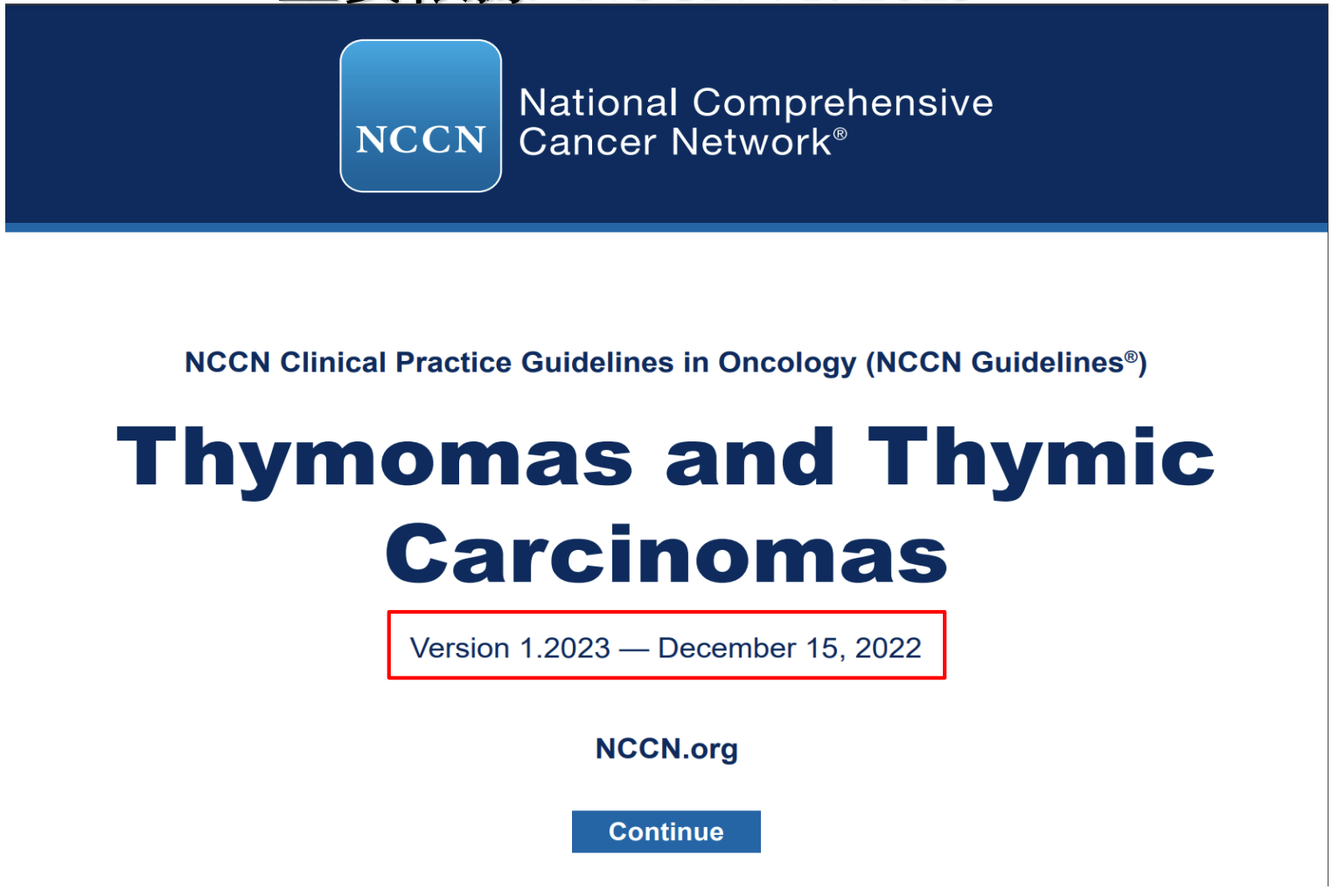
- Everolimus[10]
- 5-FU and leucovorin[11]
- Gemcitabine ± capecitabine[12,13]
- Lenvatinib[c,19]
- Paclitaxel[17]
- Pembrolizumab[d,20,21]
- Pemetrexed[18]
- Sunitinib[22]

Useful in Certain Circumstances

- Etoposide[4,8,9]
- Ifosfamide[14]

[b] Nuclear medicine scan to assess for octreotide-avid disease.
[c] There is a high risk for side effects and frequent dose reductions may be needed.
[d] Pembrolizumab is not recommended for patients with thymoma. In patients with thymic carcinoma, there is concern for a higher rate of immune-related adverse events than seen in most other malignancies treated with PD-1/PD-L1 inhibitor therapy. For example, grade 3–4 myocarditis has been reported in 5%–9% of patients receiving pembrolizumab.

台北榮總胸腺癌診療共識
主要依據- NCCN v1. 2023



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