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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

# Thymomas and Thymic Carcinomas

Version 2.2025 — May 19, 2025

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# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

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**NCCN Categories of Preference:** All recommendations are considered appropriate.

See [NCCN Categories of Preference](#).

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# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### Updates in Version 2.2025 of the NCCN Guidelines for Thymomas and Thymic Carcinomas from Version 1.2025 include:

#### **MS-1**

- The Discussion was updated to reflect the changes in the algorithm.

### Updates in Version 1.2025 of the NCCN Guidelines for Thymomas and Thymic Carcinomas from Version 1.2024 include:

#### **THYM-2**

- Footnote d modified: 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. (also applies to THYM-4)

#### **THYM-A 1 of 2**

- Bullet 5 modified: If an R0 resection appears unlikely *is considered uncertain*, patient should be considered for neoadjuvant systemic therapy. Debulking tumors is discouraged.

#### **THYM-C 1 of 3 (First-line Combination Chemotherapy Regimens)**

- The following regimen added as a Preferred option for Thymic Carcinoma
  - ▶ Carboplatin/paclitaxel/ramucirumab  
Ramucirumab 10 mg/kg IV day 1  
Paclitaxel 200 mg/m<sup>2</sup> IV day 1  
Carboplatin AUC 5 IV day 1  
Administered every 3 weeks, maximum of six cycles  
Ramucirumab monotherapy every 3 weeks as maintenance therapy, until progressive disease or unacceptable toxicity
- Footnote c added: 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.

#### **THYM-C 2 of 3 (Second-line Systemic Therapy)**

- Regimens noted in alphabetical order
- Preference stratification applied to the regimens for Thymoma
  - ▶ Moved from Other Recommended to Preferred
    - ◇ Everolimus, Gemcitabine ± capecitabine, Octreotide (including LAR) (if octreotide scan or dotatate PET/CT positive) ± prednisone, Pemetrexed
  - ▶ Moved from Other Recommended to Useful in Certain Circumstances
    - ◇ Etoposide, Ifosfamide
- The following regimen added as an Other Recommended option for Thymic Carcinoma
  - ▶ Avelumab + axitinib

#### **THYM-C 3 of 3**

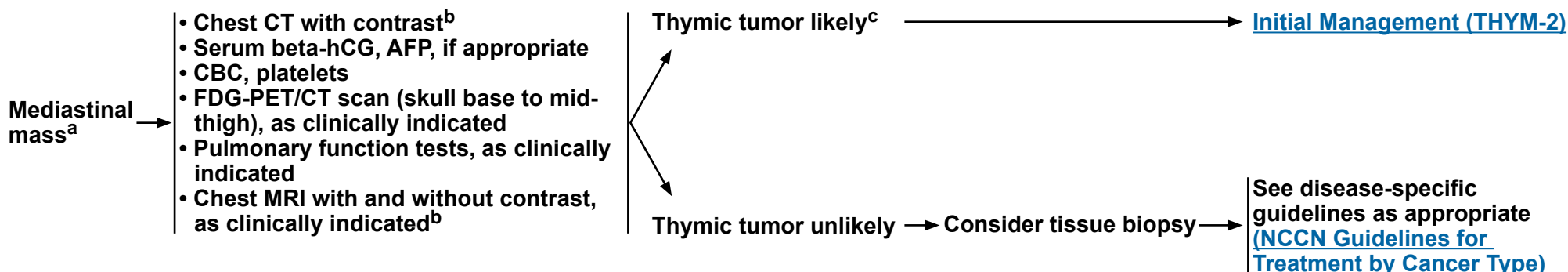
- References added
  - ▶ 6 Proto C, Ganzinelli M, Manglaviti S, et al. Efficacy and safety of ramucirumab plus carboplatin and paclitaxel in untreated metastatic thymic carcinoma: RELEVANT phase II trial (NCT03921671). Ann Oncol 2024;35:817-826.
  - ▶ 23 Conforti F, Zucali PA, Pala L, et al. Avelumab plus axitinib in unresectable or metastatic type B3 thymomas and thymic carcinomas (CAVEATT): a single-arm, multicentre, phase 2 trial. Lancet Oncol 2022;23:1287-1296.



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### INITIAL EVALUATION



<sup>a</sup> Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.

<sup>b</sup> 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.

<sup>c</sup> 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.

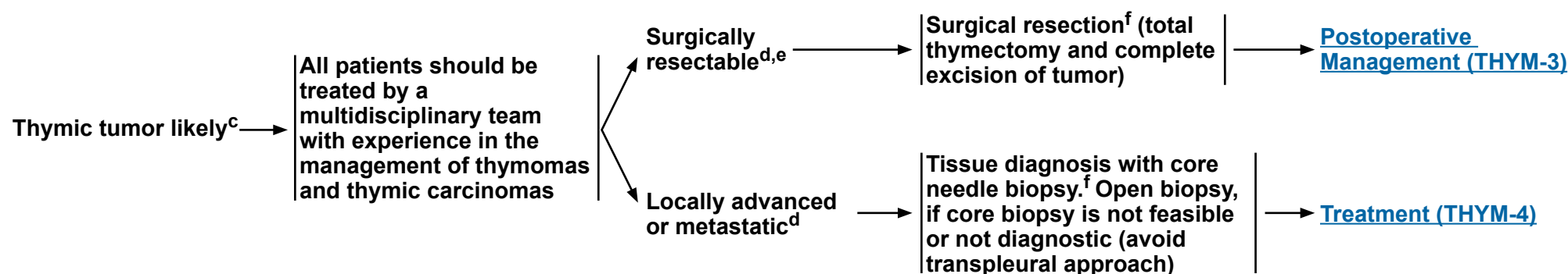
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# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### INITIAL MANAGEMENT



<sup>c</sup> 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.

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

<sup>e</sup> If R0 resection is considered uncertain, preoperative systemic therapy should be considered. See [Principles of Systemic Therapy \(THYM-C\)](#).

<sup>f</sup> [Principles of Surgical Resection \(THYM-A\)](#).

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



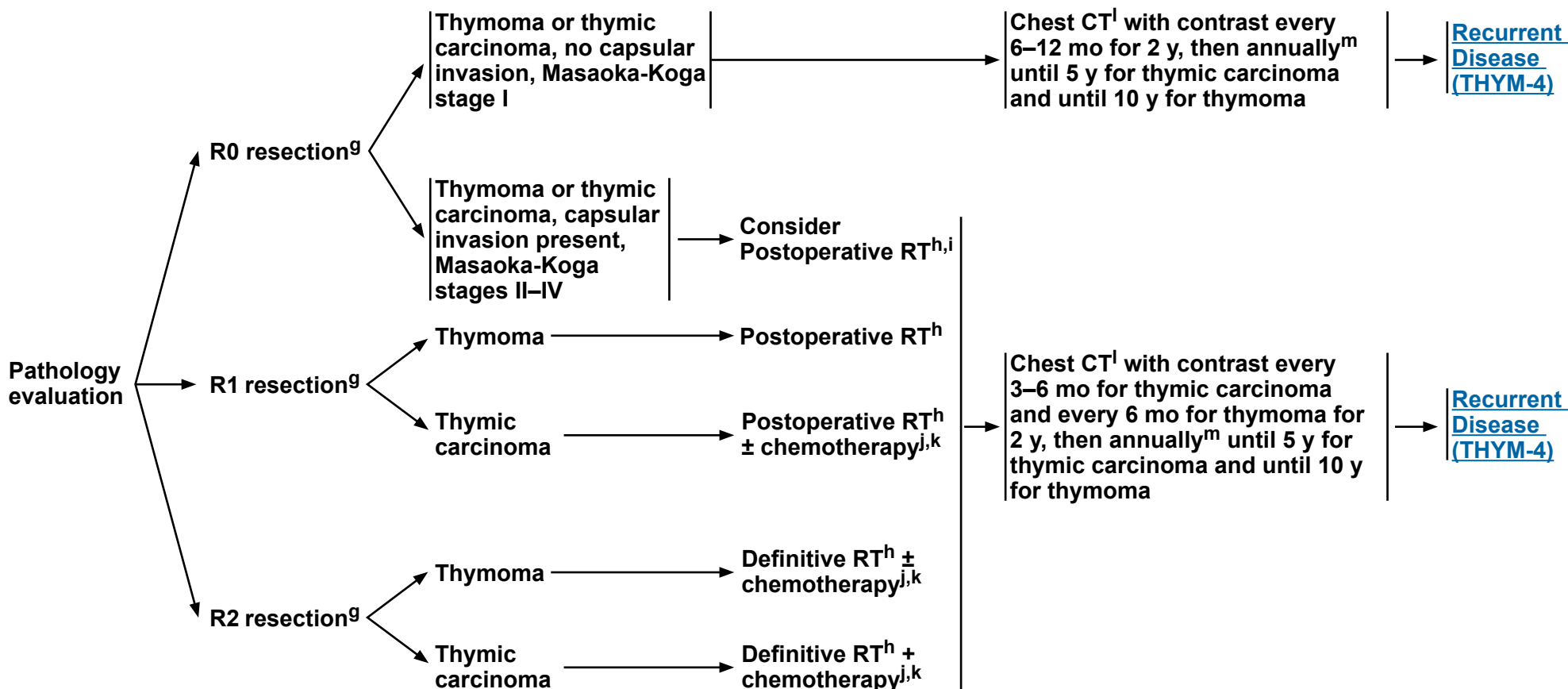
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## Thymomas and Thymic Carcinomas

### POSTOPERATIVE EVALUATION

### POSTOPERATIVE TREATMENT

### SURVEILLANCE<sup>a</sup>



<sup>a</sup> Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.

<sup>g</sup> R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.

<sup>h</sup> [Principles of Radiation Therapy \(THYM-B\)](#).

<sup>i</sup> Decisions about adjuvant radiation therapy (RT) in this setting should be based on multidisciplinary evaluation.

<sup>j</sup> [Principles of Systemic Therapy \(THYM-C\)](#).

<sup>k</sup> There is a diversity of opinion on treatment approach. Ruffini E, et al. Eur J Cardiothorac Surg 2019;55:601-609.

<sup>l</sup> MRI is an appropriate alternative to CT in certain clinical situations.

<sup>m</sup> The duration for surveillance has not been established.

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





# NCCN Guidelines Version 2.2025

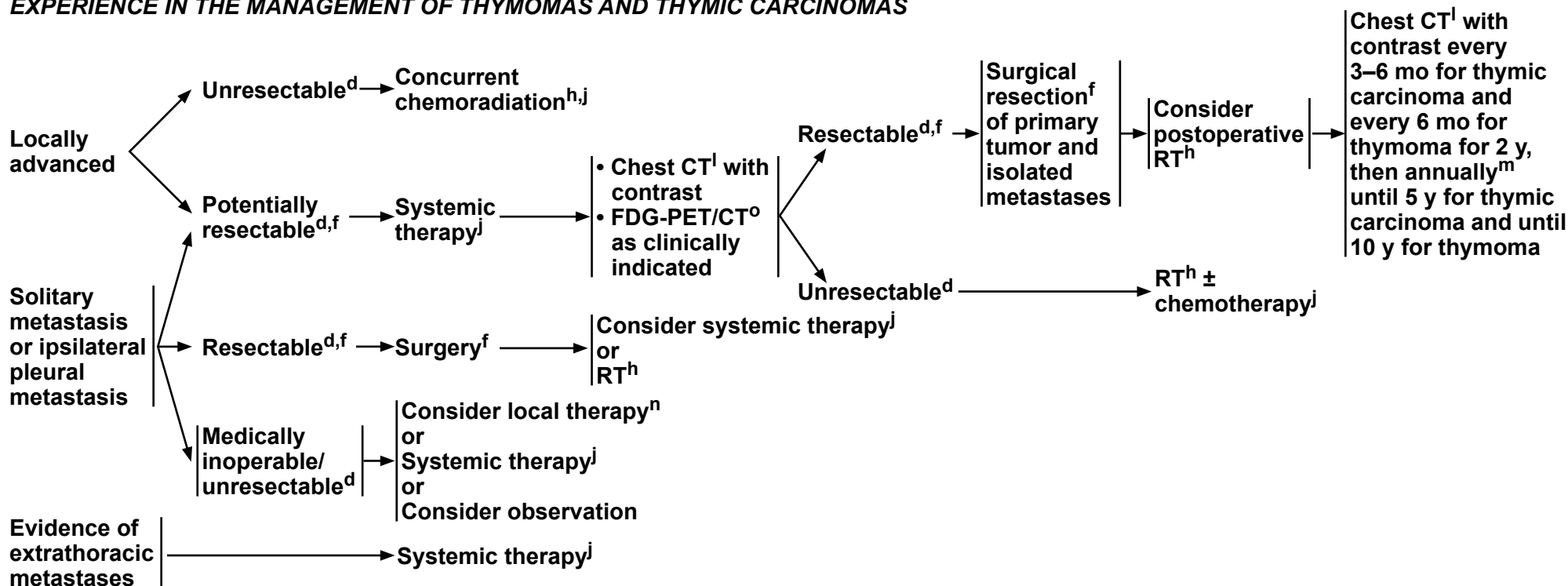
## Thymomas and Thymic Carcinomas

### RECURRENT, ADVANCED, OR METASTATIC DISEASE

### TREATMENT

### SURVEILLANCE<sup>a</sup>

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



<sup>a</sup> Patients with thymoma should be evaluated clinically for signs of myasthenia gravis and other paraneoplastic syndromes with appropriate workup and treatment.

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

<sup>f</sup> [Principles of Surgical Resection \(THYM-A\)](#).

<sup>h</sup> [Principles of Radiation Therapy \(THYM-B\)](#).

<sup>j</sup> [Principles of Systemic Therapy \(THYM-C\)](#).

<sup>l</sup> MRI is an appropriate alternative to CT in certain clinical situations.

<sup>m</sup> The duration for surveillance has not been established.

<sup>n</sup> Local therapies can include image-guided thermal ablation or RT.

<sup>o</sup> FDG-PET/CT includes skull-base to mid-thigh.

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





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## Thymomas and Thymic Carcinomas

### PRINCIPLES OF SURGICAL RESECTION

- **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 thymoma 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.**
- **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 RT 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.<sup>1-14</sup>**

[References on THYM-A 2 OF 2](#)

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



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## Thymomas and Thymic Carcinomas

### PRINCIPLES OF SURGICAL RESECTION – REFERENCES

- <sup>1</sup> Pennathur A, Qureshi I, Schubert MJ, et al. Comparison of surgical techniques for early stage thymoma: feasibility of minimally invasive thymectomy and comparison with open resection. *J Thorac Cardiovasc Surg* 2011;141:694-701.
- <sup>2</sup> Ye B, Tantai JC, Ge XX, et al. Surgical techniques for early-stage thymoma: video-assisted thorascopic thymectomy versus transsternal thymectomy. *J Thorac Cardiovasc Surg* 2014;147:1599-1603.
- <sup>3</sup> Sakamaki Y, Oda T, Kanazawa G, et al. Intermediate-term oncologic outcomes after video-assisted thorascopic thymectomy for early-stage thymoma. *J Thorac Cardiovasc Surg* 2014;148:1230-1237.
- <sup>4</sup> Manoly I, Whistance RN, Sreekumar R, et al. Early and mid-term outcomes of trans-sternal and video-assisted thorascopic surgery for thymoma. *Eur J Cardiothorac Surg* 2014;45:e187-193.
- <sup>5</sup> Liu TJ, Lin MW, Hsieh MS, et al. Video-assisted thorascopic surgical thymectomy to treat early thymoma: a comparison with the conventional transsternal approach. *Ann Surg Oncol* 2014;322-328.
- <sup>6</sup> Friedant AJ, Handorf EA, Su S, Scott WJ. Minimally invasive versus open thymectomy for thymic malignancies: systematic review and meta-analysis. *J Thorac Oncol* 2016;11:30-38.
- <sup>7</sup> Burt BM, Yao X, Shrager J, et al. Determinants of complete resection of thymoma by minimally invasive and open thymectomy: Analysis of an International Registry. *J Thorac Oncol* 2017;12:129-136.
- <sup>8</sup> Jurado J, Javidfar J, Newmark A, et al. Minimally invasive thymectomy and open thymectomy: outcome analysis of 263 patients. *Ann Thorac Surg* 2012;94:974-981.
- <sup>9</sup> Hess N, Sarkaria I, Pennathur A, et al. Minimally invasive versus open thymectomy: A systematic review of surgical techniques, patient demographics, and perioperative outcomes. *Ann Cardiothorac Surg* 2016; 5:1-9.
- <sup>10</sup> Rowse P, Roden A, Corl F, et al. Minimally invasive thymectomy: The Mayo Clinic experience. *Ann Cardiothorac Surg* 2015;4:519-526.
- <sup>11</sup> Hwang SK, Lee GD, Kang CH, et al. Long-term outcome of minimally invasive thymectomy versus open thymectomy for locally advanced cases. *Eur J Cardiothorac Surg* 2022;62:ezac238.
- <sup>12</sup> Yang C-F, Hurd J, Shah SA, et al. A national analysis of open versus minimally invasive thymectomy for stage I to III thymoma. *J Thorac Cardiovasc Surg* 2020;160:555-567.
- <sup>13</sup> Hurd J, Haridas C, Potter A, et al. A national analysis of open versus minimally invasive thymectomy for stage I–III thymic carcinoma. *Eur J Cardiothorac Surg* 2020;62:ezac159.
- <sup>14</sup> Gu Z, Chen C, Wang Y, et al. Video-assisted thorascopic surgery versus open surgery for Stage I thymic epithelial tumours: a propensity score-matched study. *Eur J Cardiothorac Surg* 2018;54:1037-1044.

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### PRINCIPLES OF RADIATION THERAPY<sup>1,2</sup>

#### 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 to 70 Gy should be given to patients with unresectable disease.
- For adjuvant treatment, the radiation dose consists of 45 to 50 Gy for clear/close margins and 54 Gy for microscopically positive resection margins. A total dose of 60–70 Gy should be given to patients with gross residual disease (similar to patients with unresectable disease),<sup>3,4,5</sup> 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.

#### 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 (ENI) (entire mediastinum and bilateral supraclavicular nodal regions) is not recommended, as thymomas do not commonly metastasize to regional lymph nodes.<sup>6</sup>
- 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.

[Radiation Techniques THYM-B 2 of 3](#)  
[References THYM-B 3 of 3](#)

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### PRINCIPLES OF RADIATION THERAPY

#### Radiation Techniques

- Target motion should be managed using the Principles of Radiation Therapy in the [NCCN Guidelines for Non-Small Cell Lung Cancer](#). Intravenous contrast is beneficial in the unresectable setting.
- In addition to following the normal tissue constraints recommendation using the Principles of Radiation Therapy in the [NCCN Guidelines 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 mean total dose to the heart should be as low as reasonably achievable to potentially maximize survival.
- A minimum technological standard for RT is CT-planned 3D conformal RT (3D-CRT). More advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) 4D-CT and/or PET/CT simulation, intensity-modulated RT (IMRT)/volumetric modulated arc therapy (VMAT), image-guided RT (IGRT), motion management, and proton therapy. In particular, IMRT is preferred over 3D-CRT. Compared to IMRT, proton therapy has been shown to improve dosimetry, thus allowing for better sparing of normal organs (lungs, heart, and esophagus)<sup>7</sup> with favorable local control and toxicity, and is appropriate.<sup>8</sup>

[General Principles, Radiation Dose, and Radiation Volume THYM-B 1 of 3](#)

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### PRINCIPLES OF RADIATION THERAPY — REFERENCES

- <sup>1</sup> Gomez D, Komaki R, Yu J, et al. Radiation therapy definitions and reporting guidelines for thymic malignancies. *J Thorac Oncol* 2011;6:S1743-1748.
- <sup>2</sup> Gomez D, Komaki R. Technical advances of radiation therapy for thymic malignancies. *J Thorac Oncol* 2010;5:S336-343.
- <sup>3</sup> Mornex F, Resbeut M, Richaud P, et al. Radiotherapy and chemotherapy for invasive thymomas: a multicentric retrospective review of 90 cases. The FNCLCC trialists. Federation Nationale des Centres de Lutte Contre le Cancer. *Int J Radiat Oncol Biol Phys* 1995;32:651-659.
- <sup>4</sup> Myojin M, Choi NC, Wright CD, et al. Stage III thymoma: pattern of failure after surgery and postoperative radiotherapy and its implication for future study. *Int J Radiat Oncol Biol Phys* 2000;46:927-933.
- <sup>5</sup> Rimner A, Yao X, Huang J, et al. Postoperative radiation therapy is associated with longer overall survival in completely resected stage II and III thymoma – an analysis of the International Thymic Malignancies Interest Group (ITMIG) retrospective database. *J Thorac Oncol* 2016;11:1785-1792.
- <sup>6</sup> Ruffini E, Mancuso M, Oliaro A, et al. Recurrence of thymoma: analysis of clinicopathologic features, treatment, and outcome. *J Thorac Cardiovasc Surg* 1997;113:55-63.
- <sup>7</sup> Parikh RR, Rhome R, Hug E, et al. Adjuvant proton beam therapy in the management of thymoma: a dosimetric comparison and acute toxicities. *Clin Lung Cancer* 2016;17:362-366.
- <sup>8</sup> Vogel J, Berman AT, Pechet TT, et al. Prospective study of proton beam radiation therapy for adjuvant and definitive treatment of thymoma and thymic carcinoma: early response and toxicity assessment. *Radiother Oncol* 2016;118:504-509.

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### PRINCIPLES OF SYSTEMIC THERAPY

#### FIRST-LINE COMBINATION CHEMOTHERAPY REGIMENS<sup>a</sup>

##### THYMOMA

##### Preferred (Other Recommended for Thymic Carcinoma)

- CAP<sup>1</sup>
  - Cisplatin 50 mg/m<sup>2</sup> IV day 1
  - Doxorubicin 50 mg/m<sup>2</sup> IV day 1
  - Cyclophosphamide 500 mg/m<sup>2</sup> IV day 1
  - Administered every 3 weeks

##### THYMIC CARCINOMA

##### Preferred (Other Recommended for Thymoma)

- Carboplatin/paclitaxel<sup>4,5,b</sup>
  - Carboplatin AUC 6 IV day 1
  - Paclitaxel 200 mg/m<sup>2</sup> IV day 1
  - Administered every 3 weeks

##### Preferred (Thymic Carcinoma only)

- Carboplatin/paclitaxel/ramucirumab<sup>6,c</sup>
  - Ramucirumab 10 mg/kg IV day 1
  - Paclitaxel 200 mg/m<sup>2</sup> IV day 1
  - Carboplatin AUC 5 IV day 1
  - Administered every 3 weeks, maximum of six cycles
  - Ramucirumab monotherapy every 3 weeks as maintenance therapy, until progressive disease or unacceptable toxicity

#### Other Recommended for Thymic Carcinoma and Thymoma

- CAP with prednisone<sup>2</sup>
  - Cyclophosphamide 500 mg/m<sup>2</sup> IV day 1;
  - Doxorubicin, 20 mg/m<sup>2</sup>/day IV continuous infusion days 1–3;
  - Cisplatin 30 mg/m<sup>2</sup>/day IV days 1–3;
  - Prednisone 100 mg/day PO days 1–5;
  - Administered every 3 weeks
- ADOC<sup>3</sup>
  - Doxorubicin 40 mg/m<sup>2</sup> IV day 1;
  - Cisplatin 50 mg/m<sup>2</sup> IV day 1;
  - Vincristine 0.6 mg/m<sup>2</sup> IV day 3;
  - Cyclophosphamide 700 mg/m<sup>2</sup> IV day 4
  - Administered every 3 weeks

- PE<sup>7,b</sup>
  - Cisplatin 60 mg/m<sup>2</sup> IV day 1;
  - Etoposide 120 mg/m<sup>2</sup>/day IV days 1–3;
  - Administered every 3 weeks
- Etoposide/ifosfamide/cisplatin<sup>8</sup>
  - Etoposide 75 mg/m<sup>2</sup>/day IV days 1–4;
  - Ifosfamide 1.2 g/m<sup>2</sup>/day IV days 1–4;
  - Cisplatin 20 mg/m<sup>2</sup>/day IV days 1–4
  - Administered every 3 weeks

[Subsequent Therapy THYM-2 of 3](#)

[References THYM-C 3 of 3](#)

<sup>a</sup> If patients cannot tolerate first-line combination regimens, consider second-line systemic therapy options.

<sup>b</sup> Regimens can be used with RT, as definitive concurrent chemoradiation.

<sup>c</sup> 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.

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### PRINCIPLES OF SYSTEMIC THERAPY

#### SECOND-LINE SYSTEMIC THERAPY (regimens noted in alphabetical order)

##### THYMOMA

###### Preferred

- Everolimus<sup>9</sup>
- Gemcitabine ± capecitabine<sup>10,11</sup>
- Octreotide<sup>d</sup> (including LAR) (if octreotide scan or dotatate PET/CT positive) ± prednisone<sup>12,13</sup>
- Pemetrexed<sup>14</sup>

###### Other Recommended

- 5-FU and leucovorin<sup>15</sup>
- Paclitaxel<sup>16</sup>

###### Useful in Certain Circumstances

- Etoposide<sup>7,17</sup>
- Ifosfamide<sup>18</sup>

##### THYMIC CARCINOMA

###### Preferred

- Gemcitabine ± capecitabine<sup>10,11</sup>
- Lenvatinib<sup>e,19</sup>
- Pembrolizumab<sup>f,20,21</sup>
- Sunitinib<sup>22</sup>

###### Other Recommended

- Avelumab + axitinib<sup>23</sup>
- Everolimus<sup>9</sup>
- 5-FU and leucovorin<sup>15</sup>
- Paclitaxel<sup>16</sup>
- Pemetrexed<sup>14</sup>

###### Useful in Certain Circumstances

- Etoposide<sup>7,17</sup>
- Ifosfamide<sup>18</sup>

#### [References THYM-C 3 of 3](#)

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

<sup>e</sup> There is a high risk for side effects and frequent dose reductions may be needed.

<sup>f</sup> 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.

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





### PRINCIPLES OF SYSTEMIC THERAPY — REFERENCES

- <sup>1</sup> Loehrer PJ Sr, Kim K, Aisner SC, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Southeastern Cancer Study Group. *J Clin Oncol* 1994;12:1164-1168.
- <sup>2</sup> Kim ES, Putnam JB, Komaki R, et al. Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. *Lung Cancer* 2004;44:369-379.
- <sup>3</sup> Fornasiero A, Daniele O, Ghiotto C, et al. Chemotherapy for invasive thymoma. A 13-year experience. *Cancer* 1991;68:30-33.
- <sup>4</sup> Lemma GL, Lee JW, Aisner SC, et al. Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. *J Clin Oncol* 2011;29:2060-2065.
- <sup>5</sup> Hirai F, Yamanaka T, Taguchi K, et al. A multicenter phase II study of carboplatin and paclitaxel for advanced thymic carcinoma: WJOG4207L. *Ann Oncol* 2015;26:363-368.
- <sup>6</sup> Proto C, Ganzinelli M, Manglaviti S, et al. Efficacy and safety of ramucirumab plus carboplatin and paclitaxel in untreated metastatic thymic carcinoma: RELEVANT phase II trial (NCT03921671). *Ann Oncol* 2024;35:817-826.
- <sup>7</sup> Giaccone G, Ardizzoni A, Kirkpatrick A, et al. Cisplatin and etoposide combination chemotherapy for locally advanced or metastatic thymoma. A phase II study of the European Organization for Research and Treatment of Cancer Lung Cancer Cooperative Group. *J Clin Oncol* 1996;14:814-820.
- <sup>8</sup> Loehrer PJ Sr, Jiroutek M, Aisner S, et al. Combined etoposide, ifosfamide, and cisplatin in the treatment of patients with advanced thymoma and thymic carcinoma: an intergroup trial. *Cancer* 2001;91:2010-2015.
- <sup>9</sup> Zucali PA, De Pas TM, Palmieri G, et al. Phase II study of everolimus in patients with thymoma and thymic carcinoma previously treated with cisplatin-based chemotherapy. *J Clin Oncol* 2018;36:342-349.
- <sup>10</sup> Palmieri G, Merola G, Federico P, et al. Preliminary results of phase II study of capecitabine and gemcitabine (CAP-GEM) in patients with metastatic pretreated thymic epithelial tumors (TETs). *Ann Oncol* 2010;21:1168-1172.
- <sup>11</sup> Palmieri G, Buonerba C, Ottaviano M, et al. Capecitabine plus gemcitabine in thymic epithelial tumors: final analysis of a phase II trial. *Future Oncol* 2014;10:2141-2147.
- <sup>12</sup> Loehrer PJ Sr, Wang W, Johnson DH, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group Phase II Trial. *J Clin Oncol* 2004;22:293-299.
- <sup>13</sup> Kirzinger L, Boy S, Marienhagen J, et al. Octreotide LAR and prednisone as neoadjuvant treatment in patients with primary or locally recurrent unresectable thymic tumors: a phase II study. *PLoS One* 2016;11:e0168215.
- <sup>14</sup> Gbolahan OB, Porter RF, Salter JT, et al. A phase II study of pemetrexed in patients with recurrent thymoma and thymic carcinoma. *J Thorac Oncol* 2018;13:1940-1948.
- <sup>15</sup> Thomas CR, Wright CD, Loehrer PJ. Thymoma: state of the art. *J Clin Oncol* 1999;17:2280-2289.
- <sup>16</sup> Umemura S, Segawa Y, Fujiwara K, et al. A case of recurrent metastatic thymoma showing a marked response to paclitaxel monotherapy. *Jpn J Clin Oncol* 2002;32:262-265.
- <sup>17</sup> Bluthgen MV, Boutros C, Fayard F, et al. Activity and safety of oral etoposide in pretreated patients with metastatic or recurrent thymic epithelial tumors (TET): A single-institution experience. *Lung Cancer* 2016;99:111-116.
- <sup>18</sup> Highley MS, Underhill CR, Parnis FX, et al. Treatment of invasive thymoma with single-agent ifosfamide. *J Clin Oncol* 1999;17:2737-2744.
- <sup>19</sup> Sato J, Satouchi M, Itoh S, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicentre, phase 2 trial. *Lancet Oncol* 2020;21:843-850.
- <sup>20</sup> Giaccone G, Kim C, Thompson J, et al. Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. *Lancet Oncol* 2018;19:347-355.
- <sup>21</sup> Cho J, Kim HS, Ku BM, et al. Pembrolizumab for patients with refractory or relapsed thymic epithelial tumor: An open-label phase II trial. *J Clin Oncol* 2019;37:2162-2170.
- <sup>22</sup> Thomas A, Rajan A, Berman A, et al. Sunitinib in patients with chemotherapy-refractory thymoma and thymic carcinoma: an open-label phase 2 trial. *Lancet Oncol* 2015;16:177-186.
- <sup>23</sup> Conforti F, Zucali PA, Pala L, et al. Avelumab plus axitinib in unresectable or metastatic type B3 thymomas and thymic carcinomas (CAVEATT): a single-arm, multicentre, phase 2 trial. *Lancet Oncol* 2022;23:1287-1296.

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



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## Thymomas and Thymic Carcinomas

### WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION<sup>1</sup>

Thymoma subtype <sup>a</sup>	Obligatory criteria	Optional criteria
Type A	Occurrence of bland, spindle shaped epithelial cells (at least focally); paucity <sup>b</sup> 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 <sup>2</sup> ); nuclear crowding	Polygonal epithelial cells CD20+ epithelial cells
Type AB	Occurrence of bland, spindle shaped epithelial cells (at least focally); abundance <sup>b</sup> 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 <sup>c</sup>	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 <sup>d</sup>		

<sup>a</sup> For thymoma composed of two or more subtypes, components should be listed.

<sup>b</sup> 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."

<sup>c</sup> MNT, micronodular thymoma with lymphoid stroma.

<sup>d</sup> Lipofibroadenoma.

<sup>1</sup> 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). Available from: <https://tumourclassification.iarc.who.int/chapters/35>.

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### WORLD HEALTH ORGANIZATION HISTOLOGIC CLASSIFICATION<sup>1</sup>

#### **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**
- **Neuroendocrine tumors ([NCCN Guidelines for Neuroendocrine and Adrenal Tumors](#))**
  - Carcinoid tumor, NOS/neuroendocrine tumor, NOS
  - Typical carcinoid/neuroendocrine tumor, grade 1
  - Atypical carcinoid/neuroendocrine tumor, grade 2
- **Neuroendocrine carcinomas**
  - Small cell carcinoma
  - Combined small cell carcinoma
  - Large cell neuroendocrine carcinoma

<sup>1</sup> 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). Available from: <https://tumourclassification.iarc.who.int/chapters/35>.

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



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

### Staging

Table 1. Modified Masaoka clinical staging of thymoma<sup>1-3</sup>

<u>Masaoka Stage</u>	<u>Diagnostic Criteria</u>
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

<sup>1</sup> Reprinted from Wright CD. Management of thymomas. Crit Rev Oncol Hematol 2008;65:109-120, with permission from Elsevier.

<sup>2</sup> Note that the Masaoka staging system is also used to stage thymic carcinomas.

<sup>3</sup> 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.



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## Thymomas and Thymic Carcinomas

## Staging

**Table 2. Definitions for TNM<sup>\*,\*\*</sup>**

### Primary Tumor (T)

<b>TX</b>	Primary tumor cannot be assessed
<b>T0</b>	No evidence of primary tumor
<b>T1</b>	Tumor encapsulated or extending into the mediastinal fat; may involve the mediastinal pleura
T1a	Tumor with no mediastinal pleura involvement
T1b	Tumor with direct invasion of mediastinal pleura
<b>T2</b>	Tumor with direct invasion of the pericardium (either partial or full thickness)
<b>T3</b>	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
<b>T4</b>	Tumor with invasion into any of the following: aorta (ascending, arch, or descending) arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus

### Regional Lymph Nodes (N)

<b>NX</b>	Regional lymph nodes cannot be assessed
<b>N0</b>	No regional lymph node metastasis
<b>N1</b>	Metastasis in anterior (perithymic) lymph nodes
<b>N2</b>	Metastasis in deep intrathoracic or cervical lymph nodes

### Distant Metastasis (M)

<b>M0</b>	No pleural, pericardial, or distant metastasis
<b>M1</b>	Pleural, pericardial, or distant metastasis
M1a	Separate pleural or pericardial nodule(s)
M1b	Pulmonary intraparenchymal nodule or distant organ metastasis

\*Involvement must be microscopically confirmed in pathological staging, if possible.

\*\*T categories are defined by “levels” of invasion; they reflect the highest degree of invasion regardless of how many other (lower-level) structures are invaded. T1, level 1 structures: thymus, anterior mediastinal fat, mediastinal pleura; T2, level 2 structures: pericardium; T3, level 3 structures: lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, hilar pulmonary vessels; T4, level 4 structures: aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus.

### AJCC Prognostic Groups

<b>Stage I</b>	T1a,b	N0	M0
<b>Stage II</b>	T2	N0	M0
<b>Stage IIIA</b>	T3	N0	M0
<b>Stage IIIB</b>	T4	N0	M0
<b>Stage IVA</b>	Any T	N1	M0
	Any T	N0-N1	M1a
<b>Stage IVB</b>	Any T	N2	M0-M1a
	Any T	Any N	M1b

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.



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## Thymomas and Thymic Carcinomas

### ABBREVIATIONS

<b>3D-CRT</b>	<b>three-dimensional conformal radiation therapy</b>	<b>IGRT</b>	<b>image-guided radiation therapy</b>
<b>4D-CT</b>	<b>four-dimensional computed tomography</b>	<b>IMRT</b>	<b>intensity-modulated radiation therapy</b>
<b>AFP</b>	<b>alpha-fetoprotein</b>	<b>MNT</b>	<b>micronodular thymoma with lymphoid stroma</b>
<b>beta-hCG</b>	<b>beta-human chorionic gonadotropin</b>	<b>NOS</b>	<b>not otherwise specified</b>
<b>CBC</b>	<b>complete blood count</b>	<b>NUT</b>	<b>nuclear protein in testis</b>
<b>CTV</b>	<b>clinical target volume</b>	<b>PD-1</b>	<b>programmed cell death protein 1</b>
<b>EMA</b>	<b>epithelial membrane antigen</b>	<b>PD-L1</b>	<b>programmed death ligand 1</b>
<b>ENI</b>	<b>elective nodal irradiation</b>	<b>PTV</b>	<b>planning target volume</b>
<b>FDG</b>	<b>fluorodeoxyglucose</b>	<b>VMAT</b>	<b>volumetric modulated arc therapy</b>



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### NCCN Categories of Evidence and Consensus

<b>Category 1</b>	Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
<b>Category 2A</b>	Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
<b>Category 2B</b>	Based upon lower-level evidence, there is NCCN consensus (≥50%, but <85% support of the Panel) that the intervention is appropriate.
<b>Category 3</b>	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

### NCCN Categories of Preference

<b>Preferred intervention</b>	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
<b>Other recommended intervention</b>	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
<b>Useful in certain circumstances</b>	Other interventions that may be used for selected patient populations (defined with recommendation).

All recommendations are considered appropriate.





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## Thymomas and Thymic Carcinomas

**Discussion** This discussion corresponds to the NCCN Guidelines for Thymomas and Thymic Carcinomas. Last updated: May 19, 2025

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## Thymomas and Thymic Carcinomas

### Overview

Thymoma and thymic carcinoma originate in the epithelial cells of the thymus.<sup>1,2</sup> Among the generally rare tumors of the anterior mediastinum, thymomas are the most common primary tumors and occur in approximately two per million per year in the United States.<sup>3,4</sup> Thymic carcinomas are even less common, with one study estimating the annual incidence to be 0.48 per million in the United States.<sup>4</sup> Although thymomas can spread locally, they are less likely to be invasive and metastasize than thymic carcinomas.<sup>5-8</sup> Patients with thymic carcinomas often present with advanced or metastatic disease at diagnosis.<sup>6,9-11</sup> The 5-year survival rate of patients with thymomas is approximately 90%,<sup>5,12,13</sup> while the 5-year survival rates for patients with thymic carcinoma are closer to 60%.<sup>5,10</sup>

These NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) focus on thymomas and thymic carcinomas and outline the recommendations for evaluation and treatment of patients with these mediastinal tumors. These NCCN Guidelines were first published in 2007 and have been subsequently updated on an annual basis. The NCCN Guidelines® for Thymomas and Thymic Carcinomas are updated by Panel members who are also on the NCCN Guidelines for Non-Small Cell Lung Cancer Panel.

### Guidelines Update Methodology

The complete details of the Development and Update of the NCCN Guidelines are available at [www.NCCN.org](http://www.NCCN.org).

### Literature Search Criteria

Prior to the annual update of the NCCN Guidelines for Thymomas and Thymic Carcinomas, an electronic search of the PubMed database was performed to obtain key literature in thymomas and thymic carcinomas published since the previous Guidelines update, using the search terms:

thymomas, thymic carcinomas, and thymic epithelial tumors. The PubMed database was chosen because it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.<sup>14</sup>

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Practice Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these Guidelines as discussed by the Panel during the Guidelines update have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the Panel's review of lower-level evidence and expert opinion.

### Sensitive/Inclusive Language Usage

NCCN Guidelines strive to use language that advances the goals of equity, inclusion, and representation.<sup>15</sup> NCCN Guidelines endeavor to use language that is person-first; not stigmatizing; anti-racist, anti-classist, anti-misogynist, anti-ageist, anti-ableist, and anti-weight biased; and inclusive of individuals of all sexual orientations and gender identities. NCCN Guidelines incorporate non-gendered language, instead focusing on organ-specific recommendations. This language is both more accurate and more inclusive and can help fully address the needs of individuals of all sexual orientations and gender identities. NCCN Guidelines will continue to use the terms men, women, female, and male when citing statistics, recommendations, or data from organizations or sources that do not use inclusive terms. Most studies do not report how sex and gender data are collected and use these terms interchangeably or inconsistently. If sources do not differentiate gender from sex assigned at birth or organs present, the information is presumed to



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## Thymomas and Thymic Carcinomas

predominantly represent cisgender individuals. NCCN encourages researchers to collect more specific data in future studies and organizations to use more inclusive and accurate language in their future analyses.

### Mediastinal Masses

Masses in the anterior mediastinum can be neoplasms (eg, thymomas, lymphomas, thymic carcinomas, thymic carcinoids, thymolipomas, germ cell tumors, lung metastases) or non-neoplastic conditions (eg, intrathoracic goiter, thymic cysts, lymphangiomas, aortic aneurysms).<sup>16-20</sup> All patients with a mediastinal mass should be evaluated to determine the type of mass and the extent of disease before treatment (THYM-1). It is essential to differentiate between thymic malignancies and other conditions (eg, lung metastases, lymphoma, goiter, germ cell tumors) before treatment, because management differs for these conditions.<sup>2,21,22</sup> However, over half of primary cancers in the anterior mediastinum are thymomas.<sup>4,23</sup>

Among the cancers presenting in the mediastinum, there are a range of clinical presentations. Unlike thymomas, which are often indolent, lymphomas or germ cell tumors may be associated with a rapid onset of symptoms.<sup>22,24</sup> Lymphomas typically manifest as generalized disease but can also be primary anterior and/or middle mediastinal lesions (ie, nodular sclerosing Hodgkin's disease, non-Hodgkin's lymphomas [diffuse large B-cell lymphoma and acute lymphoblastic lymphoma]); patients typically have lymphadenopathy (see the NCCN Guidelines for Hodgkin Lymphoma and the NCCN Guidelines for B-Cell Lymphomas, available at [www.NCCN.org](http://www.NCCN.org)).<sup>20,25</sup> Thymic carcinoids are rare neuroendocrine tumors that can be associated with multiple endocrine neoplasia type 1 (MEN1) syndrome (see the NCCN Guidelines for Neuroendocrine and Adrenal Tumors, available at [www.NCCN.org](http://www.NCCN.org)).<sup>26,27</sup> Extragonadal germ cell tumors are rare tumors that may also occur in the mediastinum.<sup>28,29</sup>

Recommended tests for the initial evaluation of mediastinal masses include chest CT with contrast and blood chemistry studies (THYM-1).<sup>30-32</sup> On CT, a thymoma is usually a well-defined round or oval mass in the thymus without lymph node enlargement.<sup>33-35</sup> 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.<sup>36</sup> In patients who cannot tolerate iodinated contrast, chest MRI may be substituted.<sup>35</sup> FDG-PET/CT is recommended as clinically indicated and should encompass the skull base to mid-thigh. Alpha-fetoprotein (AFP) levels and beta-human chorionic gonadotropin (beta-hCG) levels may be measured to rule out germ cell tumors.<sup>37</sup> Pulmonary function tests should be performed as clinically appropriate as part of the initial evaluation.

Thymic epithelial tumors are likely if: 1) a well-defined mediastinal mass in the thymic bed that is not continuous with the thyroid gland is present; 2) tumor markers for AFP or beta-hCG are negative; and 3) no other adenopathy is present.<sup>2</sup>

### Thymic Masses

#### Diagnosis

The World Health Organization (WHO) histologic classification system can be used to distinguish between thymomas, thymic carcinomas, and thymic carcinoids.<sup>1,2</sup> The WHO classification is also used to differentiate among different histologic types of thymomas (ie, A, AB, B1, B2, B3).<sup>38</sup> Thymic carcinomas are categorized by larger subtype groups such as squamous carcinomas, adenocarcinomas, adenosquamous carcinoma, and carcinomas not otherwise specified (NOS).<sup>1,2</sup>

#### Staging

Although several staging systems exist, the Masaoka-Koga staging system has been the most widely accepted system for management and



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

determination of prognosis for both thymomas and thymic carcinomas.<sup>5,7,39-43</sup> Another staging system for thymomas and thymic carcinomas is based on a combined effort by the International Thymic Malignancy Interest Group (ITMIG) and International Association for the Study of Lung Cancer (IASLC); this staging system was used as the basis for the American Joint Committee on Cancer (AJCC) TNM system for thymic malignancies (8<sup>th</sup> edition).<sup>44-51</sup> Both the Masaoka and AJCC staging systems are provided in the NCCN Guidelines for Thymomas and Thymic Carcinomas (available at [www.NCCN.org](http://www.NCCN.org)). However, in the current Guidelines, treatment recommendations for thymoma and thymic carcinoma refer to Masaoka-Koga staging since much of the available clinical evidence was generated using this system.

### Overview of Treatment Approaches

All patients with a likely thymic tumor should be treated by a multidisciplinary team with experience in the management of thymomas and thymic carcinomas (THYM-2). The team may include radiation oncologists, thoracic surgeons, medical oncologists, neurologists, pathologists, and diagnostic imaging specialists. Many patients are likely to undergo surgery with curative intent, although those with advanced disease may be treated with a multimodal approach that consists of surgery, radiation therapy (RT), and/or systemic therapy (THYM-2, THYM-3, and THYM-4).

### Surgery

For most resectable tumors, complete excision of the lesion by total thymectomy and complete surgical excision of contiguous and noncontiguous disease is the primary oncologic goal (THYM-2).<sup>5,7,22,52-55</sup> Findings from multiple studies indicate that a complete resection is considered an important prognostic factor for patients with thymic malignancies.<sup>12,56-60</sup> A board-certified thoracic surgeon with a primary focus on thoracic oncology should be involved in determining whether

the mass can be surgically resected. If an R0 resection is deemed uncertain, the NCCN Panel recommends preoperative systemic therapy, which may improve resectability of the tumor (refer to the *Systemic Therapy* section below).<sup>61-64</sup> Surgical debulking of tumors is discouraged.<sup>65,66</sup>

The resection of adjacent structures, including the pericardium, phrenic nerve, pleura, lung, and even major vascular structures may be required for a complete resection.<sup>52</sup> Bilateral phrenic nerve resection should be avoided due to severe respiratory morbidity. During thymectomy, the pleural surfaces should be examined for metastases. To achieve a complete gross resection, removal of pleural metastases may be appropriate in some patients.<sup>67-69</sup>

Tissue diagnosis with core needle biopsy is recommended for locally advanced or metastatic thymic masses. Open biopsy may be considered if core biopsy is neither feasible nor diagnostic; a transpleural approach should be avoided. The cancer protocol for thymic tumors from the College of American Pathologists (CAP) may be useful for assessing specimens.<sup>70</sup>

Minimally invasive procedures may be considered for clinical stage I–II disease if all oncologic goals can be met and if performed in specialized centers with surgeons who have expertise in these techniques.<sup>71-83</sup> However, minimally invasive procedures are not routinely recommended, because few long-term studies are available regarding recurrence and survival.<sup>75,84-86</sup> A systematic review of 1061 patients with thymomas reported that 5-year overall survival after video-assisted thoracoscopic surgery (VATS, 83%–100% vs. open, 79%–98%) and 10-year recurrence-free survival (VATS, 89%–100% vs. open, 80%–93%) were similar in patients undergoing VATS compared to open thymectomy, although outcomes may be skewed due to selection bias.<sup>84</sup> A retrospective review in 2835 patients assessed VATS thymectomy



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compared with sternotomy in patients with thymomas.<sup>87</sup> The 5-year overall survival rate was 97.9% in the VATS group. The overall survival rates were not significantly different when comparing the VATS group versus the sternotomy group. A meta-analysis also showed that VATS was safe and patients had similar overall survival when compared with those receiving open thymectomy.<sup>88</sup> There are additional clinical data available regarding the use of other types of minimally invasive procedures, such as robotic-assisted thymectomy (RATS).<sup>89</sup>

### **Radiation Therapy**

RT is used for the treatment of thymomas or thymic carcinomas in multiple settings. RT may be given for patients with unresectable disease, 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 (THYM-3 and THYM-4).<sup>90</sup>

In patients who undergo surgery for thymoma or thymic carcinoma, a National Cancer Data Base study evaluating the impact of postoperative RT in 4006 patients found that postoperative RT was associated with longer survival, particularly among those with Masaoka-Koga stage IIB and III disease and among those with positive margins.<sup>91</sup> Data from another retrospective ITMIG database study based on 1263 patients with completely resected Masaoka or Masaoka-Koga stage II or III thymoma demonstrated that postoperative RT was associated with improved overall survival.<sup>92</sup> Patients with completely resected early-stage thymoma or thymic carcinoma are at low risk of disease recurrence; some studies suggest that the addition of postoperative RT does not provide a survival benefit.<sup>22,91,93-96</sup>

RT (with or without chemotherapy) is also an option for patients with unresectable disease or those unable to undergo surgical resection.<sup>97-99</sup> A prospective phase II study in 56 patients with unresectable thymic

epithelial tumors found that concurrent chemoradiation resulted in an objective response rate of 85.7%.<sup>97</sup> A single-center study of patients with unresectable thymic carcinoma found that the overall response rate following concurrent chemoradiation was 50% (8/16).<sup>98</sup> Another single-center retrospective study evaluating the effects of RT (with or without chemotherapy) in 42 patients with unresectable locally advanced thymoma or thymic carcinoma reported that the objective response rates were 43.8% for the RT only group, 50% for the sequential chemoradiation group, and 87.5% for the concurrent chemoradiation group.<sup>100</sup>

Recommendations for RT should be made by radiation oncologists with experience in managing thymomas and thymic carcinomas. It is important for radiation oncologists to communicate with surgeons about the operative findings and determine the target volume at risk. Additionally, radiation oncologists should consult with the pathologist regarding histology, extent of disease (eg, extracapsular extension), and surgical margins.

Use of intensity-modulated RT (IMRT) may decrease the dose to the normal tissues.<sup>101</sup> If IMRT is used, guidelines from the NCI Advanced Technology Center (ATC) and American Society for Radiation Oncology/American College of Radiology (ASTRO/ACR) should be followed.<sup>102-106</sup> ICRU-83 (International Commission on Radiation Units and Measurements Report 83) recommendations are also a useful resource.<sup>104,107</sup> Although the normal tissue constraints recommendations for non-small cell lung cancer may be used (see the *Principles of Radiation Therapy* in the NCCN Guidelines for Non-Small Cell Lung Cancer, available at [www.NCCN.org](http://www.NCCN.org)), more conservative limits are recommended to minimize the dose volumes to all the normal structures.<sup>108,109</sup> Because these patients are younger and have long





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overall survival, the mean dose to the heart should be as low as reasonably achievable to potentially maximize survival.

A minimum technological standard for RT is CT-planned 3-D conformal radiation therapy (3D-CRT). More advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) 4D-CT and/or PET/CT simulation, IMRT/volumetric modulated arc therapy (VMAT), IGRT, motion management, and proton therapy. In particular, IMRT is preferred over 3D-CRT. Compared to IMRT, proton therapy has been shown to improve the dosimetry, allowing better sparing of the normal tissues with favorable local control and toxicity.<sup>110-112</sup> Incorporating 4D-CT for motion assessment and other motion management strategies can facilitate reduction of treatment margins and permit more definitive RT dosing for durable local control in this patient population that tends to have prolonged survival both in the curative and recurrent/metastatic setting.<sup>101</sup>

### **Other Local Therapies**

The NCCN Panel states that other local therapies such as image-guided thermal ablation may be considered as a treatment option for patients with advanced, metastatic, or recurrent thymic malignancies (THYM-4). There are limited data available (primarily in the setting of thymomas) supporting use of image-guided thermal ablation. One single-center retrospective review that assessed the effect of CT-guided percutaneous cryotherapy in 19 patients with unresectable thymoma found that the median progression-free survival was 18 months.<sup>113</sup> Additionally, no severe complications involving vital organs were reported; pleural effusion was the most common side effect. The efficacy and safety of CT-guided percutaneous cryoablation in five patients with recurrent thymoma was evaluated in a retrospective study.<sup>114</sup>

### **Systemic Therapy**

Systemic therapy is recommended in the NCCN Guidelines in multiple settings for patients with thymoma and thymic carcinoma: 1) preoperative therapy for potentially resectable advanced, metastatic, or recurrent disease, 2) treatment for unresectable advanced, metastatic, or recurrent disease, and 3) postoperative therapy for incompletely resected disease.

For patients with advanced or metastatic thymoma or thymic carcinoma that is potentially resectable (ie, if an R0 resection is uncertain), preoperative systemic therapy (typically a combination chemotherapy regimen) may be used to reduce tumor size and increase the odds of obtaining a complete resection (THYM-4).<sup>61-64</sup> A meta-analysis of studies that evaluated the effect of preoperative therapy in patients with advanced thymic epithelial tumors found that the pooled rate of response to preoperative therapy was 59%; the 5-year overall survival rate was 87%.<sup>64</sup> Another analysis found that the response rates were 70% to 80% among the largest studies evaluating preoperative chemotherapy in patients with thymic epithelial tumors; complete resection was reported in approximately 50% of those treated with this approach.<sup>115,116</sup>

For patients with unresectable advanced or metastatic thymoma or thymic carcinoma, systemic therapy (with or without RT, depending on extent of disease dissemination) is recommended as the main treatment approach (THYM-4). The NCCN Panel recommends various platinum-based combination chemotherapy regimens as first-line systemic treatment options (THYM-C 1 of 3). Other types of systemic therapies are reserved for use as subsequent lines of therapy (THYM-C 2 of 3). See *Systemic Therapy for Thymoma* and *Systemic Therapy for Thymic Carcinoma* for specific regimens for each tumor type recommended in these NCCN Guidelines.



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For patients with thymoma or thymic carcinoma who have surgery and residual tumor is left behind, postoperative chemotherapy (in combination with RT) is recommended as an option by the Panel (THYM-3). Clinical evidence supporting use of postoperative chemotherapy in this setting is limited due to the lack of randomized trial data. A recent systematic review reported that data on the benefit of postoperative chemotherapy in patients with thymic malignancies are mixed and may be confounded by RT, which is frequently used in the postoperative setting in those with incomplete resection.<sup>117</sup>

### Thymomas

Thymomas typically occur in adults and are rare in children and adolescents.<sup>3,22,118</sup> The etiology of thymomas is unknown; alcohol, tobacco smoking, and ionizing radiation do not appear to be risk factors for thymomas.<sup>3</sup> It has been reported that the incidence of thymomas is higher among certain racial and ethnic subgroups (ie, Black and Asian individuals).<sup>3,119</sup>

Some patients diagnosed with thymoma may be asymptomatic, while others will present with chest pain, cough, or dyspnea. Although thymomas can be locally invasive (eg, pleura, lung), they uncommonly spread to regional lymph nodes or extrathoracic sites.<sup>7,120-122</sup>

For many patients, mortality is not related to thymoma.<sup>40</sup> A number of autoimmune paraneoplastic diseases, including myasthenia gravis, hypogammaglobulinemia, and pure red cell aplasia, are associated with thymoma.<sup>123</sup> Approximately one-third of patients with thymomas may have myasthenia gravis, the most common paraneoplastic syndrome associated with thymoma.<sup>123-125</sup> The other paraneoplastic syndromes have been estimated to occur in <10% of patients with thymoma.<sup>125</sup>

Symptoms suggestive of myasthenia gravis include ptosis, diplopia, drooping, proximal muscle weakness, hoarseness, and/or dyspnea. If

patients have myasthenia gravis, they should receive treatment by a neurologist with experience in myasthenia gravis before undergoing surgical resection.<sup>126-128</sup> The NCCN Panel recommends that patients with thymoma undergo a clinical evaluation for signs of autoimmune paraneoplastic disorders (THYM-1).

### Surgically Resectable Thymoma

Completeness of resection is an important predictor of outcome for patients with thymoma.<sup>12,56,57,129</sup> For example, one study found that the 10-year survival rate of patients with thymoma and complete resection was significantly higher than those with incomplete resection or biopsy (76% vs 28%).<sup>56</sup> The NCCN Panel recommends surgery (ie, total thymectomy and complete excision of tumor) for all patients with resectable thymoma who can tolerate the procedure (THYM-2).<sup>23,130,131</sup> Among patients with resected thymoma in one study, the 10-year survival rates were approximately 90%, 70%, 55%, and 35% for Masaoka stage I, II, III, and IVa disease, respectively.<sup>132</sup>

Surgical biopsy should be avoided if a resectable thymoma is strongly suspected based on clinical and radiologic features (eg, patients have myasthenia gravis and a characteristic mass on CT).<sup>22</sup> A transpleural approach should be avoided during biopsy of a possible thymoma.<sup>127,133</sup> Small biopsy sampling (fine-needle or core needle biopsy) does not indicate whether invasion is present.<sup>134</sup> ITMIG and CAP have established procedures for reporting the surgical and pathologic findings from resection specimens.<sup>70,135</sup>

Postoperative treatment recommendations are dependent on disease stage and completeness of resection (THYM-3). The NCCN Panel does not recommend adjuvant therapy for patients with completely resected (R0) Masaoka-Koga stage I thymomas (no capsular invasion) due to low





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recurrence risk and the absence of a survival benefit for this group.<sup>22,91,93-95</sup>

There are conflicting data on whether patients with Masaoka stage II thymoma with complete resection will derive benefit from postoperative radiation.<sup>91,93-95,136</sup> Higher stage thymomas have a greater risk of disease recurrence and therefore postoperative therapy may be warranted even after complete resection.<sup>91,92,94,137,138</sup> The NCCN Panel recommends that RT after surgery can be considered if there is no residual tumor (R0) in patients with thymomas who have capsular invasion or Masaoka-Koga stage II–IV disease. If surgical margins are positive, the NCCN Panel recommends postoperative RT (if R1 resection) or definitive RT (with or without chemotherapy; if R2 resection), regardless of thymoma stage.<sup>91,139,140</sup> Decisions about postoperative treatment should be made by a multidisciplinary team.

For adjuvant RT, a dose of 45 to 50 Gy is recommended for clear or close margins; a dose of 54 Gy is recommended for microscopically positive resection margins.<sup>90,101,141</sup> However, a total dose of 60 to 70 Gy (1.8–2 Gy/fraction per day) is recommended for patients with gross residual disease after surgery.<sup>142,143</sup> Extensive elective nodal radiation is not recommended, because thymomas do not typically metastasize to regional lymph nodes.<sup>7,144</sup>

### Advanced, Metastatic, or Recurrent Thymoma

Although the majority of patients with thymoma have early-stage disease at presentation, there are patients who may be diagnosed with stage III or IV disease.<sup>5,56</sup> A multidisciplinary discussion is recommended before initiating treatment for advanced or metastatic thymoma as different treatment modalities may be necessary. The NCCN Panel recommends that if the disease is deemed resectable in the advanced or metastatic

setting, then surgery may be performed if the patient is able to tolerate the procedure (THYM-4).

For patients with thymoma with limited metastases that are potentially resectable, the NCCN Panel recommends a multimodal approach with the goal of long-term survival. Resectability is defined as complete (R0) resection. This strategy consists of preoperative systemic therapy, followed by surgery, if deemed resectable based on imaging.<sup>145,146</sup> If the primary tumor and any isolated metastases are resected, postoperative RT can be considered.<sup>62,147</sup> Definitive RT with or without chemotherapy is also an option, especially if the disease is deemed unresectable after systemic therapy.<sup>97</sup>

Treatment options for patients with unresectable localized thymomas may include concurrent chemoradiation, systemic therapy, or observation.<sup>97,148,149</sup> Local therapies, such as image-guided thermal ablation or RT, can also be considered.<sup>97,99,113,114,149</sup>

It is difficult to specify RT dosing regimens for advanced or metastatic disease given the broad range of scenarios that are possible. In general, a definitive dose of 60 to 70 Gy is recommended for patients with unresectable disease.<sup>99</sup> Stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), may be appropriate for limited focal metastases, whereas conventional fractionation is appropriate for larger metastases. In the palliative setting, typical palliative doses may be used—8 Gy in a single fraction, 20 Gy in 5 fractions, or 30 Gy in 10 fractions—depending on the treatment objectives. However, RT dosing can extend up to definitive doses for more durable local control. Highly conformal techniques may be appropriate for limited volume metastases, given the relatively long natural history of metastatic thymoma.<sup>150</sup>



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If there is evidence of extrathoracic metastases, the NCCN Panel recommends systemic therapy as a means to alleviate symptoms and achieve disease control.<sup>151-153</sup> Refer to *Systemic Therapy for Thymoma* below for information about specific regimens.

The proportion of patients with early-stage thymoma following complete resection who will experience disease recurrence is thought to be low, although overall thymoma recurrence rates reported in studies vary widely.<sup>5,56,154</sup> Treatment recommendations for recurrent thymoma are similar to those for newly diagnosed locally advanced or metastatic thymoma (THYM-4). As thymoma disease progression is often locoregional (eg, pleural or pulmonary) rather than extrathoracic in nature, surgery or RT may be considered if deemed clinically feasible.<sup>13,56,155-158</sup>

### Systemic Therapy for Thymoma

Thymomas are considered chemosensitive<sup>159</sup>; the Guidelines recommend several chemotherapy regimens for patients with thymoma (THYM-C 1 of 3).

The NCCN Panel has preference stratified the first-line combination chemotherapy treatment options for patients with thymomas. The preferred first-line regimen is cisplatin/doxorubicin/cyclophosphamide (CAP).<sup>160</sup> A 50% overall response rate was reported among 29 patients with advanced or recurrent thymoma (and 1 with thymic carcinoma) who received CAP in a clinical trial; 3 complete and 12 partial responses were documented.<sup>160</sup> Additionally, CAP was associated with a higher objective response rate than other regimens (44% versus 17%, as exclusive systemic therapy) in patients with advanced thymoma or thymic carcinoma based on data from the RYTHMIC prospective database study.<sup>153</sup>

Non-anthracycline regimens (eg, cisplatin/etoposide [with or without ifosfamide], carboplatin/paclitaxel) may be useful for patients who cannot tolerate the preferred regimen.<sup>161-164</sup>

The NCCN Panel has designated the following as “Other Recommended Regimens” for patients with thymomas: CAP with prednisone, doxorubicin/cisplatin/vincristine/cyclophosphamide (ADOC), cisplatin/etoposide (PE), etoposide/ifosfamide/cisplatin, and carboplatin/paclitaxel.<sup>62,161,162,164,165</sup> If patients are unable to tolerate the recommended first-line combination regimens, second-line systemic therapy options described below can be considered. Carboplatin/paclitaxel and PE can be used in combination with RT as definitive concurrent radiation.

Multiple systemic therapy regimens can be considered for treating thymomas in the second-line setting (THYM-C 2 of 3). The NCCN Panel has designated the following as preferred second-line systemic therapy options for the treatment of thymomas: everolimus, gemcitabine (with or without capecitabine), octreotide (if octreotide scan or dotatate PET/CT positive, with or without prednisone), or pemetrexed.<sup>166-170</sup> Other recommended regimens in the second-line setting for thymoma are 5-FU in combination with leucovorin and single-agent paclitaxel.<sup>125,171</sup> Single-agent etoposide and single-agent ifosfamide have been deemed by the Panel as subsequent therapy regimens that may be useful in certain circumstances.<sup>172,173</sup>

Treatment of thymoma with anti-PD-1/PD-L1 therapies is not recommended due to concerns about immune-related adverse events in a population of patients who are already predisposed to paraneoplastic autoimmune disorders.<sup>174,175</sup> Among the patients with thymoma who received pembrolizumab in a phase II trial, 71% (5/7) experienced grade 3 or higher immune-related adverse events, including myocarditis.<sup>176</sup>

### Surveillance: Thymoma

Despite excellent survival rates, surveillance remains essential for patients with thymoma as a wide range of recurrence rates has been



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reported.<sup>5,56,154</sup> Late recurrences occurring 10 years or later after surgical resection have been documented,<sup>56</sup> which may be due to the indolent growth of some thymomas.

For patients with completely resected Masaoka-Koga stage I thymoma (and no capsular invasion), the NCCN Panel recommends that surveillance for thymoma recurrence should include chest CT with contrast every 6 to 12 months for 2 years, then annually until 10 years. For all other patients with thymoma, surveillance should include chest CT with contrast every 6 months for 2 years, then annually until 10 years. MRI may be used for surveillance for certain clinical situations, including: 1) if patients cannot tolerate contrast; and 2) to decrease radiation if patients are young and will be screened for many years.<sup>35</sup>

The NCCN Panel notes that the duration, frequency, and type of imaging for surveillance for patients with thymomas have not been prospectively evaluated. Patients with thymoma have an increased risk for second malignancies, although no particular screening studies are recommended.<sup>3,4,177,178</sup>

### Thymic Carcinomas

Thymic carcinomas are rare aggressive tumors that often metastasize to regional lymph nodes and extrathoracic sites.<sup>5,13,19,179-181</sup> These tumors differ from thymomas because of their malignant histologic features and their different immunohistochemical and genetic features.<sup>1,2,18,182</sup> They are predominantly squamous cell carcinomas. However, thymic carcinomas should be differentiated from primary lung malignancies that metastasize to the thymus and may have a similar histologic appearance.<sup>183</sup>

Symptoms that patients with thymic carcinoma may experience include dyspnea, chest pain, superior vena cava syndrome, and others related to

mass effect.<sup>11</sup> Thymic carcinomas often cause pericardial and pleural effusions.

Thymic carcinomas are associated with a different clinical course from thymomas.<sup>152,182,184</sup> Unlike patients with thymomas, paraneoplastic syndromes (eg, myasthenia gravis) are rare in patients with thymic carcinoma.<sup>9,123,141</sup> If myasthenia gravis is diagnosed, then the diagnosis of thymic carcinoma should be reassessed, as the patient may have thymoma.<sup>9,11</sup> In contrast to thymomas (which mainly occur in adults), thymic carcinomas occur over a wide age range (including adolescents).<sup>9,11</sup>

### Surgically Resectable Thymic Carcinoma

The NCCN Panel recommends surgery for all patients with resectable thymic carcinoma who can tolerate the procedure (THYM-2). Complete resection is associated with better survival outcomes than incomplete resection or unresectable thymic carcinoma.<sup>185,186</sup> The 5-year survival rate of patients who have an R0 resection is estimated to be around 60% to 70%.<sup>9,10</sup> For completely resected (R0) Masaoka-Koga stage I thymic carcinomas with no capsular invasion, postoperative therapy is not recommended by the NCCN Panel.<sup>91,187</sup>

RT can be used to maximize local control after surgery for higher stage disease or if there are positive margins. A recent retrospective analysis evaluated the impact of postoperative RT in 462 patients with thymic carcinoma from the ITMIG/European Society of Thoracic Surgeons (ESTS) database.<sup>187</sup> Surgery followed by postoperative RT was associated with a significantly higher 5-year overall survival rate than surgery alone for patients with Masaoka stage III or IV thymic carcinoma, regardless of resection margin status. Addition of postoperative RT was associated with better survival outcomes than the absence of postoperative RT among patients who had R1 or R2 margins after



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surgery. Use of postoperative RT for stage II thymic carcinoma has historically been controversial; however, there are some data that suggest RT may have clinical benefit in this setting.<sup>10,11,136</sup>

For patients with Masaoka-Koga stage II–IV thymic carcinoma and R0 margins after surgery, postoperative RT can be considered. For patients with positive margins after surgical resection (regardless of disease stage), postoperative management options recommended by the NCCN Panel include RT alone or in combination with chemotherapy.<sup>9,10,90,136,179,186,188</sup> However, the Panel acknowledges that there is a diversity of opinion on the optimal treatment approach in this setting.<sup>146</sup>

For adjuvant RT, a dose of 45 to 50 Gy is recommended for clear or close margins; a dose of 54 Gy is recommended for microscopically positive resection margins (see *Principles of Radiation Therapy* in the full Guidelines at [www.NCCN.org](http://www.NCCN.org)).<sup>90,99,101,141,142</sup> However, a total dose of 60 to 70 Gy (1.8–2 Gy/fraction per day) is recommended for patients with gross residual disease after surgery.<sup>99,142,143</sup>

### Advanced, Metastatic, or Recurrent Thymic Carcinoma

Many patients with thymic carcinoma may have advanced or metastatic disease at presentation. In two separate studies, over three-quarters of patients with thymic carcinoma were diagnosed with Masaoka stage III or IV disease.<sup>9,10</sup> Patients treated for thymic carcinoma are also at significant risk of disease recurrence. In a retrospective analysis of 1042 patients with thymic carcinoma from the ITMIG/ESTS database, the cumulative incidence of recurrence (CIR) at 5 years was 35%, while the 10-year CIR was 40%.<sup>10</sup>

The paradigm for treating advanced, metastatic, or recurrent thymic carcinoma is like that used for thymomas (THYM-4). The NCCN Panel recommends that patients with advanced, metastatic, or recurrent thymic

carcinoma should be evaluated by a multidisciplinary team to determine the most appropriate treatment approach. If the disease is resectable and the patient is considered medically operable, then surgery is recommended, followed by postoperative therapy with RT or systemic therapy to reduce risk of recurrence after surgery. A complete (R0) resection is a critical prognostic factor.<sup>185,186,189</sup> Among patients with thymic carcinoma whose outcomes were analyzed in a retrospective study, the 5-year survival rate of those with complete resection (66.9%) was higher than those with subtotal resection (30.1%) or whose disease was considered inoperable (24.2%).<sup>5</sup>

For potentially resectable disease, the NCCN Panel recommends multimodal therapy consisting of neoadjuvant systemic therapy to increase the odds of a complete resection, followed by surgical resection of the primary tumor and any isolated metastases (if resectable), and/or RT (with or without chemotherapy).<sup>9,10,145,146,148</sup> Determination of resectability, defined as a complete (R0) resection, should be made by a thoracic surgeon together with multidisciplinary consultation as needed.

Treatment for unresectable disease should be individualized based on disease dissemination and other patient specific factors; recommended treatments in this setting may include concurrent chemoradiation, systemic therapy, observation, or local therapies (THYM-4).<sup>97,99,149</sup> A definitive RT dose of 60 to 70 Gy is recommended for patients with unresectable thymic carcinomas.<sup>97,99</sup> Local therapy options for focal metastatic lesions can include RT or image-guided thermal ablation.<sup>99,113,114</sup>

The spread of thymic carcinoma to distant sites such as brain, liver, bone, and lung has been documented.<sup>13,179</sup> If there is evidence of extrathoracic metastases in patients with thymic carcinoma, the NCCN Panel recommends systemic therapy. Refer to the *Systemic Therapy for Thymic Carcinoma* below for recommended regimens.





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### Systemic Therapy for Thymic Carcinoma

Several types of systemic therapy have clinical activity in thymic carcinomas, although these tumors are considered less chemosensitive than thymomas in general.<sup>163</sup> The NCCN Panel consensus is that carboplatin/paclitaxel (with or without ramucirumab) is the preferred first-line combination chemotherapy regimen for patients with thymic carcinoma, due to the response rates reported in prospective clinical trials (THYM-C 1 of 3).<sup>161,190,191</sup>

A phase II clinical trial reported an overall response rate of 36% among 39 patients with chemo-naïve advanced thymic carcinoma who received carboplatin/paclitaxel; this included 1 complete response and 13 partial responses.<sup>190</sup> The median progression-free survival reported was 7.5 months and the 2-year overall survival rate was 71%. A different prospective multicenter study reported an overall response rate of 21.7% among 23 patients with unresectable thymic carcinoma who were treated with carboplatin/paclitaxel; 5 partial responses were reported.<sup>161</sup> The median overall survival was 20 months.

Carboplatin/paclitaxel in combination with the vascular endothelial growth factor (VEGF) pathway inhibitor ramucirumab was recently added to the Guidelines as a preferred first-line systemic therapy option based on data from the single-arm phase II RELEVANT trial in patients with treatment-naïve advanced or metastatic thymic carcinoma.<sup>191</sup> The objective response rate was 80% based on investigator assessment and 57.6% based on central review among 35 patients who received carboplatin/paclitaxel/ramucirumab. At a median follow-up of 31.6 months, the median overall survival was 43.8 months. In the phase II S1701 study, 21 patients with unresectable, locally advanced, metastatic, or recurrent thymic carcinoma were randomized to receive carboplatin/paclitaxel with or without ramucirumab.<sup>192</sup> The carboplatin/paclitaxel/ramucirumab group had a higher response rate

than the carboplatin/paclitaxel group (88% versus 40%). However, clinicians should be aware that patients with untreated brain metastases or major standard contraindications to anti-angiogenics were not included in the RELEVANT or S1701 study populations. There is no published experience using carboplatin/paclitaxel/ramucirumab as a preoperative therapy.

The NCCN Panel has designated the following as “Other Recommended” first-line systemic therapy options for patients with thymic carcinomas: CAP with or without prednisone, ADOC, PE, and etoposide/ifosfamide/cisplatin.<sup>62,160,162,164,165</sup> Although the CAP and ADOC regimens have demonstrated efficacy in the treatment of thymic carcinomas, they are not preferred due to their toxicity. Carboplatin/paclitaxel and PE are regimens that can be used in combination with RT as definitive concurrent chemoradiation.

For thymic carcinomas, data on systemic therapy in the second-line setting are limited. The following are categorized by the NCCN Panel as “Preferred” second-line systemic therapy options: gemcitabine with or without capecitabine, lenvatinib, pembrolizumab, and sunitinib (THYM-C 2 of 3).<sup>167,193-196</sup>

Pembrolizumab is active (response rate, 22.5%) as a second-line therapy in patients with thymic carcinomas but is associated with a high rate of severe immune-related adverse events (15%).<sup>194,197</sup> For example, grade 3–4 myocarditis has been reported in 5% to 9% of patients with thymic carcinomas receiving pembrolizumab, which is higher than the rate reported in patients with other malignancies who receive pembrolizumab.<sup>176,194</sup>

Sunitinib is recommended for patients with thymic carcinoma regardless of *c-Kit* mutation status based on data from an open-label phase II study.<sup>195</sup> Out of 23 patients with chemotherapy-refractory thymic



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carcinoma, a partial response with sunitinib was observed in 6 individuals (26%). The single-arm phase II STYLE trial also evaluated sunitinib as subsequent therapy in patients with advanced or recurrent type B3 thymoma and thymic carcinoma.<sup>196</sup> The overall response rate was 21.4% among 28 assessable patients with thymic carcinoma in the intention-to-treat population; the median overall survival was 27.8 months.

Based on data from the single-arm phase II REMORA trial, the objective response rate was 38% among 42 patients with metastatic or recurrent thymic carcinoma who received lenvatinib.<sup>193</sup> The NCCN Panel notes that there is a risk for intolerable adverse effects with lenvatinib and dose reductions may be needed.

“Other Recommended” second-line treatment options for thymic carcinoma include avelumab in combination with axitinib, everolimus, 5-FU in combination with leucovorin, paclitaxel, and pemetrexed.<sup>125,166,170,171,198,199</sup> Avelumab in combination with axitinib was recently added to the Guidelines as a second-line treatment option for thymic carcinoma based on data from the single-arm phase II CAVEATT trial in patients whose advanced thymic carcinoma or type B3 thymoma had progressed after at least one line of platinum-containing chemotherapy.<sup>199</sup> Out of 32 patients in the study, 27 had thymic carcinoma. Prior use of anti-angiogenics was permitted; 4 patients in the study previously received ramucirumab. The overall response rate of those treated with avelumab/axitinib was 34%; however, the response rate of patients who previously received an anti-angiogenic was lower than that of those who had not (15% versus 47%).

Single-agent etoposide and single-agent ifosfamide are recommended by the NCCN Panel as second-line treatment options that may be useful in certain circumstances.<sup>172,200</sup>

Recent data suggest that other systemic regimens may also have activity in patients with advanced, metastatic, or recurrent thymic carcinoma.<sup>201</sup> The NCCN Panel will continue to evaluate emerging clinical evidence on an annual basis to determine if additional systemic therapy options should be recommended in these Guidelines.

### Surveillance: Thymic Carcinoma

Due to the aggressive nature of the disease, patients with thymic carcinoma are at higher risk of recurrence than those diagnosed with thymoma. In a subgroup of patients whose tumor was completely resected, one study found that 51.2% of patients with thymic carcinoma developed disease recurrence compared with 7.8% of patients with thymoma.<sup>5</sup> Additionally, progression to distant sites may occur more frequently in patients with thymic carcinoma than those with thymoma.<sup>13</sup>

A wide range of time to recurrence has been reported. For instance, one study reported that the time to recurrence ranged from 2 to 108 months, with a median of 11 months, among 40 patients with thymic carcinoma who had undergone surgical resection with curative intent.<sup>9</sup>

For patients with completely resected Masaoka-Koga stage I thymic carcinoma (and no capsular invasion), the NCCN Panel recommends that surveillance imaging should consist of chest CT with contrast every 6 to 12 months for 2 years, then annually until 5 years. Surveillance for all other patients treated for thymic carcinoma should include chest CT every 3 to 6 months for 2 years, then annually for 5 years. However, the NCCN Panel notes that the duration, frequency, and type of imaging for surveillance for thymic carcinomas have not been evaluated in prospective studies.



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## Thymomas and Thymic Carcinomas

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### Summary

Thymomas and thymic carcinomas are rare thymic epithelial tumors that originate in the thymus. These NCCN Guidelines outline the evaluation, treatment, and surveillance recommendations for patients with thymomas and thymic carcinomas. Involvement of a multidisciplinary team that includes radiation oncologists, thoracic surgeons, medical oncologists, pathologists, neurologists, and diagnostic imaging specialists is critical for the optimal care of patients with thymomas or thymic carcinomas. If clinically feasible, surgery is recommended since a complete resection is considered a key prognostic factor. A multimodal treatment approach that includes surgery, RT, and/or systemic therapy may be needed for those with poor prognosis and/or advanced disease. The NCCN Panel will continue to update these Guidelines annually based on clinical evidence and consensus.





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### References

1. Marx A, Chan JKC, Chalabreysse L, et al. The 2021 WHO Classification of tumors of the thymus and mediastinum: what is new in thymic epithelial, germ cell, and mesenchymal tumors? J Thorac Oncol 2022;17:200-213. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34695605>.
2. Marx A, Detterbeck F, Marom EM. Tumors of the Thymus. WHO Classification of Tumours Editorial Board. Thoracic Tumours, 5th ed. Vol. 7: World Health Organization; 2021.
3. Engels EA. Epidemiology of thymoma and associated malignancies. J Thorac Oncol 2010;5:S260-265. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859116>.
4. Gerber TS, Strobl S, Marx A, et al. Epidemiology of thymomas and thymic carcinomas in the United States and Germany, 1999-2019. Front Oncol 2023;13:1308989. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/38264756>.
5. Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. Ann Thorac Surg 2003;76:878-884; discussion 884-885. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12963221>.
6. Mariano C, Ionescu DN, Cheung WY, et al. Thymoma: a population-based study of the management and outcomes for the province of British Columbia. J Thorac Oncol 2013;8:109-117. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23242441>.
7. Masaoka A. Staging system of thymoma. J Thorac Oncol 2010;5:S304-312. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859124>.
8. Proceedings of the first international conference on thymic malignancies. August 20-21, 2009. Bethesda, Maryland, USA. J Thorac Oncol 2010;5:S259-370. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21275152>.
9. Litvak AM, Woo K, Hayes S, et al. Clinical characteristics and outcomes for patients with thymic carcinoma: evaluation of Masaoka staging. J Thorac Oncol 2014;9:1810-1815. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25393794>.
10. Ahmad U, Yao X, Detterbeck F, et al. Thymic carcinoma outcomes and prognosis: results of an international analysis. J Thorac Cardiovasc Surg 2015;149:95-100, 101.e101-102. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25524678>.
11. Roden AC, Ahmad U, Cardillo G, et al. Thymic carcinomas-a concise multidisciplinary update on recent developments from the Thymic Carcinoma Working Group of the International Thymic Malignancy Interest Group. J Thorac Oncol 2022;17:637-650. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35227908>.
12. Zhao Y, Shi J, Fan L, et al. Surgical treatment of thymoma: an 11-year experience with 761 patients. Eur J Cardiothorac Surg 2016;49:1144-1149. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26324679>.
13. Huang J, Rizk NP, Travis WD, et al. Comparison of patterns of relapse in thymic carcinoma and thymoma. J Thorac Cardiovasc Surg 2009;138:26-31. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19577051>.
14. PubMed. Available at: <https://pubmed.ncbi.nlm.nih.gov/about/>. Accessed April 24, 2025.
15. Freedman-Cass DA, Fischer T, Alpert AB, et al. The value and process of inclusion: using sensitive, respectful, and inclusive language and images in NCCN content. J Natl Compr Canc Netw 2023;21:434-441. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37156485>.
16. den Bakker MA, Marx A, Mukai K, Strobel P. Mesenchymal tumours of the mediastinum--part I. Virchows Arch 2015;467:487-500. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26358059>.
17. Araki T, Nishino M, Gao W, et al. Anterior mediastinal masses in the Framingham Heart study: prevalence and CT image characteristics. Eur J Radiol Open 2015;2:26-31. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25705709>.
18. Marchevsky A, Marx A, Strobel P, et al. Policies and reporting guidelines for small biopsy specimens of mediastinal masses. J Thorac Oncol 2011;6:S1724-1729. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847054>.
19. Strollo DC, Rosado de Christenson ML, Jett JR. Primary mediastinal tumors. Part 1: tumors of the anterior mediastinum. Chest 1997;112:511-522. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9266892>.
20. Strollo DC, Rosado-de-Christenson ML, Jett JR. Primary mediastinal tumors: part II. Tumors of the middle and posterior mediastinum. Chest



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

1997;112:1344-1357. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/9367479>.

21. Rashid OM, Cassano AD, Takabe K. Thymic neoplasm: a rare disease with a complex clinical presentation. *J Thorac Dis* 2013;5:173-183. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23585946>.

22. Detterbeck FC, Parsons AM. Management of stage I and II thymoma. *Thorac Surg Clin* 2011;21:59-67, vi-vii. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21070987>.

23. Detterbeck FC, Zeeshan A. Thymoma: current diagnosis and treatment. *Chin Med J (Engl)* 2013;126:2186-2191. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23769581>.

24. Almeida P, Heller D. Anterior Mediastinal Mass. [Updated 2024 Apr 19] StatPearls [Internet]: Treasure Island (FL): StatPearls Publishing. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK546608/>. Accessed April 24, 2025.

25. Barth TFE, Leithäuser F, Joos S, et al. Mediastinal (thymic) large B-cell lymphoma: where do we stand? *Lancet Oncol* 2002;3:229-234. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12067685>.

26. Ferolla P, Falchetti A, Filosso P, et al. Thymic neuroendocrine carcinoma (carcinoid) in multiple endocrine neoplasia type 1 syndrome: the Italian series. *J Clin Endocrinol Metab* 2005;90:2603-2609. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15713725>.

27. Teh BT. Thymic carcinoids in multiple endocrine neoplasia type 1. *J Intern Med* 1998;243:501-504. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9681849>.

28. Moran CA, Suster S. Primary germ cell tumors of the mediastinum: I. Analysis of 322 cases with special emphasis on teratomatous lesions and a proposal for histopathologic classification and clinical staging. *Cancer* 1997;80:681-690. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9264351>.

29. McKenney JK, Heerema-McKenney A, Rouse RV. Extragonadal germ cell tumors: a review with emphasis on pathologic features, clinical prognostic variables, and differential diagnostic considerations. *Adv Anat Pathol* 2007;14:69-92. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17471115>.

30. Yokoi K, Kondo K, Fujimoto K, et al. JLCS medical practice guidelines for thymic tumors: summary of recommendations. *Jpn J Clin*

*Oncol* 2017;47:1119-1122. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/29036455>.

31. Strange CD, Truong MT, Ahuja J, et al. Imaging evaluation of thymic tumors. *Mediastinum* 2023;7:28. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37701637>.

32. Strange CD, Ahuja J, Shroff GS, et al. Imaging evaluation of thymoma and thymic carcinoma. *Front Oncol* 2021;11:810419. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35047412>.

33. Quint LE, Reddy RM, Lin J, et al. Imaging in thoracic oncology: case studies from Multidisciplinary Thoracic Tumor Board: (part 2 of 2 part series). *Cancer Imaging* 2013;13:440-447. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24325879>.

34. Marom EM, Rosado-de-Christenson ML, Bruzzi JF, et al. Standard report terms for chest computed tomography reports of anterior mediastinal masses suspicious for thymoma. *J Thorac Oncol* 2011;6:S1717-1723. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847053>.

35. Marom EM. Imaging thymoma. *J Thorac Oncol* 2010;5:S296-303. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859123>.

36. Carter BW, Lichtenberger JP, 3rd, Benveniste MF. MR imaging of thymic epithelial neoplasms. *Top Magn Reson Imaging* 2018;27:65-71. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29613961>.

37. Carter BW, Marom EM, Detterbeck FC. Approaching the patient with an anterior mediastinal mass: a guide for clinicians. *J Thorac Oncol* 2014;9:S102-109. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25396306>.

38. Moran CA, Weissferdt A, Kalhor N, et al. Thymomas I: a clinicopathologic correlation of 250 cases with emphasis on the World Health Organization schema. *Am J Clin Pathol* 2012;137:444-450. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22338057>.

39. 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:S1710-1716. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847052>.

40. Huang J, Detterbeck FC, Wang Z, Loehrer PJ, Sr. Standard outcome measures for thymic malignancies. *J Thorac Oncol* 2011;6:S1691-1697. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847049>.



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

41. Moran CA, Walsh G, Suster S, Kaiser L. Thymomas II: a clinicopathologic correlation of 250 cases with a proposed staging system with emphasis on pathologic assessment. *Am J Clin Pathol* 2012;137:451-461. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22338058>.
42. Kondo K. Tumor-node metastasis staging system for thymic epithelial tumors. *J Thorac Oncol* 2010;5:S352-356. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859132>.
43. Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymomas with special reference to their clinical stages. *Cancer* 1981;48:2485-2492. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7296496>.
44. Benveniste MFK, Betancourt Cuellar SL, Carter BW, et al. Thymic epithelial neoplasms: Tumor-Node-Metastasis staging. *Radiol Clin North Am* 2021;59:183-192. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33551080>.
45. Amin MB, Edge SB, Greene FL, et al. *AJCC Cancer Staging Manual*, 8th edition: Springer International Publishing; 2017:1-1032.
46. Carter BW, Benveniste MF, Madan R, et al. IASLC/ITMIG staging system and lymph node map for thymic epithelial neoplasms. *Radiographics* 2017;37:758-776. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28493800>.
47. Meurgey A, Girard N, Merveilleux du Vignaux C, et al. Assessment of the ITMIG Statement on the WHO Histological Classification and of the Eighth TNM Staging of Thymic Epithelial Tumors of a Series of 188 Thymic Epithelial Tumors. *J Thorac Oncol* 2017;12:1571-1581. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28694035>.
48. Detterbeck FC, Stratton K, Giroux D, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposal for an evidence-based stage classification system for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol* 2014;9:S65-72. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25396314>.
49. Roden AC, Yi ES, Jenkins SM, et al. Reproducibility of 3 histologic classifications and 3 staging systems for thymic epithelial neoplasms and its effect on prognosis. *Am J Surg Pathol* 2015;39:427-441. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25634747>.
50. Fukui T, Fukumoto K, Okasaka T, et al. Clinical evaluation of a new tumour-node-metastasis staging system for thymic malignancies

- proposed by the International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee and the International Thymic Malignancy Interest Group. *Eur J Cardiothorac Surg* 2016;49:574-579. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26547095>.
51. Bhora FY, Chen DJ, Detterbeck FC, et al. The ITMIG/IASLC thymic epithelial tumors staging project: a proposed lymph node map for thymic epithelial tumors in the forthcoming 8th edition of the TNM Classification of malignant tumors. *J Thorac Oncol* 2014;9:S88-96. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25396317>.
52. Liou DZ, Berry MF, Brown LM, et al. The Society of Thoracic Surgeons expert consensus document on the surgical management of thymomas. *Ann Thorac Surg* 2024;118:975-1004. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/38718878>.
53. Fiorelli A, Natale G, Freda C, Santini M. Is thymectomy equivalent to complete thymectomy in non-myasthenic patients with early-stage thymoma? *Interact Cardiovasc Thorac Surg* 2019;28:399-403. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30188996>.
54. Kondo K. Optimal therapy for thymoma. *J Med Invest* 2008;55:17-28. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18319541>.
55. Detterbeck FC, Parsons AM. Thymic tumors. *Ann Thorac Surg* 2004;77:1860-1869. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15111216>.
56. Regnard JF, Magdeleinat P, Dromer C, et al. Prognostic factors and long-term results after thymoma resection: a series of 307 patients. *J Thorac Cardiovasc Surg* 1996;112:376-384. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8751506>.
57. Nakagawa K, Asamura H, Matsuno Y, et al. Thymoma: a clinicopathologic study based on the new World Health Organization classification. *J Thorac Cardiovasc Surg* 2003;126:1134-1140. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14566259>.
58. Rea F, Marulli G, Girardi R, et al. Long-term survival and prognostic factors in thymic epithelial tumours. *Eur J Cardiothorac Surg* 2004;26:412-418. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15296907>.
59. Detterbeck F, Youssef S, Ruffini E, Okumura M. A review of prognostic factors in thymic malignancies. *J Thorac Oncol* 2011;6:S1698-1704. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847050>.





# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

60. Ruffini E, Detterbeck F, Van Raemdonck D, et al. Tumours of the thymus: a cohort study of prognostic factors from the European Society of Thoracic Surgeons database. *Eur J Cardiothorac Surg* 2014;46:361-368. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24482389>.

61. Riely GJ, Huang J. Induction therapy for locally advanced thymoma. *J Thorac Oncol* 2010;5:S323-326. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859127>.

62. Kim ES, Putnam JB, Komaki R, et al. Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. *Lung Cancer* 2004;44:369-379. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15140551>.

63. Kunitoh H, Tamura T, Shibata T, et al. A phase II trial of dose-dense chemotherapy, followed by surgical resection and/or thoracic radiotherapy, in locally advanced thymoma: report of a Japan Clinical Oncology Group trial (JCOG 9606). *Br J Cancer* 2010;103:6-11. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20551960>.

64. Hamaji M, Ali SO, Burt BM. A meta-analysis of induction therapy for advanced thymic epithelial tumors. *Ann Thorac Surg* 2015;99:1848-1856. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25770014>.

65. Attaran S, Acharya M, Anderson JR, Punjabi PP. Does surgical debulking for advanced stages of thymoma improve survival? *Interact Cardiovasc Thorac Surg* 2012;15:494-497. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22700684>.

66. Weksler B, Dhupar R, Parikh V, et al. Thymic carcinoma: a multivariate analysis of factors predictive of survival in 290 patients. *Ann Thorac Surg* 2013;95:299-303. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23141529>.

67. Wright CD. Stage IVA thymoma: patterns of spread and surgical management. *Thorac Surg Clin* 2011;21:93-97, vii. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21070990>.

68. Wright CD. Extended resections for thymic malignancies. *J Thorac Oncol* 2010;5:S344-347. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859130>.

69. Huang J, Rizk NP, Travis WD, et al. Feasibility of multimodality therapy including extended resections in stage IVA thymoma. *J Thorac*

*Cardiovasc Surg* 2007;134:1477-1483; discussion 1483-1474. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18023668>.

70. Raparia K, Schneider F, Roden A, Dacic S. Protocol for the examination of specimens from patients with thymic tumors.: College of American Pathologists; 2024. Available at: [https://documents.cap.org/protocols/Thymus\\_5.0.0.0.REL.CAPCP.pdf](https://documents.cap.org/protocols/Thymus_5.0.0.0.REL.CAPCP.pdf).

71. Pennathur A, Qureshi I, Schuchert MJ, et al. Comparison of surgical techniques for early-stage thymoma: feasibility of minimally invasive thymectomy and comparison with open resection. *J Thorac Cardiovasc Surg* 2011;141:694-701. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21255798>.

72. Ye B, Tantai JC, Ge XX, et al. Surgical techniques for early-stage thymoma: video-assisted thoracoscopic thymectomy versus transsternal thymectomy. *J Thorac Cardiovasc Surg* 2014;147:1599-1603. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24290709>.

73. Sakamaki Y, Oda T, Kanazawa G, et al. Intermediate-term oncologic outcomes after video-assisted thoracoscopic thymectomy for early-stage thymoma. *J Thorac Cardiovasc Surg* 2014;148:1230-1237.e1231. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24560416>.

74. Manoly I, Whistance RN, Sreekumar R, et al. Early and mid-term outcomes of trans-sternal and video-assisted thoracoscopic surgery for thymoma. *Eur J Cardiothorac Surg* 2014;45:e187-193. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24616388>.

75. Liu TJ, Lin MW, Hsieh MS, et al. Video-assisted thoracoscopic surgical thymectomy to treat early thymoma: a comparison with the conventional transsternal approach. *Ann Surg Oncol* 2014;21:322-328. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23982255>.

76. Friedant AJ, Handorf EA, Su S, Scott WJ. Minimally Invasive versus Open Thymectomy for Thymic Malignancies: Systematic Review and Meta-Analysis. *J Thorac Oncol* 2016;11:30-38. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26762737>.

77. Burt BM, Yao X, Shrager J, et al. Determinants of complete resection of thymoma by minimally invasive and open thymectomy: analysis of an international registry. *J Thorac Oncol* 2017;12:129-136. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27566187>.

78. Jurado J, Javidfar J, Newmark A, et al. Minimally invasive thymectomy and open thymectomy: outcome analysis of 263 patients.



## NCCN Guidelines Version 2.2025

### Thymomas and Thymic Carcinomas

Ann Thorac Surg 2012;94:974-981; discussion 981-972. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22748641>.

79. Hess NR, Sarkaria IS, Pennathur A, et al. Minimally invasive versus open thymectomy: a systematic review of surgical techniques, patient demographics, and perioperative outcomes. Ann Cardiothorac Surg 2016;5:1-9. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/26904425>.

80. Yang CJ, Hurd J, Shah SA, et al. A national analysis of open versus minimally invasive thymectomy for stage I to III thymoma. J Thorac Cardiovasc Surg 2020;160:555-567 e515. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32245668>.

81. Hurd J, Haridas C, Potter A, et al. A national analysis of open versus minimally invasive thymectomy for stage I-III thymic carcinoma. Eur J Cardiothorac Surg 2022;62. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/35259241>.

82. Gu Z, Chen C, Wang Y, et al. Video-assisted thoracoscopic surgery versus open surgery for Stage I thymic epithelial tumours: a propensity score-matched study. Eur J Cardiothorac Surg 2018;54:1037-1044.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30016438>.

83. Rowse PG, Roden AC, Corl FM, et al. Minimally invasive thymectomy: the Mayo Clinic experience. Ann Cardiothorac Surg 2015;4:519-526. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/26693147>.

84. Xie A, Tjahjono R, Phan K, Yan TD. Video-assisted thoracoscopic surgery versus open thymectomy for thymoma: a systematic review. Ann Cardiothorac Surg 2015;4:495-508. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/26693145>.

85. Chao YK, Liu YH, Hsieh MJ, et al. Long-term outcomes after thoracoscopic resection of stage I and II thymoma: a propensity-matched study. Ann Surg Oncol 2015;22:1371-1376. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25256127>.

86. Hwang SK, Lee GD, Kang CH, et al. Long-term outcome of minimally invasive thymectomy versus open thymectomy for locally advanced cases. Eur J Cardiothorac Surg 2022;62. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/35445251>.

87. Agatsuma H, Yoshida K, Yoshino I, et al. Video-assisted thoracic surgery thymectomy versus sternotomy thymectomy in patients with

thymoma. Ann Thorac Surg 2017;104:1047-1053. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/28619540>.

88. Yang Y, Dong J, Huang Y. Thoracoscopic thymectomy versus open thymectomy for the treatment of thymoma: A meta-analysis. Eur J Surg Oncol 2016;42:1720-1728. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27139936>.

89. Patel AJ, Smith A, Group ETCS, et al. Robotic-assisted versus video-assisted thoracoscopic surgery for thymic epithelial tumours, from the European Society of Thoracic Surgeons Database. Eur J Cardiothorac Surg 2024;66. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/39325852>.

90. Gomez D, Komaki R, Yu J, et al. Radiation therapy definitions and reporting guidelines for thymic malignancies. J Thorac Oncol 2011;6:S1743-1748. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21847057>.

91. Jackson MW, Palma DA, Camidge DR, et al. The impact of postoperative radiotherapy for thymoma and thymic carcinoma. J Thorac Oncol 2017;12:734-744. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/28126540>.

92. Rimner A, Yao X, Huang J, et al. Postoperative radiation therapy is associated with longer overall survival in completely resected stage II and III thymoma-an analysis of the International Thymic Malignancies Interest Group Retrospective database. J Thorac Oncol 2016;11:1785-1792. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27346413>.

93. Singhal S, Shrager JB, Rosenthal DI, et al. Comparison of stages I-II thymoma treated by complete resection with or without adjuvant radiation. Ann Thorac Surg 2003;76:1635-1641; discussion 1641-1642.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14602300>.

94. Forquer JA, Rong N, Fakiris AJ, et al. Postoperative radiotherapy after surgical resection of thymoma: differing roles in localized and regional disease. Int J Radiat Oncol Biol Phys 2010;76:440-445.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19427738>.

95. Utsumi T, Shiono H, Kadota Y, et al. Postoperative radiation therapy after complete resection of thymoma has little impact on survival. Cancer 2009;115:5413-5420. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19685527>.

96. Korst RJ, Kansler AL, Christos PJ, Mandal S. Adjuvant radiotherapy for thymic epithelial tumors: a systematic review and meta-analysis. Ann



## NCCN Guidelines Version 2.2025

### Thymomas and Thymic Carcinomas

Thorac Surg 2009;87:1641-1647. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19379938>.

97. Fan XW, Yang Y, Wang HB, et al. Intensity modulated radiation therapy plus etoposide/cisplatin for patients with limited advanced unresectable thymic epithelial tumors: a prospective phase 2 study. Int J Radiat Oncol Biol Phys 2020;107:98-105. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/31987968>.

98. Chen YY, Huang CH, Tang Y, Eng HL. Concurrent chemoradiotherapy for unresectable thymic carcinoma. Chang Gung Med J 2004;27:515-522. Available at:

99. Chun SG, Rimner A, Amini A, et al. American Radium Society Appropriate Use Criteria for radiation therapy in the multidisciplinary management of thymic carcinoma. JAMA Oncol 2023;9:971-980. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/37186595>.

100. Wang CL, Gao LT, Lv CX, et al. Outcome of nonsurgical treatment for locally advanced thymic tumors. J Thorac Dis 2016;8:705-710. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27114838>.

101. Gomez D, Komaki R. Technical advances of radiation therapy for thymic malignancies. J Thorac Oncol 2010;5:S336-343. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20859129>.

102. Hartford AC, Palisca MG, Eichler TJ, et al. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guidelines for intensity-modulated radiation therapy (IMRT). Int J Radiat Oncol Biol Phys 2009;73:9-14. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19100920>.

103. Moran JM, Dempsey M, Eisbruch A, et al. Safety considerations for IMRT: executive summary. Med Phys 2011;38:5067-5072. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21978051>.

104. Gregoire V, Mackie TR. State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83). Cancer Radiother 2011;15:555-559. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21802333>.

105. Group IDW, Holmes T, Das R, et al. American Society of Radiation Oncology recommendations for documenting intensity-modulated radiation therapy treatments. Int J Radiat Oncol Biol Phys 2009;74:1311-1318. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19616738>.

106. ATC Guidelines for the use of IMRT (including intra-thoracic treatments). May 31, 2006. Available at:

<http://rrp.cancer.gov/content/docs/imrt.doc>.

107. ICRU Report 83: prescribing, recording, and reporting intensity modulated photon beam therapy (IMRT). Journal of the ICRU 2010;10. Available at:

<http://jicru.oxfordjournals.org/content/10/1.toc>.

108. Kong FM, Pan C, Eisbruch A, Ten Haken RK. Physical models and simpler dosimetric descriptors of radiation late toxicity. Semin Radiat Oncol 2007;17:108-120. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/17395041>.

109. Milano MT, Constine LS, Okunieff P. Normal tissue tolerance dose metrics for radiation therapy of major organs. Semin Radiat Oncol 2007;17:131-140. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/17395043>.

110. Loap P, Scher N, Goudjil F, et al. Proton beam therapy for thymic carcinoma with pericardial involvement. Int J Part Ther 2021;7:65-70. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/33604417>.

111. Parikh RR, Rhome R, Hug E, et al. Adjuvant proton beam therapy in the management of thymoma: a dosimetric comparison and acute toxicities. Clin Lung Cancer 2016;17:362-366. Available at:

<https://pubmed.ncbi.nlm.nih.gov/27372386/>.

112. Vogel J, Berman AT, Lin L, et al. Prospective study of proton beam radiation therapy for adjuvant and definitive treatment of thymoma and thymic carcinoma: Early response and toxicity assessment. Radiother Oncol 2016;118:504-509. Available at:

<https://pubmed.ncbi.nlm.nih.gov/26895711/>.

113. Zhang Z, Wu B, Niu L, et al. Combination percutaneous cryotherapy and iodine-125 seed implantation for unresectable malignant thymoma: experience in 19 patients. Cryobiology 2013;67:170-174. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23846104>.

114. Abtin F, Suh RD, Nasehi L, et al. Percutaneous cryoablation for the treatment of recurrent thymoma: preliminary safety and efficacy. J Vasc Interv Radiol 2015;26:709-714. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25921453>.

115. Girard N. Thymic epithelial tumours: from basic principles to individualised treatment strategies. Eur Respir Rev 2013;22:75-87. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23457169>.





# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

116. Zucali PA, De Vincenzo F, Perrino M, et al. Systemic treatments for thymic tumors: a narrative review. *Mediastinum* 2021;5:24. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35118329>.

117. Falkson CB, Vella ET, Ellis PM, et al. Surgical, radiation, and systemic treatments of patients with thymic epithelial tumors: a systematic review. *J Thorac Oncol* 2023;18:299-312. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/36343922>.

118. Yamada Y, Yoshino I, Nakajima J, et al. Surgical outcomes of patients with stage III thymoma in the Japanese nationwide database. *Ann Thorac Surg* 2015;100:961-967. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26163354>.

119. Kelly RJ, Petrini I, Rajan A, et al. Thymic malignancies: from clinical management to targeted therapies. *J Clin Oncol* 2011;29:4820-4827. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22105817>.

120. Benveniste MF, Korst RJ, Rajan A, et al. A practical guide from the International Thymic Malignancy Interest Group (ITMIG) regarding the radiographic assessment of treatment response of thymic epithelial tumors using modified RECIST criteria. *J Thorac Oncol* 2014;9:S119-124. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25396308>.

121. Hwang Y, Park IK, Park S, et al. Lymph node dissection in thymic malignancies: implication of the ITMIG lymph node map, TNM stage classification, and recommendations. *J Thorac Oncol* 2016;11:108-114. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26762745>.

122. Lewis JE, Wick MR, Scheithauer BW, et al. Thymoma. A clinicopathologic review. *Cancer* 1987;60:2727-2743. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/3677008>.

123. Padda SK, Yao X, Antonicelli A, et al. Paraneoplastic syndromes and thymic malignancies: an examination of the International Thymic Malignancy Interest Group retrospective database. *J Thorac Oncol* 2018;13:436-446. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29191778>.

124. Bernard C, Frih H, Pasquet F, et al. Thymoma associated with autoimmune diseases: 85 cases and literature review. *Autoimmun Rev* 2016;15:82-92. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26408958>.

125. Thomas CR, Wright CD, Loehrer PJ. Thymoma: state of the art. *J Clin Oncol* 1999;17:2280-2289. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10561285>.

126. Gilhus NE, Owe JF, Hoff JM, et al. Myasthenia gravis: a review of available treatment approaches. *Autoimmune Dis* 2011;2011:847393. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22007295>.

127. Mehran R, Ghosh R, Maziak D, et al. Surgical treatment of thymoma. *Can J Surg* 2002;45:25-30. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11837917>.

128. Howard FM, Lennon VA, Finley J, et al. Clinical correlations of antibodies that bind, block, or modulate human acetylcholine receptors in myasthenia gravis. *Ann N Y Acad Sci* 1987;505:526-538. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/3479935>.

129. Khorfan R, Bharat A, Odell DD. Management and Long-Term Outcomes of Advanced Stage Thymoma in the United States. *Ann Thorac Surg* 2021;111:223-230. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32659263>.

130. Bretti S, Berruti A, Loddo C, et al. Multimodal management of stages III-IVa malignant thymoma. *Lung Cancer* 2004;44:69-77. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15013585>.

131. Ried M, Potzger T, Sziklavari Z, et al. Extended surgical resections of advanced thymoma Masaoka stages III and IVa facilitate outcome. *Thorac Cardiovasc Surg* 2014;62:161-168. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23775415>.

132. Detterbeck FC. Evaluation and treatment of stage I and II thymoma. *J Thorac Oncol* 2010;5:S318-322. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859126>.

133. Murakawa T, Nakajima J, Kohno T, et al. Results from surgical treatment for thymoma. 43 years of experience. *Jpn J Thorac Cardiovasc Surg* 2000;48:89-95. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10769987>.

134. Wakely PE, Jr. Fine needle aspiration in the diagnosis of thymic epithelial neoplasms. *Hematol Oncol Clin North Am* 2008;22:433-442. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18514125>.

135. Detterbeck FC, Moran C, Huang J, et al. Which way is up? Policies and procedures for surgeons and pathologists regarding resection specimens of thymic malignancy. *J Thorac Oncol* 2011;6:S1730-1738. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847055>.

136. Omasa M, Date H, Sozu T, et al. Postoperative radiotherapy is effective for thymic carcinoma but not for thymoma in stage II and III thymic epithelial tumors: the Japanese Association for Research on the



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

Thymus Database Study. Cancer 2015;121:1008-1016. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25565590>.

137. Lim YJ, Kim HJ, Wu HG. Role of postoperative radiotherapy in nonlocalized thymoma: propensity-matched analysis of Surveillance, Epidemiology, and End Results database. J Thorac Oncol 2015;10:1357-1363. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26280586>.

138. Tateishi Y, Horita N, Namkoong H, et al. Postoperative radiotherapy for completely resected Masaoka/Masaoka-Koga stage II/III thymoma improves overall survival: an updated meta-analysis of 4746 patients. J Thorac Oncol 2021;16:677-685. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33515812>.

139. Attaran S, McCormack D, Pilling J, Harrison-Phipps K. Which stages of thymoma benefit from adjuvant chemotherapy post-thymectomy? Interact Cardiovasc Thorac Surg 2012;15:273-275. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22552797>.

140. Cowen D, Richaud P, Mornex F, et al. Thymoma: results of a multicentric retrospective series of 149 non-metastatic irradiated patients and review of the literature. FNCLCC trialists. Federation Nationale des Centres de Lutte Contre le Cancer. Radiother Oncol 1995;34:9-16. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7792406>.

141. Ruffini E, Venuta F. Management of thymic tumors: a European perspective. J Thorac Dis 2014;6 Suppl 2:S228-237. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24868441>.

142. Myojin M, Choi NC, Wright CD, et al. Stage III thymoma: pattern of failure after surgery and postoperative radiotherapy and its implication for future study. Int J Radiat Oncol Biol Phys 2000;46:927-933. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10705015>.

143. Mornex F, Resbeut M, Richaud P, et al. Radiotherapy and chemotherapy for invasive thymomas: a multicentric retrospective review of 90 cases. The FNCLCC trialists. Federation Nationale des Centres de Lutte Contre le Cancer. Int J Radiat Oncol Biol Phys 1995;32:651-659. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7790251>.

144. Ruffini E, Mancuso M, Oliaro A, et al. Recurrence of thymoma: analysis of clinicopathologic features, treatment, and outcome. J Thorac Cardiovasc Surg 1997;113:55-63. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9011702>.

145. Park S, Park IK, Kim YT, et al. Comparison of neoadjuvant chemotherapy followed by surgery to upfront surgery for thymic

malignancy. Ann Thorac Surg 2019;107:355-362. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30316850>.

146. Ruffini E, Guerrero F, Brunelli A, et al. Report from the European Society of Thoracic Surgeons prospective thymic database 2017: a powerful resource for a collaborative global effort to manage thymic tumours. Eur J Cardiothorac Surg 2019;55:601-609. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30649256>.

147. Hassan M, Seoud DE. Multimodality treatments in locally advanced stage thymomas. Hematol Oncol Stem Cell Ther 2009;2:340-344. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20118057>.

148. Rajan A, Giaccone G. Chemotherapy for thymic tumors: induction, consolidation, palliation. Thorac Surg Clin 2011;21:107-114, viii. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21070992>.

149. Chu C, Liang Y, Lin X, et al. Hypofractionated radiation therapy combined with weekly chemotherapy in patients with unresectable or recurrent thymic epithelial tumor: a prospective, single-arm phase 2 study (GASTO-1042). Int J Radiat Oncol Biol Phys 2022;114:89-98. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35598797>.

150. Basse C, Thureau S, Bota S, et al. Multidisciplinary tumor board decision making for postoperative radiotherapy in thymic epithelial tumors: insights from the RYTHMIC prospective cohort. J Thorac Oncol 2017;12:1715-1722. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28774861>.

151. Girard N, Lal R, Wakelee H, et al. Chemotherapy definitions and policies for thymic malignancies. J Thorac Oncol 2011;6:S1749-1755. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21847058>.

152. Kelly RJ. Systemic treatment of advanced thymic malignancies. Am Soc Clin Oncol Educ Book 2014:e367-373. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24857125>.

153. Merveilleux du Vignaux C, Dansin E, Mhanna L, et al. Systemic therapy in advanced thymic epithelial tumors: insights from the RYTHMIC prospective cohort. J Thorac Oncol 2018;13:1762-1770. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30138763>.

154. Mizuno T, Okumura M, Asamura H, et al. Surgical management of recurrent thymic epithelial tumors: a retrospective analysis based on the Japanese nationwide database. J Thorac Oncol 2015;10:199-205. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25247341>.



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

155. Chiappetta M, Lococo F, Zanfrini E, et al. The International Thymic Malignancy Interest Group classification of thymoma recurrence: survival analysis and perspectives. *J Thorac Oncol* 2021;16:1936-1945. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34256111>.

156. Chiappetta M, Zanfrini E, Giraldo L, et al. Prognostic factors after treatment for iterative thymoma recurrences: A multicentric experience. *Lung Cancer* 2019;138:27-34. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31606522>.

157. Chiappetta M, Grossi U, Sperduti I, et al. Which is the best treatment in recurrent thymoma? A systematic review and meta-analysis. *Cancers (Basel)* 2021;13:1559. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33805310>.

158. Mizuno T, Chen-Yoshikawa TF, Yoshino I, et al. Updated outcomes of surgical treatment for recurrent thymic tumour: a report from the Japanese nationwide database. *Interdiscip Cardiovasc Thorac Surg* 2024;38. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/38897650>.

159. Schmitt J, Loehrer PJ, Sr. The role of chemotherapy in advanced thymoma. *J Thorac Oncol* 2010;5:S357-360. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20859133>.

160. Loehrer PJ, Sr., Kim K, Aisner SC, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Southeastern Cancer Study Group. *J Clin Oncol* 1994;12:1164-1168. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8201378>.

161. Lemma GL, Lee JW, Aisner SC, et al. Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. *J Clin Oncol* 2011;29:2060-2065. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21502559>.

162. Giaccone G, Ardizzoni A, Kirkpatrick A, et al. Cisplatin and etoposide combination chemotherapy for locally advanced or metastatic thymoma. A phase II study of the European Organization for Research and Treatment of Cancer Lung Cancer Cooperative Group. *J Clin Oncol* 1996;14:814-820. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8622029>.

163. Okuma Y, Saito M, Hosomi Y, et al. Key components of chemotherapy for thymic malignancies: a systematic review and pooled analysis for anthracycline-, carboplatin- or cisplatin-based chemotherapy.

*J Cancer Res Clin Oncol* 2015;141:323-331. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25146529>.

164. Loehrer PJ, Sr., Jiroutek M, Aisner S, et al. Combined etoposide, ifosfamide, and cisplatin in the treatment of patients with advanced thymoma and thymic carcinoma: an intergroup trial. *Cancer* 2001;91:2010-2015. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11391579>.

165. Fornasiero A, Daniele O, Ghiotto C, et al. Chemotherapy for invasive thymoma. A 13-year experience. *Cancer* 1991;68:30-33. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/2049749>.

166. Zucali PA, De Pas T, Palmieri G, et al. Phase II study of everolimus in patients with thymoma and thymic carcinoma previously treated with cisplatin-based chemotherapy. *J Clin Oncol* 2018;36:342-349. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29240542>.

167. Palmieri G, Buonerba C, Ottaviano M, et al. Capecitabine plus gemcitabine in thymic epithelial tumors: final analysis of a Phase II trial. *Future Oncol* 2014;10:2141-2147. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25471029>.

168. Loehrer PJ, Sr., Wang W, Johnson DH, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group Phase II Trial. *J Clin Oncol* 2004;22:293-299. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14722038>.

169. Kirzinger L, Boy S, Marienhagen J, et al. Octreotide LAR and prednisone as neoadjuvant treatment in patients with primary or locally recurrent unresectable thymic tumors: a phase II study. *PLoS One* 2016;11:e0168215. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27992479>.

170. Gbolahan OB, Porter RF, Salter JT, et al. A phase II study of pemetrexed in patients with recurrent thymoma and thymic carcinoma. *J Thorac Oncol* 2018;13:1940-1948. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30121390>.

171. Umemura S, Segawa Y, Fujiwara K, et al. A case of recurrent metastatic thymoma showing a marked response to paclitaxel monotherapy. *Jpn J Clin Oncol* 2002;32:262-265. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12324577>.

172. Bluthgen MV, Boutros C, Fayard F, et al. Activity and safety of oral etoposide in pretreated patients with metastatic or recurrent thymic





# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

epithelial tumors (TET): A single-institution experience. Lung Cancer 2016;99:111-116. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27565923>.

173. Highley MS, Underhill CR, Parnis FX, et al. Treatment of invasive thymoma with single-agent ifosfamide. J Clin Oncol 1999;17:2737-2744. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10561348>.

174. Konstantina T, Konstantinos R, Anastasios K, et al. Fatal adverse events in two thymoma patients treated with anti-PD-1 immune check point inhibitor and literature review. Lung Cancer 2019;135:29-32. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31446999>.

175. Argentiero A, Solimando AG, Ungaro V, et al. Case report: lymphocytosis associated with fatal hepatitis in a thymoma patient treated with anti-PD1: new insight into the immune-related storm. Front Oncol 2020;10:583781. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/33381454>.

176. Cho J, Kim HS, Ku BM, et al. Pembrolizumab for patients with refractory or relapsed thymic epithelial tumor: an open-label phase II trial. J Clin Oncol 2019;37:2162-2170. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/29906252>.

177. Kumar V, Garg M, Goyal A, et al. Changing pattern of secondary cancers among patients with malignant thymoma in the USA. Future Oncol 2018;14:1943-1951. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/30081670>.

178. Pan CC, Chen PC, Wang LS, et al. Thymoma is associated with an increased risk of second malignancy. Cancer 2001;92:2406-2411.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11745297>.

179. Ogawa K, Toita T, Uno T, et al. Treatment and prognosis of thymic carcinoma: a retrospective analysis of 40 cases. Cancer 2002;94:3115-3119. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12115342>.

180. Brascia D, De Palma A, Schiavone M, et al. Lymph nodes involvement and lymphadenectomy in thymic tumors: tentative answers for unsolved questions. Cancers (Basel) 2021;13:5085. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/34680234>.

181. Wu JX, Chen HQ, Shao LD, et al. Long-term follow-up and prognostic factors for advanced thymic carcinoma. Medicine (Baltimore) 2014;93:e324. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25526488>.

182. Marx A, Rieker R, Toker A, et al. Thymic carcinoma: is it a separate entity? From molecular to clinical evidence. Thorac Surg Clin 2011;21:25-31 v-vi. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21070984>.

183. Moran CA, Suster S. Thymic carcinoma: current concepts and histologic features. Hematol Oncol Clin North Am 2008;22:393-407. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18514123>.

184. Okuma Y, Hosomi Y, Watanabe K, et al. Clinicopathological analysis of thymic malignancies with a consistent retrospective database in a single institution: from Tokyo Metropolitan Cancer Center. BMC Cancer 2014;14:349. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/24885581>.

185. Ruffini E, Detterbeck F, Van Raemdonck D, et al. Thymic carcinoma: a cohort study of patients from the European society of thoracic surgeons database. J Thorac Oncol 2014;9:541-548. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24736078>.

186. Yano M, Sasaki H, Yokoyama T, et al. Thymic carcinoma: 30 cases at a single institution. J Thorac Oncol 2008;3:265-269. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18317069>.

187. Rimner A, Ahmad U, Lobaugh SM, et al. Postoperative radiation therapy for thymic carcinoma: an analysis of the International Thymic Malignancy Interest Group/European Society of Thoracic Surgeons database. J Thorac Oncol 2024;19:626-635. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/38070599>.

188. Mao Y, Wu S. Treatment and survival analyses of completely resected thymic carcinoma patients. Onco Targets Ther 2015;8:2503-2507. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26392777>.

189. Moser B, Scharitzer M, Hacker S, et al. Thymomas and thymic carcinomas: prognostic factors and multimodal management. Thorac Cardiovasc Surg 2014;62:153-160. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23225512>.

190. Hirai F, Yamanaka T, Taguchi K, et al. A multicenter phase II study of carboplatin and paclitaxel for advanced thymic carcinoma: WJOG4207L. Ann Oncol 2015;26:363-368. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25403584>.

191. Proto C, Ganzinelli M, Manglaviti S, et al. Efficacy and safety of ramucirumab plus carboplatin and paclitaxel in untreated metastatic thymic carcinoma: RELEVANT phase II trial (NCT03921671). Ann Oncol



# NCCN Guidelines Version 2.2025

## Thymomas and Thymic Carcinomas

2024;35:817-826. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/38857846>.

192. Tsao AS, Hsieh MH, Koczywas M, et al. S1701, A Randomized Phase 2 Trial of Carboplatin-Paclitaxel With and Without Ramucirumab in Patients With Locally Advanced, Recurrent, or Metastatic Thymic Carcinoma. JTO Clin Res Rep 2024;5:100738. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/39619274>.

193. Sato J, Satouchi M, Itoh S, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicentre, phase 2 trial. Lancet Oncol 2020;21:843-850. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32502444>.

194. Giaccone G, Kim C, Thompson J, et al. Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. Lancet Oncol 2018;19:347-355. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/29395863>.

195. Thomas A, Rajan A, Berman A, et al. Sunitinib in patients with chemotherapy-refractory thymoma and thymic carcinoma: an open-label phase 2 trial. Lancet Oncol 2015;16:177-186. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25592632>.

196. Proto C, Manglaviti S, Lo Russo G, et al. STYLE (NCT03449173): a phase 2 trial of sunitinib in patients with type B3 thymoma or thymic carcinoma in second and further lines. J Thorac Oncol 2023;18:1070-1081. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37094664>.

197. Giaccone G, Kim C. Durable response in patients with thymic carcinoma treated with pembrolizumab after prolonged follow-up. J Thorac Oncol 2021;16:483-485. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/33248322>.

198. Hellyer JA, Ouseph MM, Padda SK, Wakelee HA. Everolimus in the treatment of metastatic thymic epithelial tumors. Lung Cancer 2020;149:97-102. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/33007678>.

199. Conforti F, Zucali PA, Pala L, et al. Avelumab plus axitinib in unresectable or metastatic type B3 thymomas and thymic carcinomas (CAVEATT): a single-arm, multicentre, phase 2 trial. Lancet Oncol 2022;23:1287-1296. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/36096156>.

200. Conforti F, Pala L, Vivanet G, et al. High-dose continuous-infusion ifosfamide in advanced thymic epithelial Tumors: A TYME network study.

Lung Cancer 2023;176:98-102. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/36630822>.

201. Shukuya T, Asao T, Goto Y, et al. Activity and safety of atezolizumab plus carboplatin and paclitaxel in patients with advanced or recurrent thymic carcinoma (MARBLE): a multicentre, single-arm, phase 2 trial. Lancet Oncol 2025;26:331-342. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/40049197>.