TUMEURS THYMIQUES 2023

Nicolas Girard

Institut du Thorax Curie Montsouris, Institut Curie, Paris, France

DISCLOSURE

- Recherche clinique:
- Amgen
- Astra-Zeneca
- Abbvie
- Beigene
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffmann-La Roche
- Lilly
- Merck
- MSD
- Novartis
- Sivan
- Trizell

- Symposia:
- Amgen
- Astra-Zeneca
- BMS
- Janssen
- Mirati
- MSD
- Pfizer

- Congrès:
- Astra-Zeneca
- MSD

- ITMIG: Président

- Réunions d'experts:
- Amgen
- Astra-Zeneca
- Beigene
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffman-La Roche
- Novartis
- Merck
- MSD
- Pfizer
- Sanofi
- Takeda

Déclaration publique d'intérêt
https://dpi.sante.gouv.fr/dpi-public-webapp/app/recherche/declarant

THYMIC TUMORS ARE RARE CANCERS

Incidence des Tumeurs épithéliales thymiques (TET) en France: mise à jour 2016.

Boucher ME[1], Bluthgen MV[1], Menis J[1], Dansin E[2], Kerjouan M[3], Mazieres J[4], Pichon E[5], Thillays F[6], Massard G[7], Quantin X[8], Oulkhouir Y[9], Westeel V[10], Thiberville L[11], Clement-Duchene C[12], Missy P[13], Thomas P[14], Girard N[15], Besse B[1]

[1]Département d'oncologie médicale, Gustave Roussy, Villejuif, France; [2] Département d'oncologie générale, Oscar Lambret, Lille, France; [3]Département de pneumologie, Centre Hospitalier Universitaire de Rennes, Rennes, France; [4] Département de pneumologie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [5] Département de pneumologie, Hôpital Bretonneau, Tours, France; [6] Département de radiothérapie, Institut de Cancérologie de l'ouest, Rouen, France; [7]Département de chirurgie thoracique, Centre Hospitalier Universitaire de Strasbourg, Strasbourg, France; [8] Département de pneumologie, Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [9] Département de pneumologie, Centre Hospitalier Universitaire de Caen, Caen, France; [10] Département de pneumologie, Centre Hospitalier Universitaire de Besançon, Besançon, France; [11] Département de pneumologie, Centre Hospitalier Universitaire de Rouen, Rouen, France; [12] Département d'oncologie médicale, Institut de Cancérologie de Lorraine, Nancy, France; [13]Chef de projet , Intergroupe francophone de cancérologie thoracique, Paris, France [14] Département de chirurgie thoracique, Hôpital Nord, Marseille, France; [15] Département d'oncologie médicale, Université Lyon 1,Institut Curie, Paris, France

marie-eve.boucher.6@ulaval.ca

CONTEXTE

Les **TET** sont rares avec une incidence de 0.13 à 0.32 par 100.000 personnes-années. A ce jour, la plupart de nos données sont issues de séries de cas et que d'études rétrospectives.

RYTHMIC (Réseau Tumeurs THYmiques et Cancer) est un réseau national français né à l'initiative de l'INCa (Institut National du cancer). Ses objectifs sont de coordonner la prise en charge des TET par la discussion systématique en réunion de concertation pluridisciplinaire (RCP) et de recueillir prospectivement les informations dans une base de données nationale centralisée.

OBJECTIF

Rapporter l'incidence des TET dans le réseau RYTHMIC en 2016 et son évolution par rapport à 2015 ainsi que décrire les caractéristiques cliniques et la prise en charge initiale des TET.

METHODES

- Nous avons inclus prospectivement tous les patients avec un nouveau diagnostic de TET discuté en RCP RYTHMIC entre Janvier et Décembre 2016.
-Les données épidémiologiques, cliniques, histopathologiques et chirurgicales furent enregistrées et centralisées dans la base de données.
- Le calcul de l'incidence a été réalisé en fonction des données démographiques de l'Institut national de la statistique et des études économiques (INSEE) au 1er janvier 2017

22e CONGRÈS DE PNEUMOLOGIE DE LANGUE FRANÇAISE

RESULTATS

Population

Tableau 1. Caractéristiques cliniques et prise en charge thérapeutique initiale

Caractéristiques cliniques	Fréquence N= 259	%
Age		
Médiane (interquartile)	63	
Sexe		
Homme	134	51.7%
Maladies auto-immunes	**55**	**21.2%**
Myasthénie	40	72.7%
Thrombopénie auto-immune	2	
Erythroblastopénie	1	
Anémie hémolytique	1	
Lupus érythémateux disséminé	1	
Polyarthrite rhumatoïde	1	
Autres	9	
Antécédent de cancer	**26**	**10.0%**
Sein	8	
Mélanome	7	
Prostate	5	
Poumon	2	
Lymphome	1	
Autres	4	
Modalités diagnostiques		
Exérèse chirurgicale	166	64.1%
Biopsie chirurgicale	29	11.2%
Biopsie guidée par l'imagerie	63	24.3%

Traitements	Fréquence N= 247	%
Traitement Primaire		
Chirurgie d'emblée	194	78.5%
Chimiothérapie néoadjuvante	24	10%
Chimiothérapie exclusive	25	10,1%
Chimioradiothérapie	3	1%
Radiothérapie exclusive	1	0.4%
Voie d'abord chirurgicale		
Sternotomie médiane	130	59.6%
Thoracotomie latérale	18	8.3%
Vidéothoracoscopie (VATS)	38	17.4%
Assistée par robot	12	5.5%
Cervicotomie	2	0.9%
Inconnu	18	
Régime de chimiothérapie		
CAP	28	53.8%
Carboplatine- Paclitaxel	14	26.9%
VIP	1	1.9%
Autres	9	17,4%

Figure 1.
Distribution des sous-types histologiques (OMS 2004)

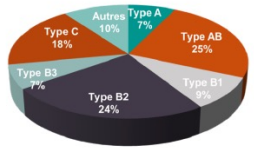
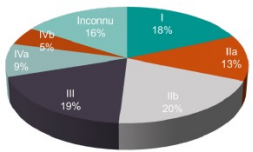
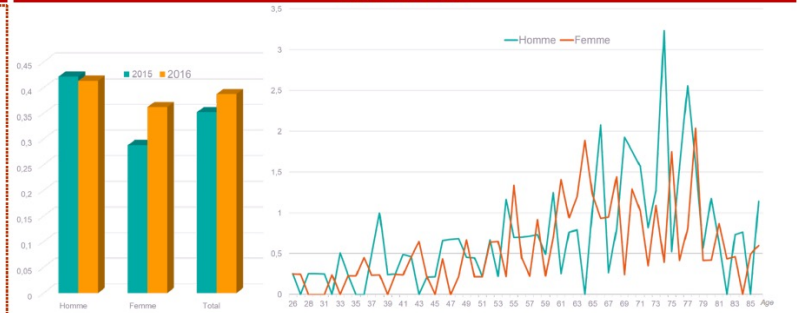


Figure 2.
Distribution du stade (Masaoka-Koga modifié par l'ITMIG)



Incidence 2015 - 2016



A. Incidence 2015 et 2016 des tumeurs thymiques observées en France (par 100.000 pers.-année) en fonction du sexe **B.** Incidence 2016 des tumeurs thymiques en fonction de l'âge et du sexe

CONCLUSIONS

Basée sur l'activité de RYTHMIC en 2016, l'incidence annuelle des TET est de 0.39 cas par 100.000 personnes. Bien que la déclaration au réseau soit obligatoire, certaines TET ne sont toujours pas déclarées et il est possible que l'on sous-estime encore l'incidence réelle. Malgré tout, l'incidence observée est supérieure aux données de la littérature. A suivre dans le future la biopsie sous imagerie et ma chirurgie mini-invasive comme éléments marquants de la prise en charge des TET.

LIENS D'INTERET

Les auteurs n'ont aucun lien d'intérêt à déclarer.

LESS RARE IN 2022

GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

#1629P

Increased incidence of Thymic Epithelial Tumors during COVID19 pandemic: A retrospective analysis from the French RYTHMIC network

Benitez JC[1], Florez-Arango J[1], Boucher ME[1], Dansin E[2], Kerjouan M[3], Bigay-Game L[4], Pichon E[5], Thillays F[5], Falcoz PE[7], Lyubimova S[8], Oulkhouir Y[9], Calcagno F[10], Thiberville L[11], Clément-Duchêne C[12], Westeel V[13], Missy P[13], Thomas P[14], Maury JM[15], Molina T[16], Girard N[17], Besse B[1]

[1]1Gustave Roussy, Villejuif, France; [2]Oscar Lambret, Lille, France; [3]Centre Hospitalier Universitaire de Rennes, Rennes, France; [4]Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [5]Hôpital Bretonneau, Tours, France; [6]Institut de Cancérologie de l'ouest, Rouen, France; [7]Centre Hospitalier Universitaire de Strasbourg, Strasbourg, France; [8]Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [9]Centre Hospitalier Universitaire de Caen, Caen, France; [10]Centre Hospitalier Universitaire de Besançon, Besançon, France; [11]Centre Hospitalier Universitaire de Rouen, Rouen, France; [12]Institut de Cancérologie de Lorraine, Nancy, France; [13]Intergroupe Francophone de Cancérologie Thoracique, Paris, France [14]Hôpital Nord, Marseille, France; [15]Department of thoracic surgery lung and heart lung transplantation , Lyon, France; [16]Hôpital Universitaire Necker Enfants Malades, Paris, France; [17]Université Lyon 1, Institut Curie, Paris, France.

Background

- TETs are rare malignancies ranging from more indolent thymoma (T) A to aggressive thymic carcinoma (TC).
- The incidence rate of TET ranges from 0.13 to 0.32 per 100 000 person/year, although limited data is available.
- Because of respiratory complications, patients with covid19 infection frequently had chest CT-scan, leading to a potential overdiagnosis of asymptomatic thoracic lesion, including TET.
- Here, we report the incidence rate of TET by year during first decade of the French RYTHMIC network.

Methods

- RYTHMIC is a French network for TETs composed of national and regional expert centers, with the objective of systematic discussion of patient's management at a single national tumor board, based on consensual guidelines.
- We conducted a retrospective analysis of 3667 patients gathered in RYTHMIC registry between January 2012 and April 2022.
- Data were prospectively collected in the registry. We aimed to assess clinic-pathological and epidemiological characteristics of TETs in RYTHMIC cohort.

josecarlos.benitez-montanez@gustaveroussy.fr
@JcbenitezMD

**First author declare no conflict of interest.*

Results

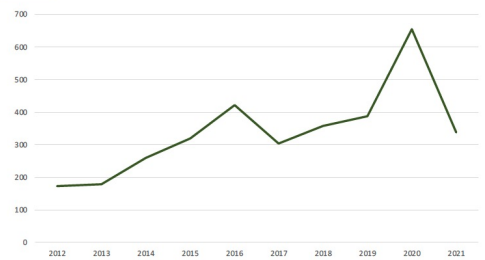


Figure 1. *Line chart representing incidence of RYTHMIC cohort from January 2012 to September 2021.* 3667 patients have been included in the analysis. Number of new patients in RYTHMIC has increased since the development of the registry due to network organization, however, we observed a pic of incidence in 2020 during SARcov-19 pandemic.

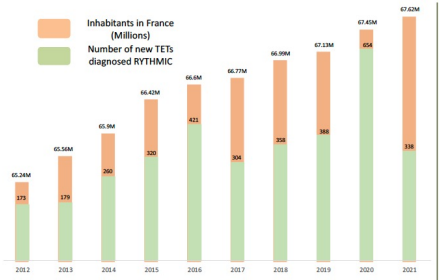


Figure 2. *Barplot representing France population and RYTHMIC cohort development.* The prevalence of TETs in France based on RYTHMIC nationwide registry was 0.0054% at 30th of March 2022 cut-off. * Data is shown until September 2021. # France population (orange) is shown in millions of inhabitants; green color represents number of patients gathered in RYTHMIC cohort.

Year	New patients (N)	France population (M)	1 year increased incidence of France population (%)	Incidence x 100.000 inhabitans	1 year increased incidence of TET in RYTHMIC (%)
2012	173	65,24	---	0,26	---
2013	179	65,56	100,51	0,27	103
2014	260	66,13	100,8	0,39	144
2015	320	66,42	100,3	0,48	123
2016	421	66,6	100,27	0,63	131
2017	304	66,77	100,31	0,45	71
2018	358	66,99	100,38	0,53	117
2019	388	67,13	100,29	0,57	107
2020	654	67,45	100,26	0,97	170
2021	338	67,62	100,17	0,49	50

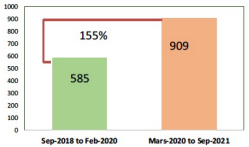


Table 2. *Cumulative incidence.* In 2020, incidence x 100 000 person/year was 0.97 an increase of 170% regarding precedent years. Between Mars 2020 to September 2021 (pic of the pandemic period) there war an 155% increased of new TETs diagnosis comparing to the same precedent period.

	Variable	N	%
Gender	Male	1882	51,3
	Female	1784	48,7
Age median (mean, range)		61, 58,6 (9-92)	
AID	Yes	552	15
Histological subtype	A	146	4
	AB	395	10,7
	B1	231	6,3
	B2	540	14,7
	B3	246	6,7
	TC	242	6,6
MK	I	358	9,8
	IIa	308	8,4
	IIb	272	7,4
	III	366	10
	IVa	182	5
	IVb	159	4,3
Resected		1156	32
Resection	R0	786	68
	R1	237	20,5
	R2	43	4

Table 1 : *RYTHMIC cohort.* The median age at diagnosis was 63.5 (range 9-91). 15% (n=552) of AIDs, mainly myasthenia Gravis (n=411, 74.4%). T B2 was the most frequent (n=540, 14.7%) followed by AB (10.7%), B3 (6.7%), TC (6.6%), B1 (6.3%) and, A (4%). Most of the pts were diagnosed encapsulated (MK I, n=358) or with invasion of the capsule (MK IIa and IIb, n= 308 and 272, respectively).

Conclusions

- Incidence of TETs in our network is higher than previously reported.
- In 2020, we observed a pic in the incidence (170% compared to the average rate), potentially due to the COVID induced CT-scans.

THYMIC TUMORS: TREATMENT STRATEGIES

THYMIC TUMORS: TREATMENT STRATEGIES

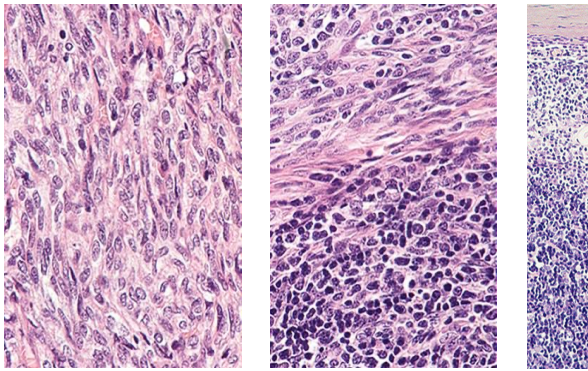
3 KEY POINTS TO KEEP IN MIND IN THE CLINIC

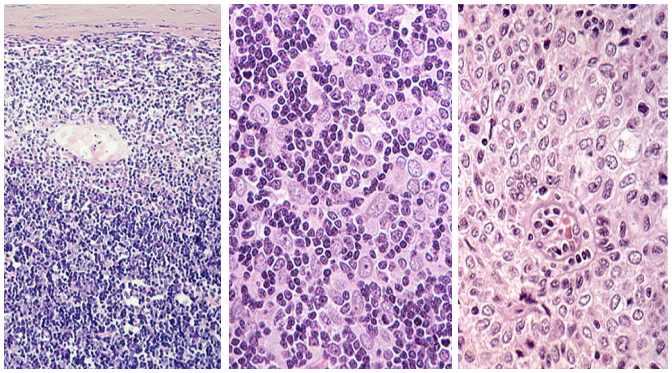
#1 MAKE SURE OF THE DIAGNOSIS

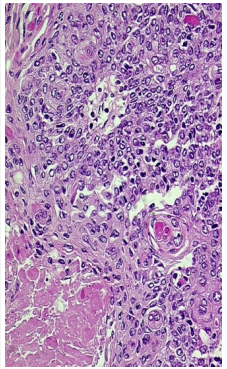
World Health Organization 2015

Thymoma | **Carcinoma**

A | **AB** | **B1** | **B2** | **B3**







"Médullary" | Mixed | "Cortical" | SCC

#1 MAKE SURE OF THE DIAGNOSIS

Pathological review

Pathological Central Review of 290 Thymic Epithelial Tumors (TET): The French National Network RYTHMIC Experience

Molina TJ[1], Bluthgen MV[2*], Chalabreysse L[3], De Montpréville VT[4], De Muret A[5], Hofman V[6], Lantuejoul S[7], Parrens M[8], Rouquette I[9], Secq V[10], Girard N[11], Marx A[12], Besse B[2]

[1]Service d'anatomie pathologique, AP-HP, Hôpital Universitaire Necker-Enfants-Malades, Université Paris Descartes, Sorbonne Paris Cité, France; [2]Department of cancer medicine, Gustave Roussy, Villejuif, France; [3]Département de pathologie, Hôpital Louis-Pradel, hospices civils de Lyon, France; [4]Service d'anatomie pathologique, Institut d'oncologie thoracique, Centre chirurgical Marie-Lannelongue, Le Plessis-Robinson, France; [5]Département de pathologie, CHU de Tours, France; [6]Laboratoire de pathologie cellulaire et expérimentale, Hôpital Pasteur, CHU de Nice, France; [7]Département d'anatomie et de cytologie pathologiques, CHU de Grenoble, France; [8]Département de pathologie, CHU de Bordeaux, France; [9]Service d'anatomie pathologique, CHU Ranguell, Toulouse, France; [10]Laboratoire d'anatomie pathologique, Hôpital Nord, AP-HM, Marseille, France; [11] Département des maladies respiratoires, Hôpital Louis-Pradel, hospices civils de Lyon, Lyon, France; Institut de Pathologie; [12]Université médicale de Mannheim, Université de Heidelberg, Mannheim, Germany. *Maria-Virginia.BLUTHGEN@gustaveroussy.fr

BACKGROUND

- RYTHMIC (Réseau tumeurs THYMiques et Cancer) is a nationwide network for TET appointed in 2012 by the French National Cancer Institute (INCa).
- The objectives of the network are territorial coverage by regional expert centers with systematic discussion of patients management at national tumor board and central pathologic review of all cases.
- RYTHMIC Tumor Board is based on initial histopathological diagnosis.

OBJECTIVE

- To evaluate the clinical impact of central pathological review of the cases discussed at clinical tumor board

PATIENTS AND METHODS

- Pathological central review of patients diagnosed with Thymoma (T) or Thymic carcinoma (TC) from January 2012 to December 2015 was made by a panel of 10 expert pathologists from the working group.
- Assessment of agreement or disagreement between the initial institution and the panel review was made according the WHO 2004/2015 and new ITMIG proposals for histologic typing and staging.
- Discordances were classified as "major" when they would have changed the therapy or management of patients according to the RYTHMIC guidelines.
- RYTHMIC Guidelines post-operative recommendations are based on histopathological subtype, Masaoka-Koga stage and resection status.

RESULTS

-Specimens from a total of 290 patients were reviewed: discordances were identified in 37.6% of the patients (n=109). Among them, 60% concerned histological diagnosis / subtype (n=65), 32% staging (n=35) and 8% both (n=9). The most frequent disagreement was the sub-diagnosis of stage III reflecting the underlying difficulty in pericardial / mediastinal pleura histological involvement recognition. (Figure 1)

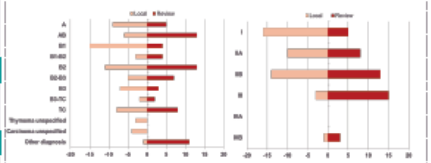


Figure 1. Description of discordances over 109 patients according to histology (left) and stage (right) before and after pathological central review

Discordances were classified as minor in 31% of the patients (n=90) and as major discordances in 6.6 % (n=19) of them. (Figure 2)

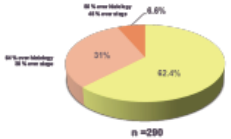


Figure 2. Description of pathological central review classified according to type of discordances.

Figure 3.Description of major discordances identified in 19 patients (6.6%).
7 patients for whom management of disease should have been modified and 12 patients for whom post-surgical treatment recommendation concerning adjuvant radiotherapy would have been changed.
Additionally, major disagreement between the initial / panel pathology's stage and subsequent interpretation by the working group at national tumor board (RCP) was found in 3 patients

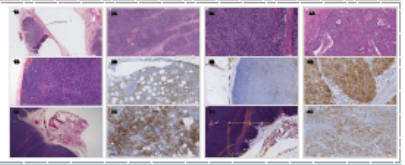


Figure 4. Sub-diagnosis of stage III TETs and AB histology sub-type were the discordances most frequently observed. 1. Stage III with pericardial (A) or mediastinal pleural invasion (B, C). 2. Thymoma AB with biphasic pattern (A),TdT + thymocytes (B) and CD20 expression in epithelial cells (C). 3. Thymoma AB with biphasic pattern (A), CD20+ (B), with minimal mediastinal fat invasion (C). 4. Thymic carcinoma (A) with epithelial expression of CD5 (B), and CD117 / C-KIT (C).

CONCLUSION

The RYTHMIC experience confirms the relevance of an expert histopathological panel diagnosis of thymic malignancies for better decision-making, in particular concerning post-operative radiotherapy to avoid over- or under-treatment of the patients.

ASCO 2016

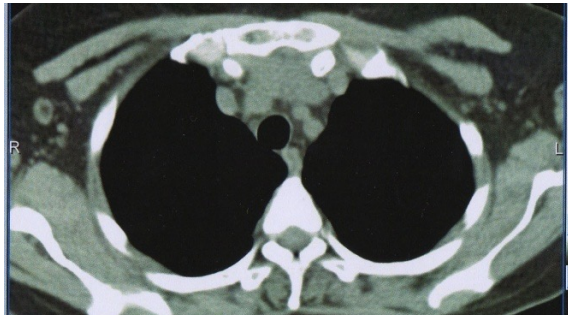
THYMIC TUMORS: TREATMENT STRATEGIES

3 KEY POINTS TO KEEP IN MIND IN THE CLINIC

#1 MAKE SURE OF THE DIAGNOSIS

- **Thymic hyperplasia**

- **CT scan:** low-attenuation, symmetric and fatty pattern, maintaining the bi-pyramidal shape of the thymus

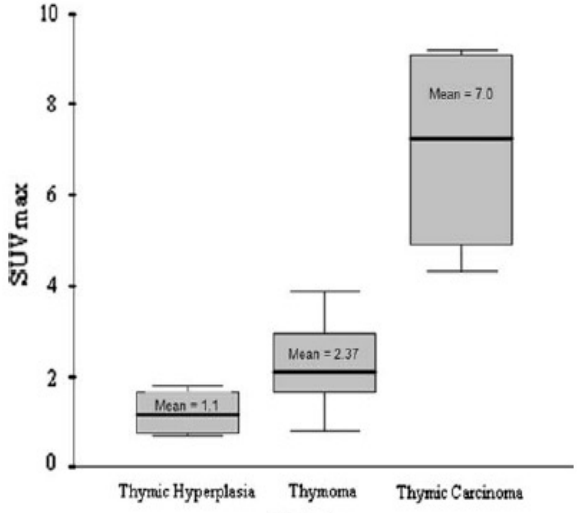


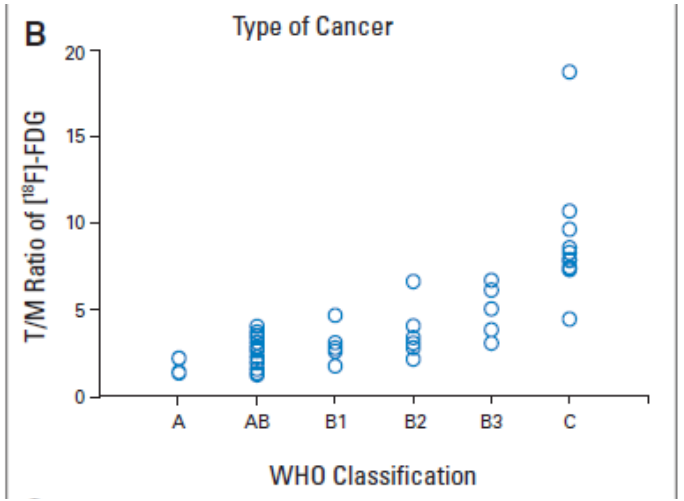
- **“Rebound” hyperplasia:**
  - stress: pneumonia, surgery, burns, corticoid treatment
  - chemotherapy:
    - 10-25% of cases, young adults, intensive treatment

- **Lymphoid hyperplasia**
  - autoimmune and inflammatory disorders
  - connective tissue diseases and vasculitis
  - myasthenia

#1 MAKE SURE OF THE DIAGNOSIS

- 18-FDG PET-scan : hyperplasia vs. thymoma vs. carcinoma



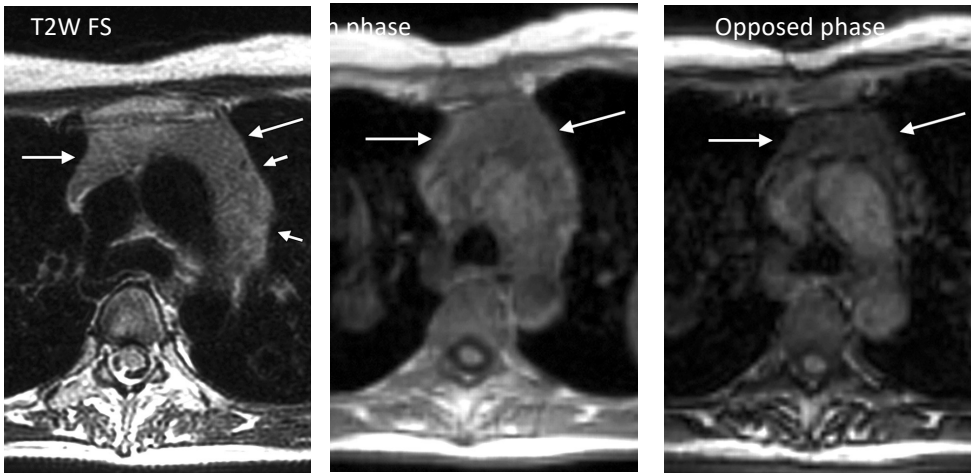


Igai et al .Eur J Cardiothor Surg 2011;40: 143
Kimar et al. Ann Nucl Med 2009; 23:569; Endo et al. Lung Cancer 2008;61:350
Kaira et al. J Clin Oncol 2011;28:3746; Shibata et al. Cancer 2009;115:2531

#1 MAKE SURE OF THE DIAGNOSIS

- Detect microscopic fatty infiltration by showing homogeneous signal decrease on opposed phase images relative to in-phase images, which is not observed in thymoma

DIXON/
Chemical shift
MRI

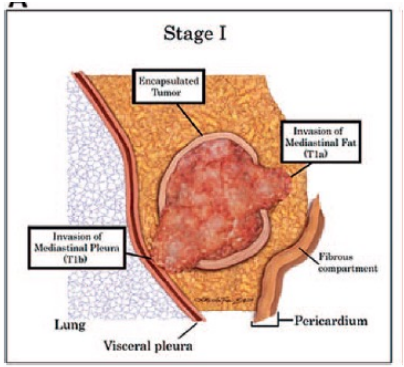


THYMIC TUMORS: TREATMENT STRATEGIES

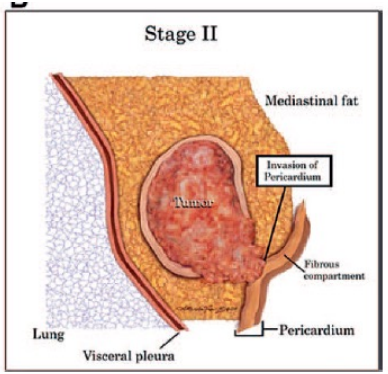
KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

#2 STAGING IS COMPLEX MASAOKA-KOGA TO TNM

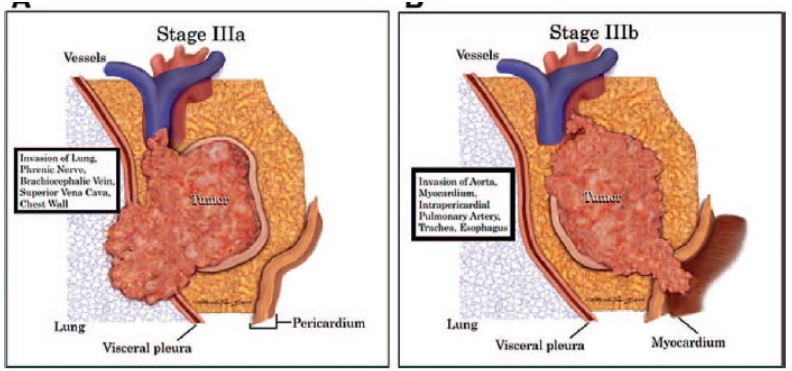
8th TNM staging system



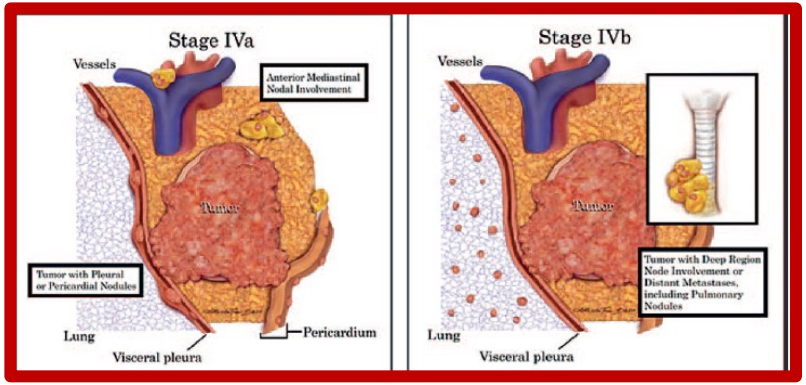
Masaoka-Koga : I, IIA, IIB, III



Masaoka-Koga : III



Masaoka-Koga : III



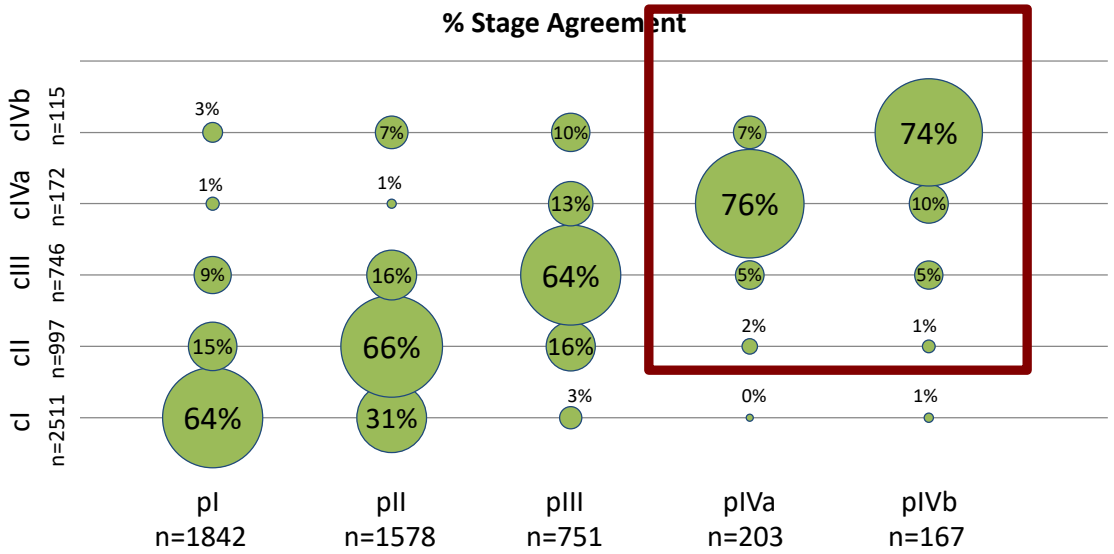
Masaoka-Koga : IVB

Detterbeck et al. J Thorac Oncol 2014;S65-72

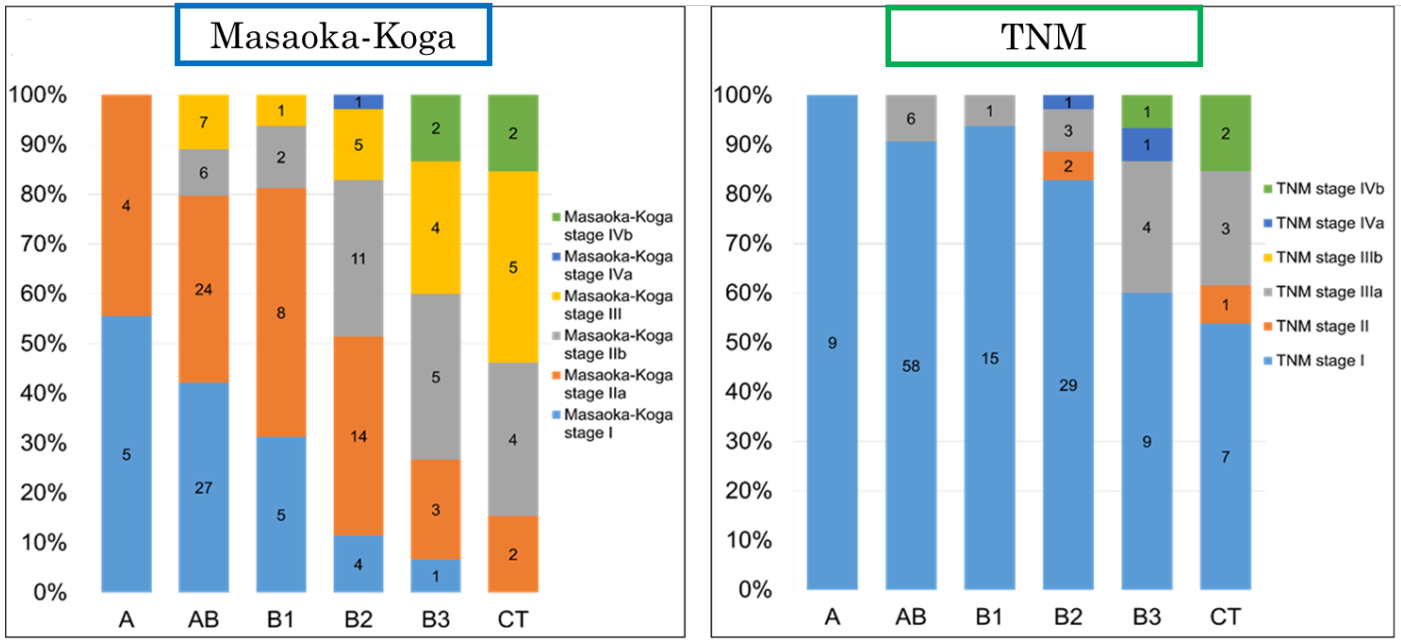
ONCOLOGISTS DO NOT OPERATE PATIENTS NEED FOR A CTNM CLASSIFICATION

Clinical & Pathologic Stage (N=4541)

M & M-K combined



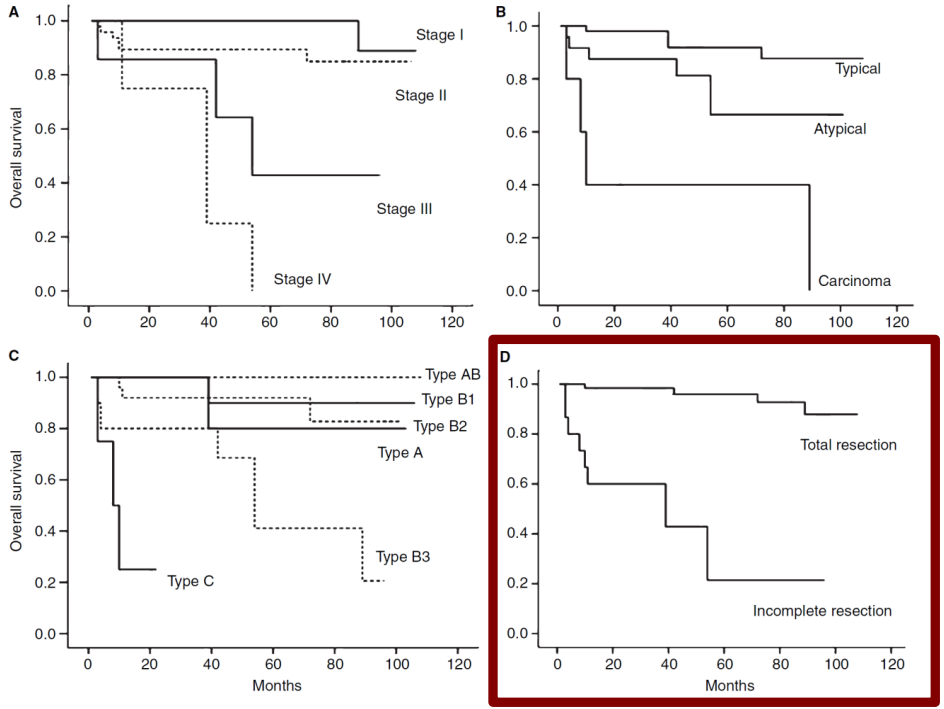
HISTOLOGY AND STAGE ARE CORRELATED MASAOKA-KOGA TO TNM



Meurgey et Girard. J Thorac oncol 2017

#2 STAGE, HISTOLOGY, OTHERS

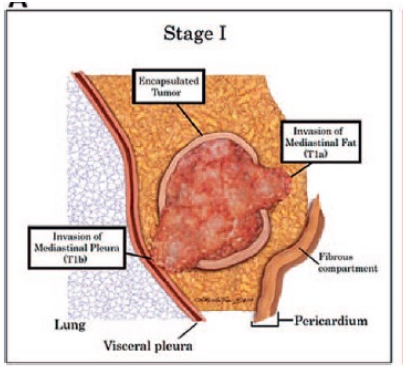
- The most significant prognostic factor in thymic malignancies is **the completion of surgical resection**, whatever classification is used.



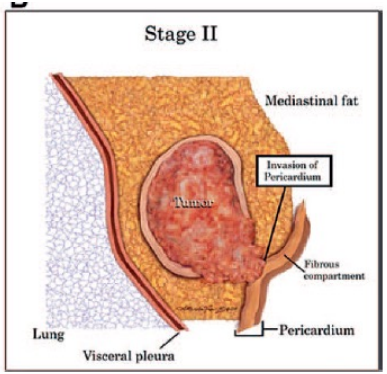
Rossi et al. Histopathology 2008;53:483

#2 STAGE IV DOES NOT EXCLUDE CURATIVE-INTENT LOCAL TREATMENT

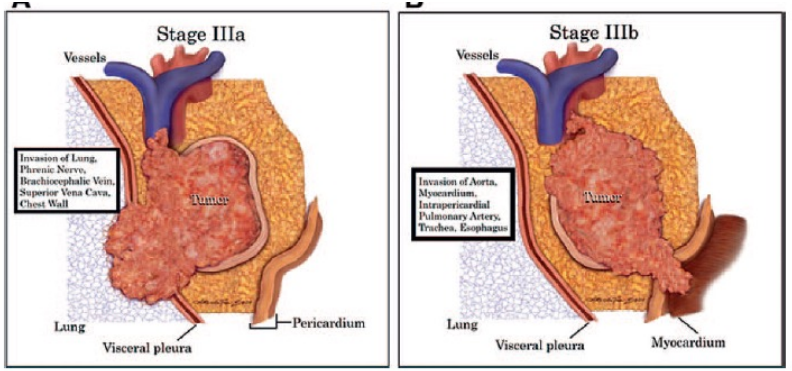
8th TNM staging system



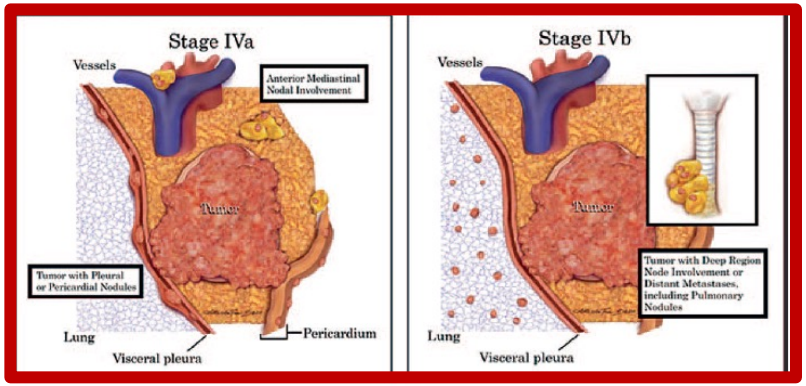
Masaoka-Koga : I, IIA, IIB, III



Masaoka-Koga : III



Masaoka-Koga : III

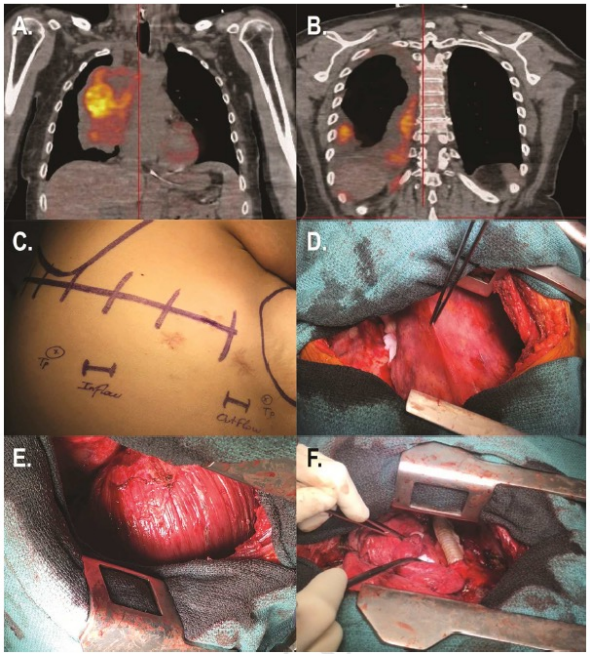


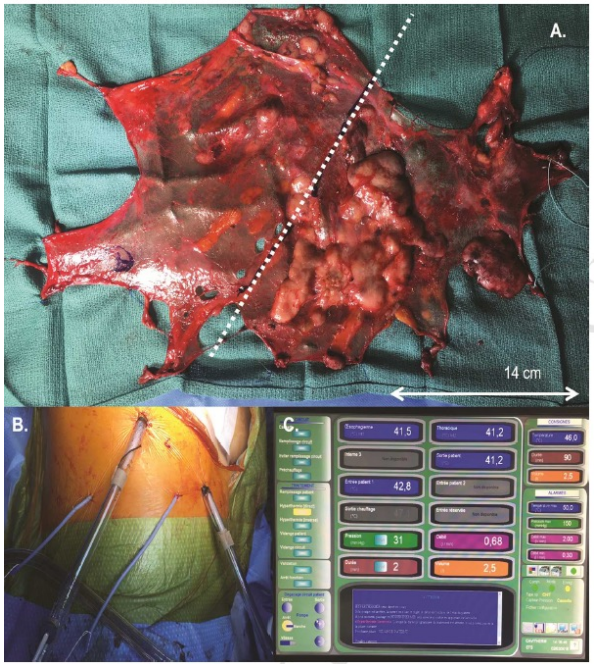
Masaoka-Koga : IVB

Detterbeck et al. J Thorac Oncol 2014;S65-72

#2 STAGE IV DOES NOT EXCLUDE CURATIVE-INTENT LOCAL TREATMENT

Stage IVA type B2 thymoma: pleurectomy and intra-thoracic chemo-hyperthermia





Maury, Girard, Ann Thorac Surg 2018;10.1016/j.athoracsur.2018.07.058

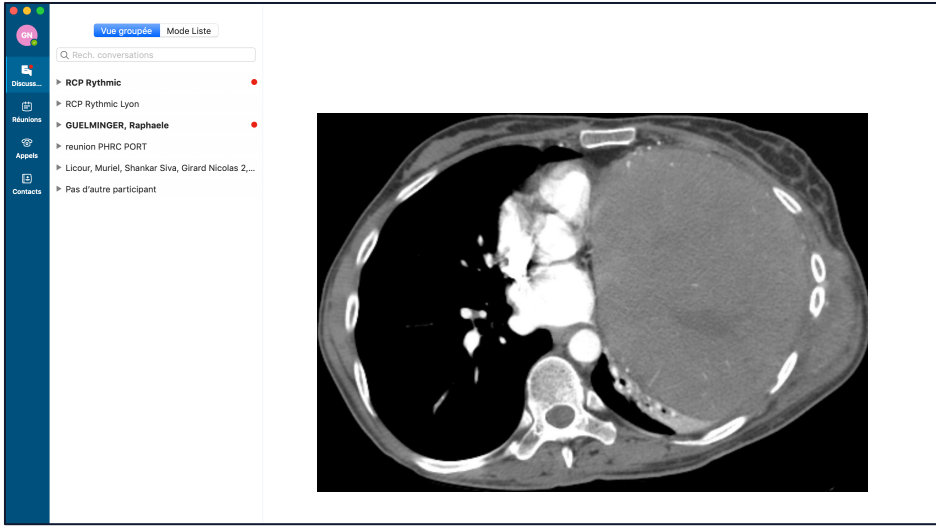
THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

#3 LEVELS OF EVIDENCE ARE LIMITED: ROOM FOR MULTIDISCIPLINARY DISCUSSION

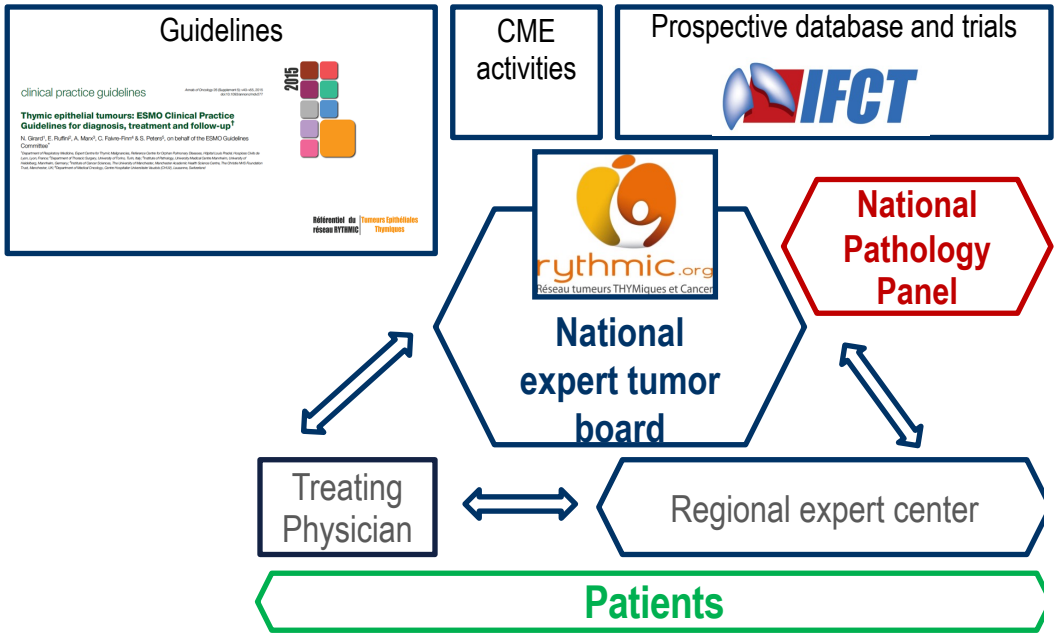
RYTHMIC network

Coordinator:
B. Besse
Gustave Roussy



#3 LEVELS OF EVIDENCE ARE LIMITED: ROOM FOR MULTIDISCIPLINARY DISCUSSION

RYTHMIC network



rythmic.org
Reseau tumeurs THYMiques et Cancer

THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

SURGERY UPFRONT IN RESECTABLE TUMORS

SURGERY PRINCIPLES

Which Way is Up? Policies and Procedures for Surgeons and Pathologists Regarding Resection Specimens of Thymic Malignancy

Frank C. Detterbeck, MD, Cesar Moran, MD,† James Huang, MD,‡ Saul Suster, MD,§ Garrett Walsh, MD,# Lawrence Kaiser, MD,‖ and Mark Wick, MD¶*

- **Median sternotomy** is the standard approach
- Complete exploration of the pleural cavities

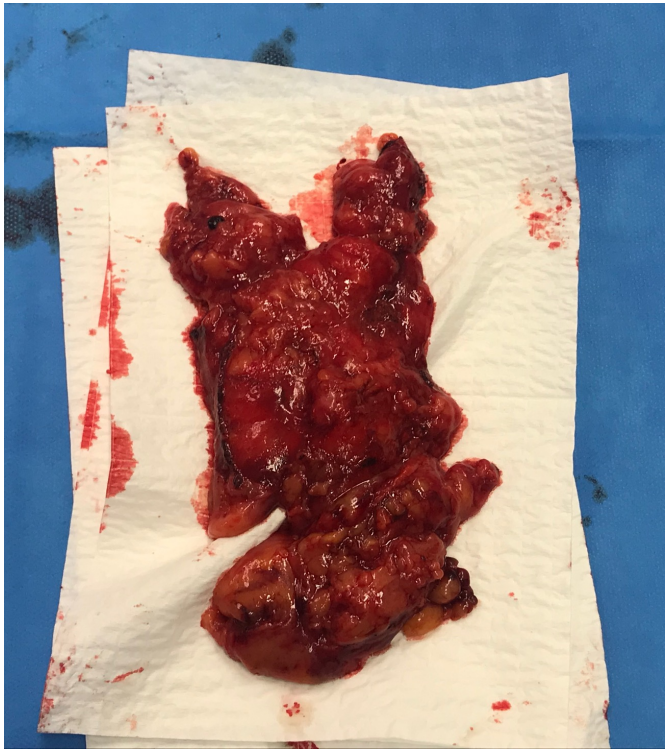
- Mediastinal nodes sampling/resection (stage III tumor/thymic carcinoma)

- **Complete thymectomy**, including tumor, normal thymus, and mediastinal fat
- *en bloc* resection of involved structures:
  - lung, vessels, pleural implants, phrenic nerves
  - surgical clips in areas of concern

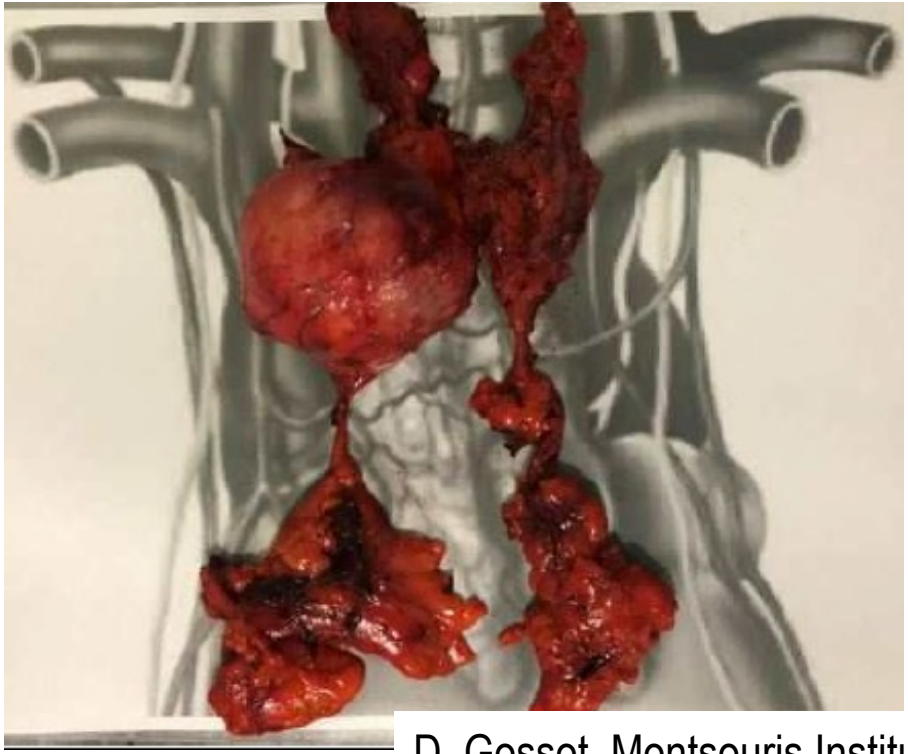
- Frozen section not recommended for margins assessment

Orientation and marking in the operative room

NO



YES



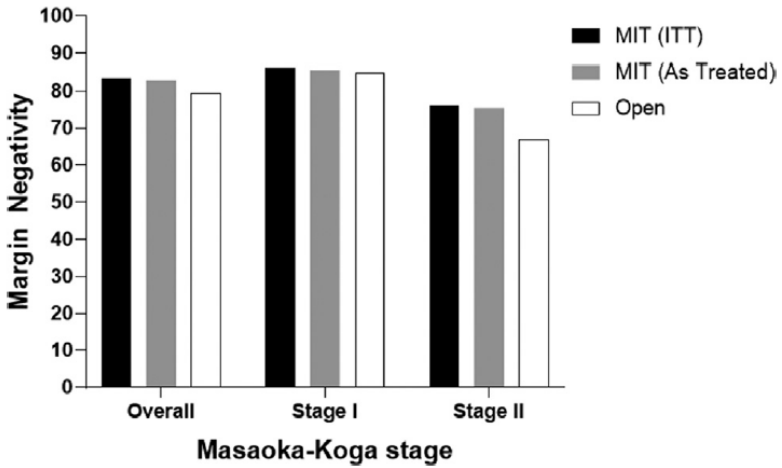
D. Gossot, Montsouris Institute

TOWARDS MINIMALLY-INVASIVE SURGERY?

Utilization of Minimally Invasive Thymectomy and Margin-Negative Resection for Early-Stage Thymoma

Bryan M. Burt, MD, Duy Nguyen, MD, Shawn S. Groth, MD, Nihanth Palivela, BA, BS, R. Taylor Ripley, MD, Konstantinos I. Makris, MD, Farhood Farjah, MD, MPH, Lorraine Cornwell, MD, and Nader N. Massarweh, MD, MPH

Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas; Division of Cardiothoracic Surgery, Surgical Outcomes Research Center, University of Washington Medical Center, Seattle, Washington; and Center for Innovations in Quality, Effectiveness, and Safety, Michael E. DeBakey VA Medical Center, Houston, Texas



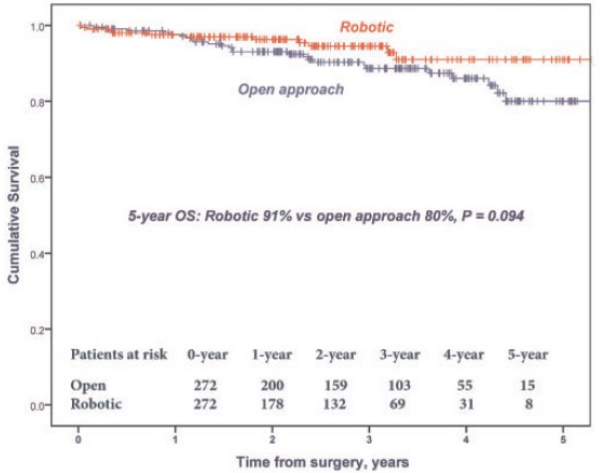
European Journal of Cardio-Thoracic Surgery 0 (2019) 1–8
doi:10.1093/ejcts/ezz111

ORIGINAL ARTICLE

Cite this article as: Kamel MK, Villena-Vargas J, Rahouma M, Lee B, Harrison S, Stiles BM *et al*. National trends and perioperative outcomes of robotic resection of thymic tumours in the United States: a propensity matching comparison with open and video-assisted thoracoscopic approaches .Eur J Cardiothorac Surg 2019; doi:10.1093/ejcts/ezz111.

National trends and perioperative outcomes of robotic resection of thymic tumours in the United States: a propensity matching comparison with open and video-assisted thoracoscopic approaches†

Mohamed K. Kamel[a,b], Jonathan Villena-Vargas[a], Mohamed Rahouma[a,b], Benjamin Lee[a], Sebron Harrison[a], Brendon M. Stiles[a], Abdelrahman M. Abdelrahman[b], Nasser K. Altorki[a] and Jeffery L. Port[a,*]



THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

SURGERY UPFRONT IN RESECTABLE TUMORS

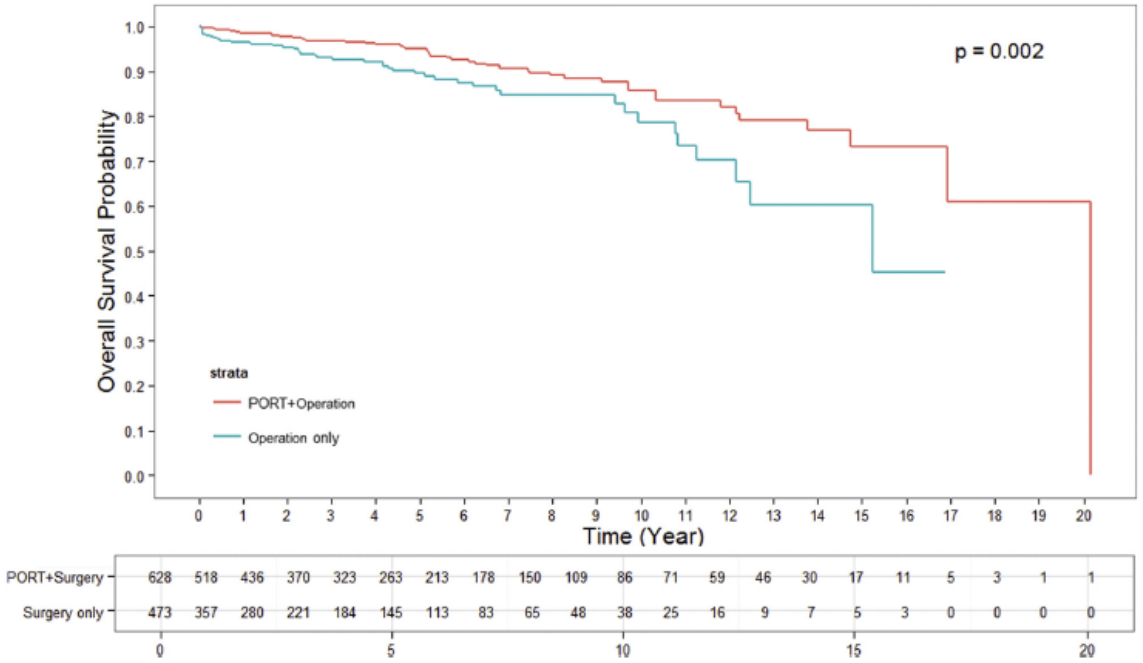
POST-OPERATIVE DECISION-MAKING

Postoperative radiotherapy: ITMIG database

ORIGINAL ARTICLE

Postoperative Radiation Therapy Is Associated with Longer Overall Survival in Completely Resected Stage II and III Thymoma—An Analysis of the International Thymic Malignancies Intere Database

Andreas Rimner, MD,[a,*] Xiaopan Yao, Phl
Alberto Antonicelli, MD,[d] Usman Ahmad
Frank Detterbeck, MD,[d] Daniel R. Gome



Rimner et al. J Thorac Oncol 2016;11:1785

Thymic carcinoma cohorts: Postoperative radiotherapy

Thymic Carcinoma: A Cohort Study of Patients from the European Society of Thoracic Surgeons Database

Enrico Ruffini, MD, Frank Detterbeck, MD,† Dirk Van Raemdonck, MD,‡ Gaetano Rocco, MD,§ Pascal Thomas, MD,‖ Walter Weder, MD,¶ Alessandro Brunelli, MD,# Francesco Guerrera, MD,* Shaf Keshavjee, MD,** Nasser Altorki, MD,†† Jan Schützner, MD,‡‡ Alex Arame, MD,§§ Lorenzo Spaggiari, MD,‖‖ Eric Lim,, MD,¶¶ Alper Toker, MD,## Federico Venuta, MD***; and the European Society of Thoracic Surgeons Thymic Working Group†††*

	Hazard Ratio	SE	p	Lower	Upper	Hazard Ratio
Overall survival—multiple imputation for missing data						
Sex (male)	1.03	0.22	(			
Age (continuous, 1 yr)	1.03	0.01	(			
Myasthenia Gravis (yes)	0.56	0.20	(			
Tumor size (continuous, 1 cm)	1.01	0.04	(			
Histology (squamous cell carcinoma vs. other)	1.11	0.34	(			
Other						
Resection status (R0 vs. R1-2)	3.28	0.74	(			
Masaoka-Koga stage ($n = 186$) I–II vs. III–IV	2.54	0.81	(			
[illegible]	[illegible]	[illegible]	[illegible]			
Postoperative (adjuvant) therapy (yes)	0.64	0.15	0.033	0.41	1.01	0.33

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 Thymus Database Study

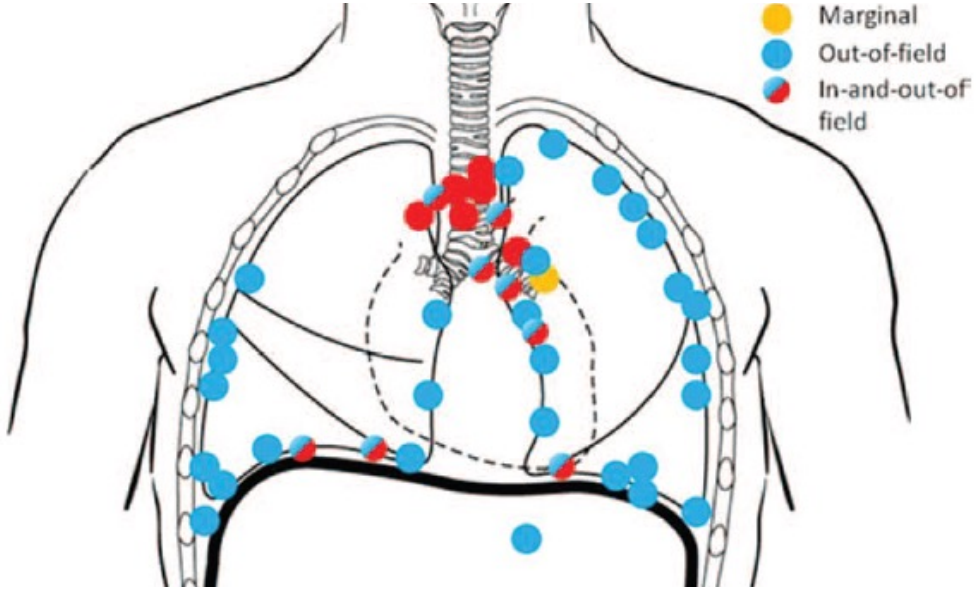
Mitsugu Omasa, MD, PhD[1]; Hiroshi Date, MD, PhD[1]; Takashi Sozu, PhD[2]; Tosiya Sato, PhD[2]; Kanji Nagai, MD, PhD[3]; Kohei Yokoi, MD, PhD[4]; Tatsuro Okamoto, MD, PhD[5]; Norihiko Ikeda, MD, PhD[6]; Fumihiro Tanaka, MD, PhD[7]; and Yoshimasa Maniwa, MD, PhD[8]; for the Japanese Association for Research on the Thymus

TABLE 3. Cox Regression Analysis for Relapse-Free Survival Adjusted for the Pathology, Masaoka Staging, and Residual Tumor

Parameter	HR (95% CI)	P
Postoperative radiotherapy (yes/no)	0.76 (0.58-1.01)	.116
[illegible]	[illegible]	[illegible]
Masaoka stage (III/II)	4.46 (3.33-5.99)	<.001
Residual tumor (yes/no)	2.14 (1.49-3.09)	<.001

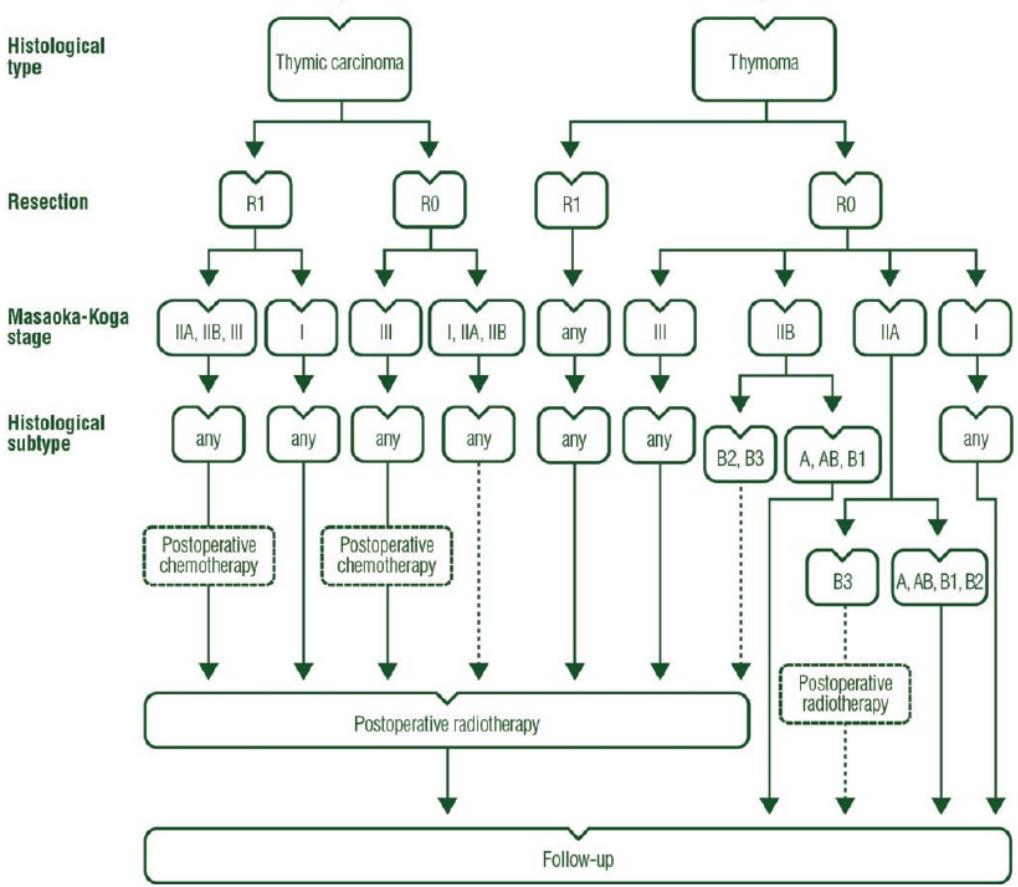
Failure Patterns Relative to Radiation Treatment Fields for Stage II–IV Thymoma

Andreas Rimner, MD, Daniel R. Gomez, MD,# Abraham J. Wu, MD,* Weiji Shi, MS,¶ Ellen D. Yorke, PhD,‖ Andre L. Moreira, MD,§ David Rice, MD,** Ritsuko Komaki, MD,# Kenneth E. Rosenzweig, MD,†† Gregory J. Riely, MD,‡ and James Huang, MD,†*



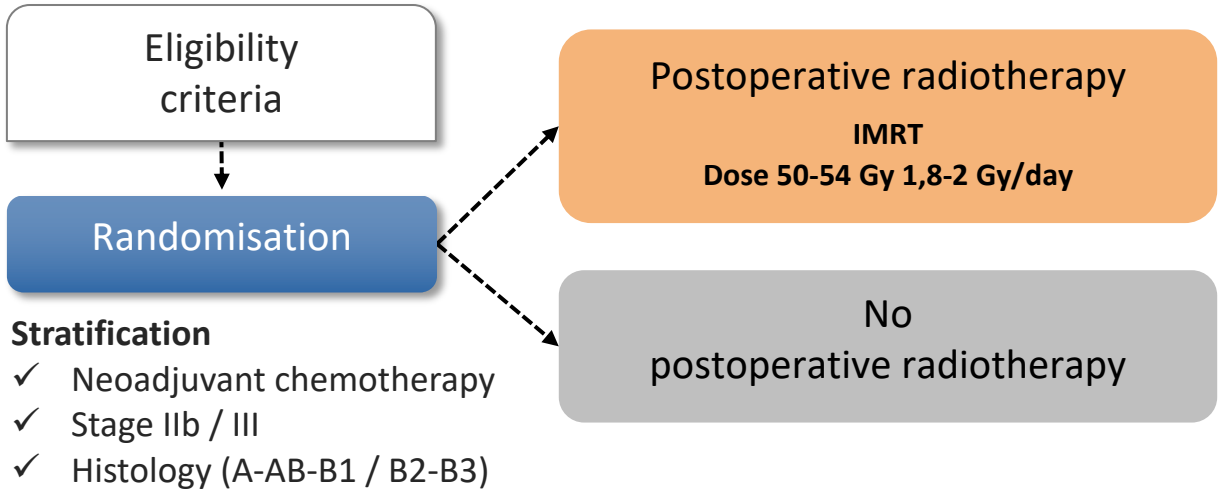
(*J Thorac Oncol.* 2014;9: 403–409)

POSTOPERATIVE RADIOTHERAPY GUIDELINES



RADIORYTHMIC: THE ONLY RANDOMIZED TRIAL IN THYMIC TUMORS

RADIORYTHMIC trial



Suivi

- ✓ As per ESMO/**RYTHMIC**
- ✓ CT-scan every 6 months for 3 years, then annual
- ✓ Minimum 3 years

Basse et al. Clin Lung Cancer 2021

THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

STRATEGIES FOR SYSTEMIC THERAPY

SURGERY UPFRONT IN RESECTABLE TUMORS

POST-OPERATIVE DECISION-MAKING

KEY QUESTION IS:
WHAT IS THE INTENT OF THE SYSTEMIC TREATMENT?

ITMIG Definitions and Policies

Chemotherapy Definitions and Policies for Thymic Malignancies

Nicolas Girard, MD, Rohit Lal, MD,† Heather Wakelee, MD,‡ Gregory J. Riely, MD,§ and Patrick J. Loehrer, MD‖*

PRIMARY CHEMOTHERAPY	EXCLUSIVE CHEMOTHERAPY	SYSTEMIC THERAPIES FOR RECURRENCES

J Thorac Oncol 2011;6(7 Suppl 3):S1749

KEY QUESTION IS:
WHAT IS THE INTENT OF THE SYSTEMIC TREATMENT?

ITMIG Definitions and Policies

Chemotherapy Definitions and Policies for Thymic Malignancies

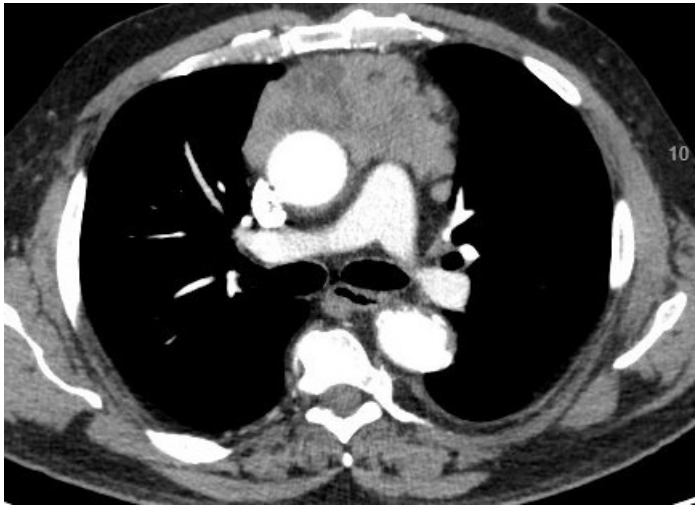
Nicolas Girard, MD, Rohit Lal, MD,† Heather Wakelee, MD,‡ Gregory J. Riely, MD,§ and Patrick J. Loehrer, MD‖*

PRIMARY CHEMOTHERAPY	EXCLUSIVE CHEMOTHERAPY	SYSTEMIC THERAPIES FOR RECURRENCES

J Thorac Oncol 2011;6(7 Suppl 3):S1749

PRIMARY CHEMOTHERAPY: CASE REPORT

27-year old male, chest pain, no myasthenia



MTB: Is upfront complete resection achievable?

Re: « Not sure »

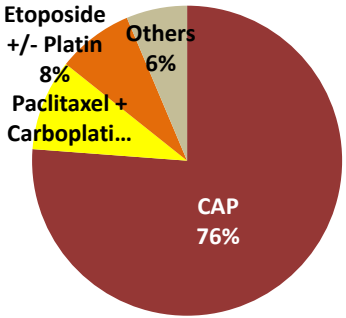
Biopsy: thymoma, type B3

PRIMARY CHEMOTHERAPY: CLINICAL EVIDENCE

Historical data

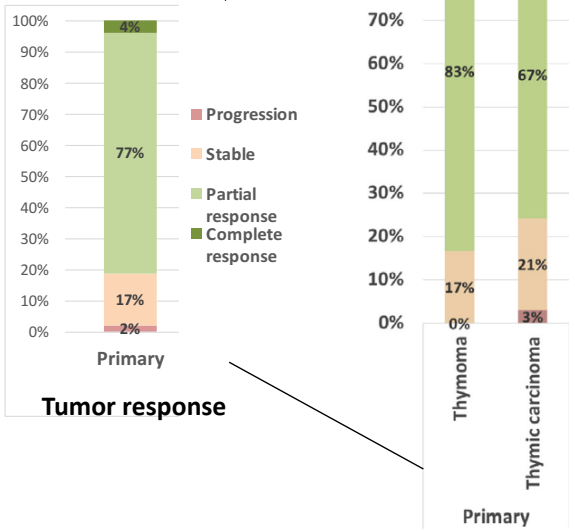
Study	Primary Chemotherapy Regimen	No. of Patients	Tumor		Design	Response Rate (%)
			Type	Stage		
Chemotherapy						
Macchiarini et al 1991[14]	CEE	7	T/TC	III	Phase II	100
Berruti et al 1993[15]	ADOC	6	T	III-IVA	Phase II	83
Rea et al 1993[16]	ADOC	16	T	III-IVA	Retrosp	100
Berruti et al 1999[17]	ADOC	16	T	III-IVA	Phase II	81
Venuta et al 2003[18]	CEE	15	T/TC	III	Retrosp	66
Bretti et al 2004[19]	ADOC/PE	25	T/TC	III-IVA	Retrosp	72
Kim et al 2004[20]	CAPP	22	T		Phase II	77
Lucchi et al 2005[21]	CEE	36	T/TC	III-IVA	Retrosp	67
Jacot et al 2005[22]	CAP	5	T/TC	III-IVA	Retrosp	75
Yokoi et al 2007[23]	CAMP	14	T/TC	III, IV	Retrosp	93
Kunitoh et al 2009[24]	CODE	21	T	III	Phase II	62

RYTHMIC data



Administered regimens

n=91



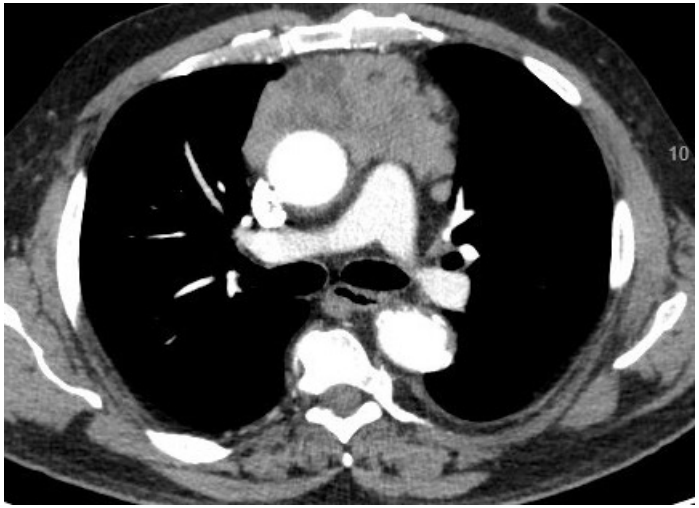
Tumor response

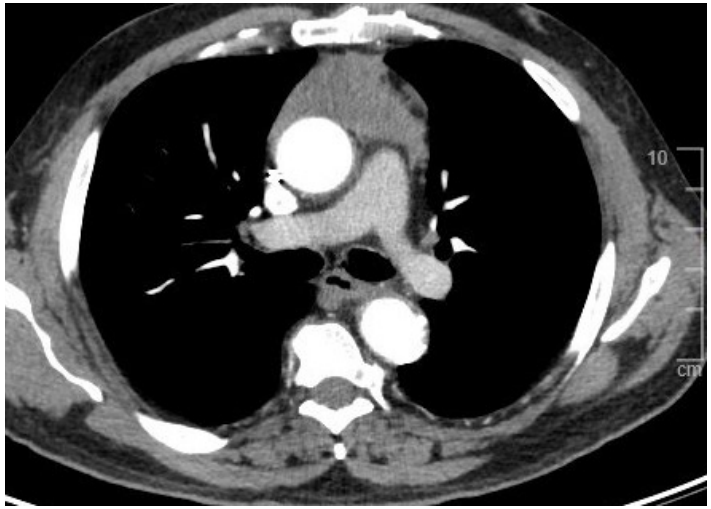
Girard N. Eur Respir Rev 2013;22:75

Merveilleux du Vignaux et al. J Thorac Oncol 2018; online first

PRIMARY CHEMOTHERAPY: CASE REPORT

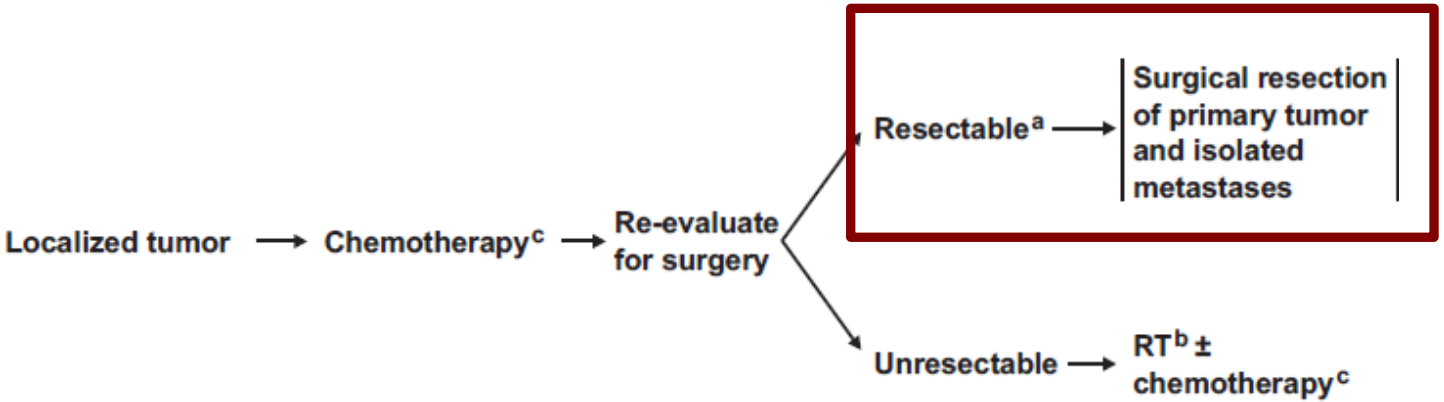
27-year old male, chest pain, no myasthenia

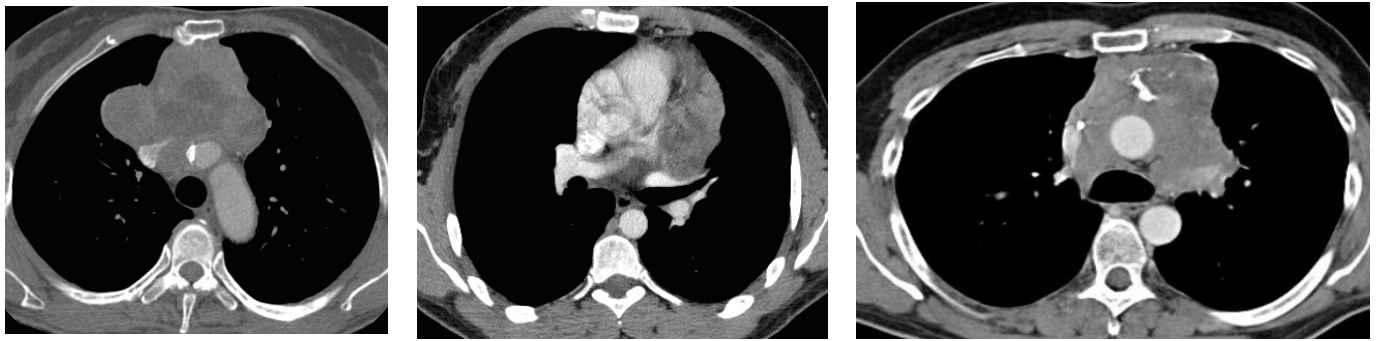




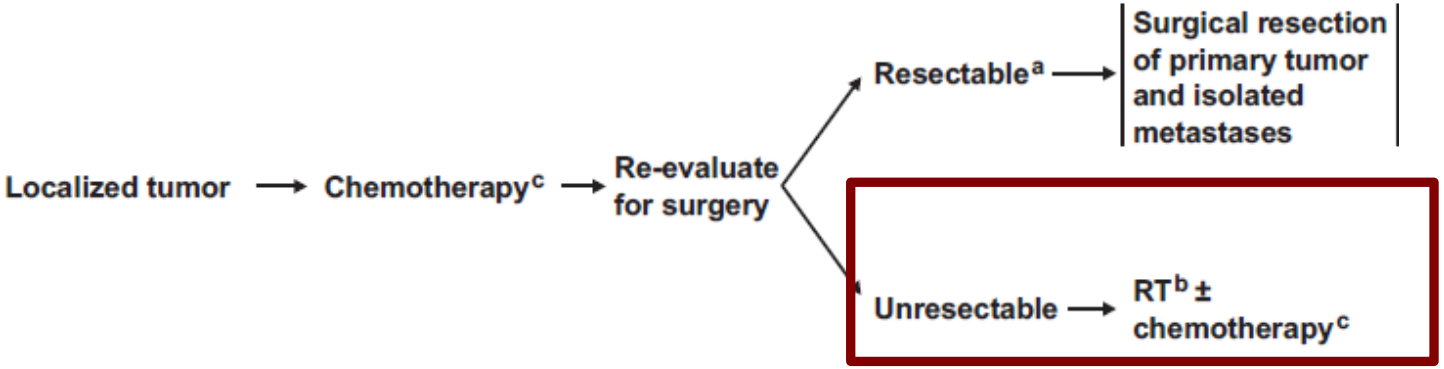
Then surgery !

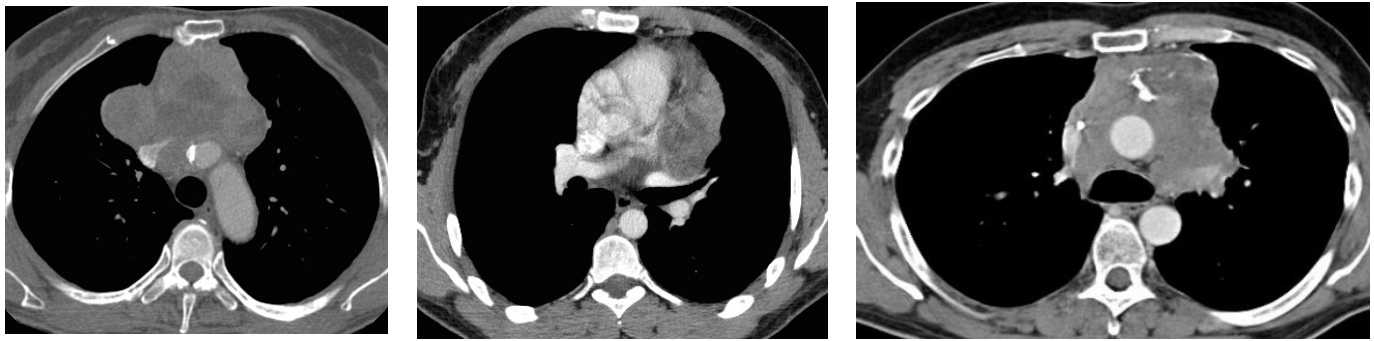
ADVANCED TUMORS: MULTIMODAL TREATMENT





ADVANCED TUMORS: MULTIMODAL TREATMENT





KEY QUESTION IS:
WHAT IS THE INTENT OF THE SYSTEMIC TREATMENT?

ITMIG Definitions and Policies

Chemotherapy Definitions and Policies for Thymic Malignancies

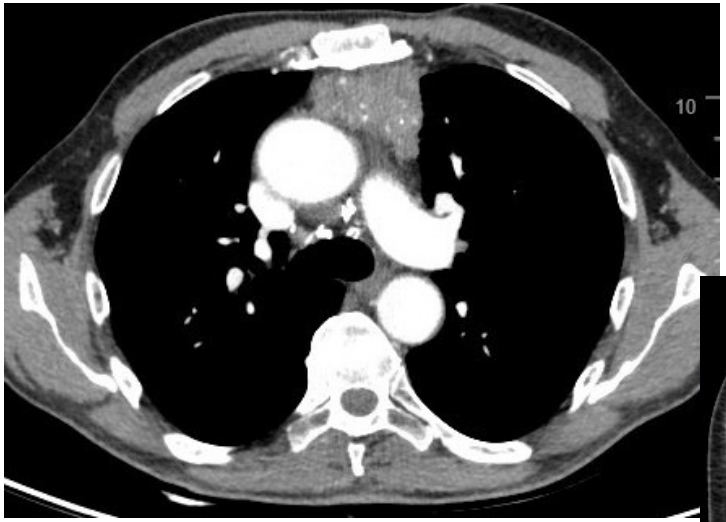
Nicolas Girard, MD, Rohit Lal, MD,† Heather Wakelee, MD,‡ Gregory J. Riely, MD,§ and Patrick J. Loehrer, MD‖*

PRIMARY CHEMOTHERAPY	EXCLUSIVE CHEMOTHERAPY	SYSTEMIC THERAPIES FOR RECURRENCES

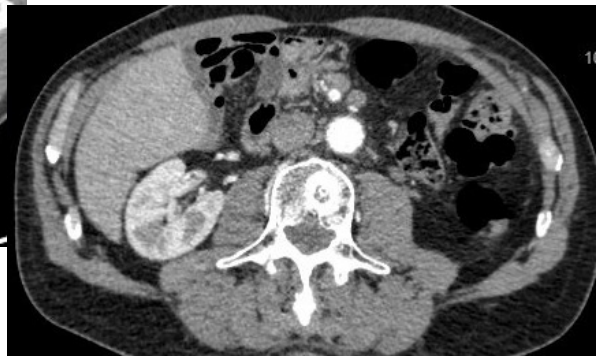
J Thorac Oncol 2011;6(7 Suppl 3):S1749

EXCLUSIVE CHEMOTHERAPY: CASE REPORT

67-year old male, lombalgia, hypercalcemia



Biopsy: thymic carcinoma, CD117+, CD5+

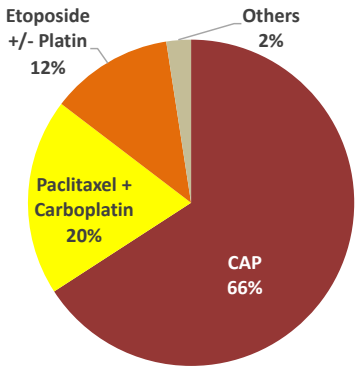


EXCLUSIVE CHEMOTHERAPY: CLINICAL EVIDENCE

Historical data

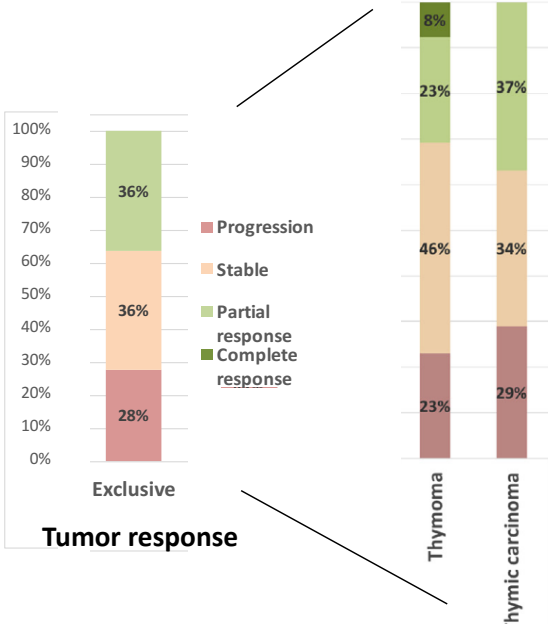
Study	No. of Patients	Period of Accrual (years)	Tumor Type	Design	Regimen	Agents	Doses	Response Rate (%)
Single-agent chemotherapy								
Bonomi et al 1993[27]	21	4	T/TC	Phase II	Cisplatin		50 mg/m^2/3 weeks	10
Highley et al 1999[28]	15	12	T/TC	Retrosp	Ifosfamide		1.5g/m^2 × 5 days/3 weeks	46
Loehrer et al 2006[29]	27	1	T/TC	Phase II	Pemetrexed		500 mg/m^2/3 weeks	17
Combination chemotherapy								
Fornasiero et al 1990[30]	32	11	T	Retrosp	ADOC	Doxorubicin	40 mg/m^2/3 weeks	91
						Cisplatin	50 mg/m^2/3 weeks	
						Vincristin	0.6 mg/m^2/3 weeks	
						Cyclophosphamide	700 mg/m^2/3 weeks	
Loehrer et al 1994[31]	30	9	T/TC	Phase II	CAP	Cisplatin	50 mg/m^2/3 weeks	51
						Doxorubicin	50 mg/m^2/3 weeks	
						Cyclophosphamide	500 mg/m^2/3 weeks	
Giaccone et al 1996[32]	16	6	T	Phase II	PE	Cisplatin	60 mg/m^2/3 weeks	56
						Etoposide	120 mg/m^2 × 3/3 weeks	
Loehrer et al 2001[33]	34	2	T/TC	Phase II	VIP	Etoposide	75 mg/m^2 × 4 days/3 weeks	32
						Ifosfamide	1.2 g/m^2 × 4 days/3 weeks	
						Cisplatin	20 mg/m^2 × 4 days/3 weeks	
Lemma et al 2011[34]	46	7	T/TC	Phase II	Carbo-Px	Carboplatin	AUC 5/3 weeks	43
						Paclitaxel	225 mg/m^2/3 weeks	
Palmieri et al 2011[35]	15	3	T/TC	Phase II	CAP-GEM	Capecitabine	650 mg/m^2 bid × 14 days/3 weeks	40
						Gemcitabine	1000 mg/m^2 × 2 days/3 weeks	
Okuma et al 2011[36]	9	8	TC	Retrosp	Cisplatin-Irinotecan	Cisplatin	80 mg/m^2/4 weeks	56
						Irinotecan	60 mg/m^2 × 3 days/4 weeks	

RYTHMIC data



Administered regimens

n=41



Tumor response

Girard N. Eur Respir Rev 2013;22:75

Merveilleux du Vignaux et al. J Thorac Oncol 2018; online first

KEY QUESTION IS:
WHAT IS THE INTENT OF THE SYSTEMIC TREATMENT?

ITMIG Definitions and Policies

Chemotherapy Definitions and Policies for Thymic Malignancies

Nicolas Girard, MD, Rohit Lal, MD,† Heather Wakelee, MD,‡ Gregory J. Riely, MD,§ and Patrick J. Loehrer, MD‖*

PRIMARY CHEMOTHERAPY	EXCLUSIVE CHEMOTHERAPY	SYSTEMIC THERAPIES FOR RECURRENCES

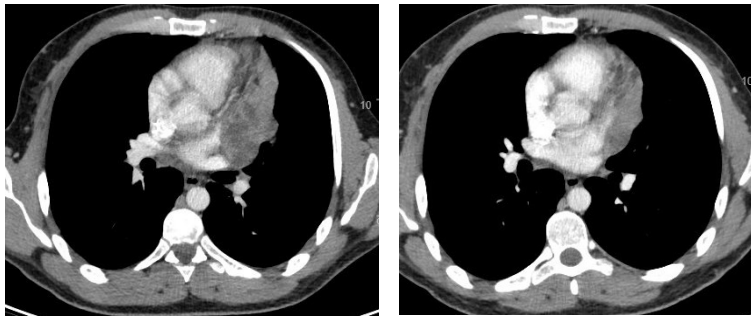
J Thorac Oncol 2011;6(7 Suppl 3):S1749

RECURRENCES: CASE REPORT

32 year-old male, Morvan syndrome

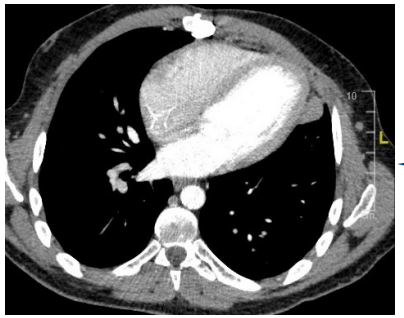
2011

chemo and resection for thymoma, type B2-B3

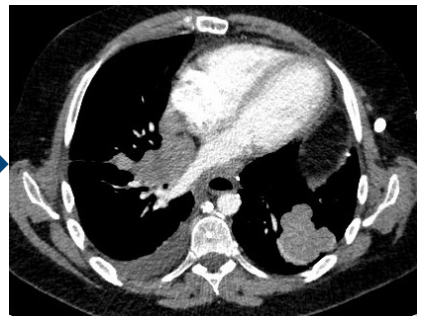


2014

Resection of implant

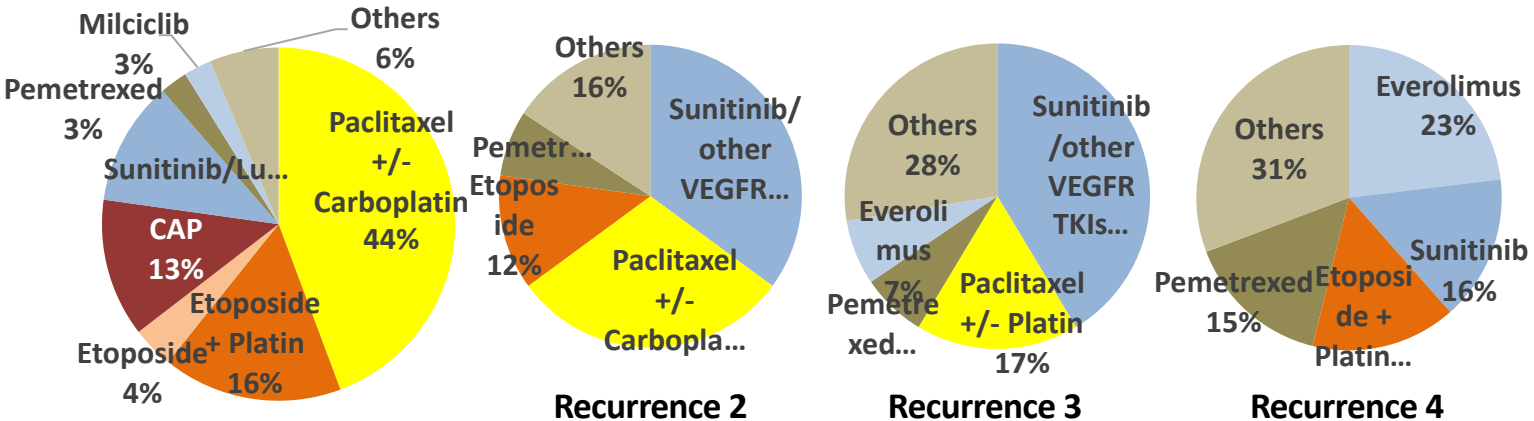


2016



RECURRENCES: CLINICAL EVIDENCE FOR SYSTEMIC TREATMENT

RYTHMIC data



Merveilleux du Vignaux et al. J Thorac Oncol 2018; online first

European Journal of Cancer 162 (2022) 118–127

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Treatment strategies for thymic carcinoma in a real-life setting. Insights from the RYTHMIC network

Arthur Petat [a,b], Eric Dansin [c], Fabien Calcagno [d], Laurent Greillier [e], Eric Pichon [f], Mallorie Kerjouan [g], Christelle Clement-Duchene [h], Bertrand Mennecier [i], Virginie Westeel [j], François Thillays [k], Xavier Quantin [l], Youssef Oulkhouir [m], Luc Thiberville [n], Charles Ricordel [g], Vincent Thomas De Montpreville [o], Lara Chalabreysse [p], Véro, Pierre Fournel [s], Laurence, Nicolas Girard [v,*]

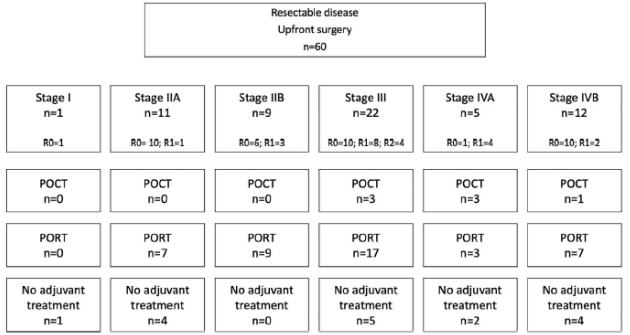


Fig. 1. Treatment strategies in 60 patients with upfront surgical resection of the tumour, possibly followed by postoperative radiotherapy (PORT) or postoperative chemotherapy (POCT).

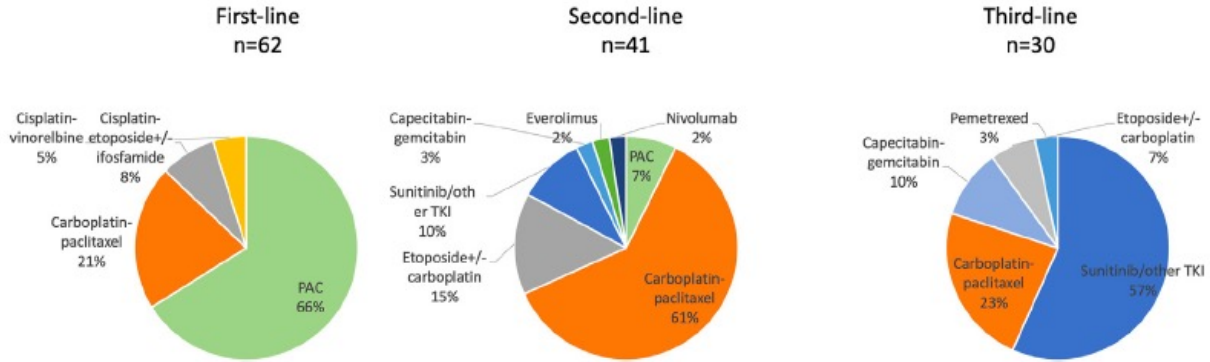


Fig. 2. Treatment strategies in 91 patients who received preoperative chemotherapy (a) and subsequently possibly were treated for recurrence (40 patients) (b). Legend: PAC: cyclophosphamide, adriamycin and cisplatin.

THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

STRATEGIES FOR SYSTEMIC THERAPY

SURGERY UPFRONT IN RESECTABLE TUMORS

PRECISION MEDICINE APPROACHES?

POST-OPERATIVE DECISION-MAKING

THYMIC CARCINOMAS FOUNDATION MEDICINE PANEL

	Adeno.	Basaloid	Lymphoepi-theliomatous	Neuro-endocrine	NOS	Squamous Cell	Sarcomatoid
Patients	7	5	5	30	54	69	4
Median Age (y)	48	58	50	48	57	57	61
Gender (% Female)	43%	60%	20%	37%	24%	34%	50%
Avg GA/tumor	4.0	2.8	1.0	3.3	4.1	4.1	4.8
Avg CRGA/tumor	0.9	0.3	--	0.9	0.8	1.0	1.0
Significant Genomic Alterations	*PDGFRA* *FGFR3* *KIT* *MET* *PTCH1*	*CDKN2A* *FBXW7*	*CDKN2A* *MEN1*	*KIT* *BRCA2* *IDH1* *ERBB2* *ERBB3*	*KIT* *PTEN* *PIK3CA*	*KIT* *FGFR3* *PIK3CA*	*ERBB2* *IDH1* *KIT*
TMB ≥10 mutations/Mb	14%	--	--	3%	5%	9%	--
TMB ≥20 mutations/Mb	0%	--	--	3%	5%	9%	--

Ross et al. ESMO 2017

THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

STRATEGIES FOR SYSTEMIC THERAPY

SURGERY UPFRONT IN RESECTABLE TUMORS

PRECISION MEDICINE APPROACHES?

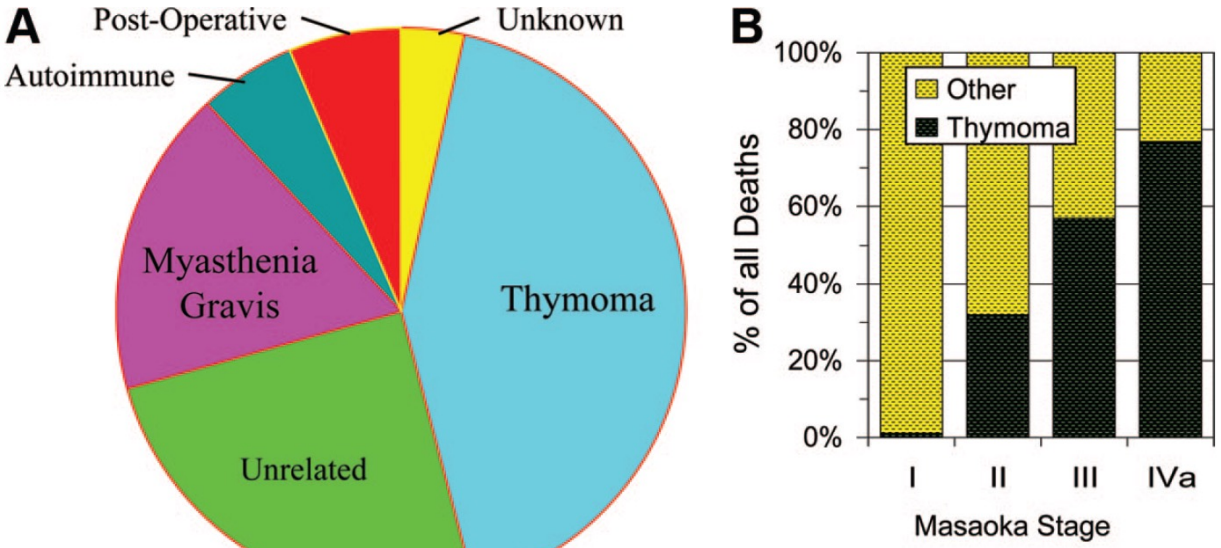
POST-OPERATIVE DECISION-MAKING

IMMUNE CHECKPOINT INHIBITORS

IMMUNOTHERAPY SHOULD *NOT* BE USED IN THYMIC TUMORS

LET'S FIRST EXCLUDE THYMOMAS

Death in thymic malignancies



Huang et al. J Thorac Oncol 2011; 5:2017

THYMOMA AS A CONTRA-INDICATION FOR IMMUNE CHECKPOINT INHIBITORS

Impressive case reports…do you want this?

CASE REPORT

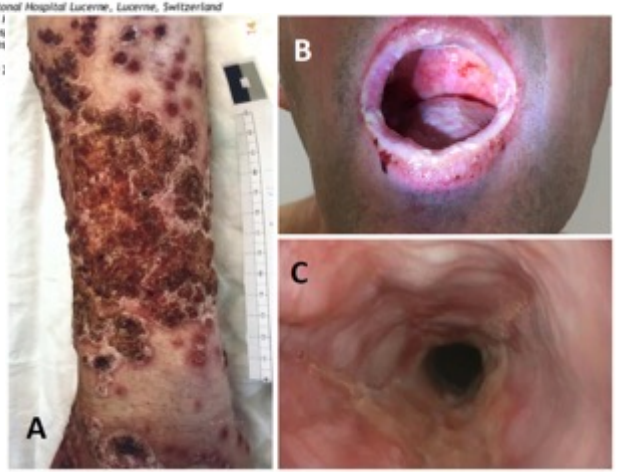
IASLC

Response to Pembrolizumab in a Patient with Relapsing Thymoma

Thilo Zander, MD,[a,*] Stefan Aebi, MD,[a] Anna Christina Rast, MD,[b] Andrea Zander, MD,[c] Ralph Winterhalder, MD,[a] Christoph Brand, MD,[b] Joachim Diebold, MD,[d] Oliver Gautschi, MD[a]

[a]Department of Medical Oncology, Cantonal Hospital Lucerne, Lucerne, Switzerland
[b]Department of Dermatology, Cantonal
[c]Department of Radiology, Cantonal Hos
[d]Department of Pathology, Cantonal Hos

Received 23 June 2016; revised 14 July
Available online - 3 August 2016

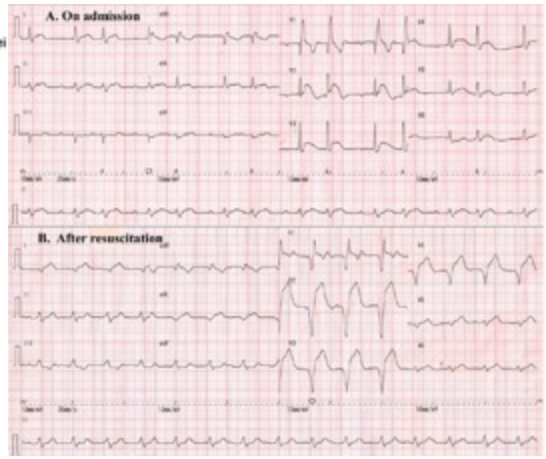


J Thorac Oncol 2016;11:e147

Clinical Toxicology

Fatal myocarditis and rhabdomyolysis induced by nivolumab during the treatment of type B3 thymoma

Qiang Chen, Dang-Sheng Huang, Li-Wei
& Hong-bin Liu



Clin toxicol 2018;56:667

IMMUNOTHERAPY SHOULD *NOT* BE USED IN THYMIC TUMORS

LET'S FIRST EXCLUDE THYMOMAS

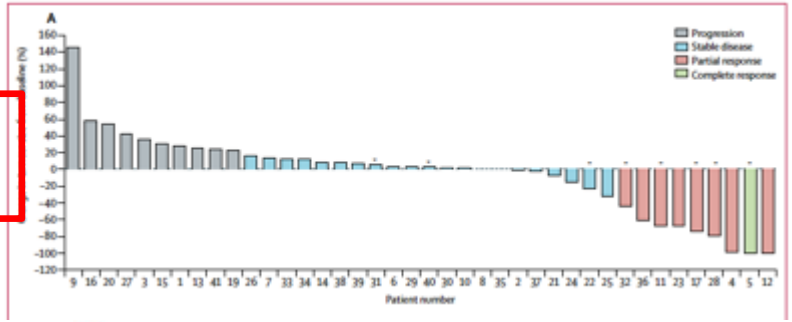
THEN LOOK AT CLINICAL TRIALS IN THYMIC CARCINOMAS

IMMUNE CHECKPOINT INHIBITORS IN THYMIC CARCINOMA

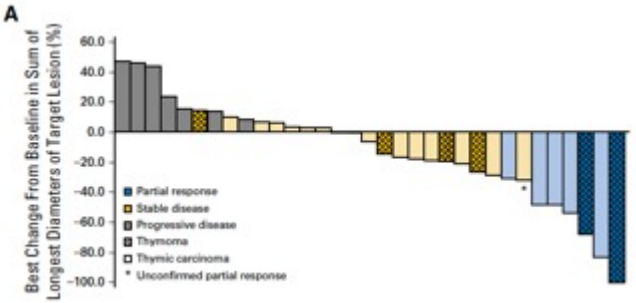
Response is consistent with pembrolizumab across 2 phase II trials BUT not reproducible with nivolumab

Pembrolizumab

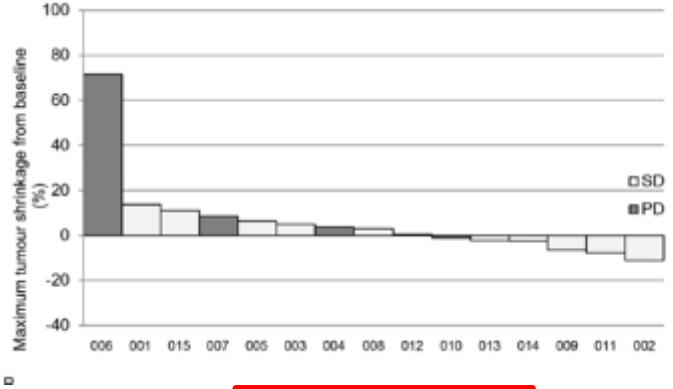
PR+CR: 23%
SD:53%



PR+CR: 19%
SD:54%



Nivolumab



No response
SD:73%

Giaccone et al. Lancet Oncol 2018;19:347
Cho et al. J Clin Oncol 2019;37:2162
Seto et al. Eur J Cancer 2019;113:78

IMMUNE CHECKPOINT INHIBITORS IN THYMIC CARCINOMA

Major toxicities: 15-20% of patients

Polymyositis/myocarditis/hepatitis

A [illegible] year-old Caucasian female, with a performance status of 0, developed severe asthenia, dysp
muscle aches after 2 cycles of pembrolizumab. Hospitalization was required. Severe transaminiti
and myocarditis were diagnosed with complete A-V block which necessitated high-dose steroids
maker placement. Patient recovered completely in a few weeks and was able to undergo further a
treatment. The patient progressed on CT scan after 2 cycles of pembrolizumab.

Hepatitis/pancreatitis/Diabetes mellitus type 1

A 55-year old Asian female with a performance status of 0, developed grade 4 hyperglycemia aft
of pembrolizumab. This was associated with severe increase of lipase (grade 3) and amylase (gra
grade 3 transaminitis. She was admitted briefly and received insulin. The diabetes did not resolve
continues to require insulin. The tumor was stable after 2 cycles of pembrolizumab but progresse
and she is receiving alternate therapy.

Bullous pemphigoid

A 64 year-old African American man with performance status of 1, developed severe itching and
progressive skin blistering after 10 cycles of pembrolizumab. Histological diagnosis of bullous p
was established after 12 cycles. He was treated with oral steroids and topical therapy and recover
completely after termination of pembrolizumab therapy. His tumor remained stable for 8.6 month

Polymyositis/hepatitis/myocarditis/Myasthenia Gravis

A 60 year-old Asian woman with a performance status of 1 developed severe asthenia and severe
and joint pains after 2 cycles of pembrolizumab. A diagnosis of severe myositis and hepatitis (tra
elevation grade 4) was made and the patient was hospitalized and received intravenous (IV) stero
Complete A-V block developed and she required placement of a permanent pace-maker. She reco
completely, but liver enzyme elevation recurred after 3 months and vague signs of myasthenia gr
(AchR antibody positive in blood) appeared; she was restarted on oral steroids, and pyridostigmi
added. Liver enzymes did not improve and a diagnosis of reactivation of Hepatitis B was made, t
successfully with tenofovir. Signs of myasthenia gravis worsened and required IVIG treatment a
After only 2 cycles the tumor had a partial response on CT scan and minimal activity on FDG-PE
is still ongoing after 15 months from the last cycle.

Polymyositis/hepatitis

A 36 year-old Caucasian man with a performance status of 0 developed severe asthenia and respi
symptoms and grade 3 transaminitis after 4 cycles of pembrolizumab. He was hospitalized and pl
IV steroids. He slowly recovered. Autoantibodies against muscle AchR binding and muscle AchR
modulatory (neurological autoimmunity) were detected, but a definite diagnosis of myasthenia gr

	Grade 1-2	Grade 3	Grade 4
Fatigue	16 (40%)	3 (8%)	0
Aspartate aminotransferase increased	11 (28%)	3 (8%)	2 (5%)
Alanine aminotransferase increased	5 (13%)	4 (10%)	1 (3%)
Alkaline phosphatase increased	10 (25%)	0	0
Diarrhoea	9 (23%)	0	0
Arthralgia	4 (10%)	1 (3%)	0
Fever	5 (13%)	0	0
Hypothyroidism	5 (13%)	0	0
Rhinitis	4 (10%)	0	0
Anaemia	2 (5%)	2 (5%)	0
Nausea	4 (10%)	0	0
Rash	4 (10%)	0	0
Dyspnoea	0	3 (8%)	0
Myalgia or myositis	0	3 (8%)	0
Creatine phosphokinase increased	0	1 (3%)	2 (5%)
Bilirubin increased	2 (5%)	0	0
Blurred vision	1 (3%)	1 (3%)	0
Dry mouth	2 (5%)	0	0
Flu-like symptoms	2 (5%)	0	0
Hyperthyroidism	2 (5%)	0	0
Hyperuricaemia	2 (5%)	0	0
Myocarditis	0	0	2 (5%)
Neutropenia	2 (5%)	0	0
Amylase increased	1 (3%)	0	0
Dehydration	1 (3%)	0	0
Watering eyes	1 (3%)	0	0
Hyperglycaemia	0	0	1 (3%)
Hypokalaemia	1 (3%)	0	0
Leucocytopenia	1 (3%)	0	0
Lipase increased	0	1 (3%)	0
Localised oedema (facial swelling)	1 (3%)	0	0
Palpitations	1 (3%)	0	0
Skin and subcutaneous tissue disorders	1 (3%)	0	0
Thrombocytopenia	0	1 (3%)	0

Table 3. All Adverse Events Regardless of Their Causality to Pembrolizumab

	Observed in ≥ 5% of Patients in Any Histologic Group				
Adverse Event	All Grade	Grade 1	Grade 2	Grade 3	Grade 4
Dyspnea	11 (33)	6 (18)	5 (15)	0	0
Chest wall pain	10 (30)	6 (18)	4 (12)	0	0
Anorexia	7 (21)	6 (18)	1 (3)	0	0
Fatigue	7 (21)	5 (15)	2 (6)	0	0
Cough	6 (18)	4 (12)	2 (6)	0	0
Back pain	4 (12)	4 (12)	0	0	0
Hepatitis	4 (12)	0	0	3 (9)	1 (3)
Anemia	3 (9)	0	2 (6)	1 (3)	0
Myalgia*	3 (9)	3 (9)	0	0	0
Myasthenia gravis	3 (9)	0	1 (3)	1 (3)	1 (3)
Myocarditis	3 (9)				
Sensory neuropathy	3 (9)				
Thyroiditis	3 (9)				
Pruritus	3 (9)				
Dermatitis	2 (6)				
Edema	2 (6)				
General weakness	2 (6)				
Lower extremity pain	2 (6)				
Pelvic pain	2 (6)				
Skin rash	2 (6)				

Table 4. Immune-Related Adverse Events at Any Frequency

	Thymoma (n = 7)		Thymic Carcinoma (n = 26)	
Adverse Event	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Hepatitis		2 (28.6)	0	2 (7.7)
Myasthenia gravis	(14.3)	0	0	2 (7.7)
Myocarditis		3 (42.9)	0	0
Thyroiditis	(14.3)	1 (14.3)	1 (3.8)	0
Dermatitis	(28.6)	0	0	0
Colitis		1 (14.3)	0	0
Conjunctivitis		1 (14.3)	0	0
Nephritis		1 (14.3)	0	0
Subacute myoclonus		0	0	1 (3.8)
Pruritus		0	3 (11.5)	0
Skin rash		0	2 (7.7)	0

NOTE: Data presented as No. (%).

Giaccone et al. Lancet Oncol 2018;19:347
Cho et al. J Clin Oncol 2019;37:2162

ESMO Congress– Sep 9–13, 2022. Abstract #1023

1640TiP - PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma

Jordi Remon[1], Nicolas Girard[2], Paolo Bironzo[3], Silvia Novello[3], Javier de Castro[4], Laurence Bigay-Game[5], Reyes Bernabé[6], Laurent Greillier[7], Joaquin Mosquera[8], Sophie Cousin[9], Oscar Juan[10], Miguel Sampayo[11], Benjamin Besse[12]

[1] Department of Medical Oncology, Centro Integral Oncológico Clara Campal (HM-CIOCC), Hospital HM Delfos, HM Hospitales, Barcelona, Spain; [2] Institut du thorax Curie Montsouris, Institut Curie Paris France UVSQ, Paris Saclay University, Paris, France; [3] Department of Oncology, University of Turin, S. Luigi Gonzaga Hospital, Orbassano, TO, Italy; [4] Department of Medical Oncology, Hospital La Paz, Madrid, Spain; [5] Department of Pneumology and Thoracic Oncology, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [6] Department of Medical Oncology, Hospital Virgen del Rocío, Seville, Spain; [7] Aix Marseille Univ, APHM, INSERM, CNRS, CRCM, Hôpital du Nord, Multidisciplinary Oncology and Therapeutic Innovations Department, Marseille, France; [8] Department of Medical Oncology, Hospital Universitario de A Coruña, A Coruña, Spain; [9] Department of Medical Oncology, Institut Bergonié, Bordeaux, France; [10] Department of Medical Oncology, Hospital La Fe, Valencia, Spain; [11] Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain; [12] Department of Cancer Medicine, Gustave Roussy, Villejuif, France; (13) Université Paris-Saclay, Orsay, France

BACKGROUND

- First-line platinum-based chemotherapy is the standard of care treatment for advanced B3-thymoma (B3-T) and thymic carcinoma (TC) [1]. However, the optimal treatment in patients with platinum refractory tumors is not yet defined.
- In the setting of platinum-refractory thymic epithelial tumors; two phase 2 trials have reported a meaningful clinical benefit in patients with TC when treated with the multi-tyrosine kinase inhibitors with antiangiogenic properties sunitinib [2] and lenvatinib [3]. Recently, immune checkpoint inhibitors (ICI), such as pembrolizumab [4-6], nivolumab [7], and avelumab [8] have also demonstrated encouraging antitumor activity with durable response. Despite recent advances, many patients still have a poor outcome with lack of alternative treatment options.
- Combination of ICI and antiangiogenic drugs is a novel approach that may provide greater antitumor activity compared to single-agent alone. Indeed, combination of pembrolizumab and lenvatinib has reported synergistic activity in other solid tumors [9,10].

OBJECTIVE

- PECATI evaluates the safety and efficacy of lenvatinib combined with pembrolizumab in patients with advanced B3-T or TC who progressed on or after at least one previous line of platinum-based chemotherapy.

METHODS

STUDY ENDPOINTS

Primary Endpoint

- To evaluate the efficacy in terms of investigator-assessed 5-months progression-free survival (PFS).

Secondary Endpoints

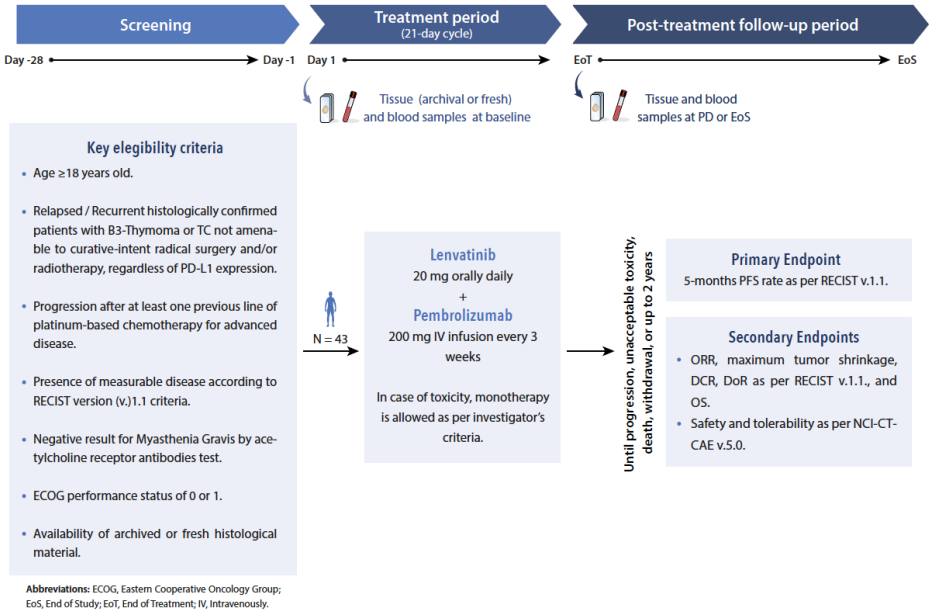
- To assess the efficacy in terms of investigator-assessed overall response rate (ORR), maximum tumor shrinkage, disease control rate (DCR), duration of response (DoR) as per RECISTv.1.1., and overall survival (OS).
- To evaluate the safety and tolerability of lenvatinib in combination with pembrolizumab as per National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) v.5.0.

Exploratory Endpoints

- To identify an optimal cut-off value by PD-L1 protein expression (22C3 anti-PD-L1 monoclonal antibody assay).
- To investigate blood tumor mutational burden by next-generation sequencing (NGS) at baseline and at the time of disease progression.
- To analyze genomic profile by NGS through a liquid biopsy test at baseline and at the time of disease progression.
- To determine immune-related gene signatures at baseline and at the time of disease progression.

STUDY DESIGN

Figure 1. PECATI Trial Design



Abbreviations: ECOG, Eastern Cooperative Oncology Group; EoS, End of Study; EoT, End of Treatment; IV, Intravenously.

THYMIC TUMORS: TREATMENT STRATEGIES

KEY FACTORS TO CONSIDER BEFORE TREATING PATIENTS

STRATEGIES FOR SYSTEMIC THERAPY

SURGERY UPFRONT IN RESECTABLE TUMORS

PRECISION MEDICINE APPROACHES?

POST-OPERATIVE DECISION-MAKING

IMMUNE CHECKPOINT INHIBITORS

Merci!

E-Mail: nicolas.girard2@curie.fr @nicogirardcurie