Les tumeurs rares intra-thoraciques

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rythmic.org
Reseau tumeurs THYMiques et Cancer

Les tumeurs rares intra-thoraciques

Définitions

Les tumeurs rares intra-thoraciques

- **Tumeurs primitives rares intra-thoraciques**
  - développées dans le thorax (poumon, plèvre, médiastin, cœur)
  - bénignes ou malignes
  - définies par leur très faible prévalence

- Métastases pulmonaires de tumeurs rares extra-thoraciques
- Formes inhabituelles et sous-groupes rares de tumeurs fréquentes

- **Spécificité thoracique:**
  - explorations diagnostiques (imagerie, endoscopie, chirurgie)
  - thérapeutique (chirurgie, radiothérapie)

Girard et al. Eur Respir Monograph2007;39:85
Girard et al. Murray & Nadel ’s Textbook. Elsevier. 2010

Les tumeurs rares intra-thoraciques

Définitions

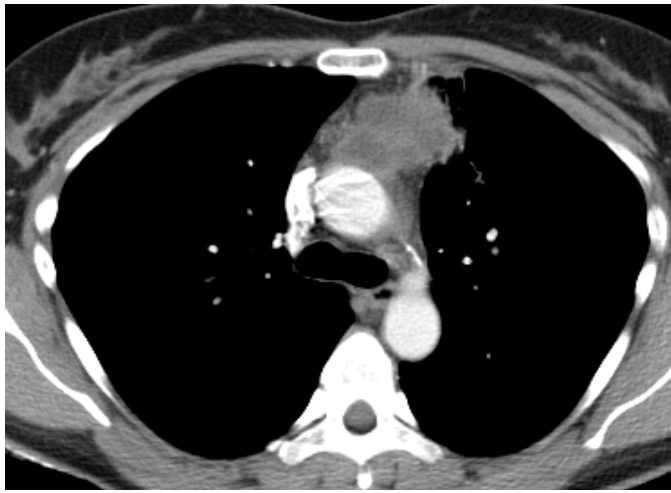
- Localisation

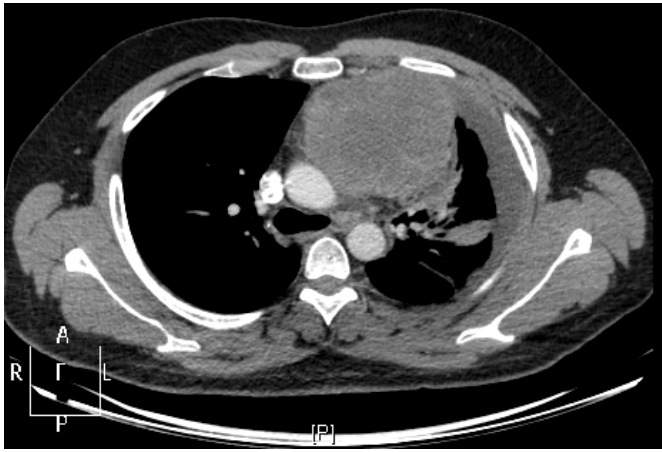
Tumeurs rares intra-thoraciques

- **<u>Définition par la localisation</u>**

  - Tumeurs du médiastin:
    - Tumeurs thymiques
    - Tumeurs germinales

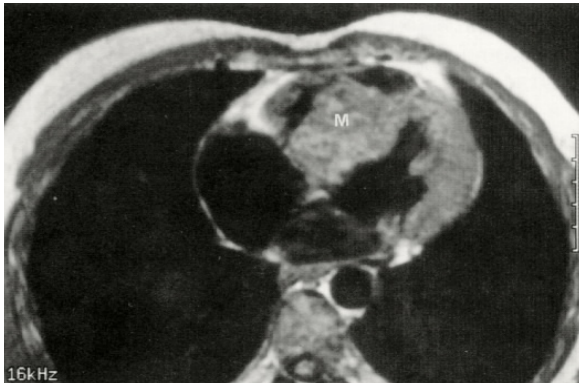
  - Tumeurs cardiaques

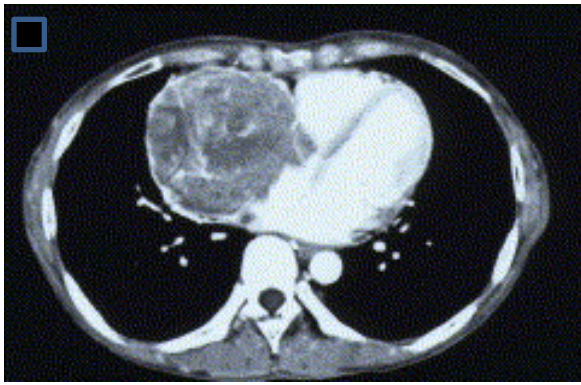




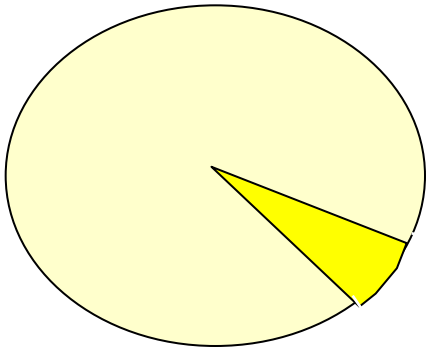
Tumeurs rares intra-thoraciques

- **<u>Définition par la localisation</u>**



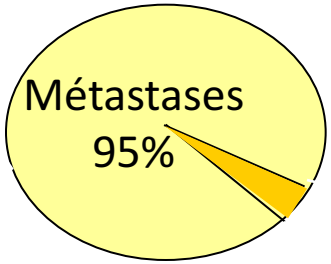


- **Tumeurs cardiaques**:
  - Incidence: 0,001% à 0,28% des cancers

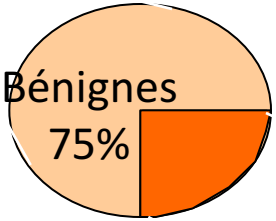


Tumeurs cardiaques 2,3-18,3%

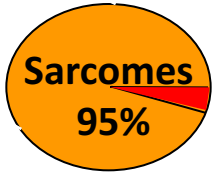
Cancers



Tumeurs primitives 3-5%



Tumeurs malignes 25%



Lymphomes 5%

Travis et al.. WHO Classification of Tumours. 2004
Laissy et al. J Radiol 2004:85:363
Araoz et al. Radiographics 1999;19:1421

Tumeurs rares intra-thoraciques

- **<u>Définition par l'histologie</u>**

  - Carcinomes bronchiques: 99% des tumeurs malignes primitives du thorax

  - **Tumeurs rares: 1% des tumeurs malignes primitives du thorax**
    - plus de 110 sous-types histo-pathologiques différents
    - grande disparité de prévalence :
      - 0,15% pour les tumeurs carcinoïdes
      - moins de 100 cas pour le mélanome pulmonaire primitif

  - **Définition complexe:**
    - évolution des classifications
    - individualisation récente de certains sous-types tumoraux:
      - carcinomes neuro-endocrines à grandes cellules

Travis et al.WHO Classification of Tumours. 2004
Girard et al. Eur Respir Monograph2007;39:85
Miller. Semin Resp Crit Care Med 1997;4:405

Les tumeurs rares intra-thoraciques

- **<u>Définition par l'histologie</u>**

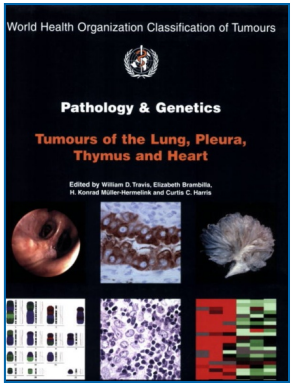
  - **Types histologiques spécifiques au thorax:**
    - hémangiome sclérosant
    - thymomes

  - **Types histologiques rares quelle que soit la localisation:**
    - blastome
    - hémangio-endothéliome épithélioïde

  - **Types histologiques plus fréquents en extra-thoracique**
    - sarcomes
    - lymphomes
    - différenciation souvent spécifique : angiosarcome, MALT

Miller. Semin Resp Crit Care Med 1997;4:405
Pierce et al. Curr Op Oncol 1993;5:343
Marchevsky. Semin Diagn Pathol 1995;12:172

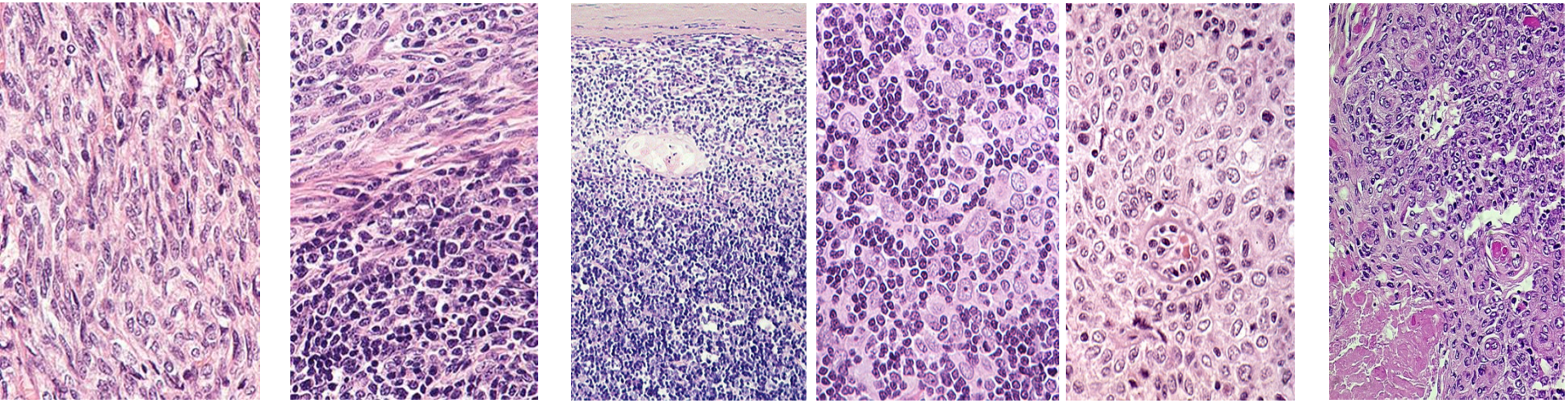
Tumeurs thymiques



- **Classification actuelle : OMS 2004**

Thymome **Carcinome**

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



"Medullaire" Mixte "Cortical" SCC

Intérêt de la double lecture anatomopathologique

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 Rangueil, 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. *Marie-Virginie.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 (NCI).
- 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)

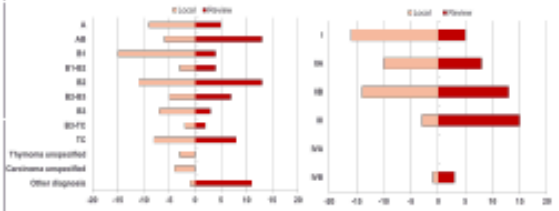


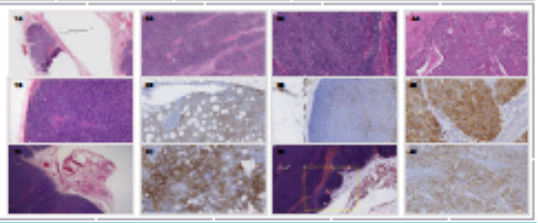
Figure 1. Description of discordances over 109 patients according to histology (left) and stage (right) before and after pathological central review

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.

Intérêt de la double lecture anatomopathologique

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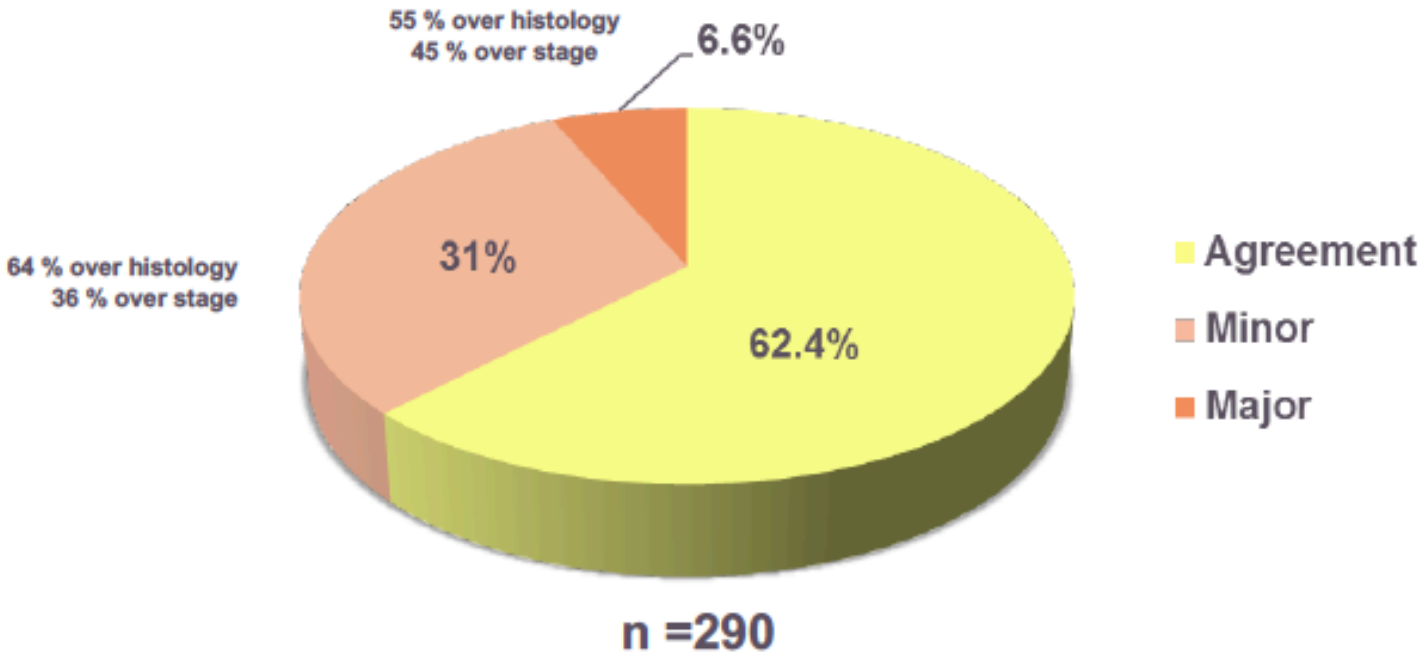


guidelines.

- RYTHMIC Guidelines post-operative recommendations are based on histopathological subtype, Masaoka-Koga stage and resection status.

n =290

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

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.

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence

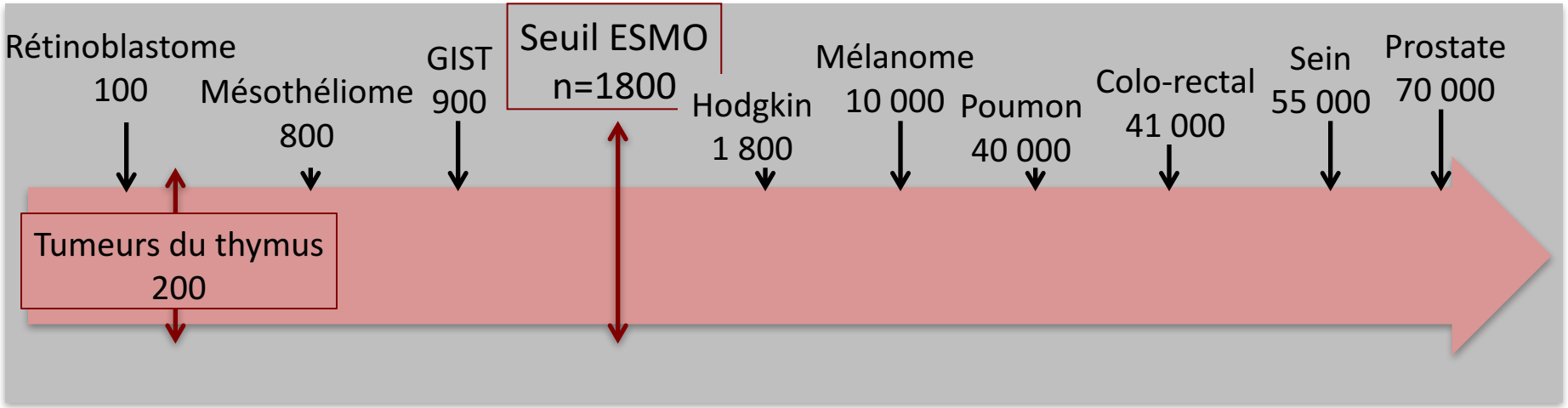
Oncologie orpheline

Tumeurs rares intra-thoraciques

- **<u>Définition par la fréquence</u>**

  - **Consensus européen ESMO/JARC:**
    - incidence **<3 ou <6/100000**, soit 1800/3600 cas en France
    … pour *chaque* sous-type tumoral
    … chaque année

Gatta et al. Lancet 2006; 7:132

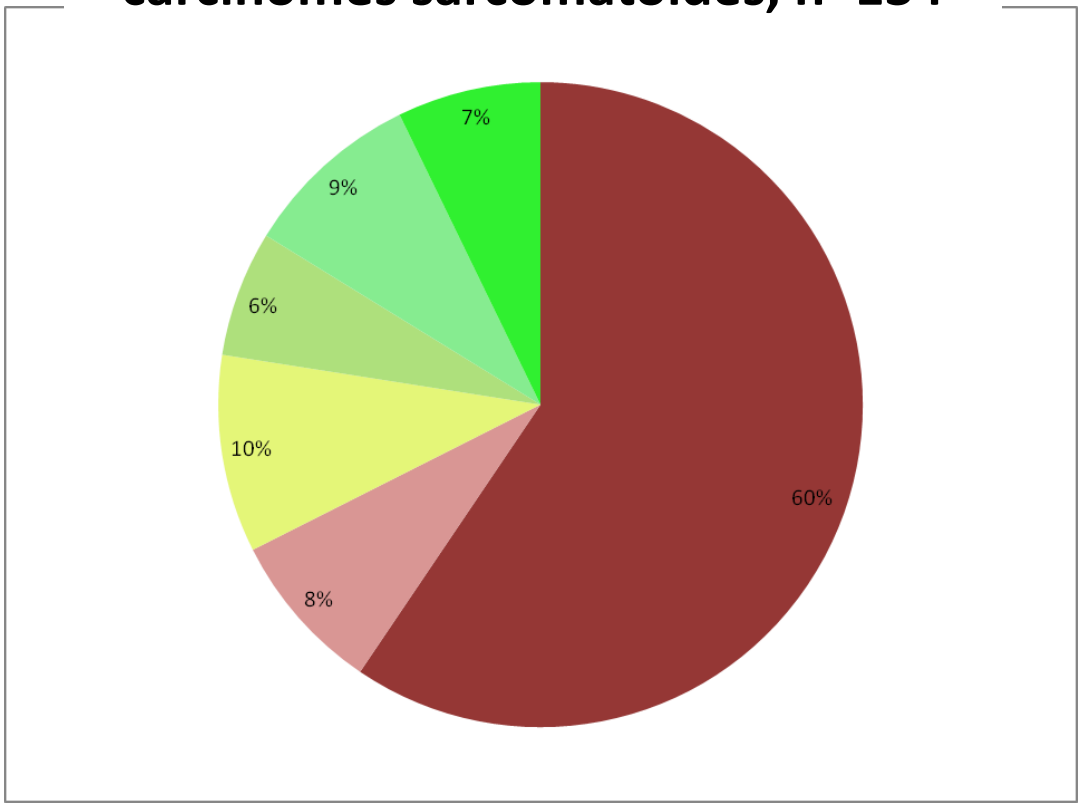


Tumeurs pulmonaires rares

- **Définition par la fréquence**

  - **Publications 1989-2013**

carcinomes sarcomatoïdes, n=134



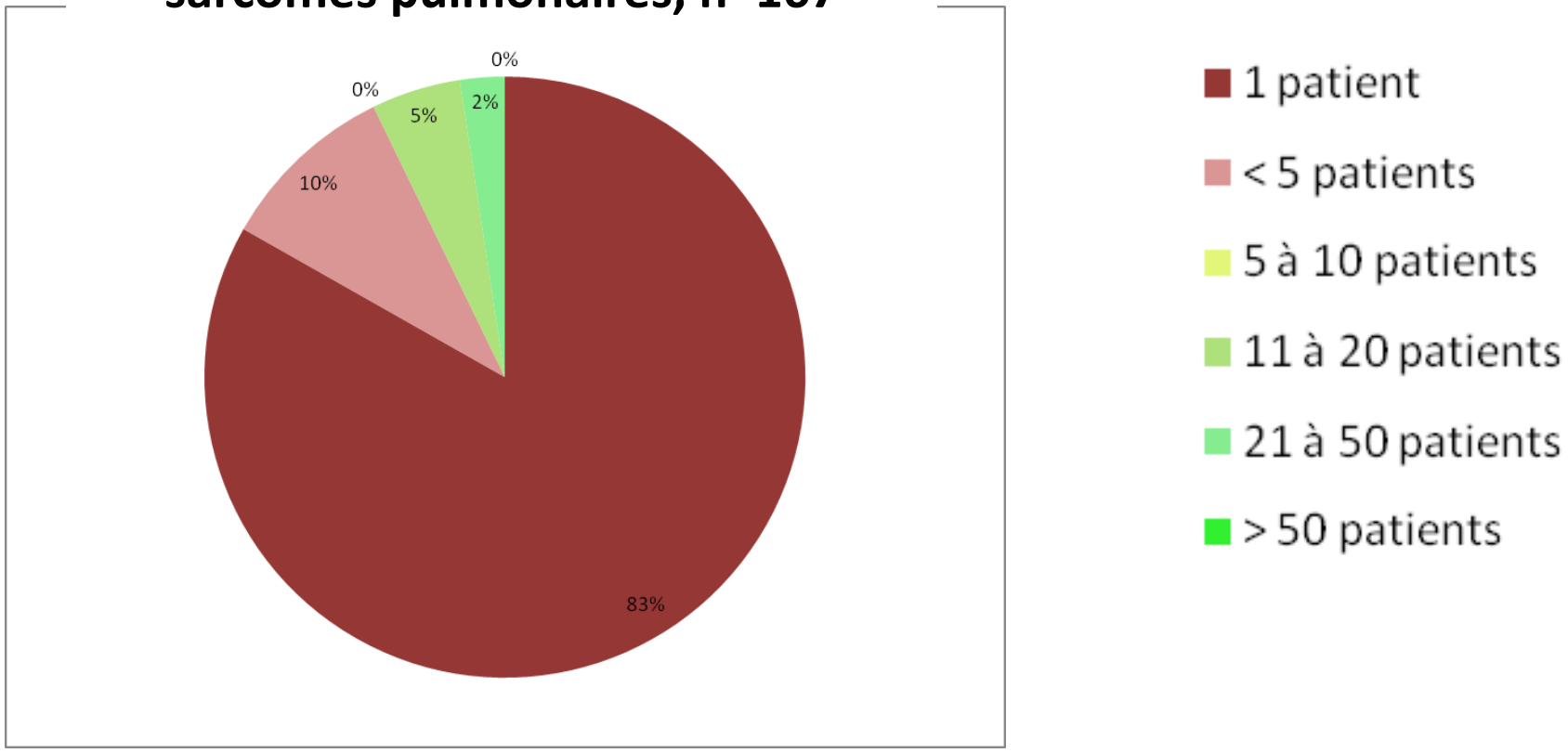
Girard et al. Eur Respir Monograph 2007;39:85

Tumeurs pulmonaires rares

- **<u>Définition par la fréquence</u>**

  - **Publications 1989-2013**

sarcomes pulmonaires, n=167



Girard et al. Eur Respir Monograph 2007;39:85

Tumeurs pulmonaires rares

- **<u>Définition par la fréquence</u>**

  - **Sous-types histologiques les plus fréquents :**
    - tumeurs carcinoïdes
    - tumeurs myofibroblastiques
    - lymphomes du *Mucosa-Associated Lymphoid Tissue* (MALT)
    - carcinomes sarcomatoïdes, dont les pneumoblastomes

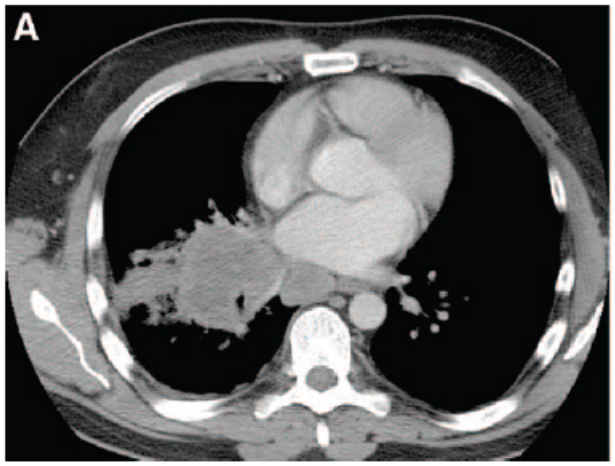
Les tumeurs rares intra-thoraciques

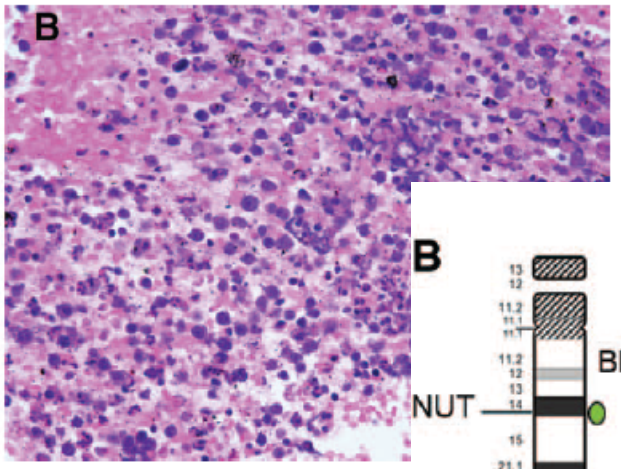
Définitions

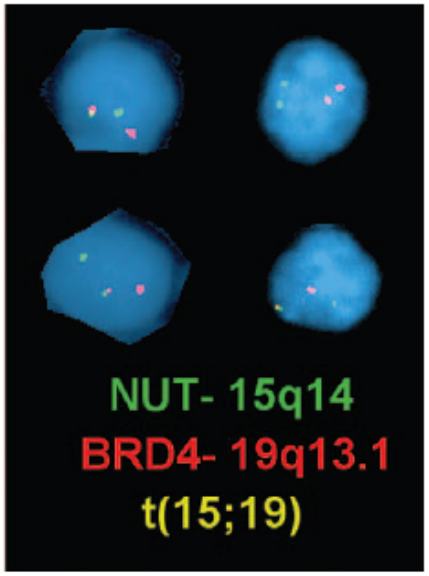
- Localisation
- Histologie
- Fréquence
- Moléculaire

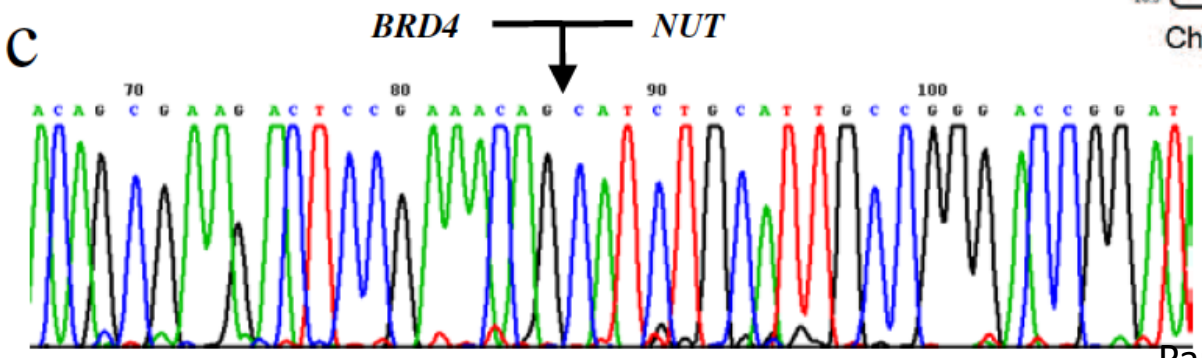
Oncologie orpheline

Carcinomes de la ligne médiane “NUT”









Engleson et al. BMC Cancer 2006, 6:69
Parikh et al. J Thorac Oncol. 2013;8: 1335
Evans, et al. Am J Surg Pathol 2012;36:1222

Carcinomes SMARC-A4 déficients

nature genetics

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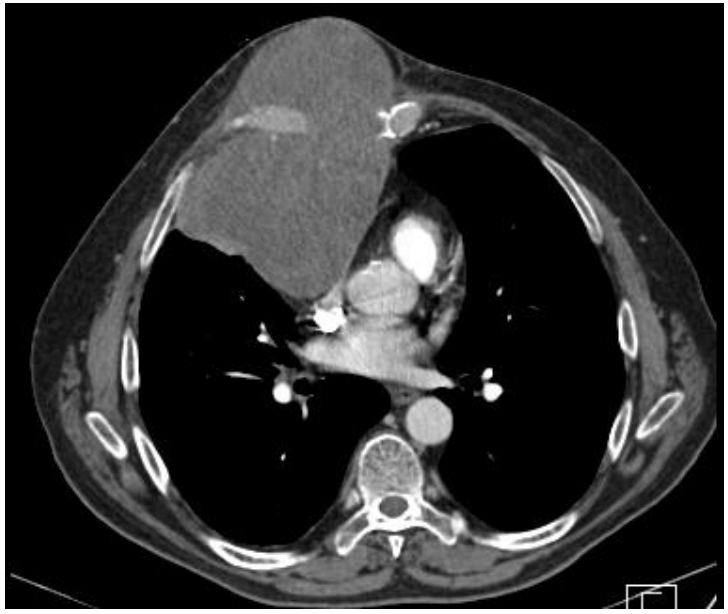
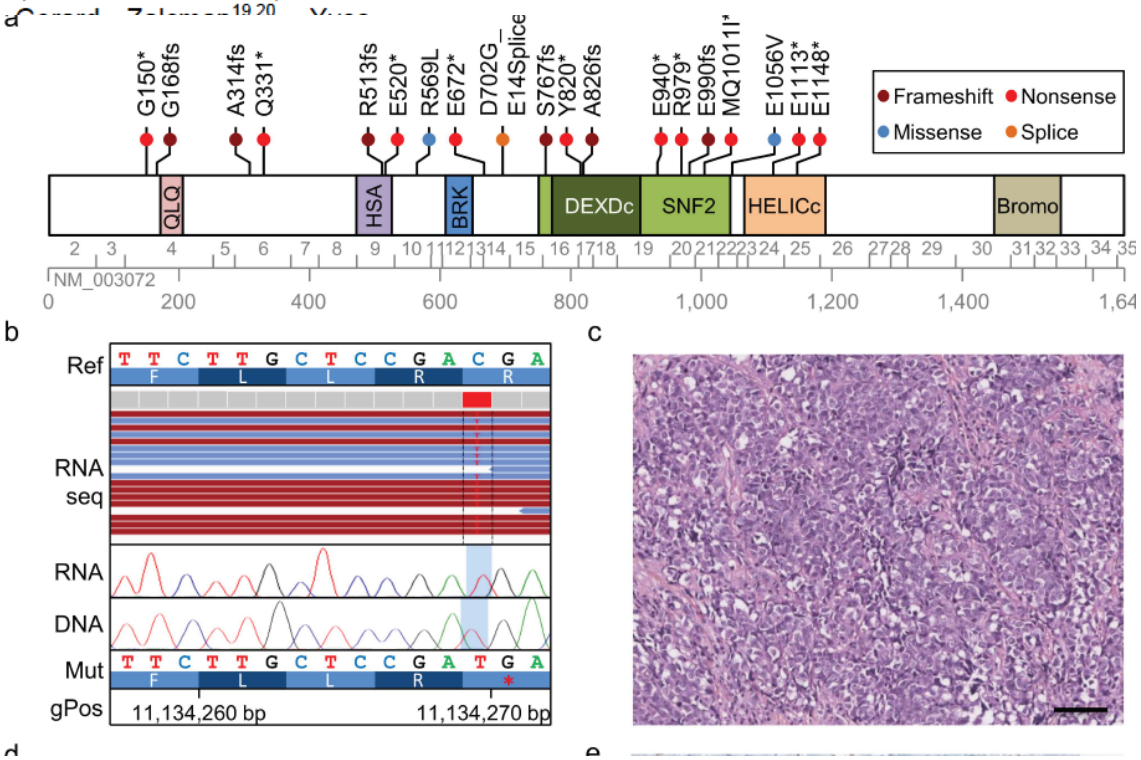
SMARCA4 inactivation defines a group of undifferentiated thoracic malignancies transcriptionally related to *BAF*-deficient sarcomas

Francois Le Loarer[1-3], Sarah Watson[4,5], Gaelle Pierron[6], Vincent Thomas de Montpreville[7], Stelly Ballet[6], Nelly Firmin[8], Aurelie Auguste[9], Daniel Pissaloux[2], Sandrine Boyault[10], Sandrine Paindavoine[2], Pierre Joseph Dechelotte[11], Benjamin Besse[12,13], Jean Michel Vignaud[14], Marie Brevet[3,15], Elie Fadel[13,16], Wilfrid Richer[4,17], Isabelle Treilleux[2], Julien Masliah-Planchon[5,6], Mojgan Devouassoux-Shisheboran[18] [illegible] Allory[21,22,23], Franck Bourdeaut[6,24], Francoise Thivolet-Beji[illegible] Nicolas Girard[3,25], Sylvie Lantuejoul[26-27], Francoise Ga[illegible]





IN PRESS

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

Oncologie orpheline

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

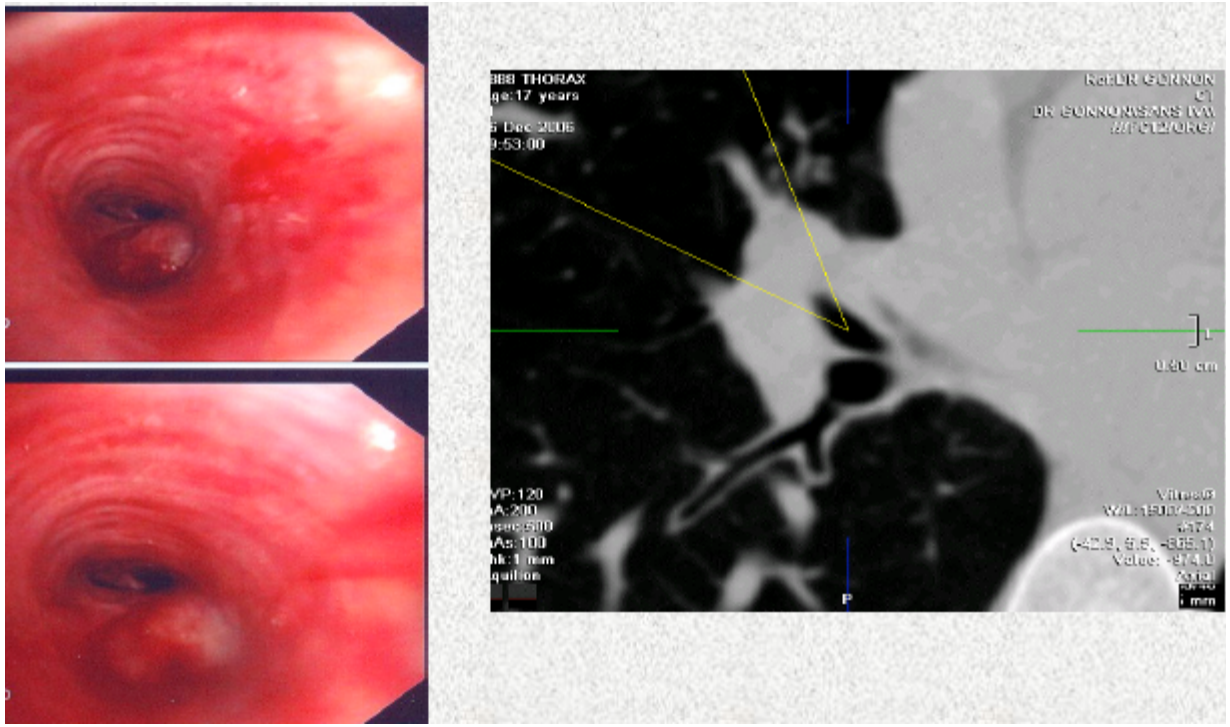
Signes évocateurs

- Aspects radiologiques

Oncologie orpheline

Quelle démarche en pratique clinique?

- **<u>Reconnaissance de signes cliniques et radiologiques évocateurs</u>**



Quelle démarche en pratique clinique?

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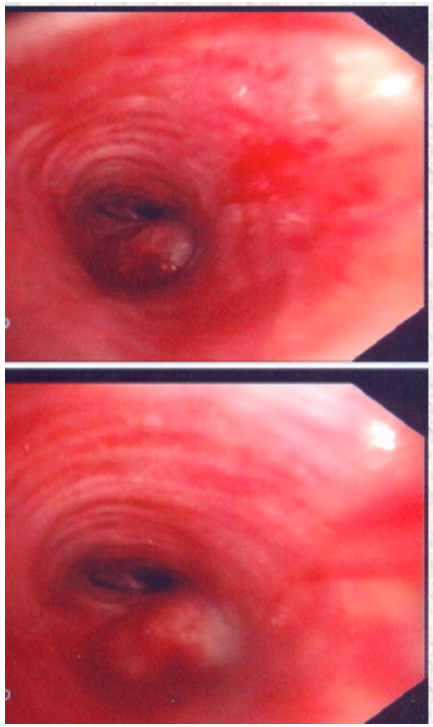

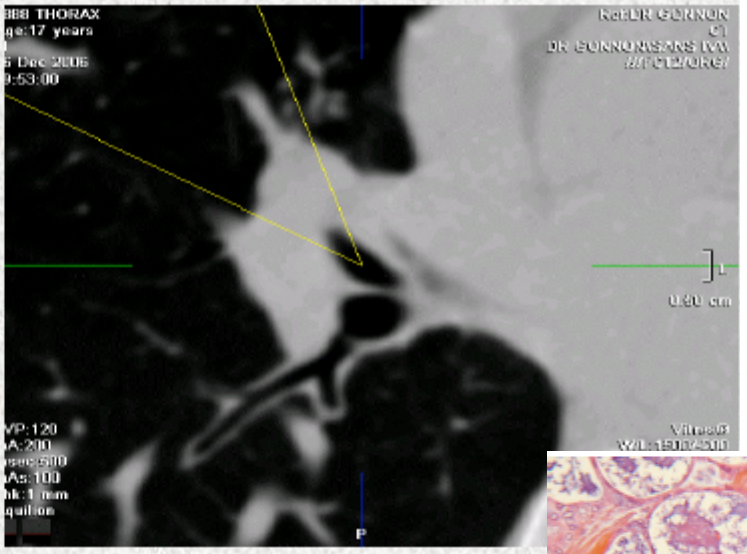

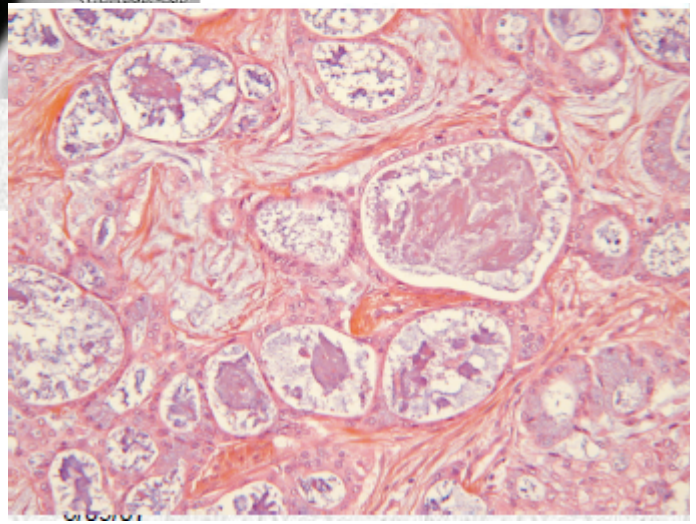

Tumeur carcinoïde

Quelle démarche en pratique clinique?

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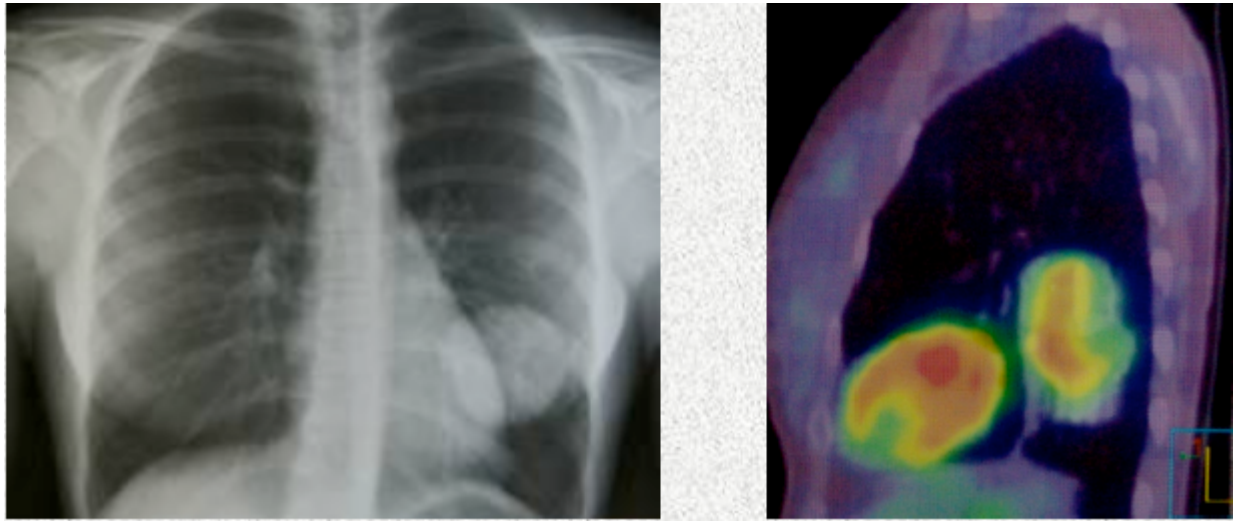

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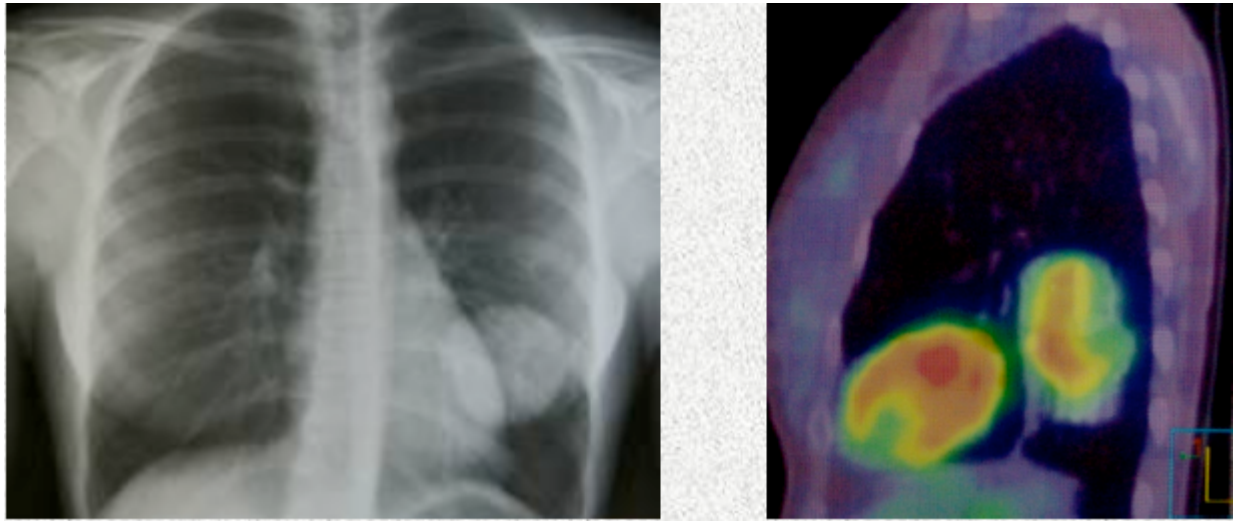
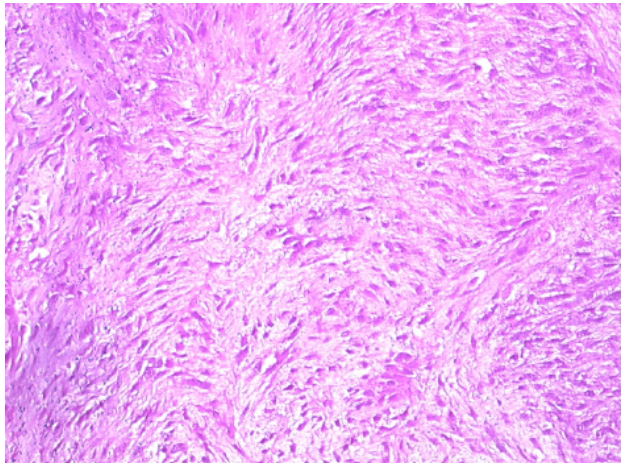


Ostéosarcome pulmonaire primitif



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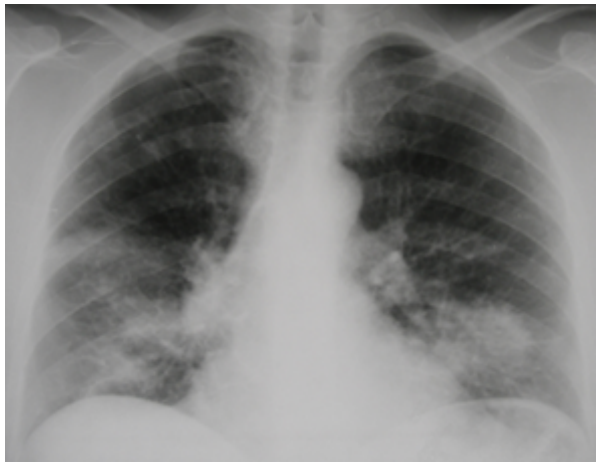

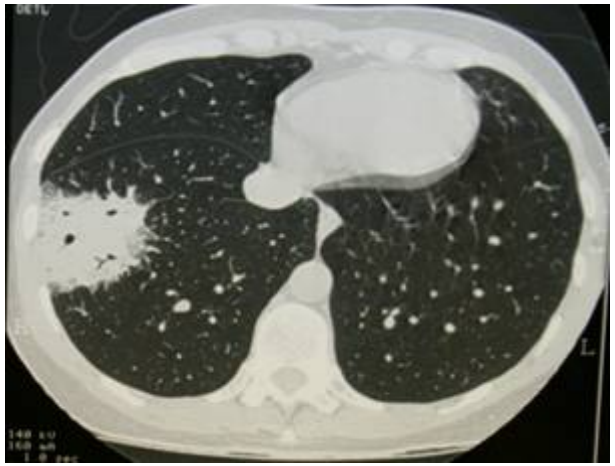

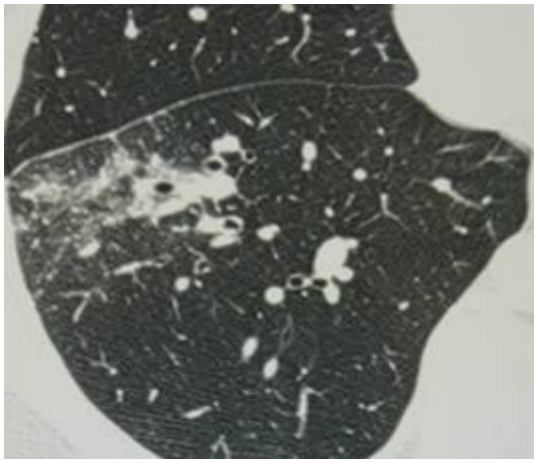

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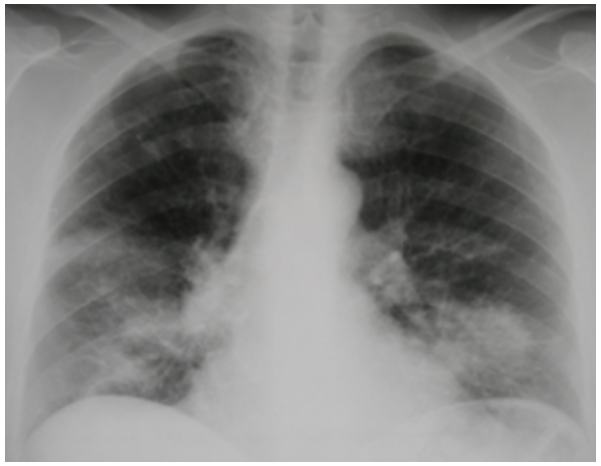
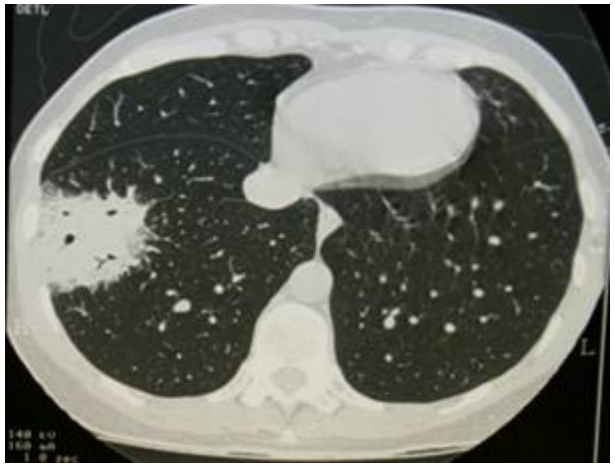
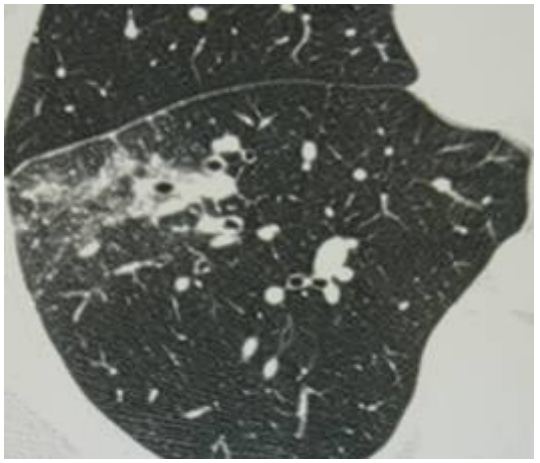
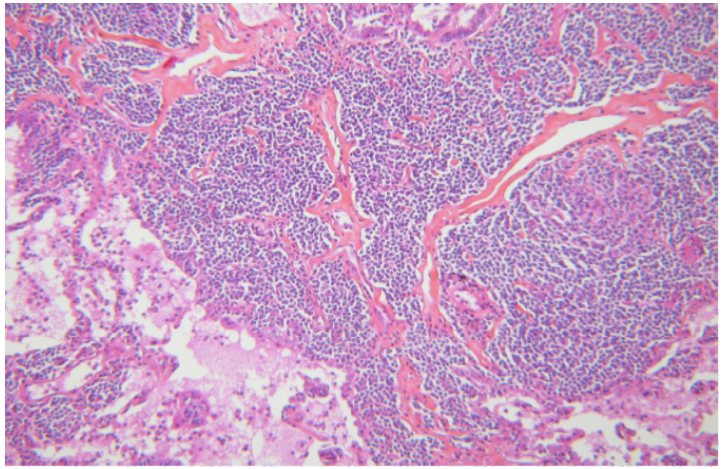
- **<u>Reconnaissance de signes cliniques et radiologiques évocateurs</u>**







Lymphome de type MALT



Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques

Oncologie orpheline

Quelle démarche en pratique clinique?

- **<u>Reconnaissance de signes cliniques évocateurs</u>**

  - Absence de tabagisme:
    - 15% des carcinomes bronchiques non à petites cellules
    - 80% des tumeurs rares

  - Age < 40 ans:
    - <10% des cancers bronchiques non à petites cellules
    - 50% des tumeurs rares

  - Syndromes paranéoplasiques

  - Localisation métastatique inhabituelle
  - Présentation « discordante »

Manifestations associées aux tumeurs thymiques

Neuromusculaires
Myasthénie
Neuropathie périphérique
Polymyosite
Dermatomyosite
Encéphalite
Myélite optique

Hématologiques
Erythroblastopénie
Anémie auto-immune
Polyglobulie
Pancytopénie
Leucémie
Myélome

Auto-immunes
Lupus
Polyarthrite rhumatoïde
Gougerot-Sjogren
Sclérodermie

Endocrinologiques
NEM
Cushing
Hyperthyroïdie

Dermatologiques
Pemphigus
Lichen plan
Candidose chronique
Alopécie

Autres
Myocardite
Syndrome néphrotique
Colite inflammatoire
Pierre-Marie
Pneumopathie interstitielle

Déficits immunologiques
Hypogammaglobulinémie
Lymphopénie

Manifestations spécifiques

- **Neuropathie et encéphalite limbique, anticorps anti-CV2**

- **Carcinome bronchiolo-alvéolaire**

ORIGINAL ARTICLES

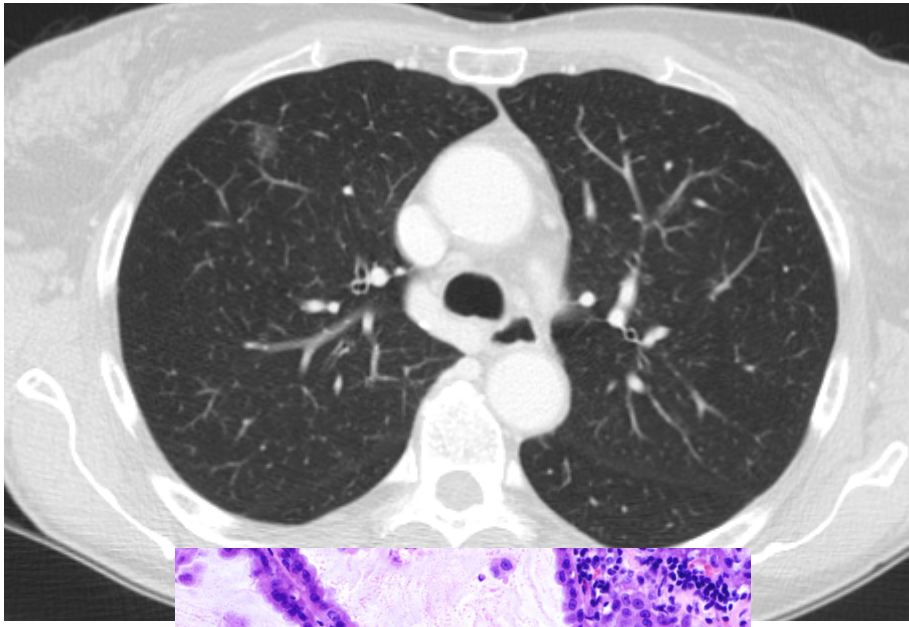
CRMP-5 Neuronal Autoantibody: Marker of Lung Cancer and Thymoma-Related Autoimmunity

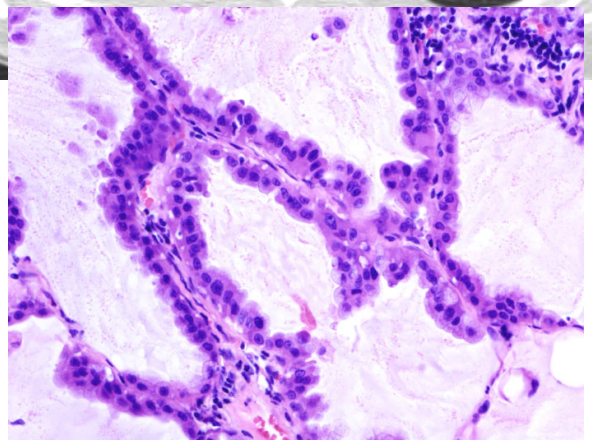
Zhiya Yu, MD, PhD,[1] Thomas J. Kryzer, AS,[1,3] Guy E. Griesmann, MS,[1,3] Kwang-kuk Kim, MD, PhD,[2] Eduardo E. Benarroch, MD,[2] and Vanda A. Lennon, MD, PhD[1–3]

Table 2. Neoplasms Found in 116 CRMP-5–Seropositive Patients[a]

No. Patients	Neoplasm
89	Lung carcinoma[b]
(74)	Histologically proven
(15)	Imaged
7	Thymoma[c]
9	Other neoplasms[d]
11	None[e]

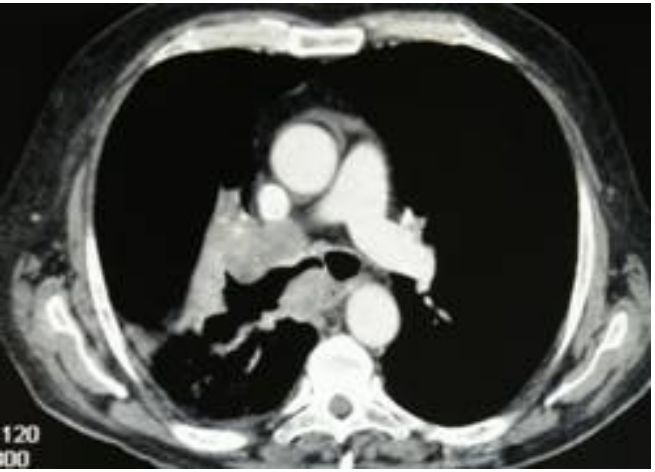
Ann Neurol 2001;49:146–154

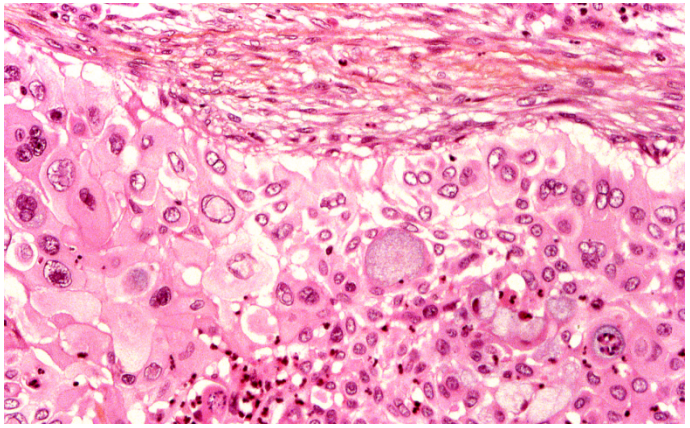




Quelle démarche en pratique clinique?

- **Présentation discordante**





Quelle démarche en pratique clinique?

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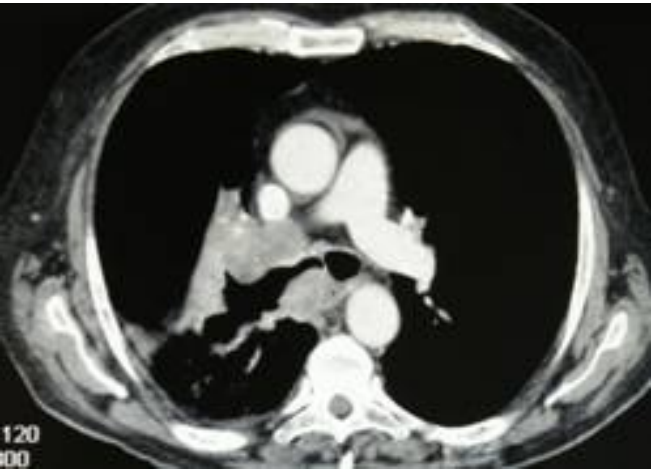
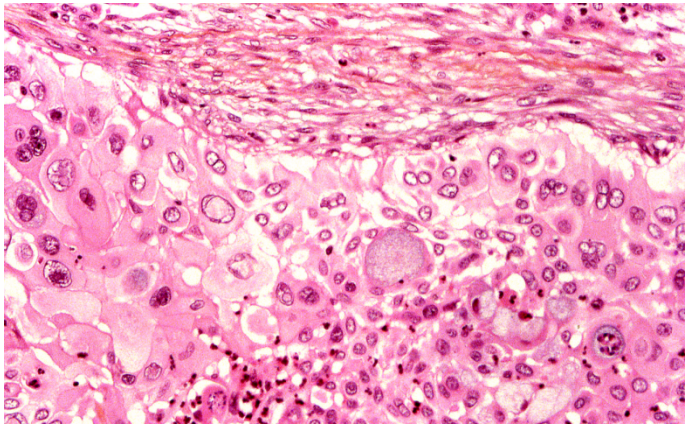
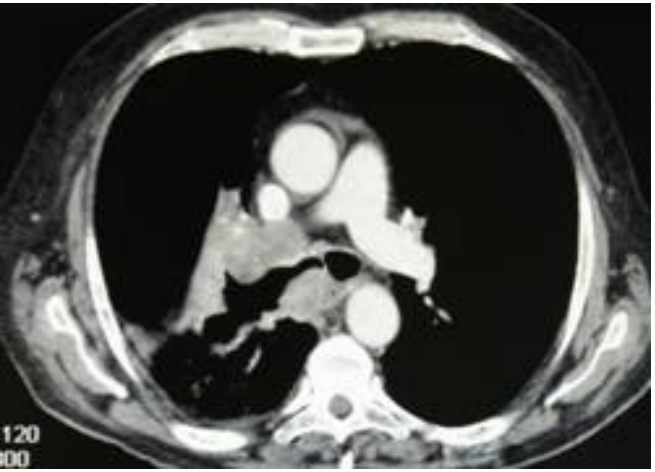


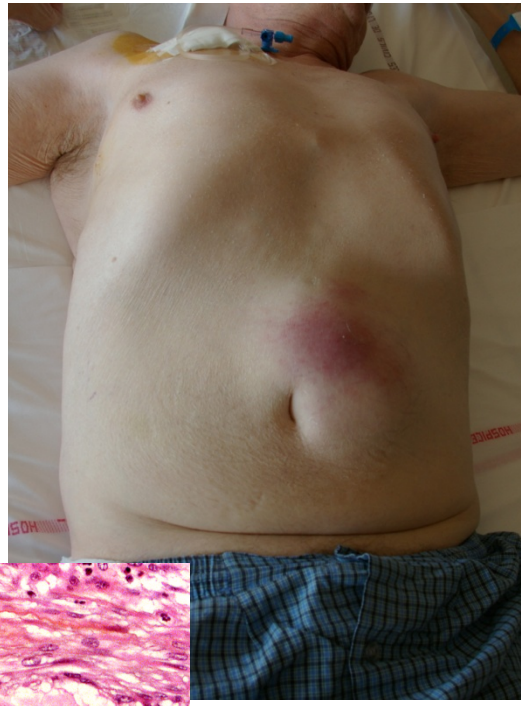


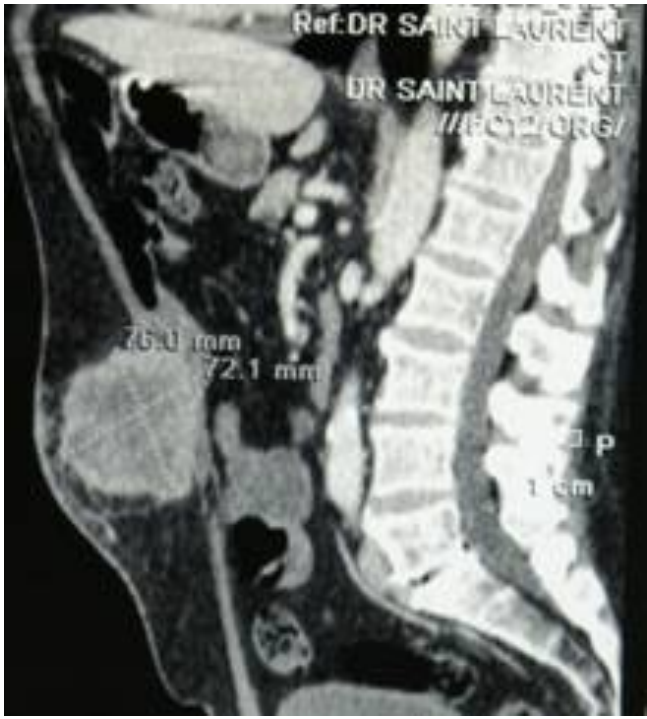
Carcinome épidermoïde

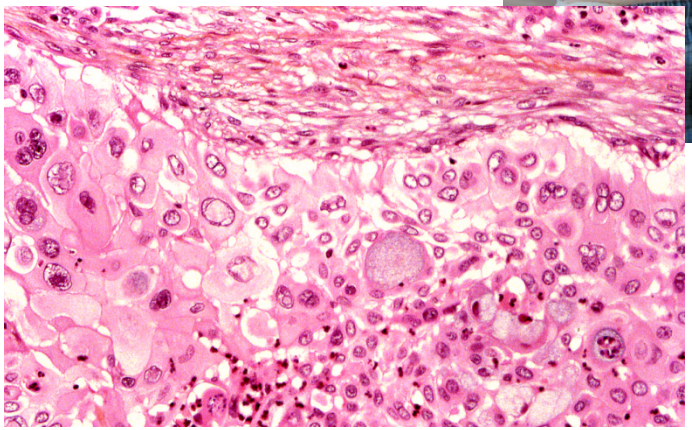
Quelle démarche en pratique clinique?

- **Présentation discordante**









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Quelle démarche en pratique clinique?

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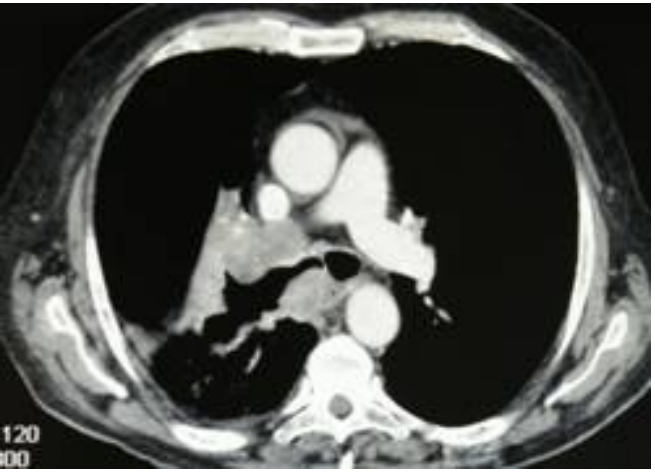
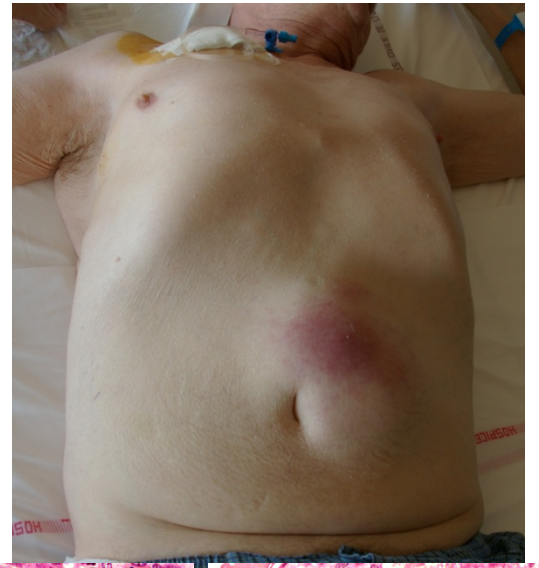
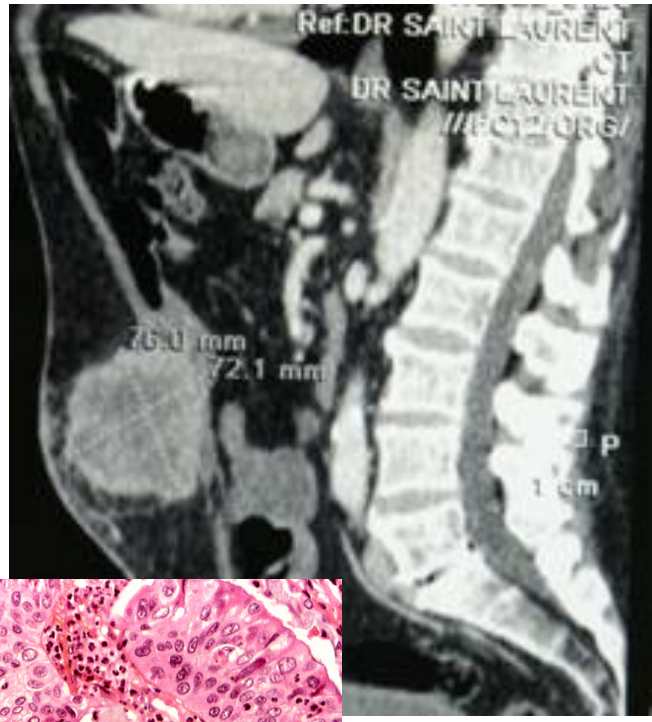
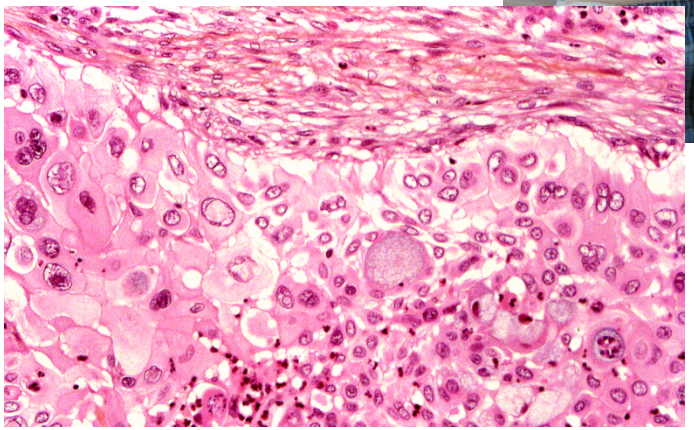
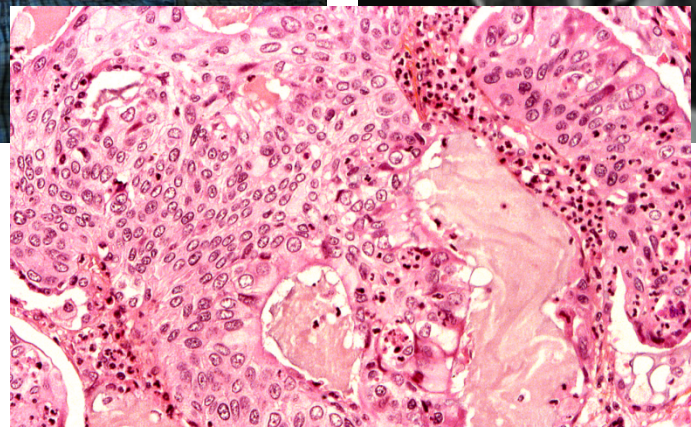






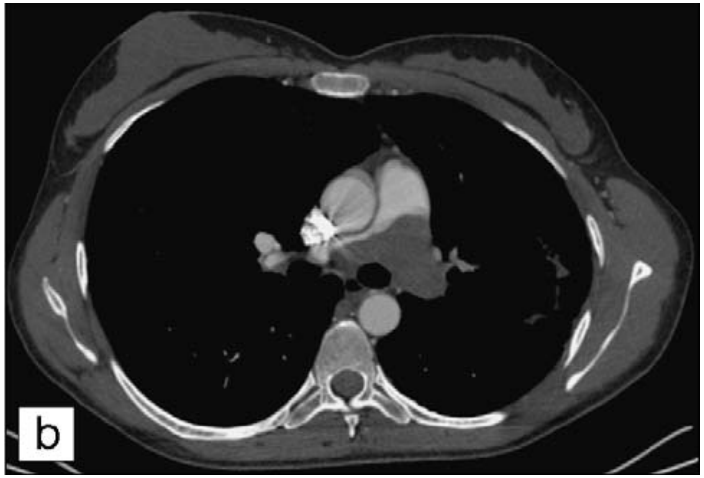




Carcinome muco-épidermoïde

Quelle démarche en pratique clinique?

- **<u>Reconnaissance de signes cliniques et radiologiques évocateurs</u>**



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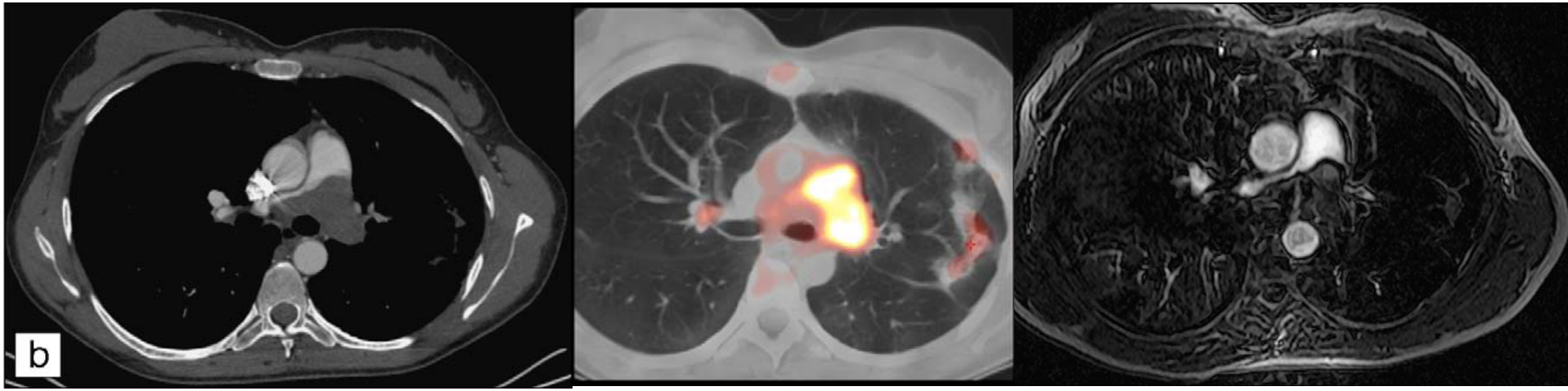

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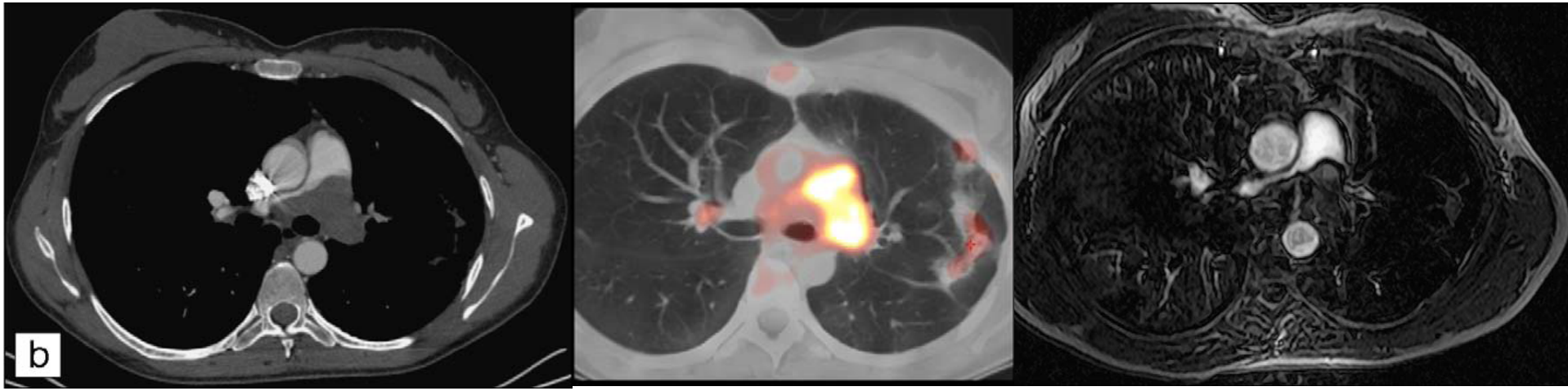
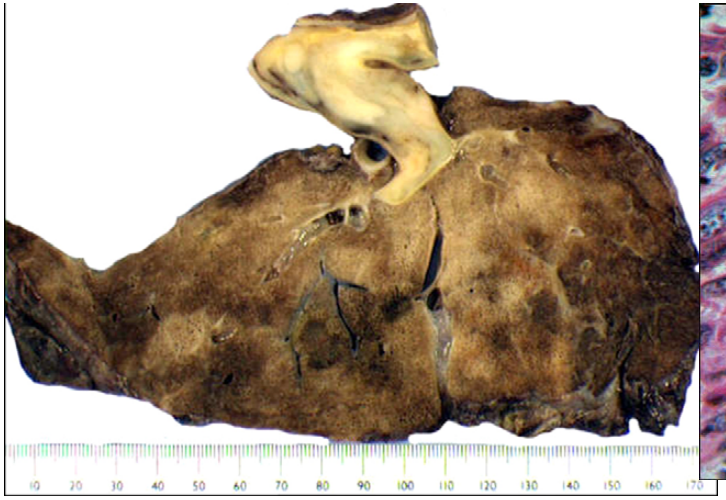
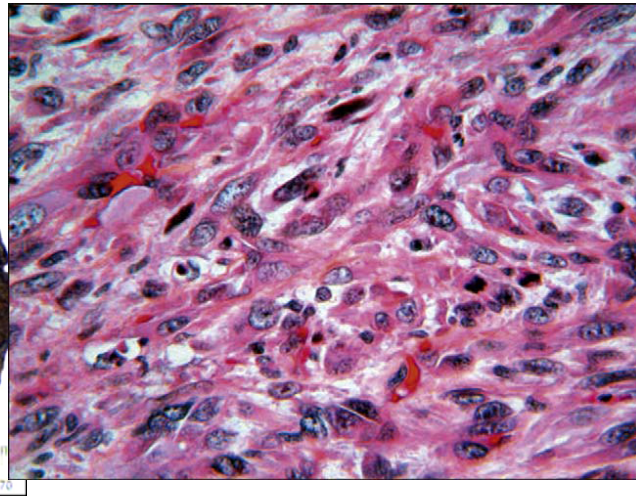


Angiosarcome de l'artère pulmonaire





Girard et al. Presse Med 2009;38:1167

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
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Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Oncologie orpheline

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 26), pp: 42428-42437

Research Paper

MET exon 14 mutations as targets in routine molecular analysis of primary sarcomatoid carcinoma of the lung

Raphaël Saffroy[1,2,*], Vincent Fallet[3,4,*], Nicolas Girard[5], Julien Mazieres[6], Denis Moro Sibilot[7], Sylvie Lantuejoul[8], Isabelle Rouquette[9], Françoise Thivolet-Bejui[10], Thibaut Vieira[3,4], Martine Antoine[3,11], Jacques Cadranel[3,4], Antoinette Lemoine[1,2,*] and Marie Wislez[3,4,*]

Table 1: Studies assessing MET mutations in sarcomatoid carcinoma.

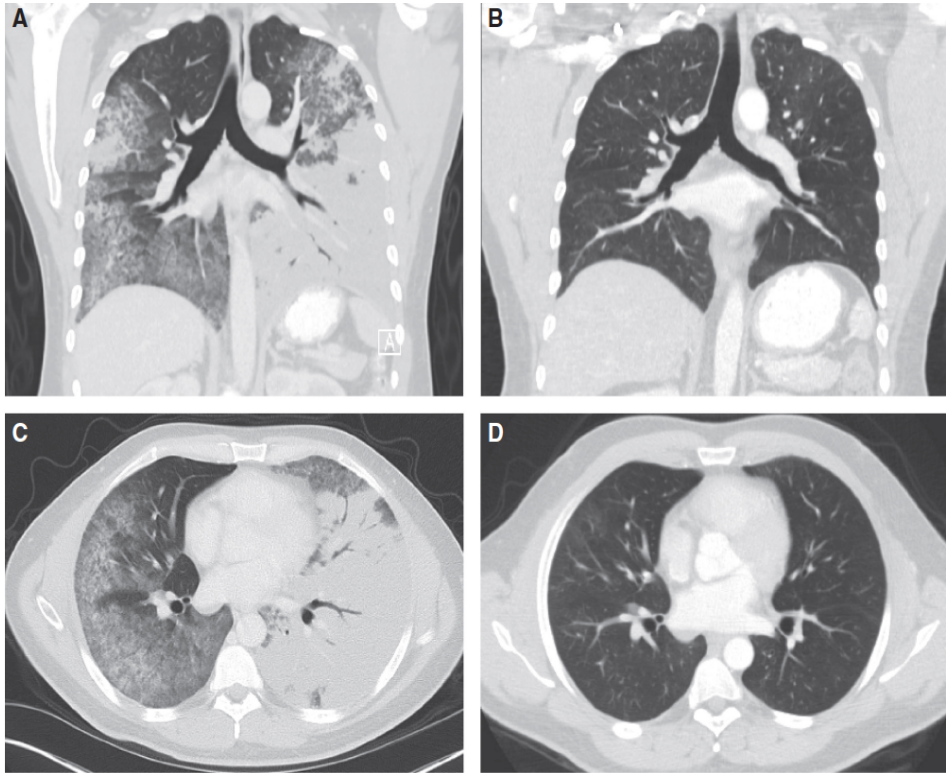
Study	Number of pts *N*=	Histological Subtypes of SC	Controls *N*=	MET ex 14 analysis	MET ex 14 frequency in SC *N* (%)	MET ex 14 frequency in controls *N* (%)
Saffroy *et al* 2016	81	PC (77.8%) Others (22.2%)	ADC (N=150)	Whole met ex 14 and flanking intronic regions (14 +/- n bp) MassArray and HRM Paraffin embedded tumors	4 (4.9%)	8 (5.3%)
Schrock *et al* 2016	104	PC and others	NSCLC (N=11 101) including ADC (N=7140)	NGS - Capture hybrydization including intronic regions Paraffin embedded tumors	8 (7.7%)	NSCLC : 290 (2.14%) ADC : 205 (2.8%)
Tong *et al* 2016	22	ND	NSCLC (N=665) including ADC (N=392)	Whole met ex 14 and flanking intronic regions (14 +/- n bp) Sanger sequencing Paraffin embedded tumors	7 (31.8 %)	NSCLC : 1 (0.3%) ADC : 10 (2.6%)
Awad *et al* 2016	15	ND	NSLC (N=1126) including ADC (N=873)	NGS (22 genes)	4 (26.7%)	NSCLC : 6 (2.4%) ADC : 18 (2.1%)
Liu *et al* 2015	36	ND carcinosarcoma and blastoma excluded	Not studied	Whole-exome sequencing Targeting exome sequencing (Truseq panel, Illumina) Sanger sequencing half frozen & half paraffin embedded tumors	8 (22%)	Not studied
Vieira *et al* 2014	77	PC (78%) Others (22%)	Not studied	Sizing analysis of fluorescently labeled PCR products (only 3'-splice site of MET ex 14 deletions) Formalin-fixed paraffin-embedded samples	2 (3%)	Not studied

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

ROS1 Rearrangements Define a Unique Molecular Class of Lung Cancers

Kristin Bergethon, Alice T. Shaw, Sai-Hong Ignatius Ou, Ryohei Katayama, Christine M. Lovly, Nerina T. McDonald, Pierre P. Massion, Christina Siwak-Tapp, Adriana Gonzalez, Rong Fang, Eugene J. Mark, Julie M. Batten, Haiquan Chen, Keith D. Wilner, Eunice L. Kwak, Jeffrey W. Clark, David P. Carbone, Hongbin Ji, Jeffrey A. Engelman, Mari Mino-Kenudson, William Pao, and A. John Iafrate



J Clin Oncol 2012;30:863

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

Oncologie orpheline

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Définitions

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- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif

Oncologie orpheline

Quelle démarche en pratique clinique?

- **<u>Prise en charge diagnostique</u>**

  - Les questions posées évoluent au cours de la prise en charge :

Présentation initiale → **Chirurgie** → **Récidive**

↑

- Tumoral ou non-tumoral ?
- Bénin ou malin ?

Quelle démarche en pratique clinique?

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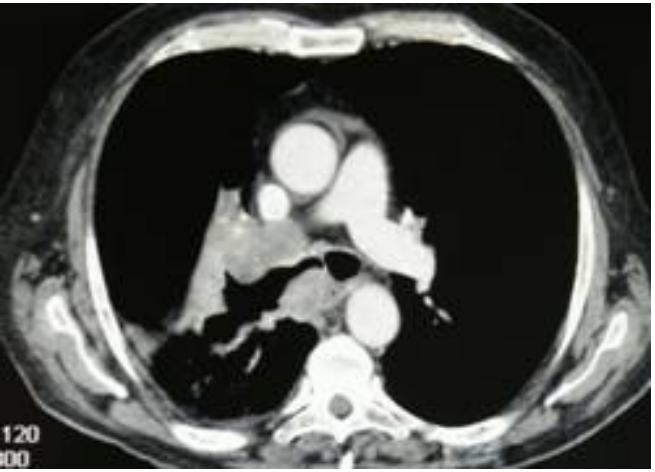
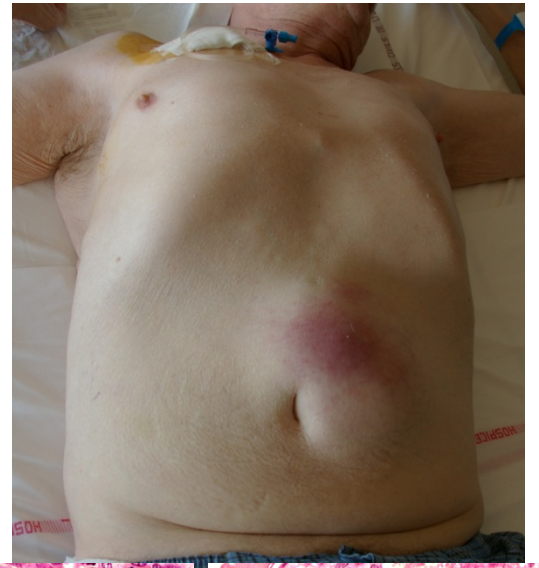
- **Cancer bronchique ou tumeur rare?**

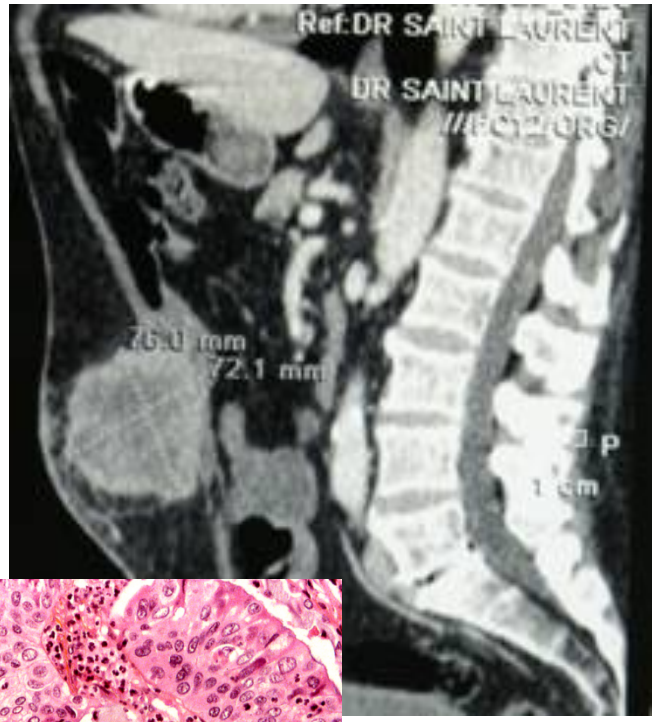
- PROBLÉMATIQUES: - valeur des biopsies / tumeurs biphasiques

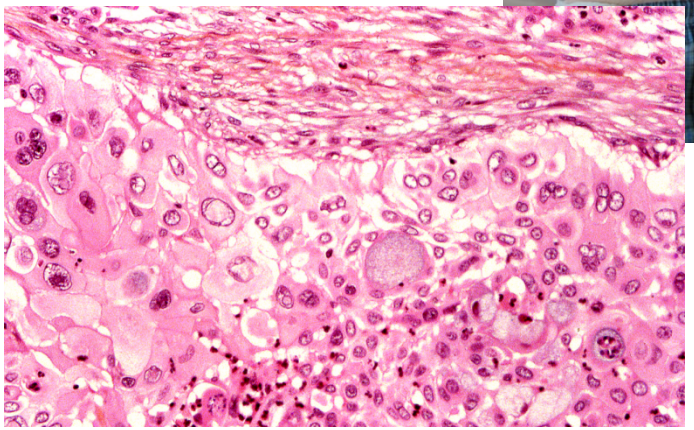
Quelle démarche en pratique clinique?

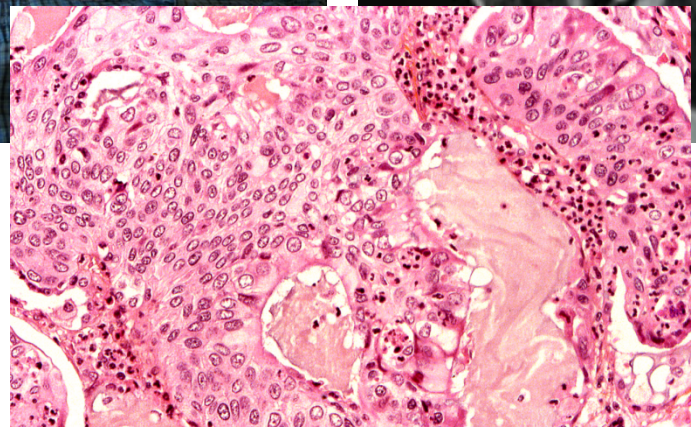
- **Reconnaissance de signes cliniques et radiologiques évocateurs**











Carcinome muco-épidermoïde

Diagnostic sur biopsies de petite taille

Eur Respir J 2009; 34: 1408–1416
DOI: 10.1183/09031936.00039309

Clinical characteristics and prognostic factors of pulmonary MALT lymphoma

R. Borie, M. Wislez, G. Thabut, M. Antoine, A. Rabbat, L-J. Couderc, I. Monnet, H. Nunes, F-X. Blanc, H. Mal, A. Bergeron, D. Dusser, D. Israël-Biet, B. Crestani and J. Cadranel

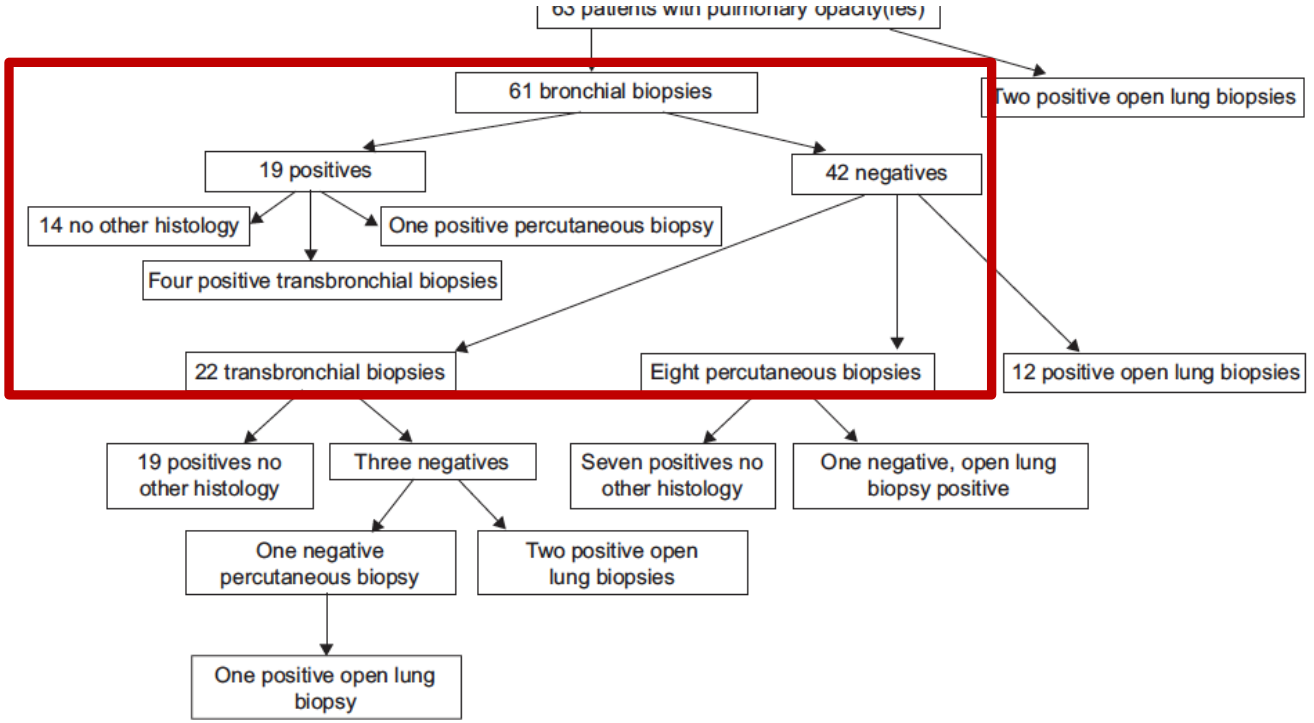


FIGURE 1. Strategy for pathological diagnosis in pulmonary mucosa-associated lymphoid tissue-derived (MALT) lymphoma. 63 patients were referred for diagnosis of pulmonary opacity(ies). 61 had bronchial biopsies during fibreoptic bronchoscopy, among which transbronchial biopsies were performed in the same procedure in 26 cases (42.6%). In a second step, 10 patients had computed tomography (CT)-guided percutaneous transparietal biopsies. One supplementary patient had CT scan biopsies, whereas re-reading of the bronchial biopsy revealed MALT lymphoma. In a third step, the diagnosis was made by open lung biopsy in 18 patients.

Quelle démarche en pratique clinique?

- **<u>Prise en charge diagnostique</u>**

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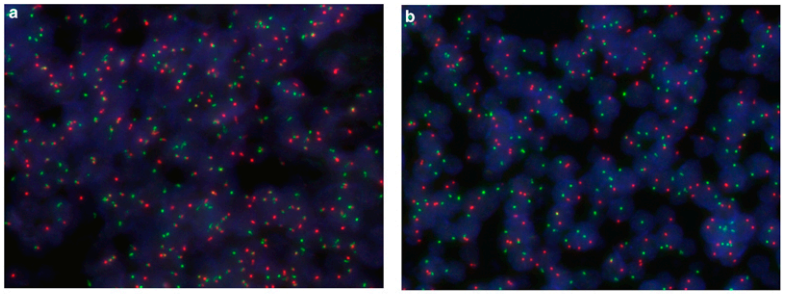
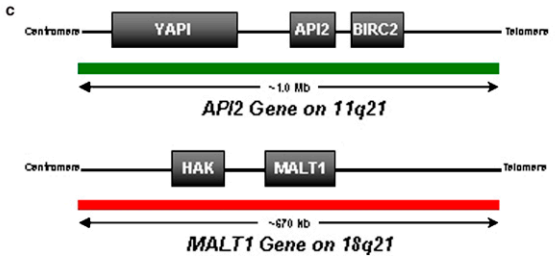
- Cancer bronchique ou tumeur rare?

- PROBLÉMATIQUES:
  - valeur des biopsies / tumeurs biphasiques
  - techniques spécifiques: IHC / cytogénétique

Lymphome de type MALT





Clonality and phenotyping analysis of alveolar lymphocytes is suggestive of pulmonary MALT lymphoma

Raphael Borie [a,b], Marie Wislez [a,c,*], Martine Antoine [d], Jocelyne Fleury-Feith [c,e], Gabriel Thabut [f,g], Bruno Crestani [b,g], Isabelle Monnet [h], Hilario Nunes [i,j], Marie-Helene Delfau-Larue [k,l], Jacques Cadranel [a,c]

TABLE 2 Main cytogenetic abnormalities involved in marginal zone lymphoma

Cytogenetic abnormality	Site (frequency)
t(11;18)(q21;q21) *API2-MALT1*	Lung (30–50%) Intestine (~40%) Stomach (5–~30%) Ocular adnexa (0–5%)
t(14;18)(q32;q21) *IgH-MALT1*	Ocular adnexa, skin, salivary glands and liver (frequent) Lung (10%) Stomach (rare)
t(1;14)(p22;q32) *BCL10-IgH*	Stomach (5%) Lung (rare)
t(3;14)(p14.1;q32) *FOXP1-IgH*	All sites (10%) Thyroid (50%) Ocular adnexa (20%) Skin (10%)
Trisomy 3, 12, 18	Intestine Salivary glands Ocular adnexa

Alvéolite Lymphocytaire 84%

Population de lymphocytes B clonaux 82%

Sensibilité : 82%
Spécificité: 90%

Recherche de translocations diagnostiques

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2012
Soft Tissue Sarcoma

NCCN Guidelines Index
Soft Tissue Sarcoma, Table of Contents
Discussion

PRINCIPLES OF ANCILLARY TECHNIQUES USEFUL IN THE DIAGNOSIS OF SARCOMAS

TUMOR	ABERRATION	GENE(S) INVOLVED
Other Sarcomas–(continued)		
Extraskeletal myxoid chondrosarcoma	t(9;22)(q22;q12) t(9;17)(q22;q11) t(9;15)(q22;q21) t(3;9)(q11;q22)	*EWSR1-NR4A3* *TAF2N-NR4A3* *TCF12-NR4A3* *TFG-NR4A3*
Sporadic and familial GIST Carney-Stratakis syndrome (gastric GIST and paragaglioma)	Activating kinase mutations Krebs cycle mutation	*KIT or PDGFRA* *germline SDH* subunit mutations
Inflammatory myofibroblastic tumor	t(1;2)(q22;p23) t(2;19)(p23;p13) t(2;17)(p23;q23) t(2;2)(p23;q13) t(2;11)(p23;p15) inv(2)(p23;q35)	*TPM3-ALK* *TPM4-ALK* *CLTC-ALK* *RANBP2-ALK* *CARS-ALK* *ATIC-ALK*
Leiomyosarcoma	Complex alterations	Unknown
Low grade fibromyxoid sarcoma	t(7;16)(q33;p11) t(11;16)(p11;p11)	*FUS-CREB3L2* *FUS-CREB3L1*
Malignant peripheral nerve sheath tumor	Complex alterations	Unknown
Synovial sarcoma	t(X;18)(p11;q11) t(X;18)(p11;q11) t(X;18)(p11;q11)	*SS18-SSX1* *SS18-SSX2* *SS18-SSX4*
Tenosynovial giant cell tumor/pigmented villonodular synovitis (TGCT/PVNS)	t(1;2)(p13;q35)	*CSF1*

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
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- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Oncologie orpheline

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire

Quelle démarche en pratique clinique?

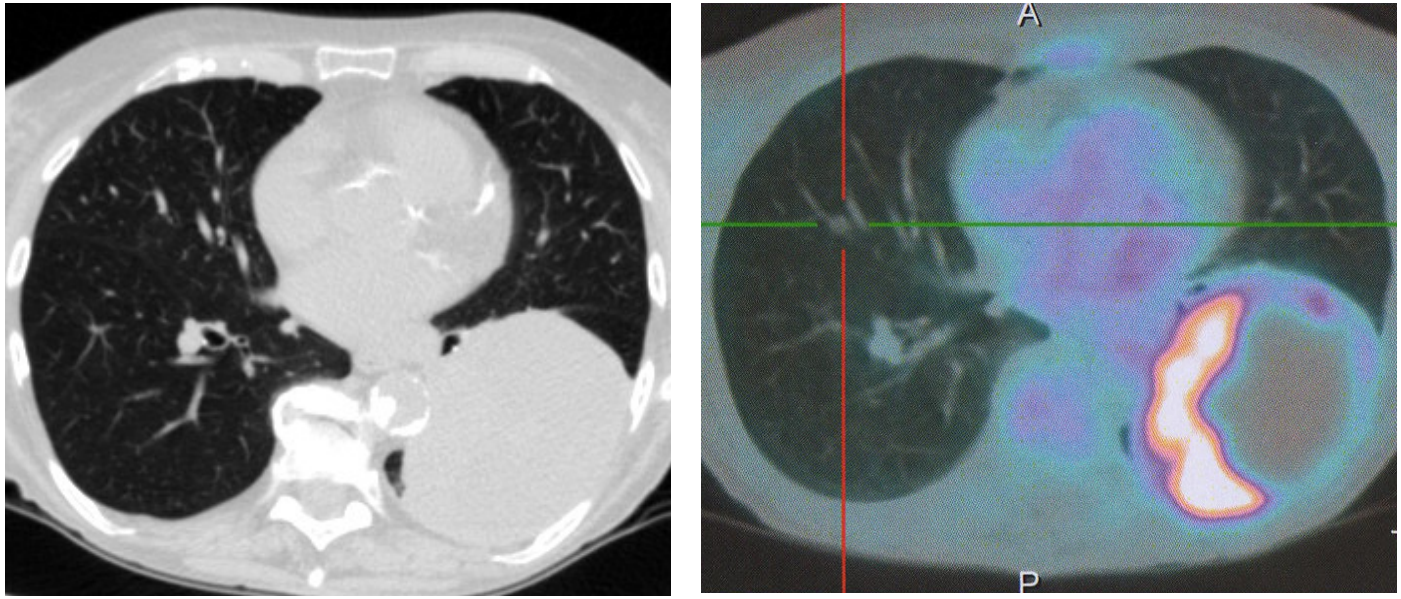
- **<u>Définition du caractère primitif ou secondaire</u>**

  - **La majorité des tumeurs rares intra-thoraciques sont des métastases de tumeurs primitives extra-thoraciques**

Quelle démarche en pratique clinique?

- **<u>Définition du caractère primitif ou secondaire</u>**

- La majorité des tumeurs rares intra-thoraciques sont des métastases de tumeurs primitives extra-thoraciques

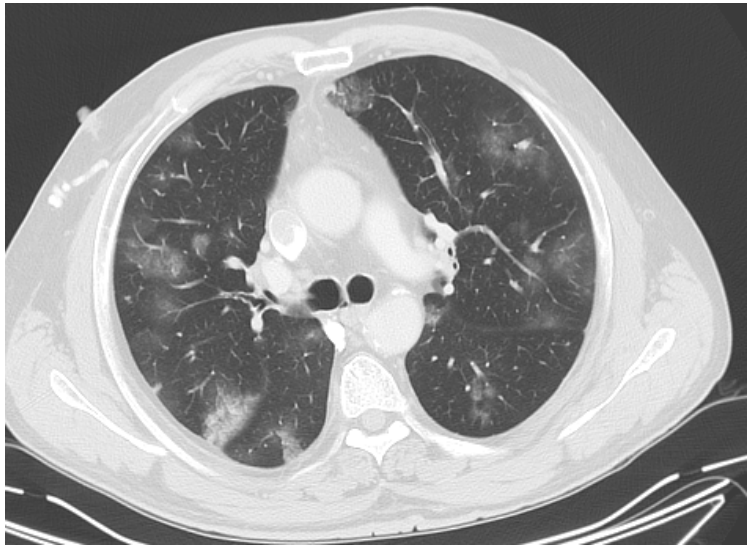


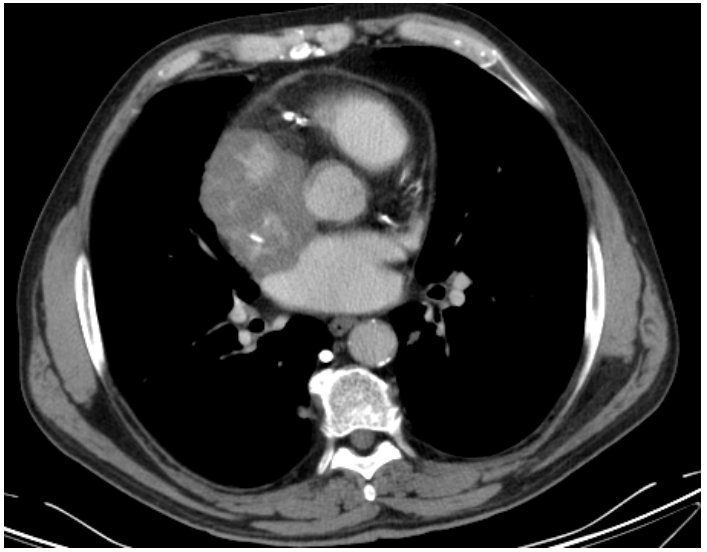
Fibrosarcome de la parotide

Quelle démarche en pratique clinique?

- **<u>Définition du caractère primitif ou secondaire</u>**

- La majorité des tumeurs rares intra-thoraciques sont des métastases de tumeurs primitives extra-thoraciques

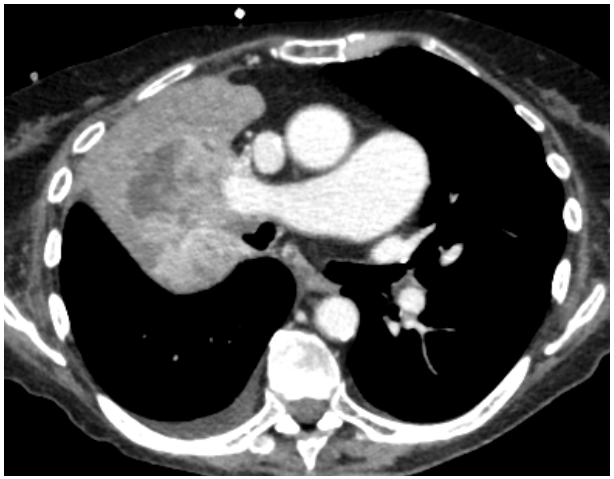


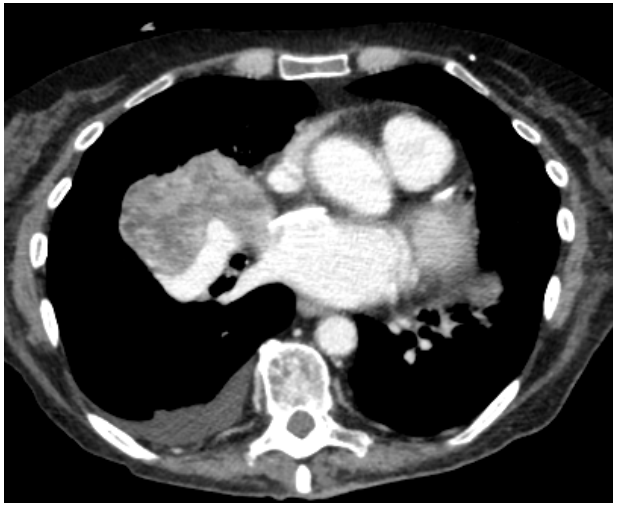


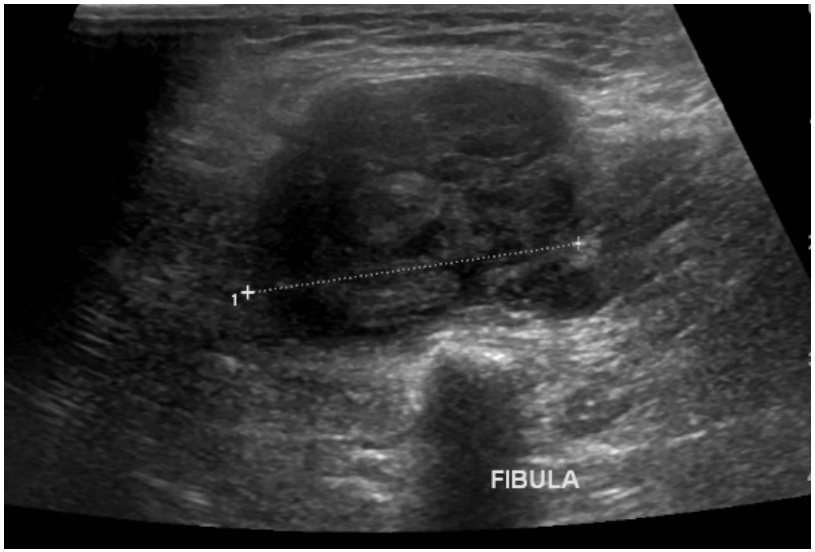
Angiosarcome cardiaque

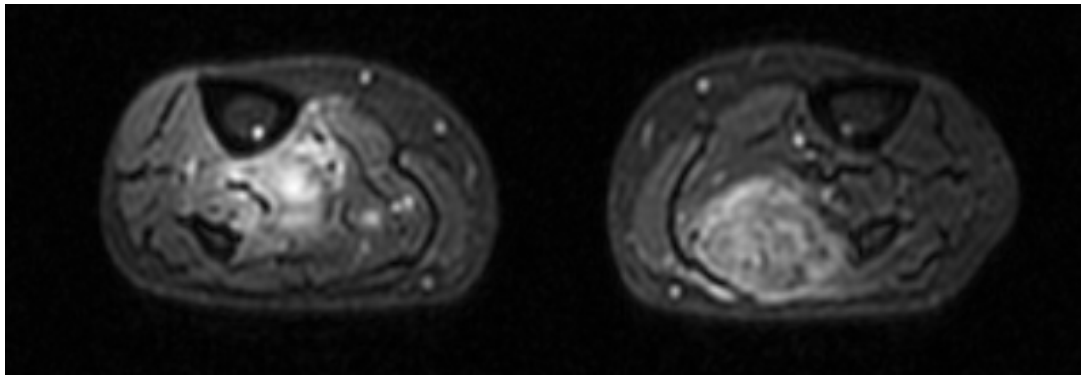
Synovialosarcome pulmonaire

- **<u>Définition du caractère primitif ou secondaire</u>**





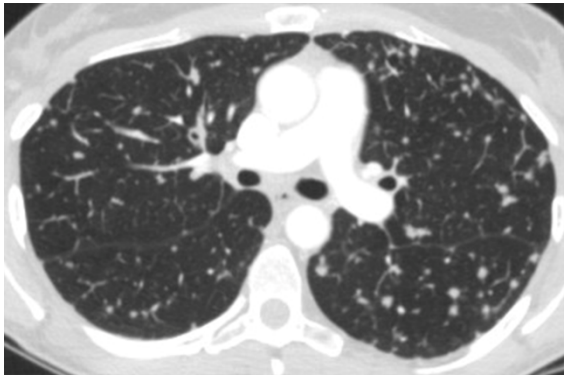




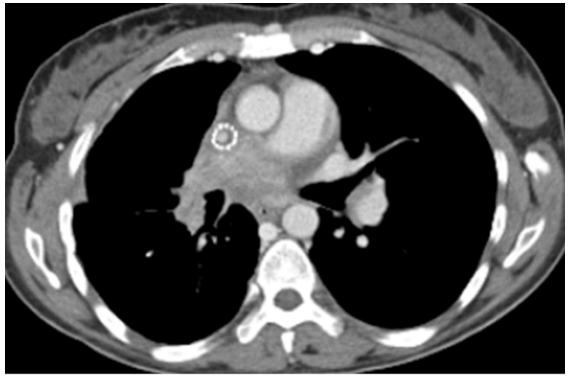
Quelle démarche en pratique clinique?

- **<u>Définition du caractère primitif ou secondaire</u>**

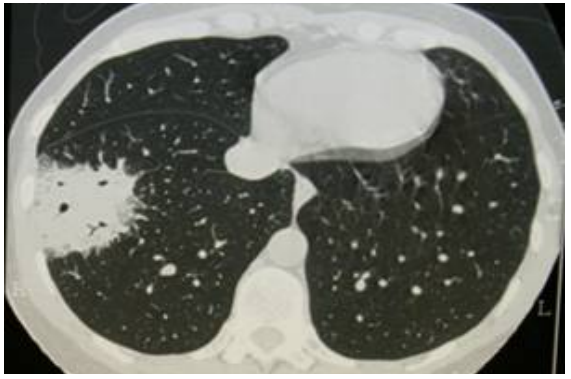
- Utilisation du 18-FDG-PET scan ?



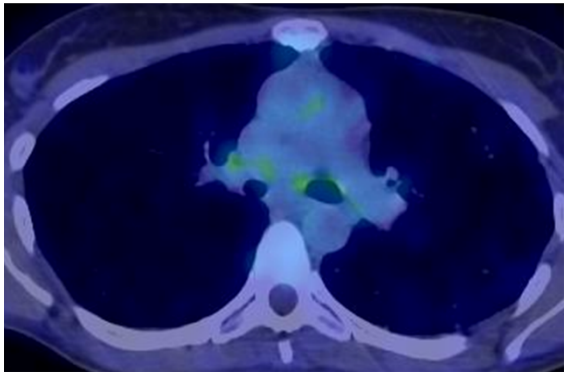
Hémangio-endothéliome épithélioïde

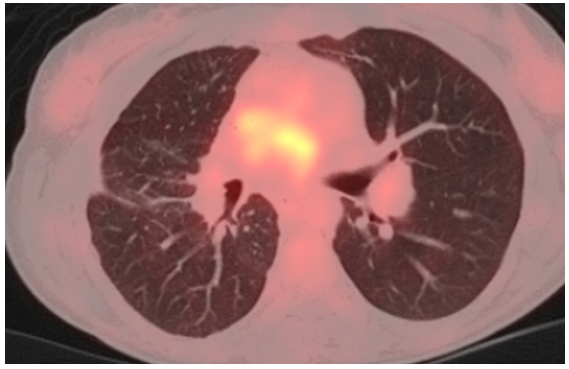


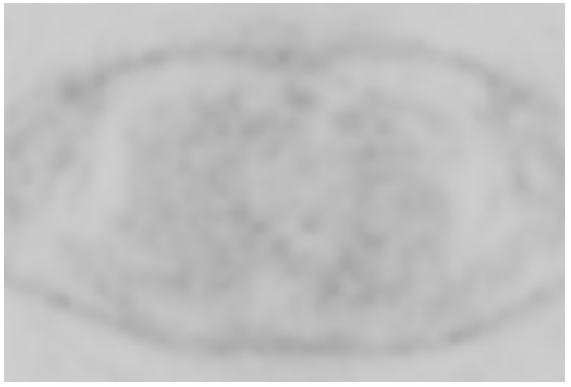
Pseudo-tumeur inflammatoire



Lymphome du MALT







Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire

Oncologie orpheline

Management of rare thoracic malignancies

- **<u>Defining the primary or the secondary nature of a rare tumor</u>**

  - Entities with uncertain primary intrathoracic origin

Clinical characteristics and prognostic factors of pulmonary MALT lymphoma

R. Borie, M. Wislez, G. Thabut, M. Antoine, A. Rabbat, I. Monnet, H. Nunes, F-X. Blanc, H. Mal, A. Bergeron, D. Israël-Biet, B. Crestani and J. Cadranel

TABLE 2 Staging of the 63 patients with pulmonary mucosa-associated lymphoid tissue-derived (MALT) lymphoma

Pulmonary CT scan evaluation[#]	
Unilateral	33 (52)
One lobe	25 (39)
Mediastinal adenopathy	10 (16)
Pleural effusion	7 (11)
Extrapulmonary evaluation[¶]	
Total	29 (46)
Mucosal site	19 (30)
Stomach	15 (19)
Skin	2 (3)
Bowel	2 (3)
Conjunctiva	1 (1.5)
Cavum	1 (1.5)
Parotid	1 (1.5)
Lymphoid organs	14 (22)
Bone marrow	8 (13)
Nodal	4 (6)
Spleen	4 (6)

Eur Respir J 2009; 34:1408

Lymphomes de type MALT

More than a third of non-gastric malt lymphomas are disseminated at diagnosis: a single center survey

Mirjana Sretenovic, Milica Colovic, Gradimir Jankovic, Nada Suvajdzic, Biljana Mihaljevic, Natasa Colovic, Milena Todorovic, Henry Dushan E. Atkinson

Institute of Haematology Clinical Center of Serbia, Koste Todorovica 2, Belgrade, Serbia

Table 2 Primary extranodal MALT involvement of 51 patients with non-gastric MALT lymphoma

MALT organ involvement	No. patients (%)
Single MALT site	36 (70.5)
Two MALT sites	7 (13.7)
Three MALT sites	8 (15.6)
Orbit/lachrymal glands/conjunctiva	8 (15.7)
Waldeyer's ring	9/51 (17.64)
Salivary glands	12/51 (23.52)
Lung/pleura	8/51 (15.7)
Thyroid gland	5/51 (9.80)
Small intestine/colon	4/51 (7.8)
Urogenital	4/51 (7.8)
Central nervous system (dura)	1/51 (1.9)

MALT, mucosa-associated lymphoid tissue

European Journal of Haematology ISSN 0902-4441

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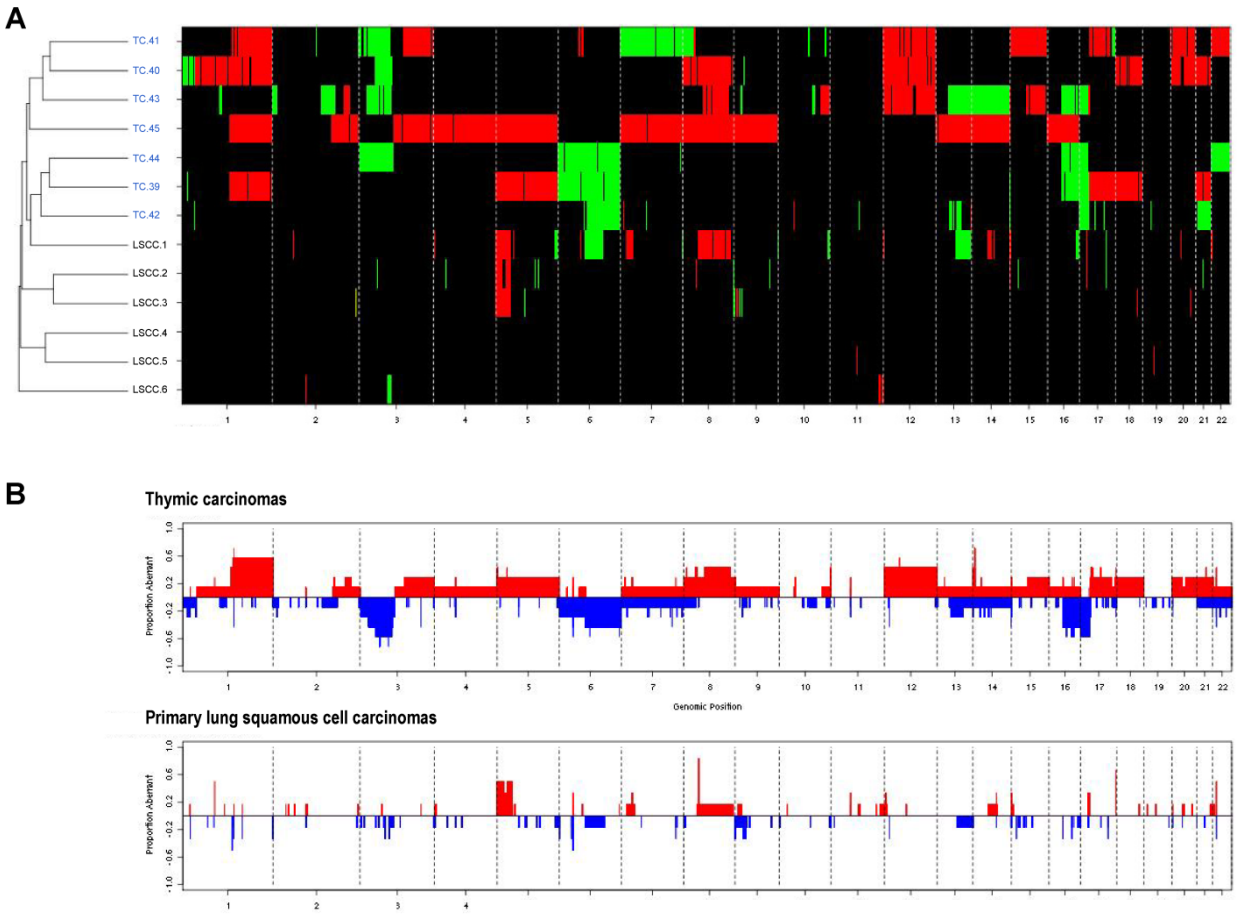
Oncologie orpheline

Aspects moléculaires

- **Carcinome thymique vs. Carcinome broncho-pulmonaire**

  - Différentiation épidermoïde

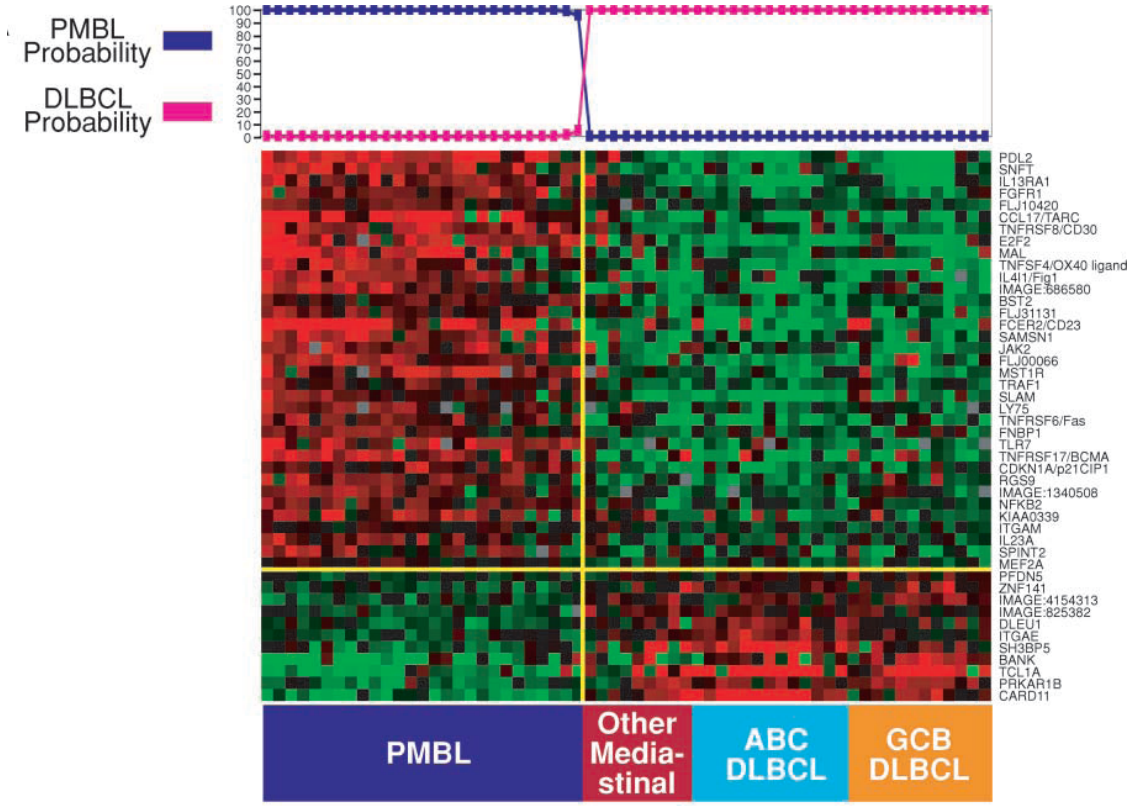


Girard et al. Clin Cancer Res 2009; 15:6790

Aspects moléculaires

- **Lymphome du médiastin vs. Lymphome diffus à grandes cellules B**

  - Origine: lymphocytes thymiques

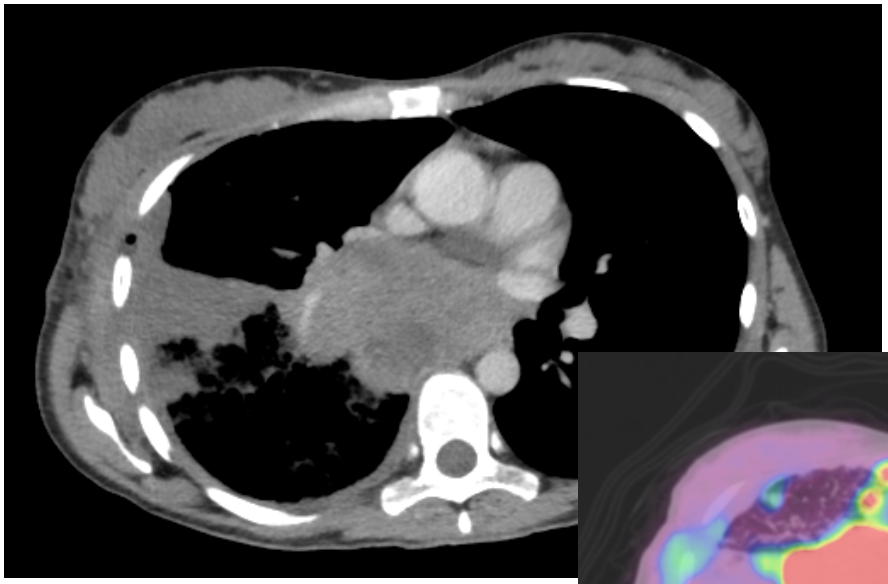


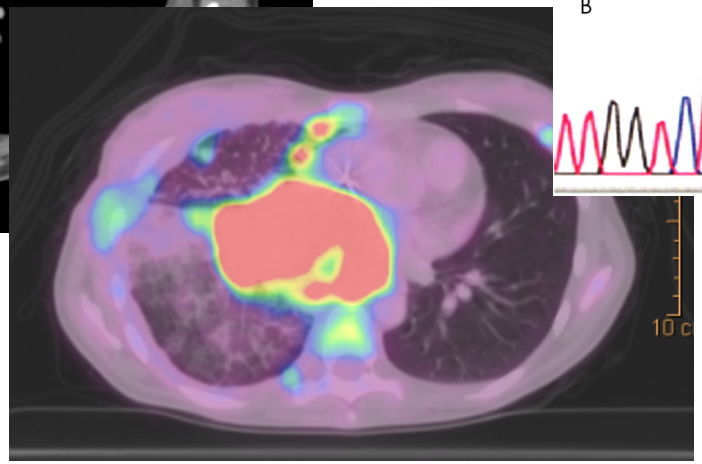
Rosenwald et al. J Exp Med 2003;198:851

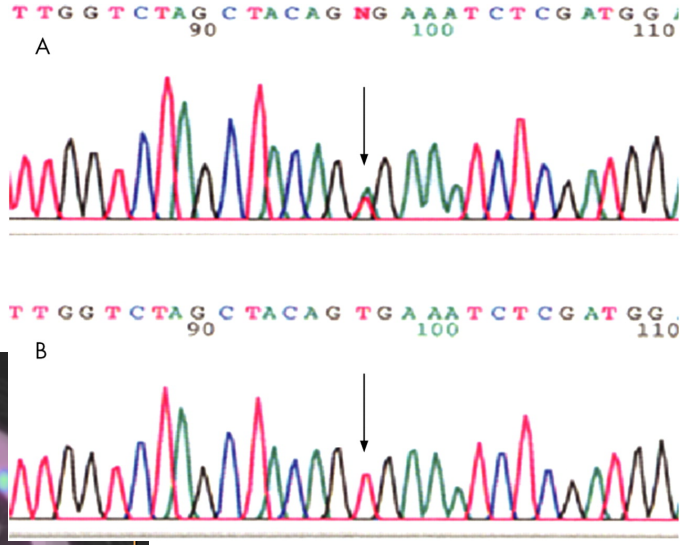
Tumeur cardiaque

- **Insuffisance cardiaque aigue: tumeur oreillette droite**

  - Profilage mutationnel: mutation de BRAF V600E
  - Mélanome sans primitif retrouvé







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- Données moléculaires

Oncologie orpheline

Prise en charge

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire
- Données moléculaires

Oncologie orpheline

Prise en charge

- Diagnostic incident

Quelle démarche en pratique clinique?

A) <u>Diagnostic chirurgical « incident »</u>

- **Les tumeurs pulmonaires rares sont souvent limitées lors du diagnostic**:
    - séries chirurgicales
    - valeur du diagnostic pré-opératoire?
        - diagnostic de malignité ou de bénignité
        - *extension de la résection chirurgicale?*

- **Pas de traitement post-opératoire**:
    - tumeurs carcinoïdes typiques
    - tumeurs myofibroblastiques ?

- **Problématiques:**
    - *Modalités de suivi?*
    - *Prise en charge de la récidive?*

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Traitement

- Diagnostic incident
- Contexte spécifique

Oncologie orpheline

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire
- Données moléculaires

Quelle démarche en pratique clinique?

B) <u>Présentation clinico-radiologique spécifique</u>

- Démarche diagnostique et thérapeutique précise

- **lymphomes du MALT**
- carcinoïdes
- sarcomes pulmonaires et vasculaires
- tumeurs neuro-endocrines
- tumeurs germinales

- Problématiques:

- données souvent rétrospectives
- applicabilité des stratégies établies pour d'autres localisations
  - lymphomes
  - sarcomes

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Addition of Rituximab to Chlorambucil Produces Superior Event-Free Survival in the Treatment of Patients With Extranodal Marginal-Zone B-Cell Lymphoma: 5-Year Analysis of the IELSG-19 Randomized Study

Emanuele Zucca, Annarita Conconi, Daniele Laszlo, Armando López-Guillermo, Reda Bouabdallah, Bertrand Coiffier, Catherine Sebban, Fabrice Jardin, Umberto Vitolo, Franck Morschhauser, Stefano A. Pileri, Christiane Copie-Bergman, Elias Campo, Andrew Jack, Irene Floriani, Peter Johnson, Maurizio Martelli, Franco Cavalli, Giovanni Martinelli, and Catherine Thieblemont

Table 1. Baseline Patient Characteristics

Characteristic	All Patients (N = 231) No.	%	Chlorambucil (arm A) (n = 116) No.	%	Chlorambucil Plus Rituximab (arm B) (n = 115) No.	%	*P**
Male sex	122	53	65	56	57	50	.33
Age, years							
Median	59.8		60.4		59.2		.68
Range	26-81		28-81		26-81		
Ann Arbor stage > II	96	42	44	38	52	45	.26
ECOG PS ≥ 2	4	2	3	3	1	1	.62
Presence of "B" symptoms	21	9	6	5	15	13	.037
Increased serum LDH	17	7	7	6	10	9	.44
Two or more extranodal sites	81	35	40	34	41	36	.85
Nodal involvement	88	38	44	38	44	38	.96
Bone marrow involvement	50	22	20	17	30	26	.10
Prior local therapy†	24	10	14	12	10	9	.40
Primary gastric site‡	96	42	50	43	46	40	.63
IPI risk							.65
Low	135	58	71	61	64	56	
Low-intermediate	49	21	21	18	28	24	
Intermediate-high	40	17	21	18	19	17	
High	7	3	3	3	4	3	
Primary extranodal site							
Stomach	86	37	44	38	42	37	.83
Pharynx	4	2	2	2	2	2	1.00
Orbit	17	7	7	6	10	9	.44
Salivary glands	19	8	11	9	8	7	.49
Lung	21	9	14	12	7	6	.11

Quelle démarche en pratique clinique?

B) <u>Présentation clinico-radiologique spécifique</u>

- Démarche diagnostique et thérapeutique précise

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- **carcinoïdes**
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- tumeurs germinales

- Problématiques:

- données souvent rétrospectives
- applicabilité des stratégies établies pour d'autres localisations
    - lymphomes
    - sarcomes

Classification des tumeurs neuro-endocrines pulmonaires

WHO 2004	Typical carcinoid	Atypical carcinoid	Large cell neuroendocrine carcinoma	Small cell neuro-endocrine carcinoma
Differentiation	Well	Well	Poor	Poor
Cell size			>20 µm	< 20 µm
Necrosis	Absent	Possible, focal	Jsual, extensive	Frequent
Mitotic index	< 2 mitoses /10 HPF (2 mm²)	2 – 10 mitoses /10 HPF (2 mm²)	> 10 mitoses /10 HPF (2 mm²)	> 10 mitoses /10 HPF (2 mm²)

Pulmonary neuroendocrine (carcinoid) tumors: European Neuroendocrine Tumor Society expert consensus and recommendations for best practice for typical and atypical pulmonary carcinoids

M. E. Caplin[1*], E. Baudin[2], P. Ferolla[3], P. Filosso[4], M. Garcia-Yuste[5], E. Lim[6], K. Oberg[7], G. Pelosi[8], A. Perren[9], R. E. Rossi[1,10] & W. D. Travis[11] the ENETS consensus conference participants[†]

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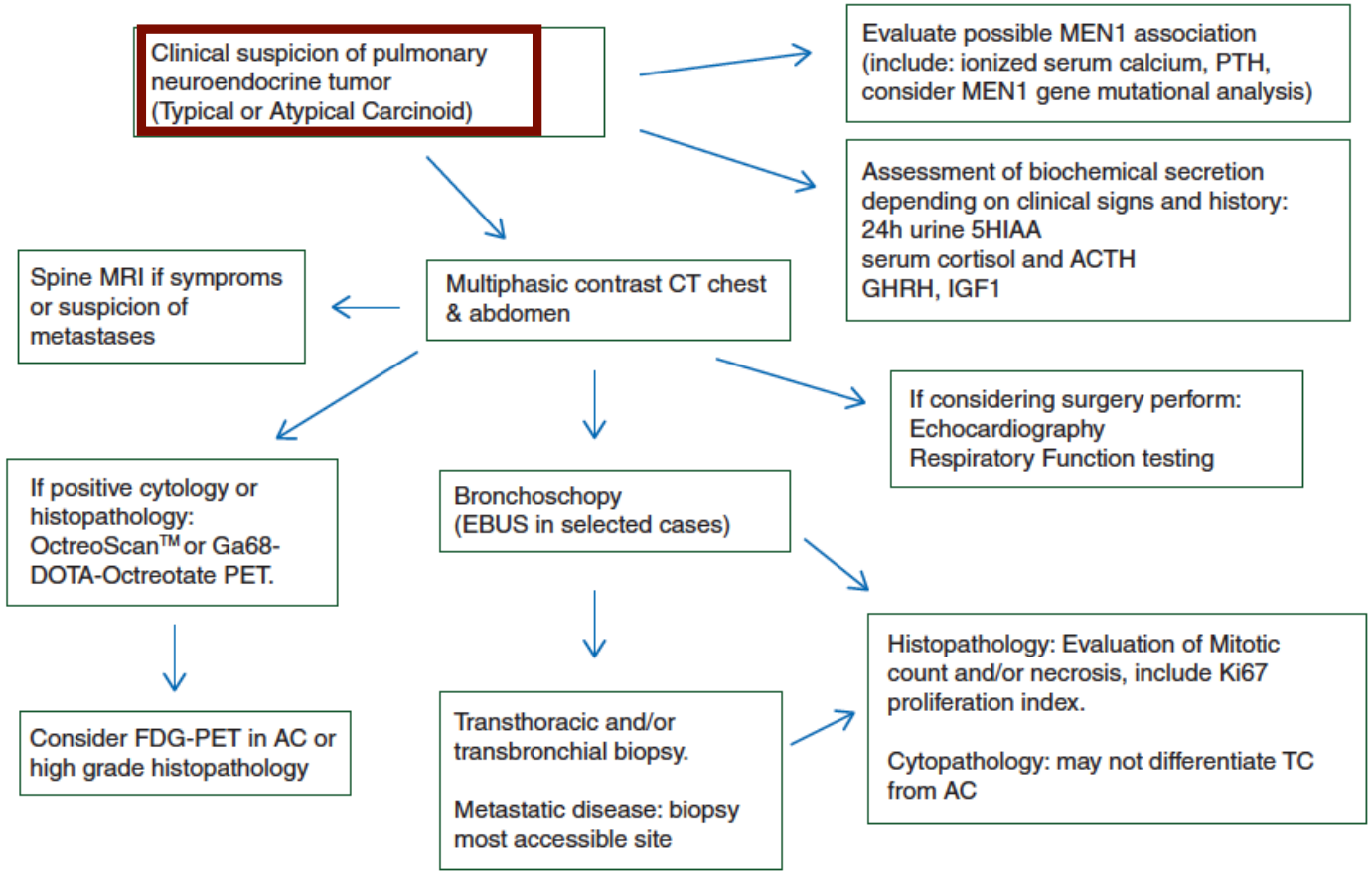

Figure 1. Algorithm for diagnosis of pulmonary neuroendocrine tumor.

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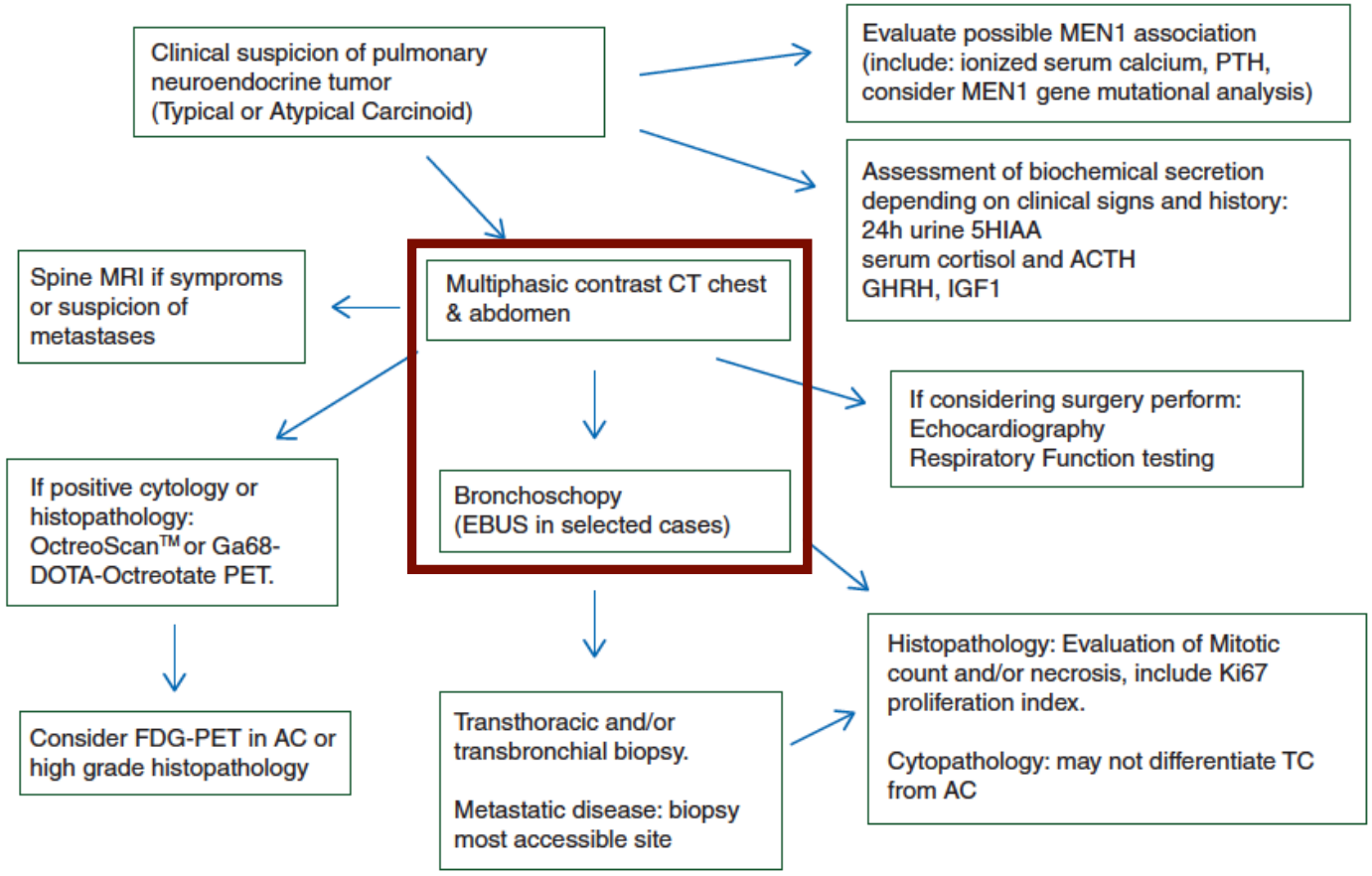

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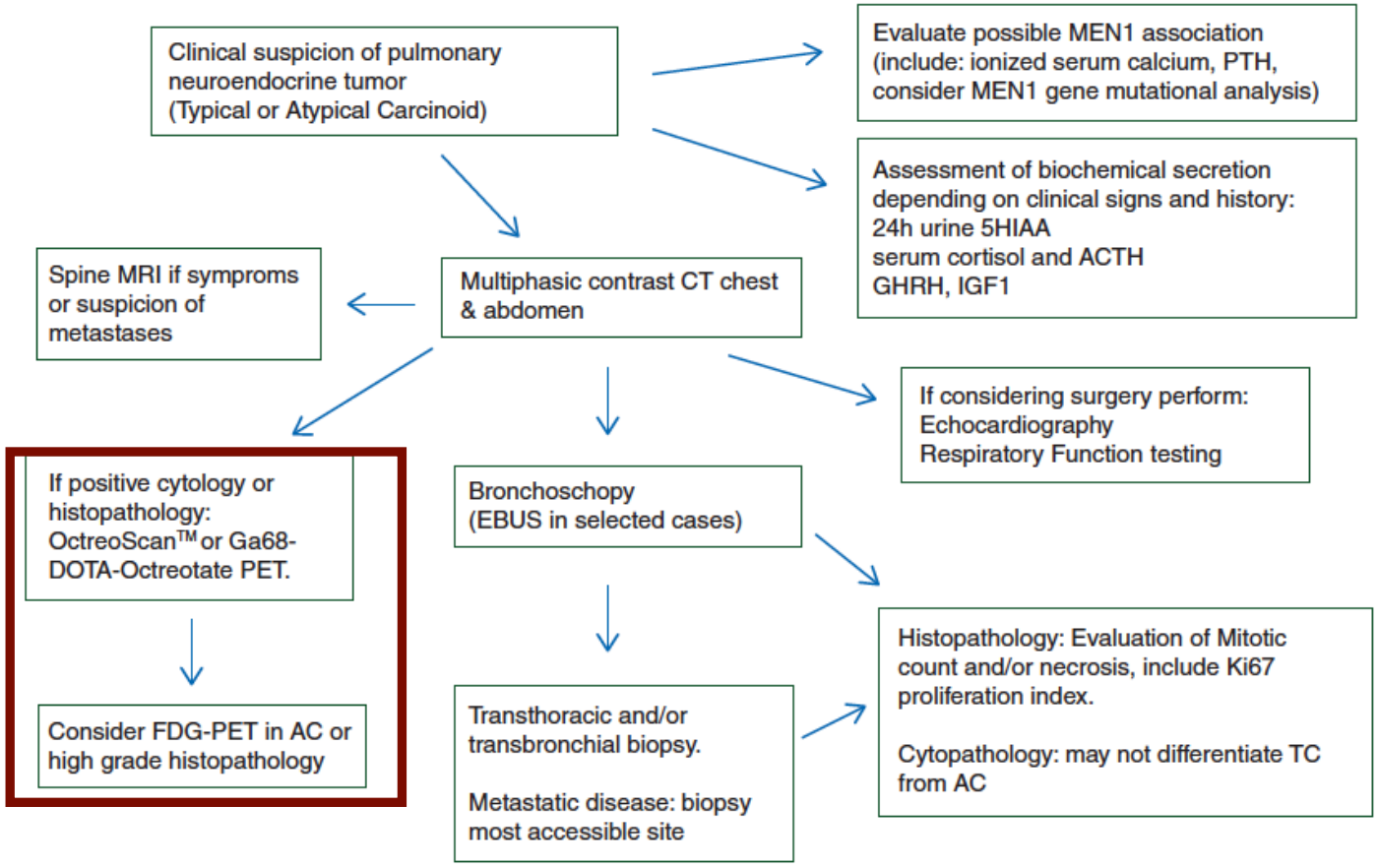

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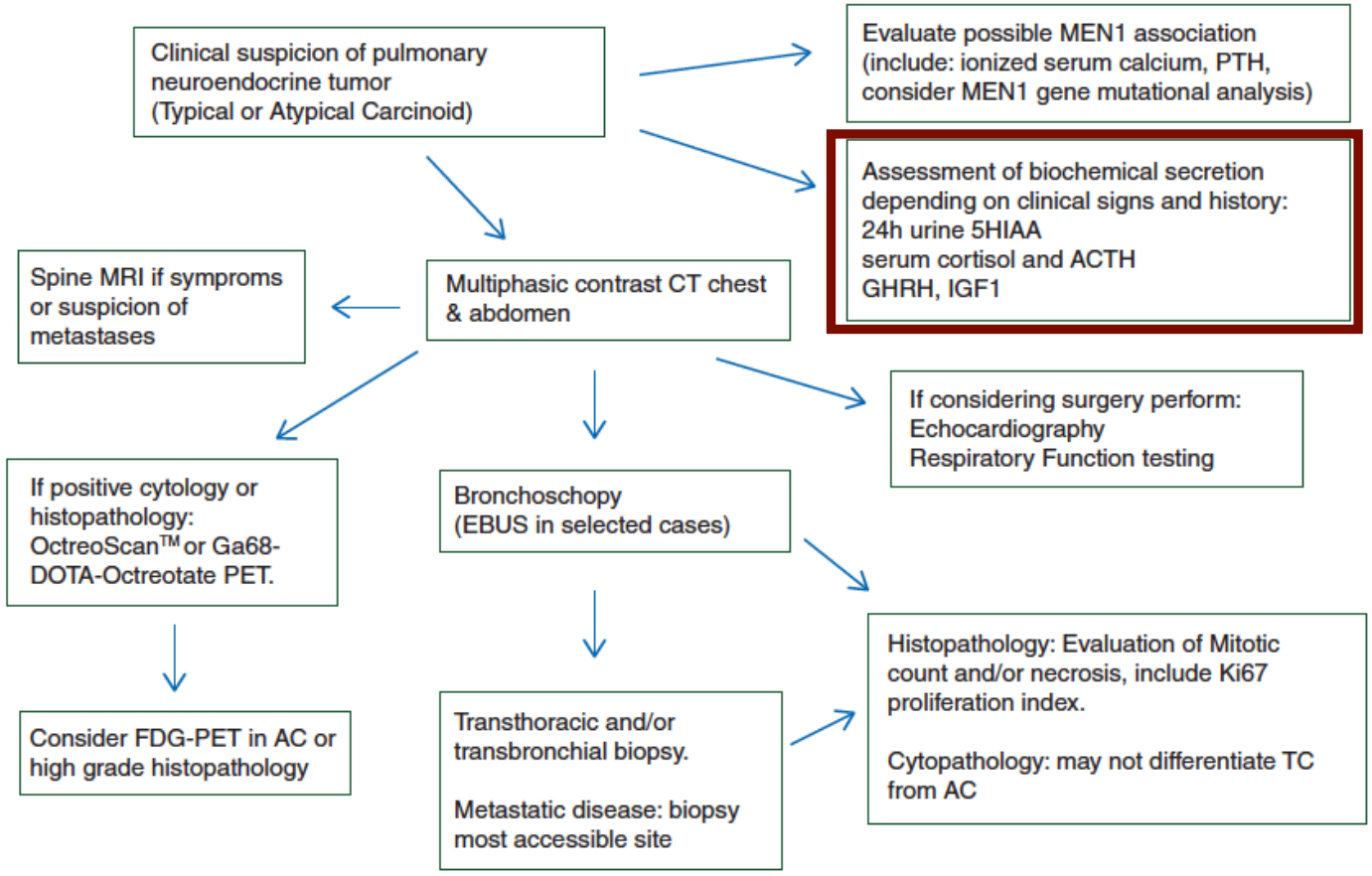

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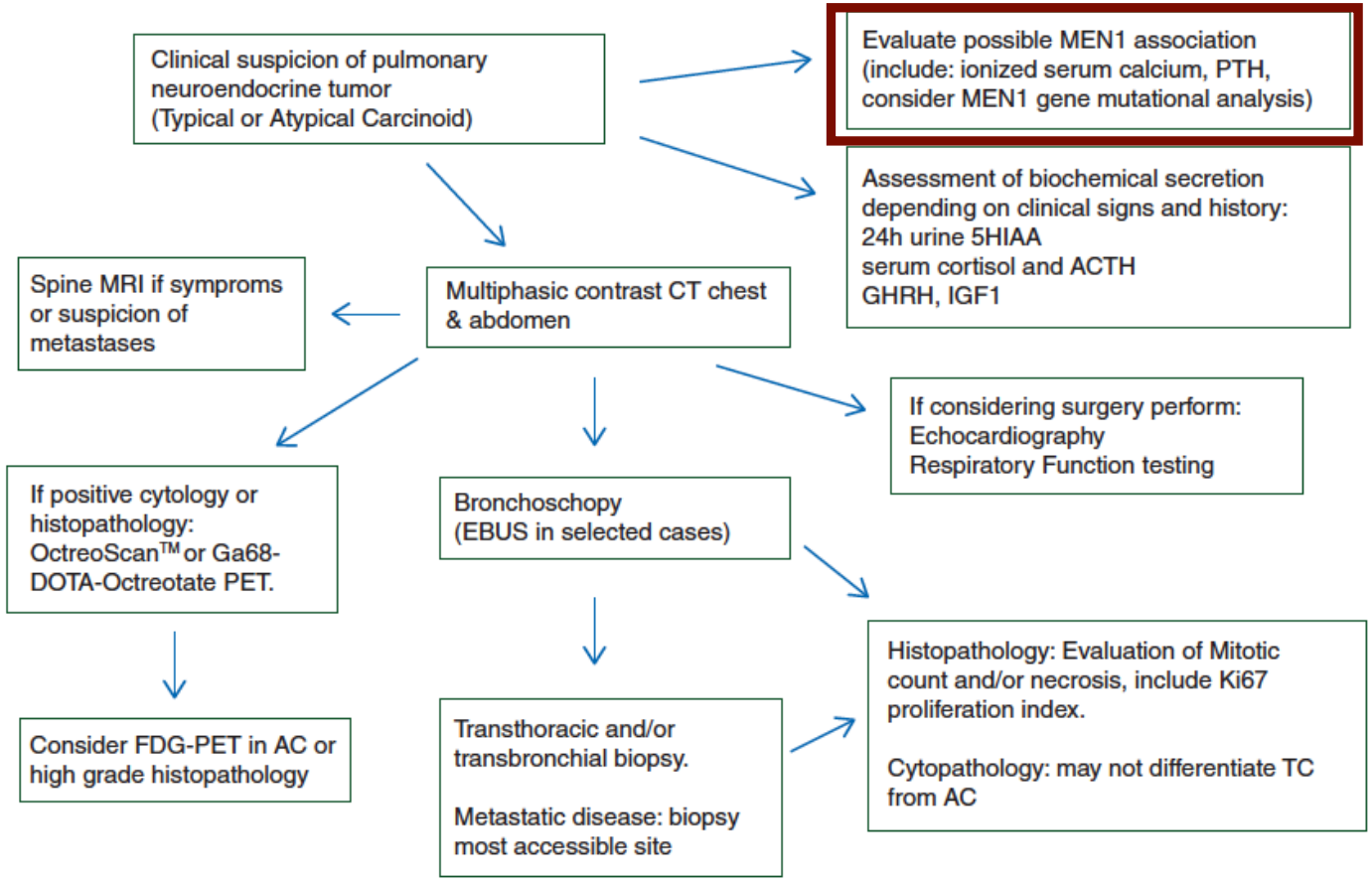

Figure 1. Algorithm for diagnosis of pulmonary neuroendocrine tumor.

Tumeurs carcinoïdes : stades avancés

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Fréquence des métastases hépatiques

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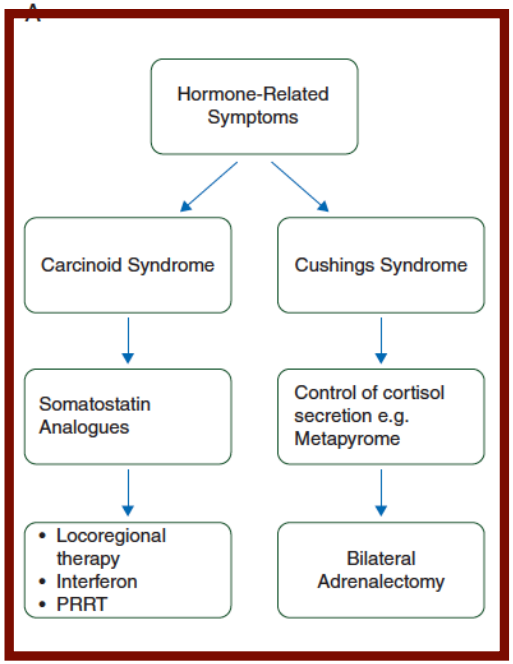

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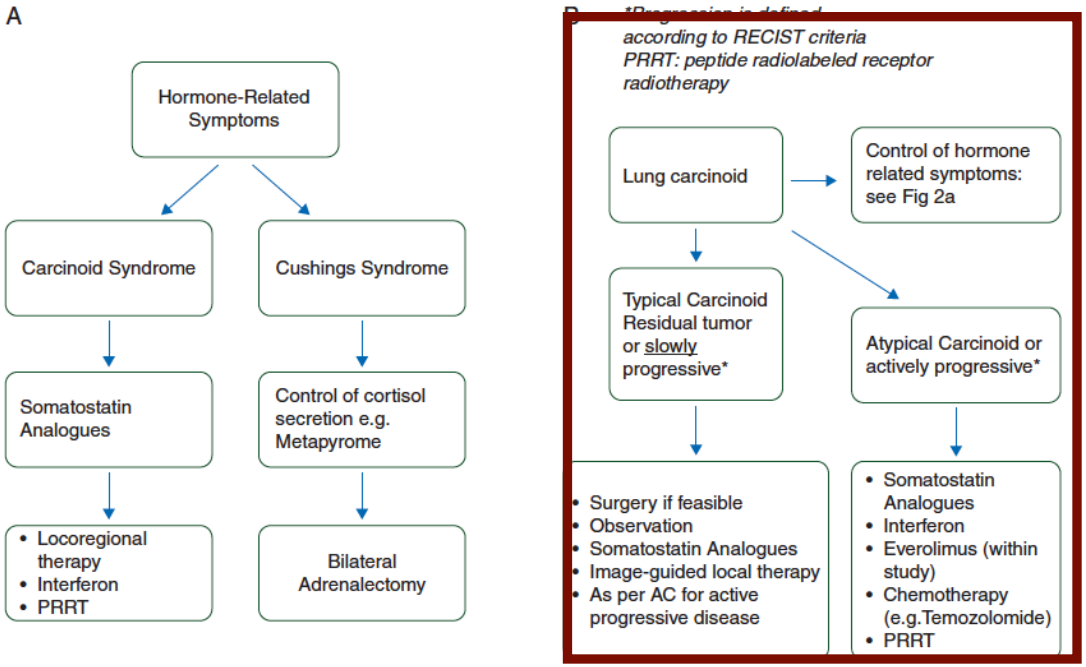

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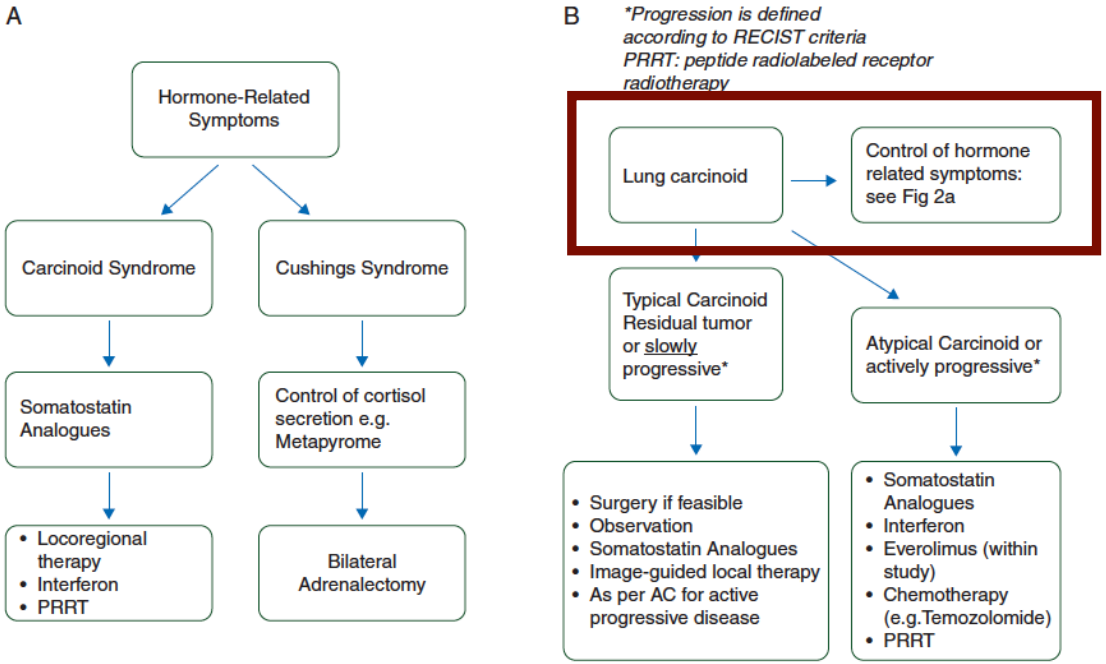

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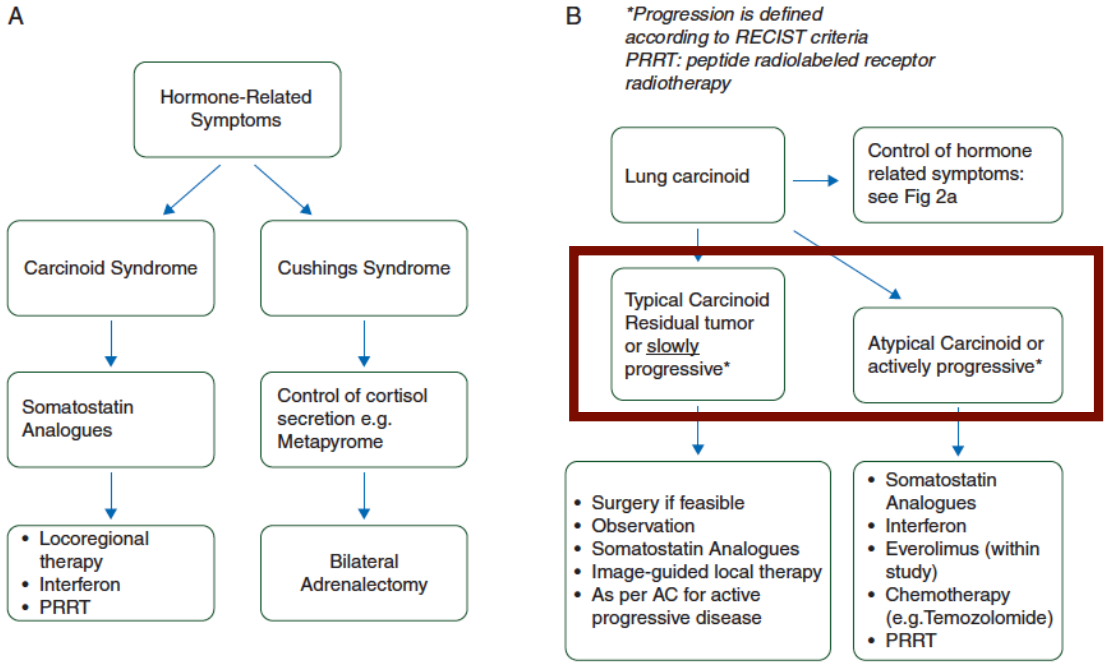

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Tumeurs carcinoïdes : stades avancés

G1

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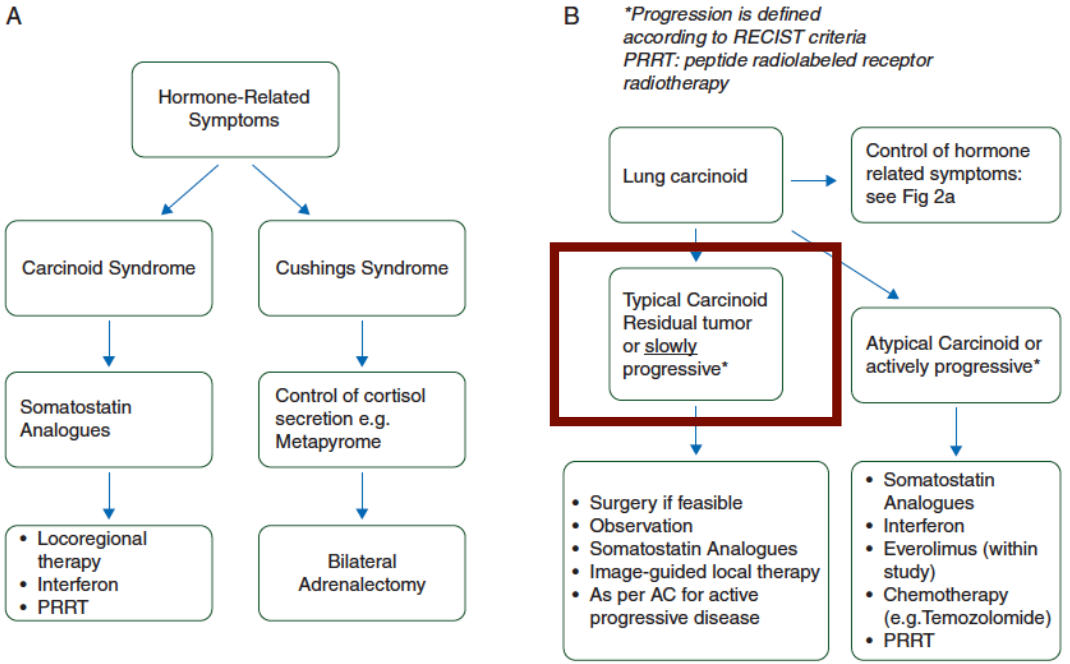

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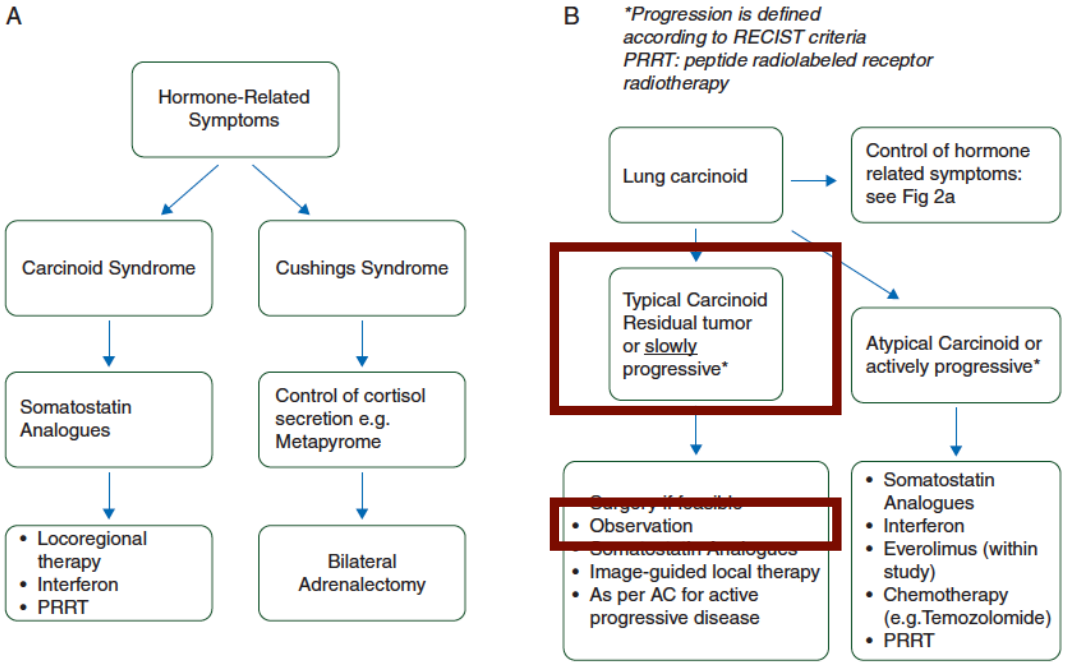

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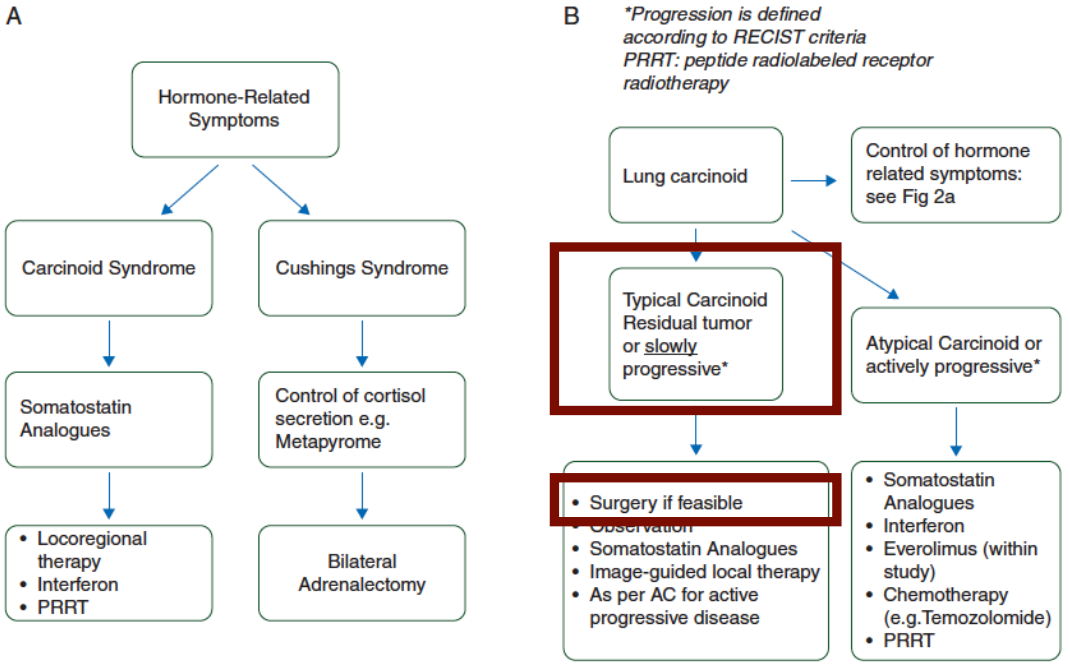

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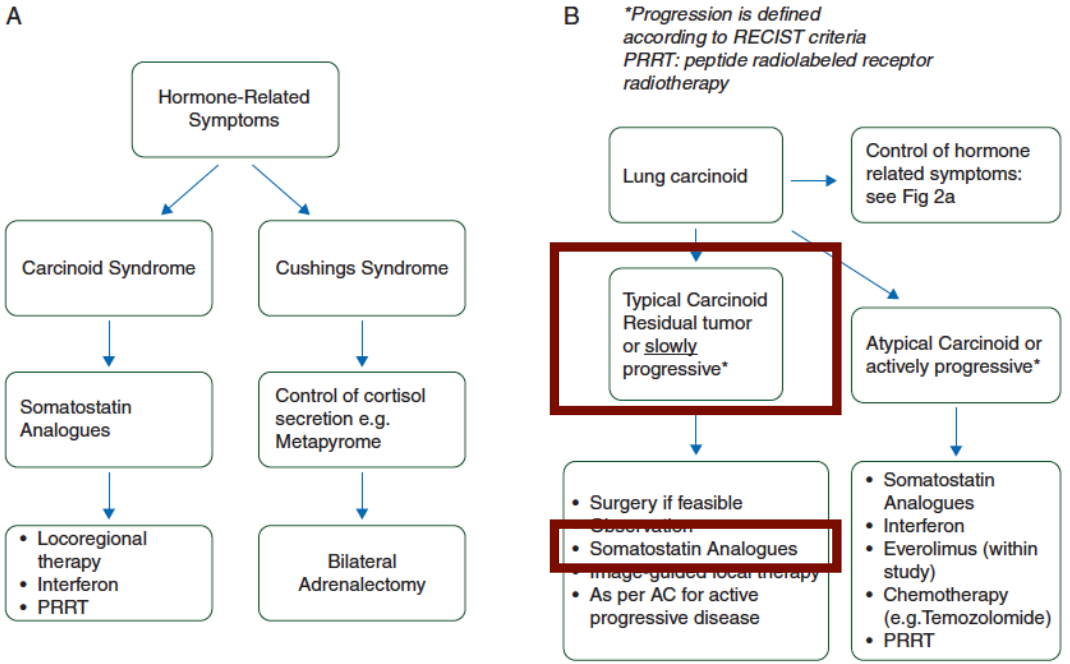

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Analogues de la somatostatine: essai PROMID

VOLUME 27 · NUMBER 28 · OCTOBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Placebo-Controlled, Double-Blind, Prospective, Randomized Study on the Effect of Octreotide LAR in the Control of Tumor Growth in Patients With Metastatic Neuroendocrine Midgut Tumors: A Report From the PROMID Study Group

Anja Rinke, Hans-Helge Müller, Carmen Schade-Brittinger, Klaus-Jochen Klose, Peter Barth, Matthias Wied, Christina Mayer, Behnaz Aminossadati, Ulrich-Frank Pape, Michael Bläker, Jan Harder, Christian Arnold, Thomas Gress, and Rudolf Arnold

Table 1. Baseline Patient Demographics and Clinical Characteristics

Demographic or Clinical Characteristic	Octreotide LAR (n = 42)		Placebo (n = 43)		Total (N = 85)		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	*P*
Carcinoid syndrome	17	40.5	16	37.2	33	38.8	.8256
Resection of primary tumor	29	69.1	27	62.8	56	65.9	.6487
Ki-67 up to 2%	41	97.6	40	93.0	81	95.3	.6160
Octreoscan							.8806
Positive	32	76.2	31	72.1	63	74.1	
Negative	4	9.5	6	14.0	10	11.8	

Tumeurs sécrétantes: 40%
Octreoscan positif: 75%

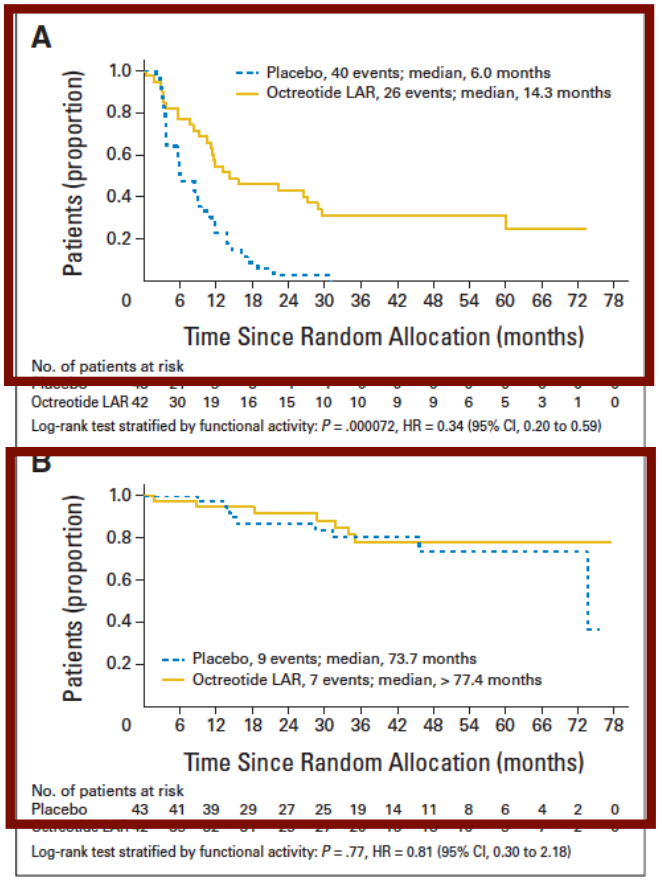

Fig 2. (A) Conservative intent-to-treat analysis of time to progression or tumor-related death. (B) Intent-to-treat analysis of overall survival. HR, hazard ratio.

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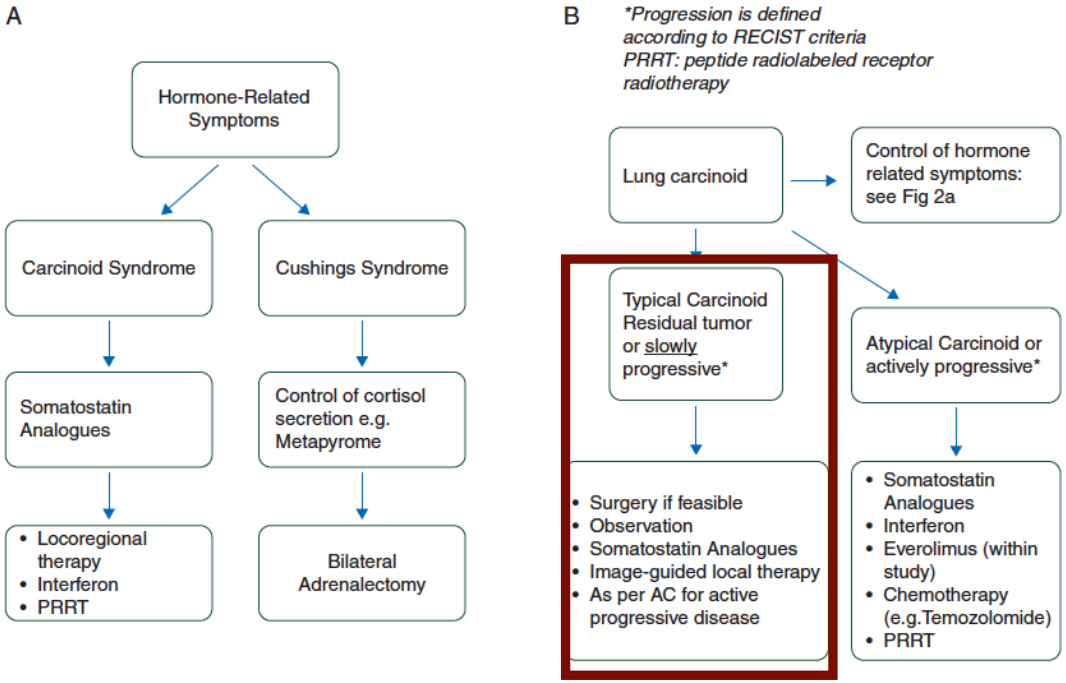

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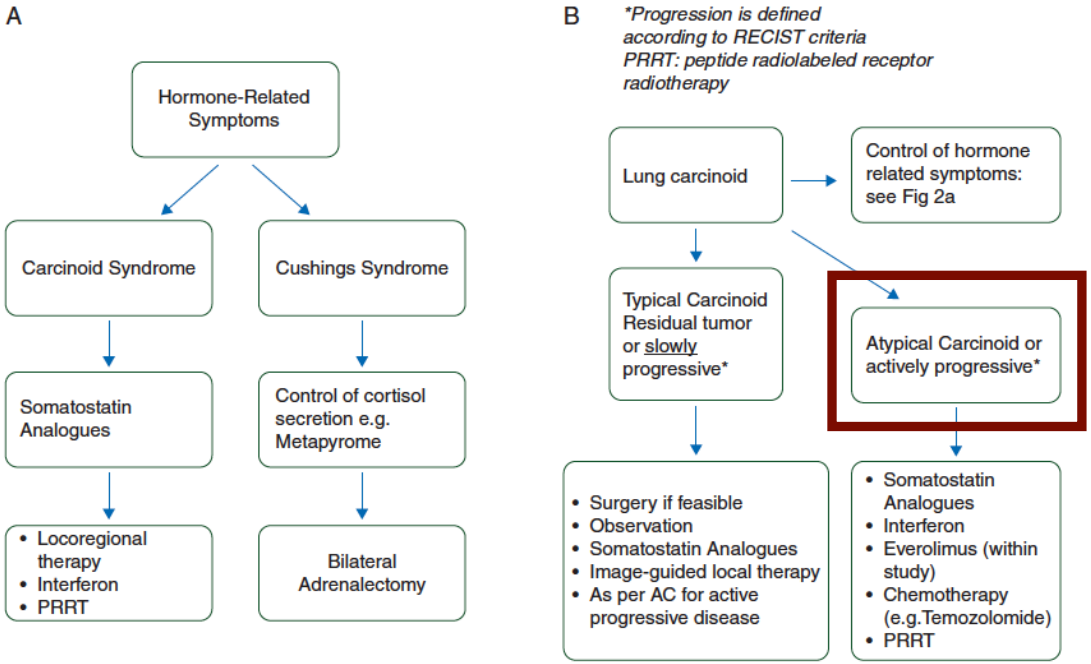

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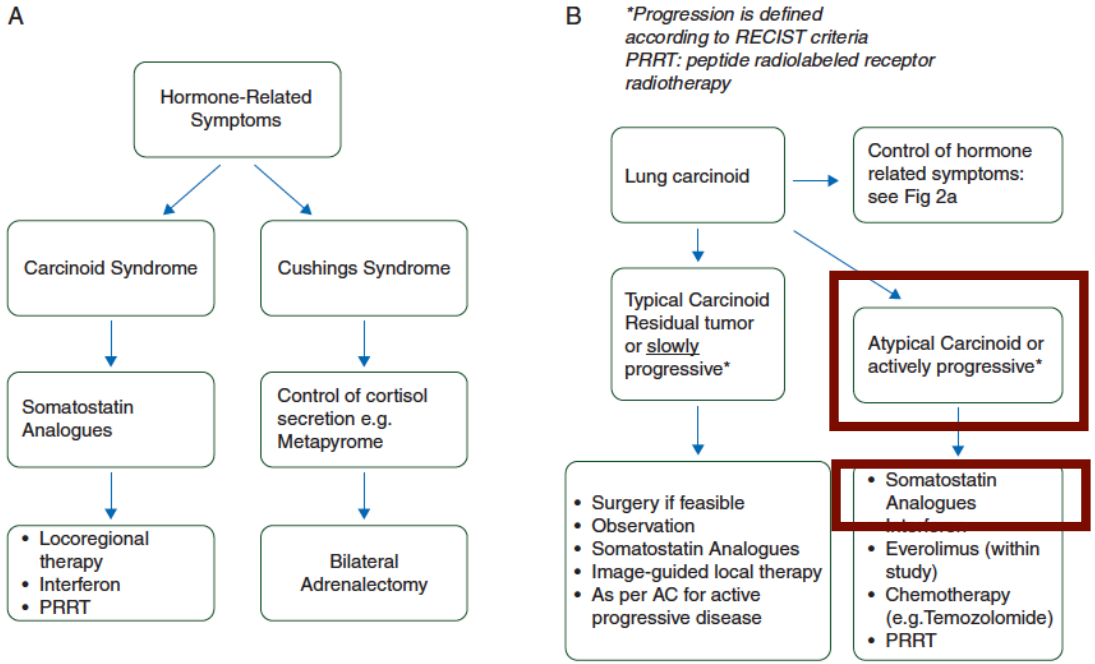

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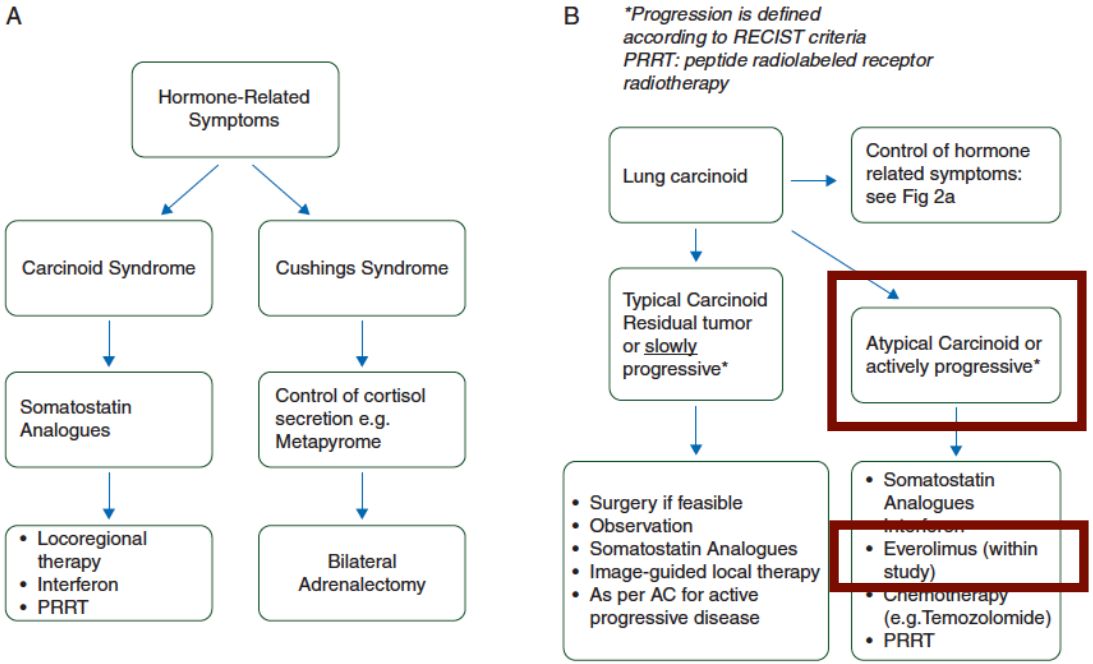

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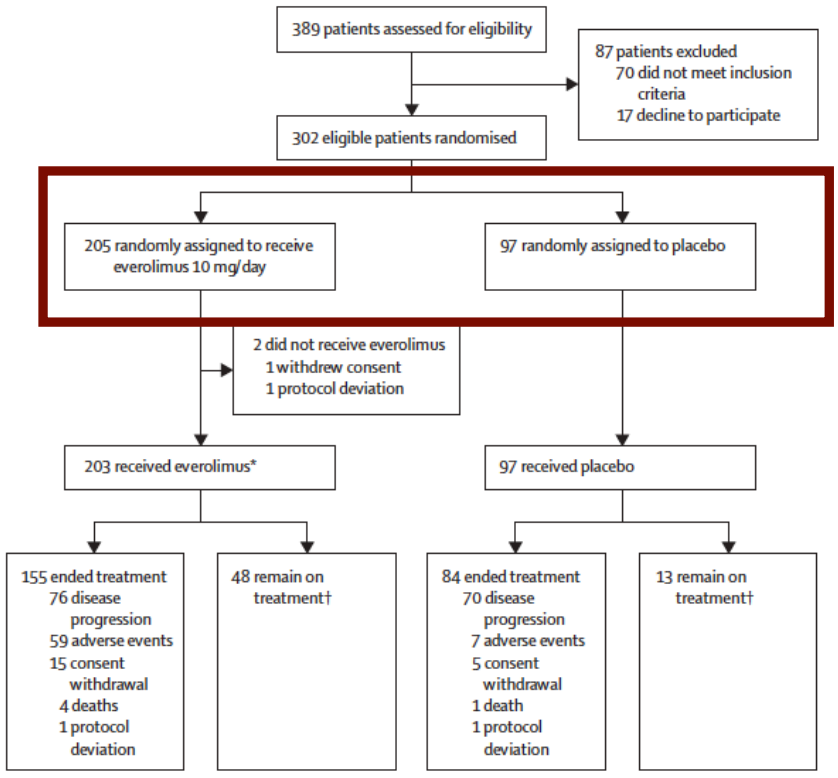
Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study

*James C Yao, Nicola Fazio, Simron Singh, Roberto Buzzoni, Carlo Carnaghi, Edward Wolin, Jiri Tomasek, Markus Raderer, Harald Lahner, Maurizio Voi, Lida Bubuteishvili Pacaud, Nicolas Rouyrre, Carolin Sachs, Juan W Valle, Gianfranco Delle Fave, Eric Van Cutsem, Margot Tesselaar, Yasuhiro Shimada, Do-Youn Oh, Jonathan Strosberg, Matthew H Kulke, Marianne E Pavel, for the RAD001 in Advanced Neuroendocrine Tumours, Fourth Trial (RADIANT-4) Study Group**



	Everolimus (n=205)	Placebo (n=97)
Age, years	65 (22–86)	60 (24–83)
Sex		
Men	89 (43%)	53 (55%)
Women	116 (57%)	44 (45%)
WHO performance status*		
0	149 (73%)	73 (75%)
1	55 (27%)	24 (25%)
Primary tumour site		
Lung	63 (31%)	27 (28%)
Ileum	47 (23%)	24 (25%)
Rectum	25 (12%)	15 (16%)
Neuroendocrine tumour of unknown primary origin†	23 (11%)	13 (13%)
Jejunum	16 (8%)	6 (6%)
Stomach	7 (3%)	4 (4%)
Duodenum	8 (4%)	2 (2%)
Colon	5 (2%)	3 (3%)
Other‡	6 (3%)	2 (2%)
Caecum	4 (2%)	1 (1%)
Appendix	1 (1%)	0

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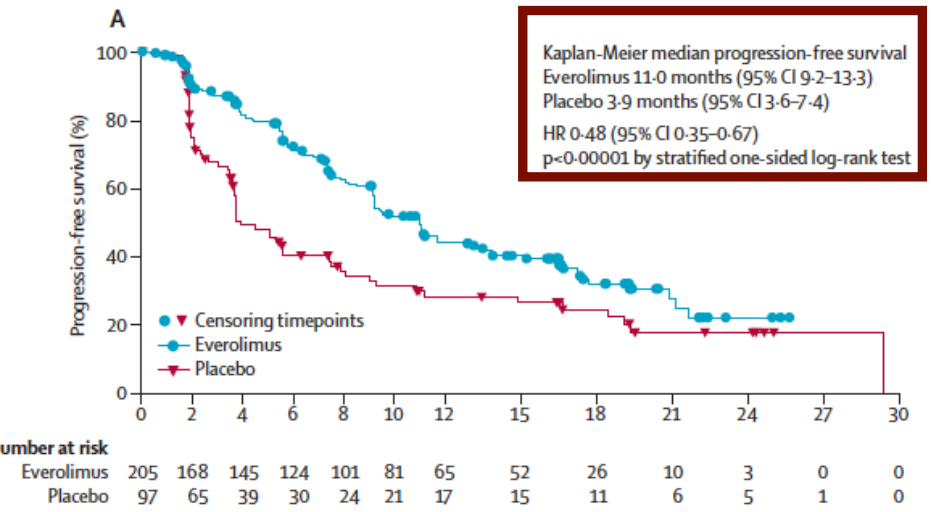

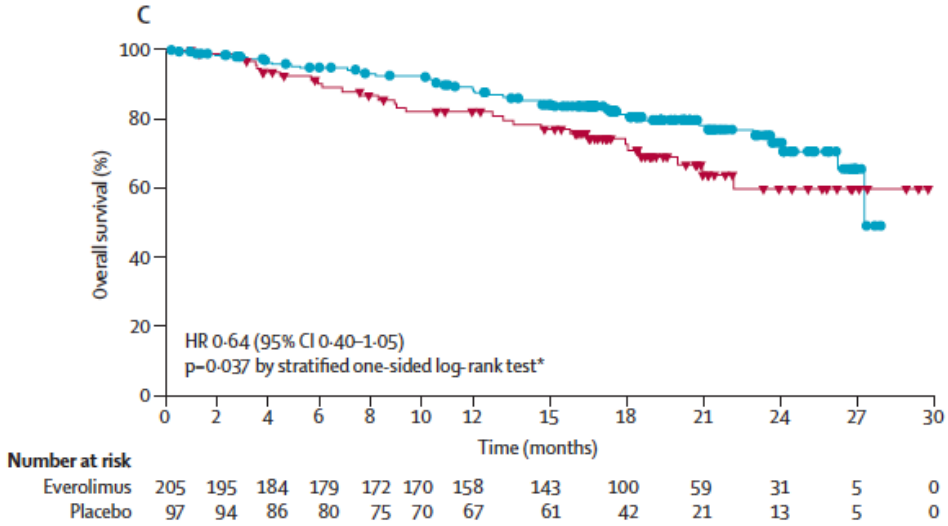

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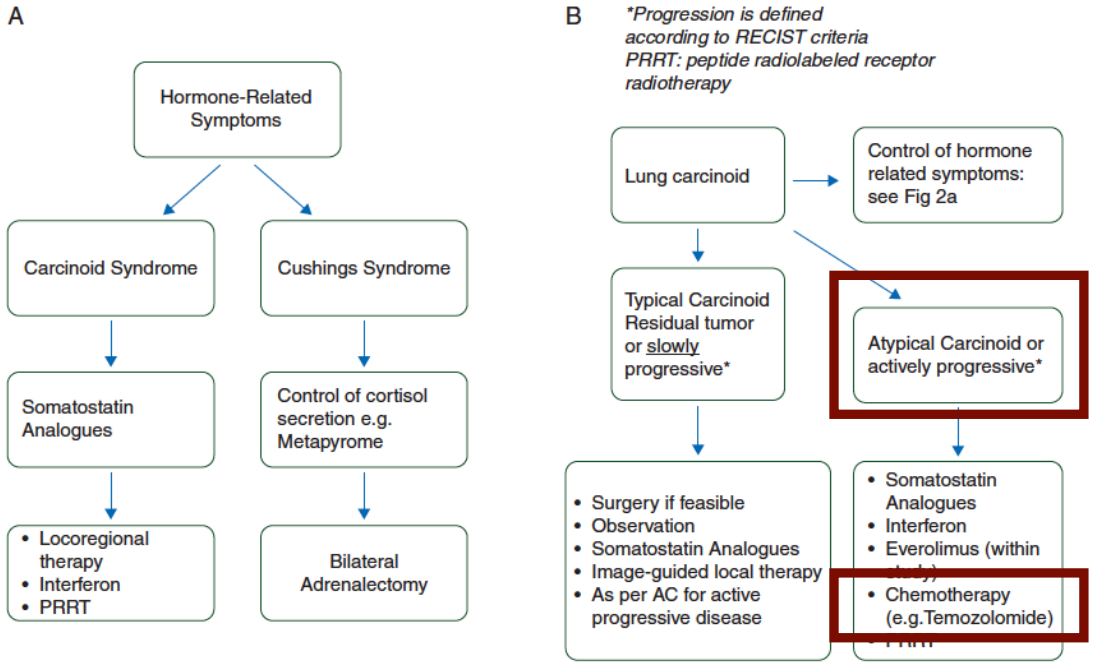

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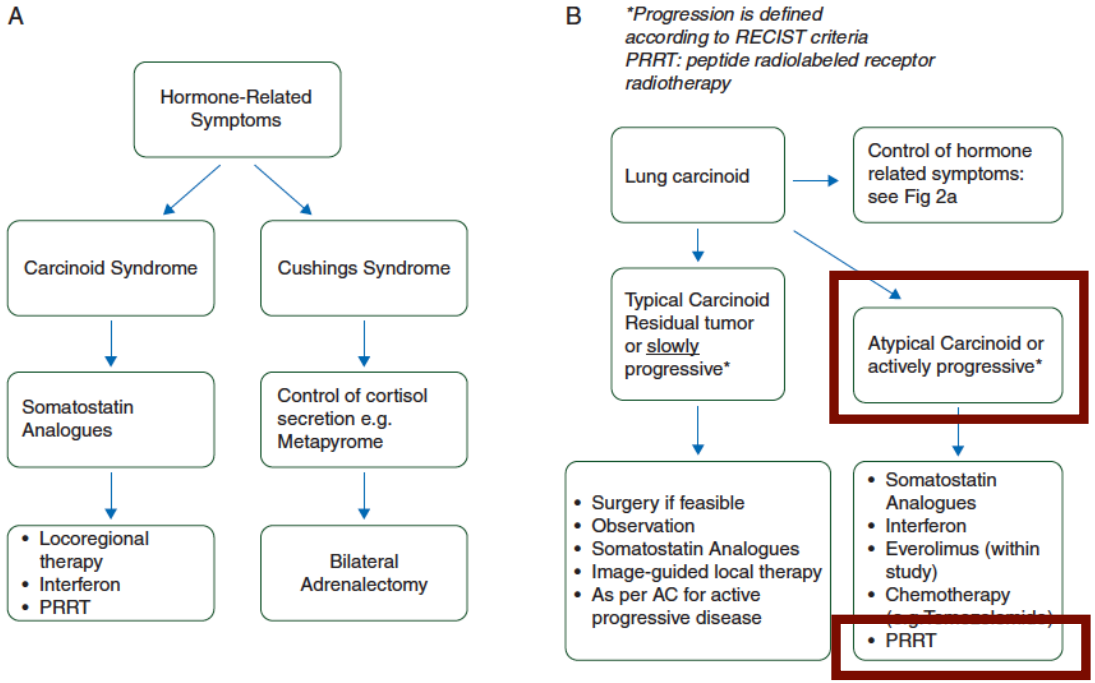

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Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire
- Données moléculaires

Oncologie orpheline

Traitement

- Diagnostic incident
- Contexte spécifique
- Contexte orphelin

Quelle démarche en pratique clinique?

C) <u>Diagnostic inattendu, implications incertaines</u>

- **Rôle du consensus d'experts et de la réunion de concertation pluri-disciplinaire dédiée**

- **Intérêt de la caractérisation complète des observations**
  - médecine personnalisée
  - imagerie, biologie moléculaire

- **Problématiques:**
  - Facteurs pronostiques: survie souvent surestimée
  - **Traitements adjuvants:**
    - similaires aux cancers bronchiques non à petites cellules?
    - basés sur les stratégies de traitement d'autres localisations?

Hémangioendothéliome épithélioïde

CHEST Original Research
CANCER

Clinical Patterns and Outcome in Epithelioid Hemangioendothelioma With or Without Pulmonary Involvement

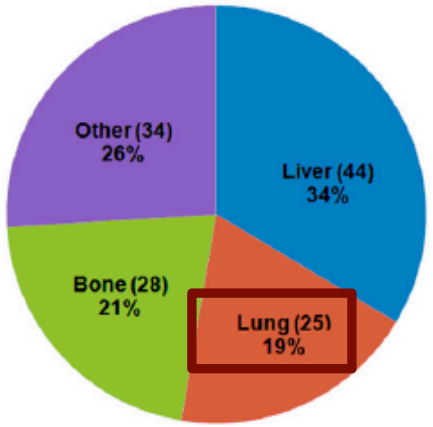
Insights From an Internet Registry in the Study of a Rare Cancer

Kenneth Lau, MD; Malek Massad, MD, FCCP; Cynthia Pollak; Charles Rubin, MD; Joannie Yeh, MD; Jing Wang, PhD; Guy Edelman, MD; Jenny Yeh, MD; Sunil Prasad, MD; and Guy Weinberg, MD

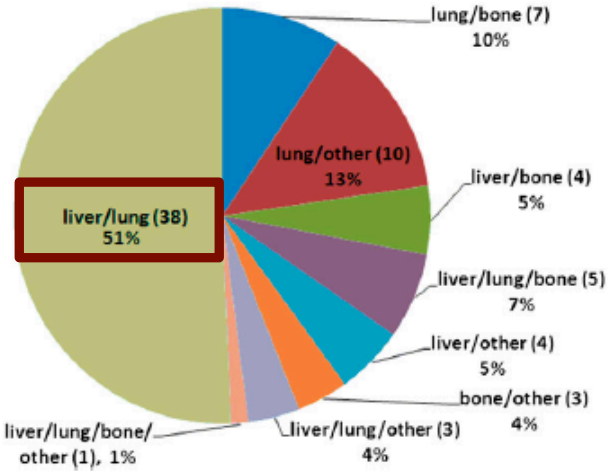
Table 1—*Distribution of Signs and Symptoms*

Presenting Signs and Symptoms	No.	%
Asymptomatic	42	28.2
Symptomatic	107	71.8
Abdominal pain	28	18.8
Anorexia	1	0.7
Ascites	2	1.3
Back pain	11	7.4
Chest pain	9	6.0
Cough	13	8.7
Dyspepsia	4	2.7
Dysphagia	1	0.7
Dyspnea	4	2.7
Fatigue	5	3.4
Fever	2	1.3
Fracture	4	2.7
Hemoptysis	6	4.0
Pain, NOS	31	20.8
Palpable mass	8	5.4
Pleural effusion	6	4.0
Pneumonia, URTI	4	2.7
Vision problems	1	0.7
Weakness/numbness	3	2.0

Single-organ involvement (n=131)



Multi-organ involvement (n=75)



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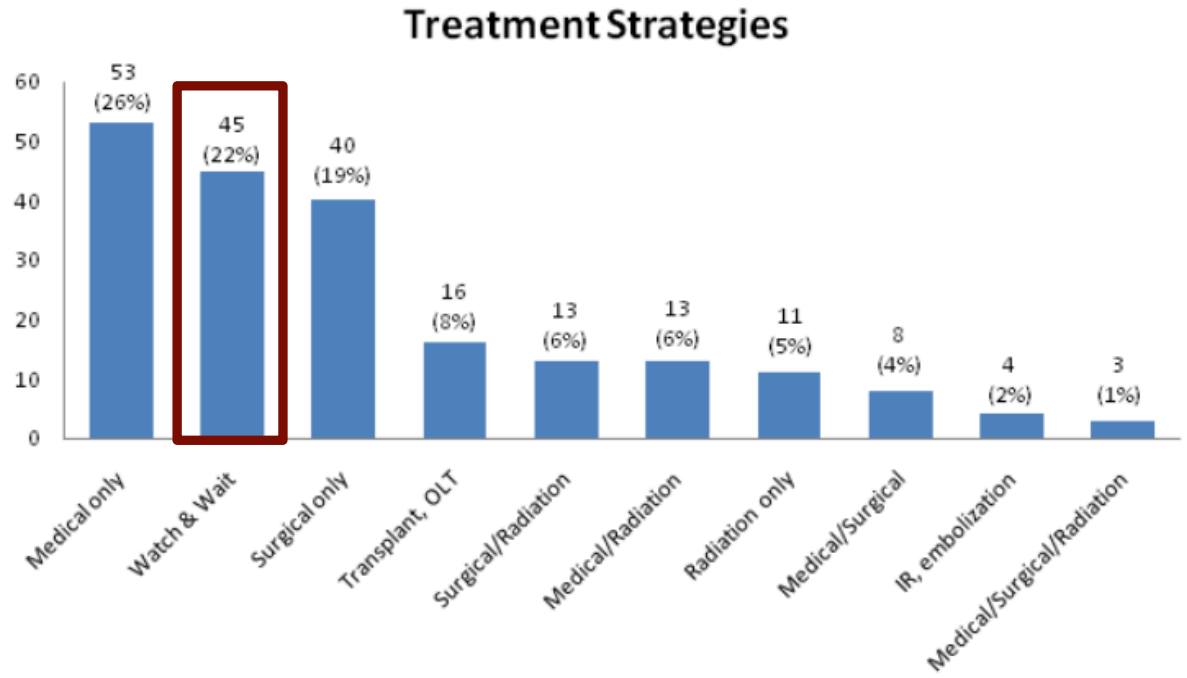

Les tumeurs rares intra-thoraciques

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- Histologie
- Fréquence
- Moléculaire

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- Données moléculaires

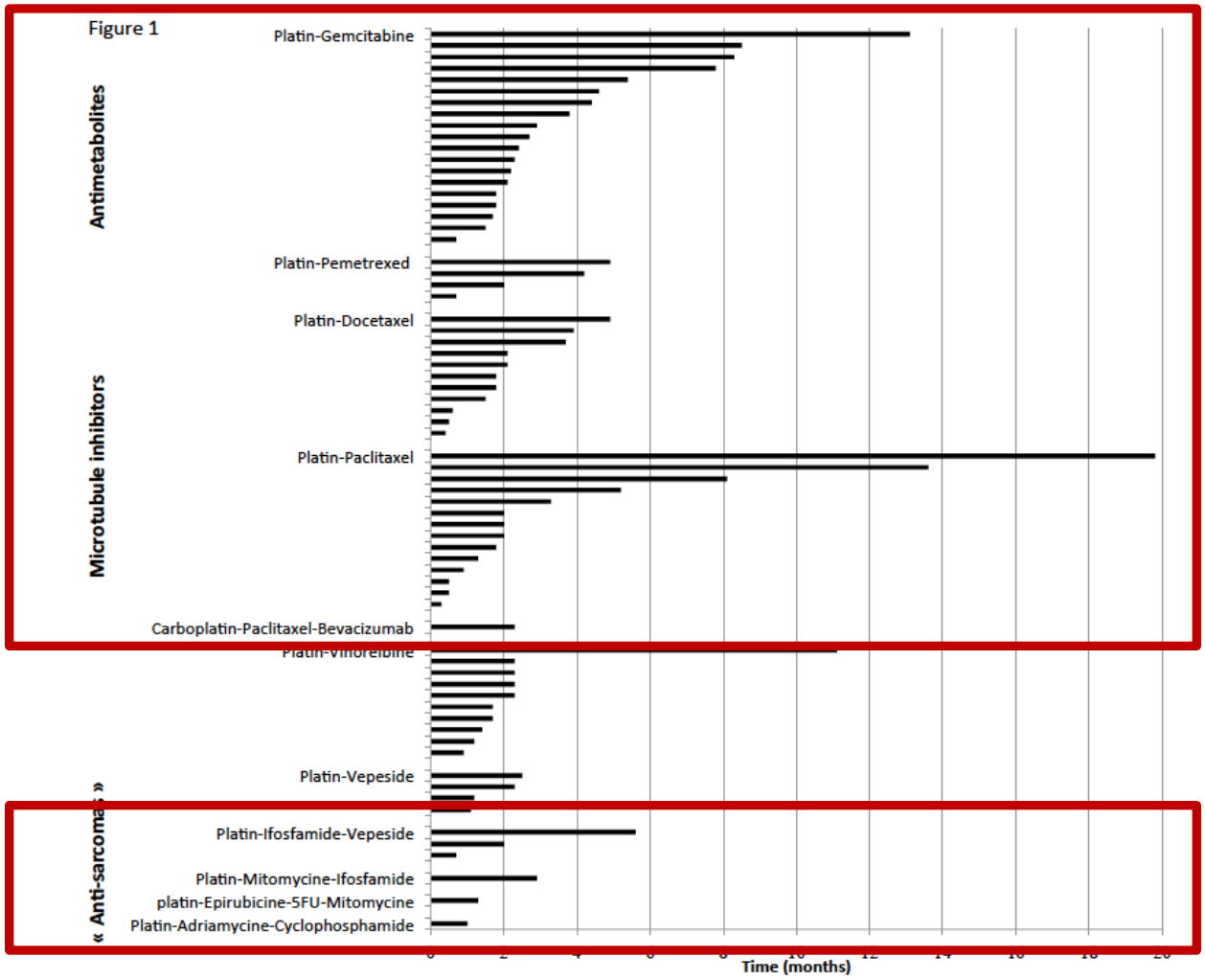
Oncologie orpheline

Traitement

- Diagnostic incident
- Contexte spécifique
- Contexte orphelin

Carcinomes sarcomatoïdes métastatiques

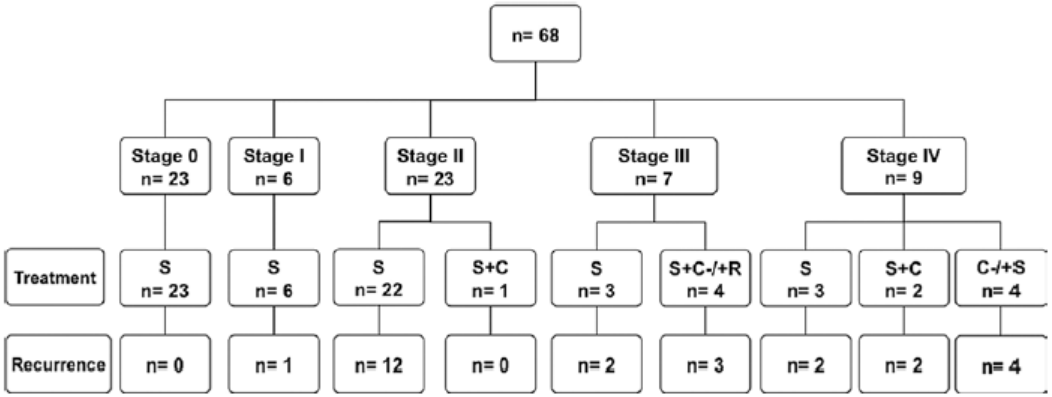
- **Série française de 97 patients**



Vieira, J Thorac Oncol. 2013 Dec;8(12):1574

Assessing the Multimodal Management of Advanced Solitary Fibrous Tumors of the Pleura in a Routine Practice Setting

Olivier Bylicki, Damien Rouvière,† Philippe Cassier,‡ Lara Chalabreysse,§ Alice Levard,‡ Jean-Michel Maury,‖ Jacques Margery,¶ Jean-Yves Blay,‡ Julien Mazières,† and Nicolas Girard, MD**



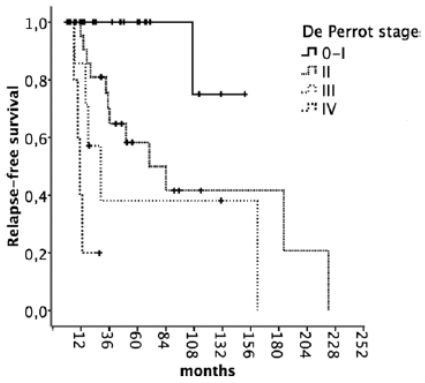


TABLE 2. Chemotherapy Treatment

	First-line[a]			Second-line			Third-line		
Treatment/Regimen	***n***	**DC (%)**	**PD (%)**	***n***	**DC (%)**	**PD (%)**	***n***	**DC (%)**	**PD (%)**
Cytotoxic agents									
MAID	6	83	17	1	0	100	0	…	…
Doxorubicine	4	25	75	4	50	50	5	20	80
Brostacilline	0	…	…	1	0	100	1	100	0
Paclitaxel weekly	0	…	…	2	0	100	1	0	100
Gemcitabine weekly	0	…	…	0	…	…	5	0	100
Gemcitabine/Dacarbazine	0	…	…	0	…	…	3	66	33
Vinorelbine	0	…	…	0	…	…	2	0	100
Docetaxel	0	…	…	1	100	0	2	0	100
Cisplatin–pemetrexed	1	100	0	…	…	…	…	…	…
Trabectedin	0	…	…	1	100	0	8	75	25
Antiangiogenic treatment									
Pazopanib	0	…	…	3	0	100	1	0	100
Sunitinib	0	…	…	1	0	100	2	0	100

J Thorac Oncol 2015; 10:309

European Journal of Cancer (2014) 50, 128–136

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Primary cardiac sarcomas: A retrospective study of the French Sarcoma Group ☆

Nicolas Isambert [a,*], Isabelle Ray-Coquard [b], Antoine Italiano [c], Maria Rios [d], Pierre Kerbrat [e], Mélanie Gauthier [a], Aurélien Blouet [f], Loïc Chaigneau [g], Florence Duffaud [h], Sophie Piperno-Neumann [i], Jean-Emmanuel Kurtz [j], Nicolas Girard [k], Olivier Collard [l], Emmanuelle Bompas [m], Nicolas Penel [n],

Treatment of patients.

	Non-metastatic disease at diagnostic ($N = 100$)	%	Metastatic disease at diagnostic ($N = 24$)
Treatment surgery	75	75.0	6
R0 resection	10	10.0	0
R1 or R2 resection	51	51.0	5
Unknown	14	14.0	1
Heart transplant	4	4.0	1
Chemotherapy	90	90.0	21
Monotherapy	19	19.0	8
Combination	70	70.0	13
Unknown	1	1.0	
Radiotherapy	24	24.0	0
Combination of treatment			
No treatment	2	2.0	2
Surgery alone	7	7.0	1
Chemotherapy alone	17	17.0	16
Surgery + chemotherapy	50	50.0	5
Surgery + radiotherapy	1	1.0	0
Chemotherapy + radiotherapy	6	6.0	0
Surgery + chemotherapy + radiotherapy	17	17.0	0

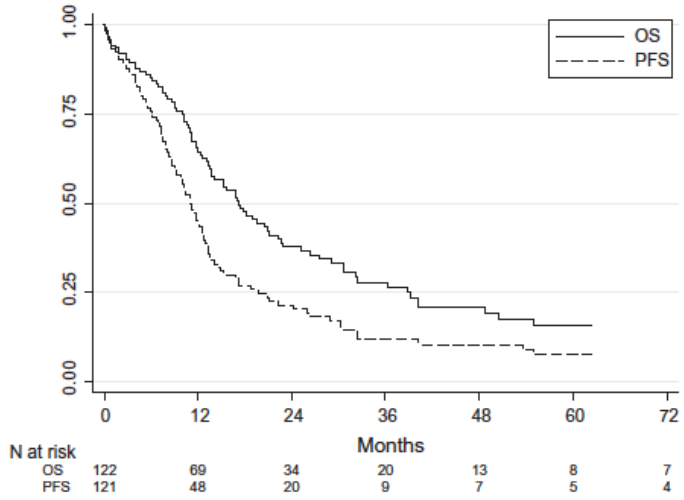


Fig. 1. Overall survival and progression free survival of the entire cohort of patients.

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

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- Diagnostic positif
- Tumeur primitive ou secondaire
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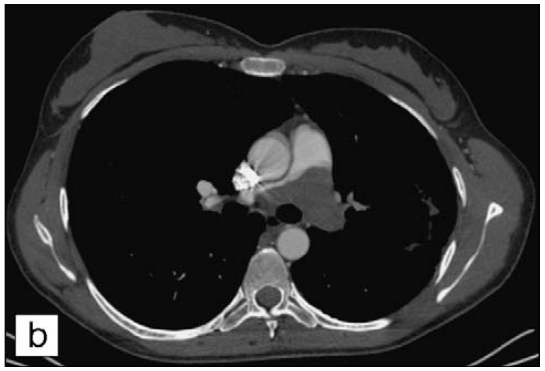
Oncologie orpheline

Traitement

- Diagnostic incident
- Contexte spécifique
- Contexte orphelin
- Approches ciblées

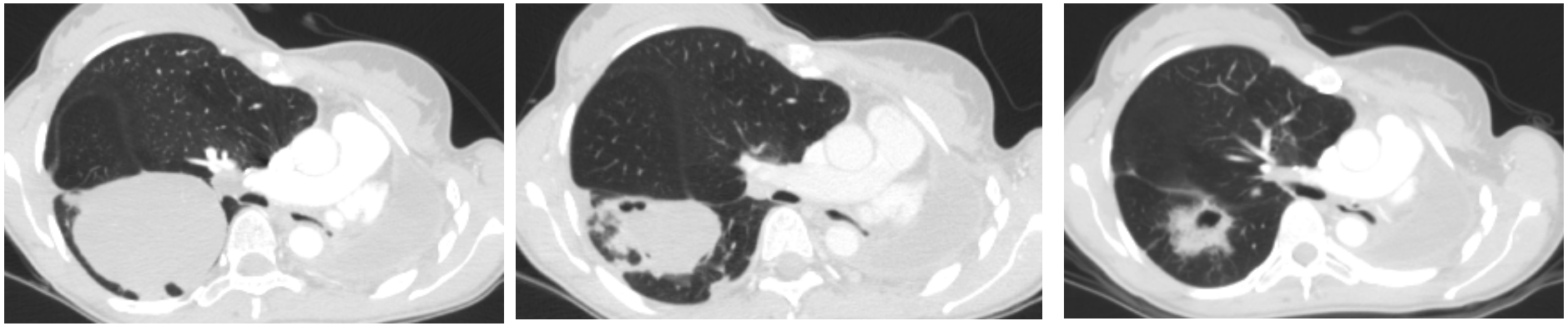
Sarcome de l’artère pulmonaire

- **Récidive pulmonaire contro-latérale, 18 mois après la pneumonectomie gauche**



Chimiothérapie MAI

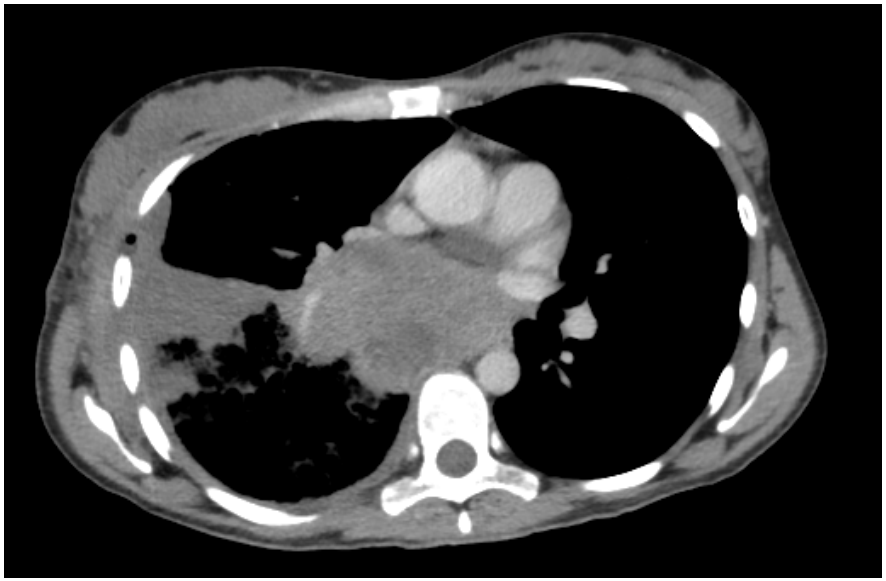
Sorafenib

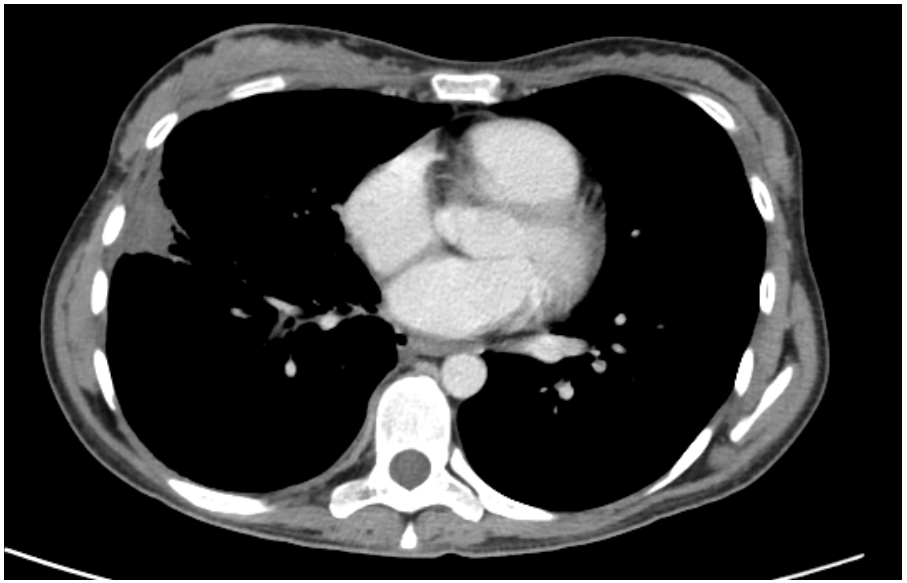


Tumeur cardiaque avec mutation de BRAF

- **Mutation BRAF V600E**

- Traitement par vemurafenib, évaluation à 6 semaines

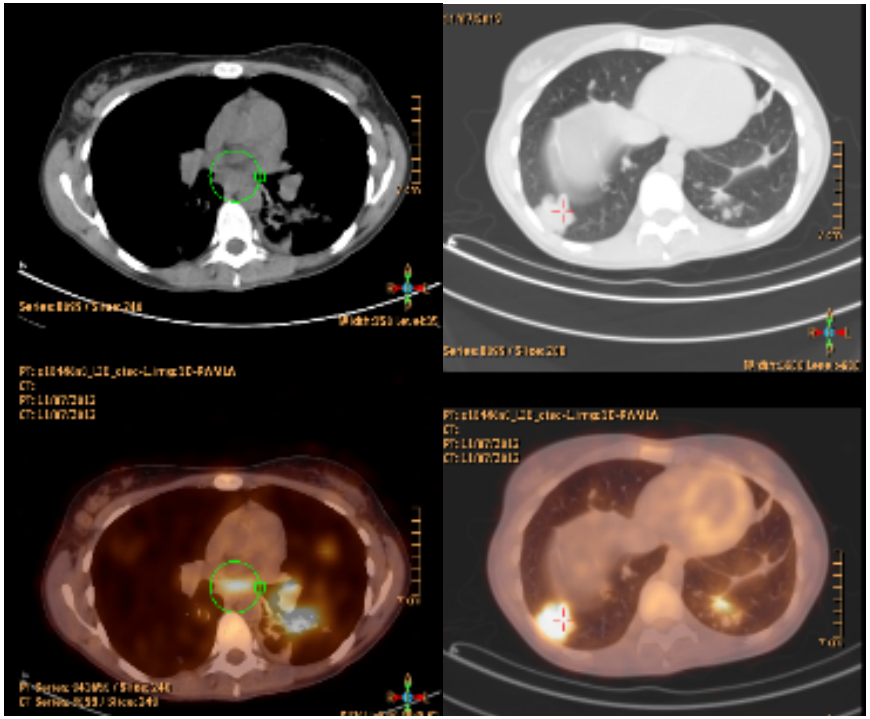


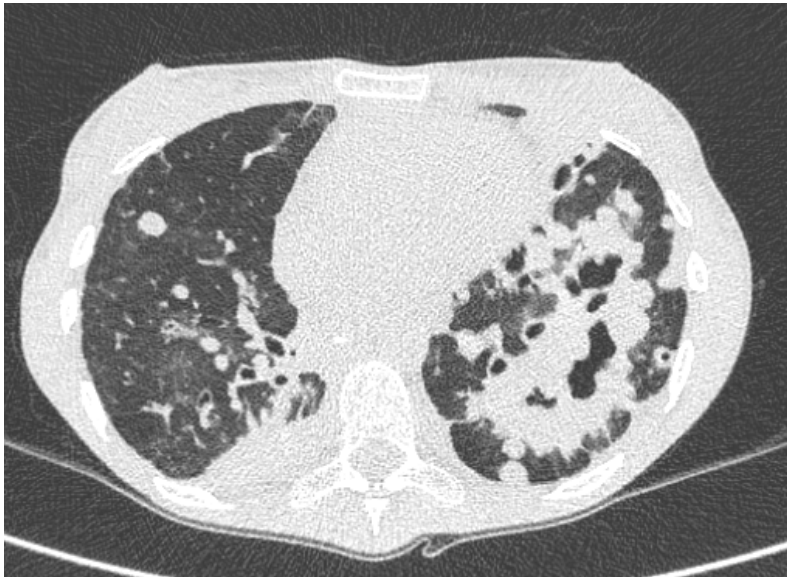


Carcinome épidermoïde/Papillomatose pulmonaire

- **Papillomatose pulmonaire et des voies aériennes supérieures**
- **Résection chirurgicale d'un carcinome épidermoïde LIG**

- **Récidive**



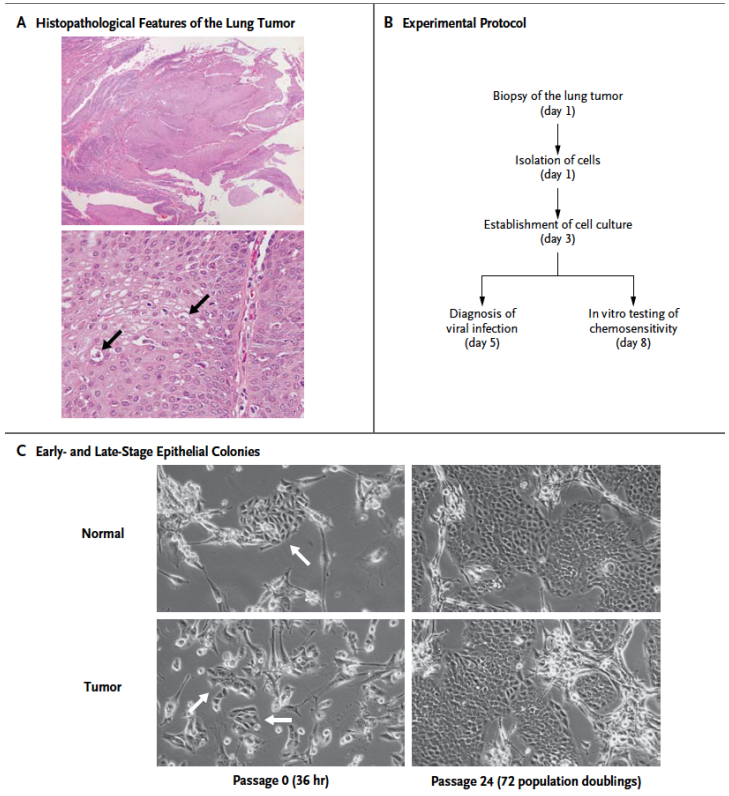


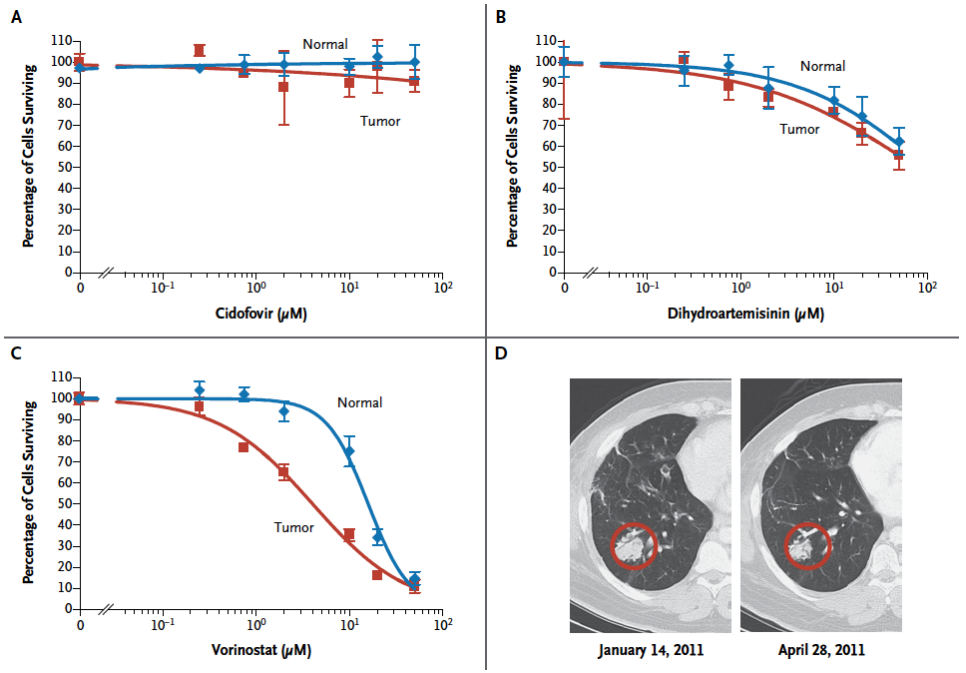
Carcinome épidermoïde/Papillomatose pulmonaire

BRIEF REPORT

Use of Reprogrammed Cells to Identify Therapy for Respiratory Papillomatosis

Hang Yuan, Ph.D., Scott Myers, M.D., Jingang Wang, Ph.D., Dan Zhou, M.S., Jennifer A. Woo, M.S., Bhaskar Kallakury, M.D., Andrew Ju, M.D., Michael Bazylewicz, M.D., Yvonne M. Carter, M.D., Christopher Albanese, Ph.D., Nazaneen Grant, M.D., Aziza Shad, M.D., Anatoly Dritschilo, M.D., Xuefeng Liu, M.D., and Richard Schlegel, M.D., Ph.D.





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- Diagnostic incident
- Contexte spécifique
- Contexte orphelin
- Approches ciblées

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Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

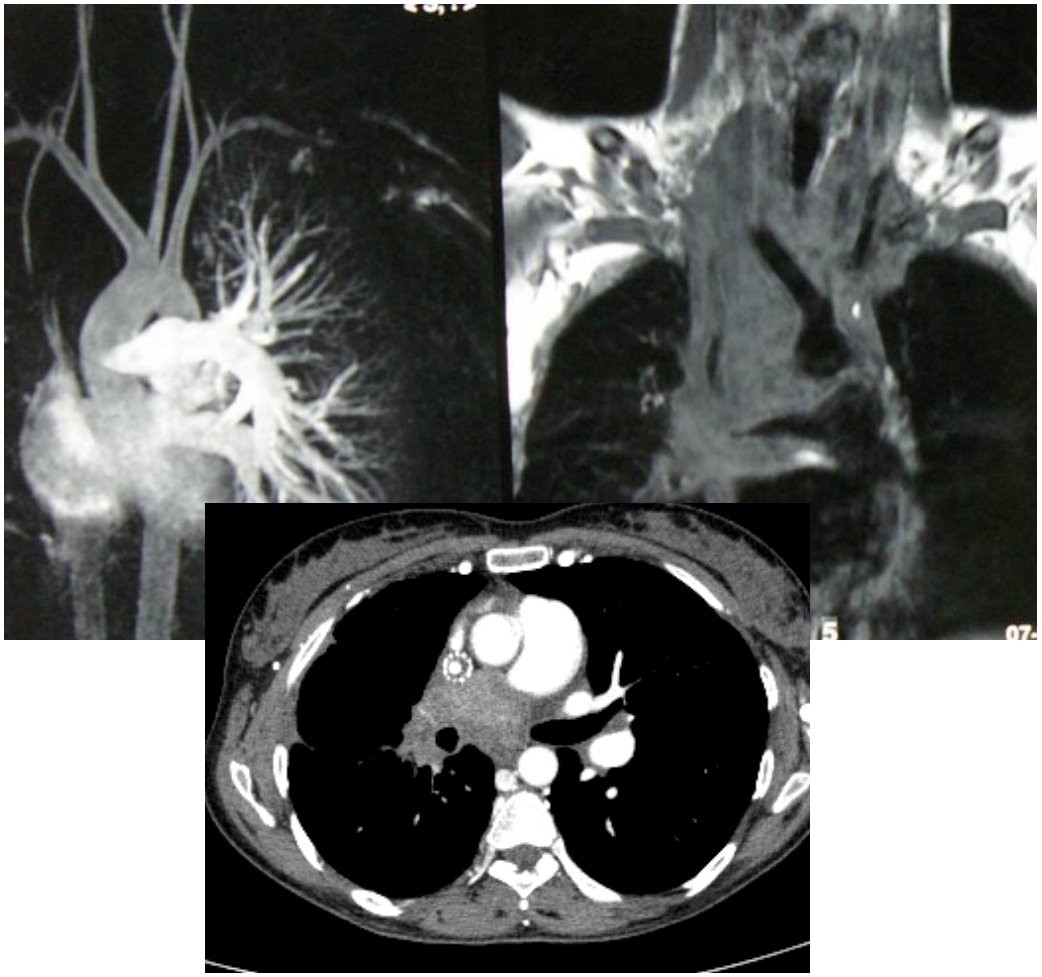
Pseudotumeurs et entités frontières

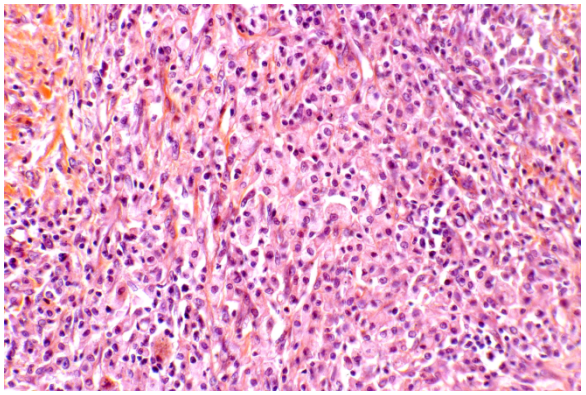
Diagnostic

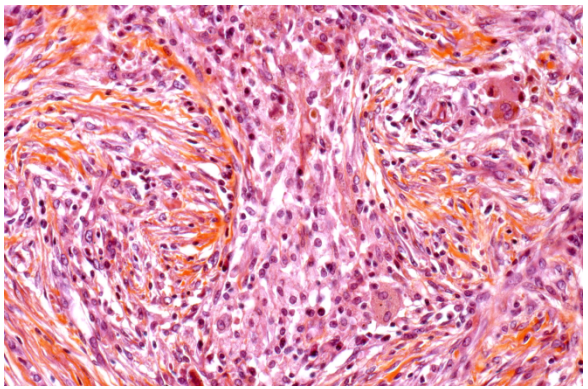
- Diagnostic positif
- Tumeur primitive ou secondaire
- Données moléculaires

Pseudo-tumeurs inflammatoires

- **Tumeur myofibroblastique/médiastinite sclérosante**

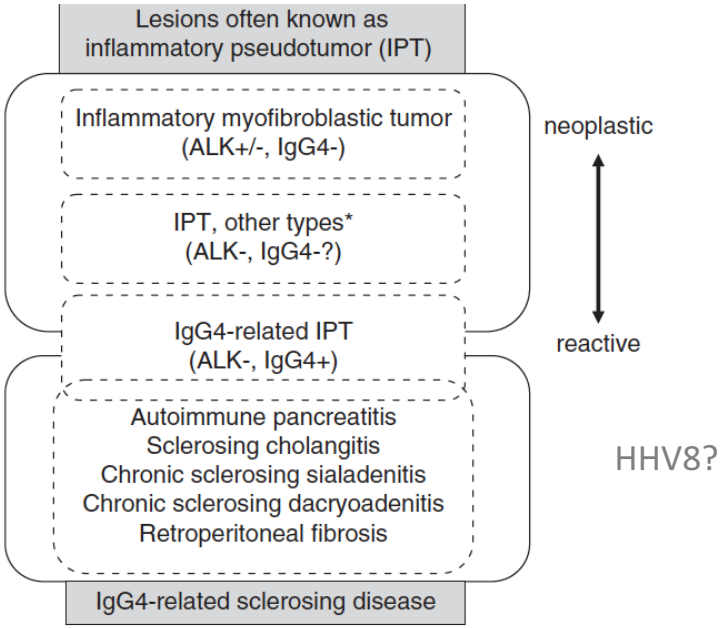






Pseudo-tumeurs inflammatoires

- **Tumeur myofibroblastique/médiastinite sclérosante**



*Other types of IPT may include IPT-like follicular dendritic cell tumor, fibrohistiocytic-type IPT, organizing pneumonia-type IPT and some infectious disease.

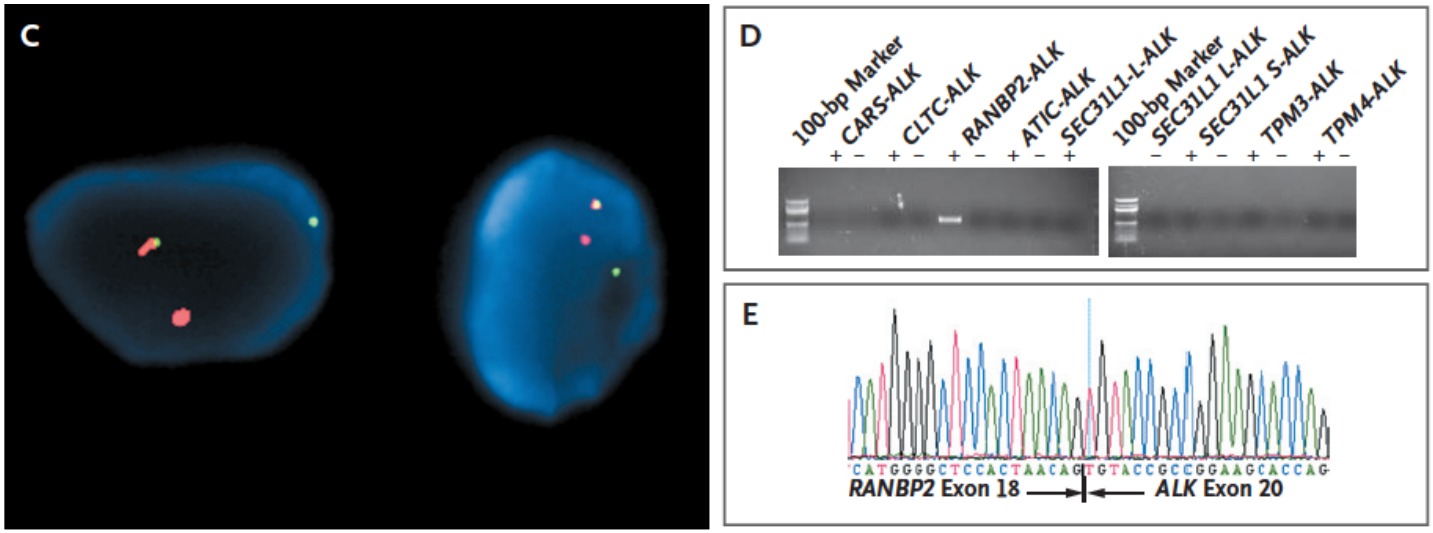
FIGURE 6. Scheme of a spectrum of the lesions often diagnosed as IPT and the relationship between IPT, inflammatory myofibroblastic tumor, and IgG4-related sclerosing disease. IgG4-related IPT morphologically belongs to the IPT group, but is etiologically a member of IgG4-related sclerosing disease. IPT indicates inflammatory pseudotumor.

Yamamoto et al. Am J Surg Pathol 2009;33:1330

Pseudo-tumeurs inflammatoires

- **Tumeur myofibroblastique/médiastinite sclérosante**

  - Pseudo-tumeurs inflammatoires/Tumeurs myofibroblastiques:
    - réarrangements chromosomiques *spécifiques* de *ALK* :
      - translocation *TPM3-ALK*
      - translocation *PPFIBP1–ALK*
    - prédiction de l'efficacité du crizotinib



Takeushi et al. Clin Cancer Res 2011;17:3341

Eyden et al. J Clin Pathol 2010;62:236; Butrynski et al. N Engl J Med 2010;363:1727

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Pseudotumeurs et entités frontières

- Tumeurs myofibroblastiques
- Histiocytose Langerhansienne

Histiocytose à cellules de Langerhans

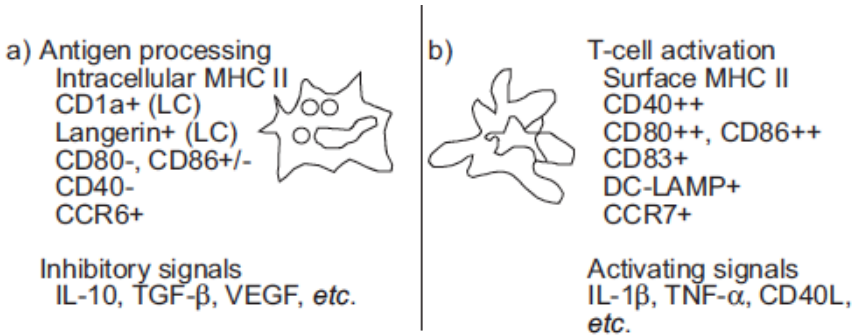
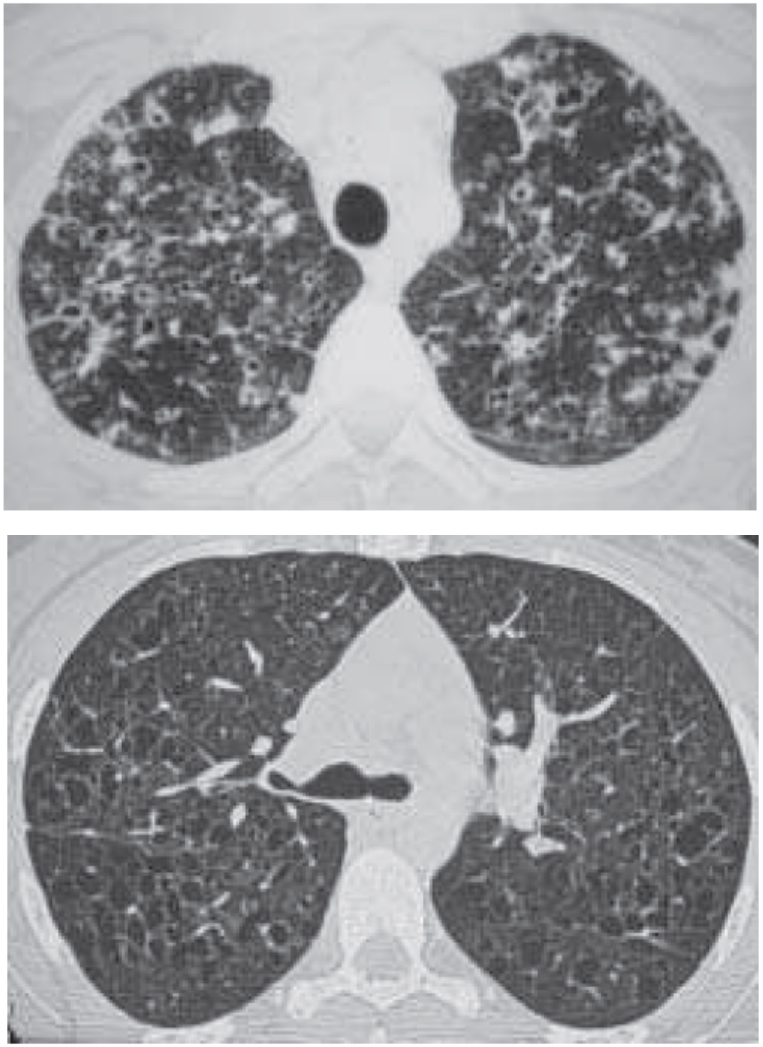


FIGURE 5. Comparison of the surface phenotype and inhibitory/activating signal micro-environment of: a) immature, and b) mature dendritic cells (DCs). MHC II: class II major histocompatibility complex; LC: Langerhans' cell; CCR: CC chemokine receptor; IL: interleukin; TGF: transforming growth factor; VEGF: vascular endothelial growth factor; LAMP: lysosome-associated membrane protein; TNF: tumour necrosis factor; CD40L: CD40 ligand.



Tazi et al Eur Respir J 2006; 27: 1272

CHEST

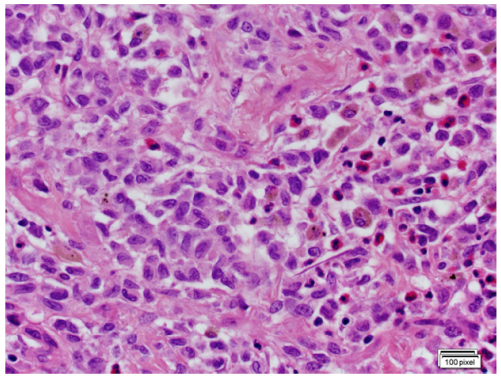
Original Research

DIFFUSE LUNG DISEASE

Pulmonary Langerhans Cell Histiocytosis

Profiling of Multifocal Tumors Using Next-Generation Sequencing Identifies Concordant Occurrence of *BRAF* V600E Mutations

Samuel A. Yousem, MD, FCCP; Sanja Dacic, MD, PhD; Yuri E. Nikiforov, MD, PhD; and Marina Nikiforova, MD



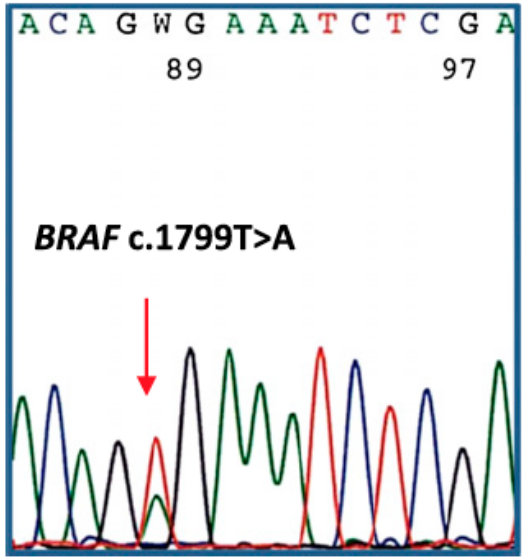


FIGURE 2. Within the stellate nodule of pulmonary Langerhans cell histiocytosis are a mixture of cells dominated by the characteristic Langerhans cell with folded reniform nuclei and eosinophilic cytoplasm. In the background are smokers-type pigmented macrophages, bilobed eosinophils, lymphocytes, and stromal myofibroblasts. There were no distinctive histologic features that separated cases with and without *BRAF* V600E mutations (hematoxylin-eosin, original magnification ×600).

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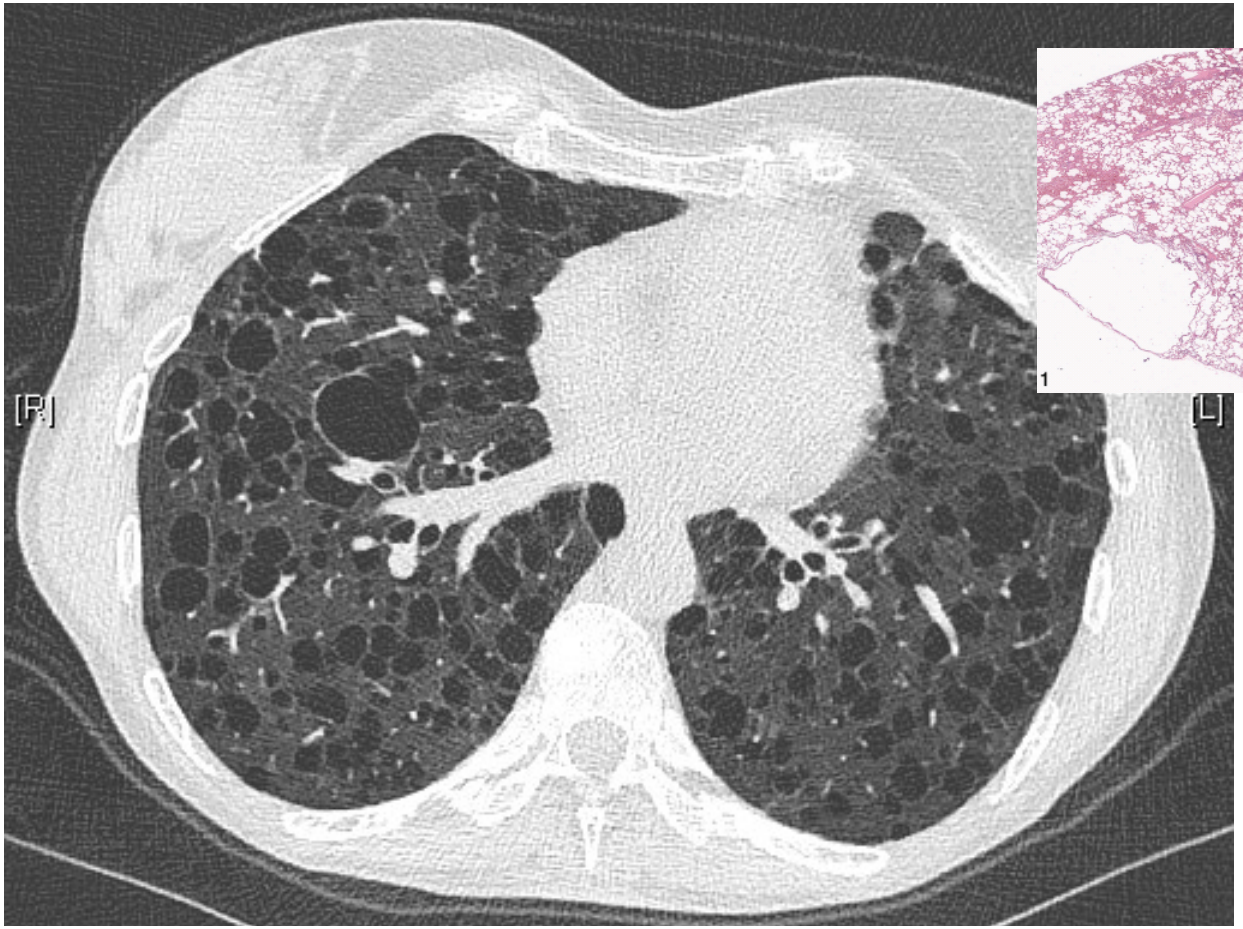
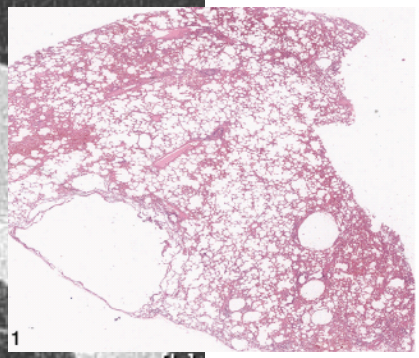
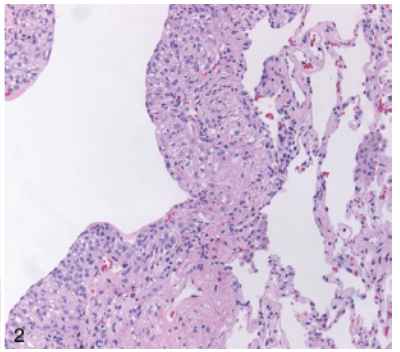
- Tumeurs myofibroblastiques
- Histiocytose Langerhansienne
- Lymphangioléiomyomatose

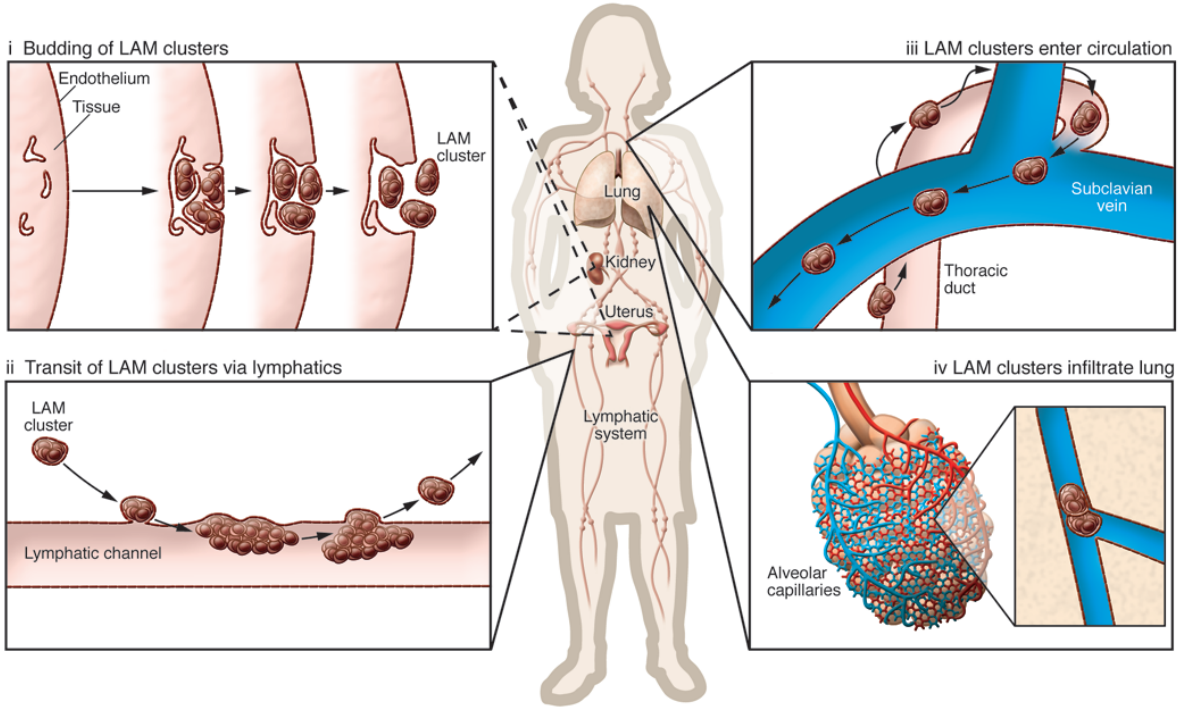
Lymphangioléiomyomatose

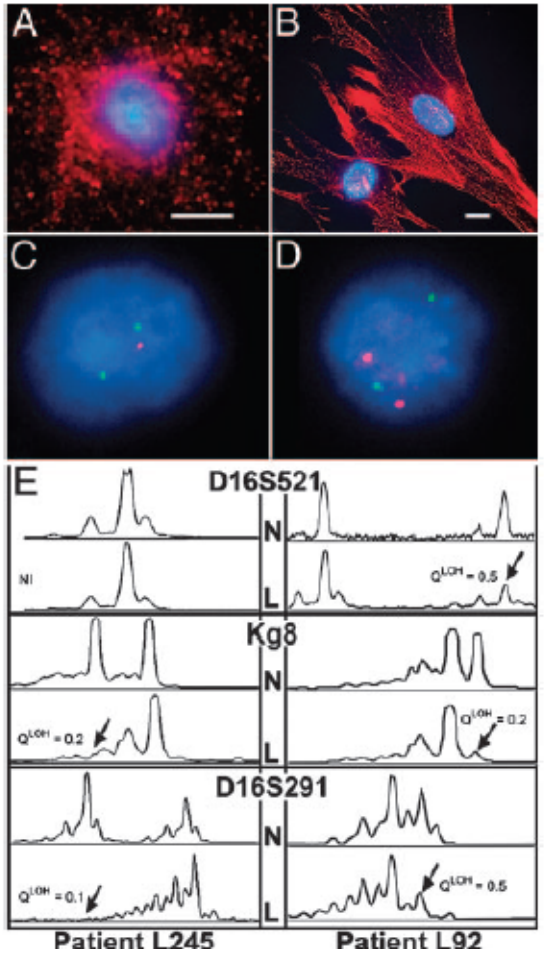






Lymphangioléiomyomatose





Henske et al. 2012

Crooks et al. PNAS 2004;101:17462

Lymphangioléiomyomatose

J Hum Genet (2002) 47:20–28

ORIGINAL ARTICLE

Teruhiko Sato · Kuniaki Seyama · Hiroaki Fujii
Hiroshi Maruyama · Yasuhiro Setoguchi
Shin-ichiro Iwakami · Yoshinosuke Fukuchi
Okio Hino

Mutation analysis of the *TSC1* and *TSC2* genes in Japanese patients with pulmonary lymphangioleiomyomatosis

Table 2. Mutations of the *TSC* genes in patients with pulmonary lymphangioleiomyomatosis

Gene	Category of mutation	Location	Nucleotide alteration	Expected protein alteration	Reference[a]
TSC-LAM					
TSC1	Germline	ex 9	T1112G	Try297stop	Strizheva et al. 2001
TSC1	Germline	ex 10	C1222A	Ser334stop	Jones et al. 1999
TSC2	Germline	ex 9	G898A	Gly294Arg	Strizheva et al. 2001
TSC2	Germline	ex 16	C1849T	Arg611Trp	Jones et al. 1999
TSC2	Germline	ex 19	T2168G	Leu717Arg	Zhang et al. 1999
TSC2	Germline	ex 23	A2701G	Met895Val	Niida et al. 1999
TSC2	Germline	ex 38	C5042T	Pro1675Leu	Franz et al. 2001
TSC2	Germline	ex 39	C5144T	Pro1709Leu	Franz et al. 2001
TSC2	Germline	ex 41	C5401T	Arg1795Cys	Strizheva et al. 2001
TSC2	Germline	ex 7	G778T	Gln254stop	Strizheva et al. 2001
TSC2	Germline	ex 19	G2127A	Trp703stop	Niida et al. 2001
TSC2	Germline	ex 29	C3460T	Gln1148stop	Strizheva et al. 2001
TSC2	Germline	ex 30	C3773	Ser1252stop	Strizheva et al. 2001
TSC2	Germline	ex 9	465-bp deletion	Large deletion	Franz et al. 2001
TSC2	Germline	ex 9	Del921-940	Met301fs → aa330stop	Franz et al. 2001
TSC2	Germline	Many exons	Large deletion	Loss of tuberin	Jones et al. 1999
TSC2	Germline	ex 18	Del1978-79	Gly654fs → aa655stop	Franz et al. 2001
TSC2	Germline	ex 24	Del2832-2833TA	Thr938fs → aa958stop	Beauchamp et al. 1998
TSC2	Germline	ex 27	Del3232A	Ser1072fs → aa1081stop	Franz et al. 2001
TSC2	Germline	ex 37	Del4891A	Met1625fs → aa1671stop	this study (LTK22)
TSC2	Germline	ex 38	Del5069-5086+16	NA[b]	Franz et al. 2001
TSC2	Germline	ex 40	Del5256-5273	6 aa in-frame deletion	Strizheva et al. 2001
TSC2	Germline	ex 9	Del993G	Multiple splicing products	Maruyama et al. 2001 and this study (LKM14)
TSC2	Germline	int 18	G2116-1A	NA [b]	Franz et al. 2001
Sporadic LAM					
TSC1	Germline	ex 6	C716A	Cys165stop	This study (LNK8)
TSC2	Somatic	ex 16	G1850A	Arg611Gln	Carsillo et al. 2000
TSC2	Somatic	ex 10	G1114T	Glu366stop	Carsillo et al. 2000
TSC2	Somatic	ex 5	Del547-550CTTC	Leu177fs → aa180stop	Carsillo et al. 2000
TSC2	Somatic	ex 18	Del2079-2091	Ser687fs → aa693stop	Carsillo et al. 2000
TSC2	Somatic	ex 33	Del4267C	Arg1417fs → aa1475stop	This study (LMJ7)
TSC2	Somatic	ex 33	Ins4109T	Ser1364fs → aa1413stop	This study (LMJ7)
TSC2	Somatic	ex 40	Ins5196-5199TGCA	His1726fs → aa1729stop	This study (LIY26)

Lymphangioléiomyomatose

ORIGINAL ARTICLE

Sirolimus for Angiomyolipoma in Tuberous Sclerosis Complex or Lymphangioleiomyomatosis

John J. Bissler, M.D., Francis X. McCormack, M.D., Lisa R. Young, M.D., Jean M. Elwing, M.D., Gail Chuck, L.M.T., Jennifer M. Leonard, R.N., Vincent J. Schmithorst, Ph.D., Tal Laor, M.D., Alan S. Brody, M.D., Judy Bean, Ph.D., Shelia Salisbury, M.S., and David N. Franz, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 28, 2011 VOL. 364 NO. 17

Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis

Francis X. McCormack, M.D., Yoshikazu Inoue, M.D., Ph.D., Joel Moss, M.D., Ph.D., Lianne G. Singer, M.D., Charlie Strange, M.D., Koh Nakata, M.D., Ph.D., Alan F. Barker, M.D., Jeffrey T. Chapman, M.D., Mark L. Brantly, M.D., James M. Stocks, M.D., Kevin K. Brown, M.D., Joseph P. Lynch, III, M.D., Hilary J. Goldberg, M.D., Lisa R. Young, M.D., Brent W. Kinder, M.D., Gregory P. Downey, M.D., Eugene J. Sullivan, M.D., Thomas V. Colby, M.D., Roy T. McKay, Ph.D., Marsha M. Cohen, M.D., Leslie Korbee, B.S., Angelo M. Taveira-DaSilva, M.D., Ph.D., Hye-Seung Lee, Ph.D., Jeffrey P. Krischer, Ph.D., and Bruce C. Trapnell, M.D., for the National Institutes of Health Rare Lung Diseases Consortium and the MILES Trial Group*

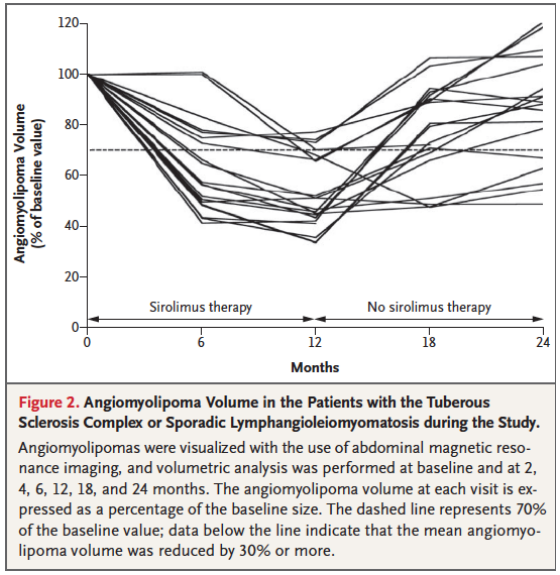
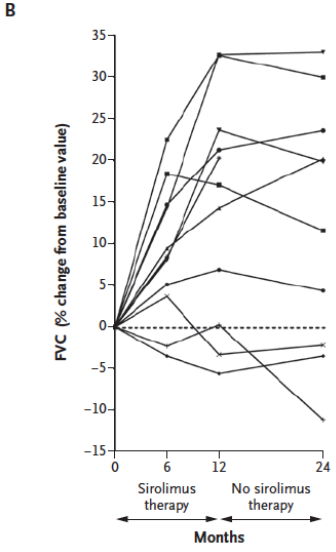
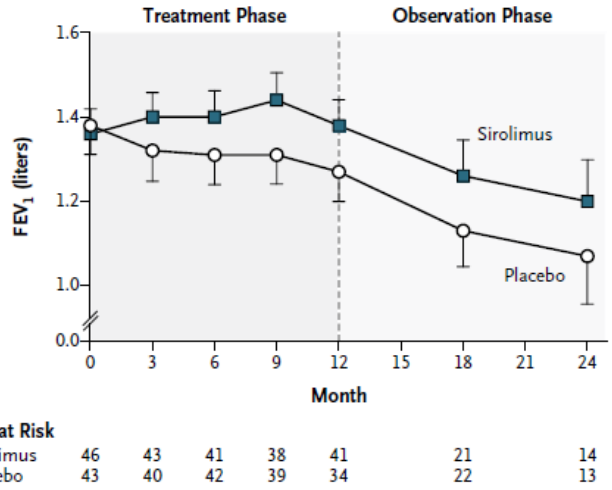


Figure 2. Angiomyolipoma Volume in the Patients with the Tuberous Sclerosis Complex or Sporadic Lymphangioleiomyomatosis during the Study.

Angiomyolipomas were visualized with the use of abdominal magnetic resonance imaging, and volumetric analysis was performed at baseline and at 2, 4, 6, 12, 18, and 24 months. The angiomyolipoma volume at each visit is expressed as a percentage of the baseline size. The dashed line represents 70% of the baseline value; data below the line indicate that the mean angiomyolipoma volume was reduced by 30% or more.





N Engl J Med 2008;358:140-51

Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histologie
- Fréquence
- Moléculaire

Signes évocateurs

- Aspects radiologiques
- Aspect cliniques
- Sous-groupes moléculaires

Diagnostic

- Diagnostic positif
- Tumeur primitive ou secondaire
- Données moléculaires

Oncologie orpheline

Traitement

- Diagnostic incident
- Contexte spécifique
- Contexte orphelin
- Approches ciblées

Pseudotumeurs et entités frontières

- Tumeurs myofibroblastiques
- Histiocytose Langerhansienne
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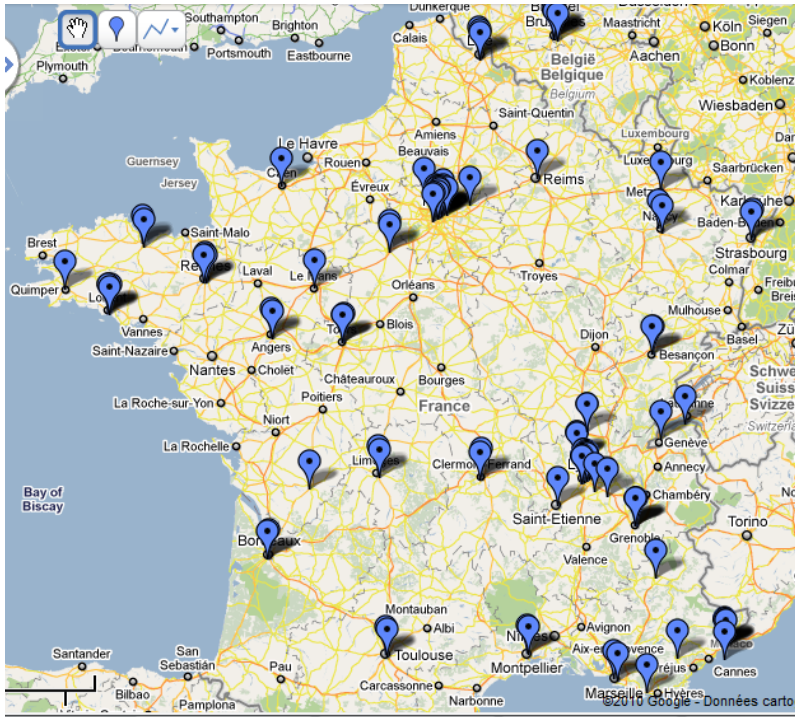
Projet oncologie orpheline thoracique
Présentation générale



- Observatoire de 932 cas de tumeurs rares intra-thoraciques

RYTHMIC: notre réseau pour les tumeurs thymiques

rythmic.org
Réseau tumeurs THYMiques et Cancer

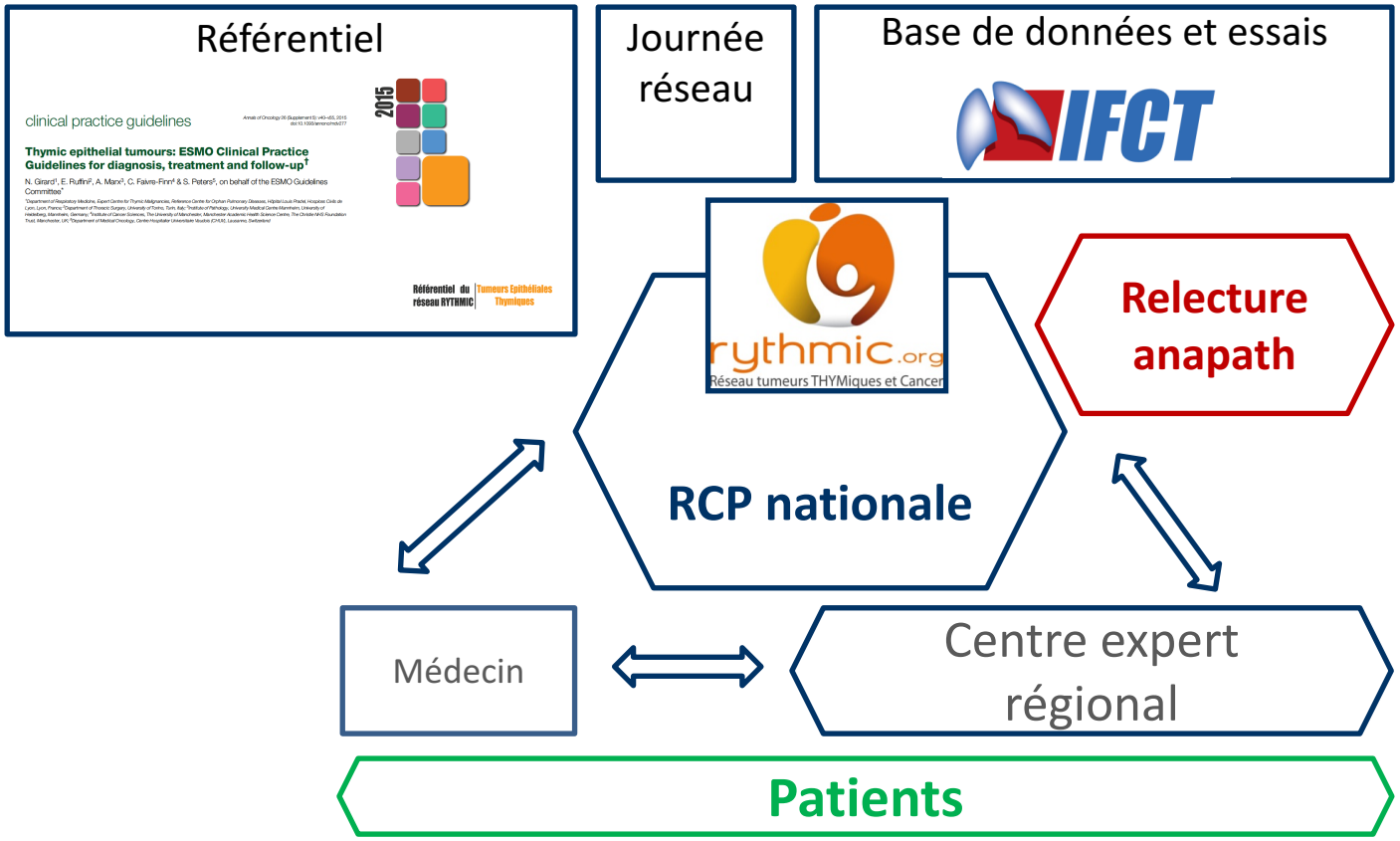
GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Hospices Civils de Lyon

Coordinateur:
B. Besse
Gustave Roussy

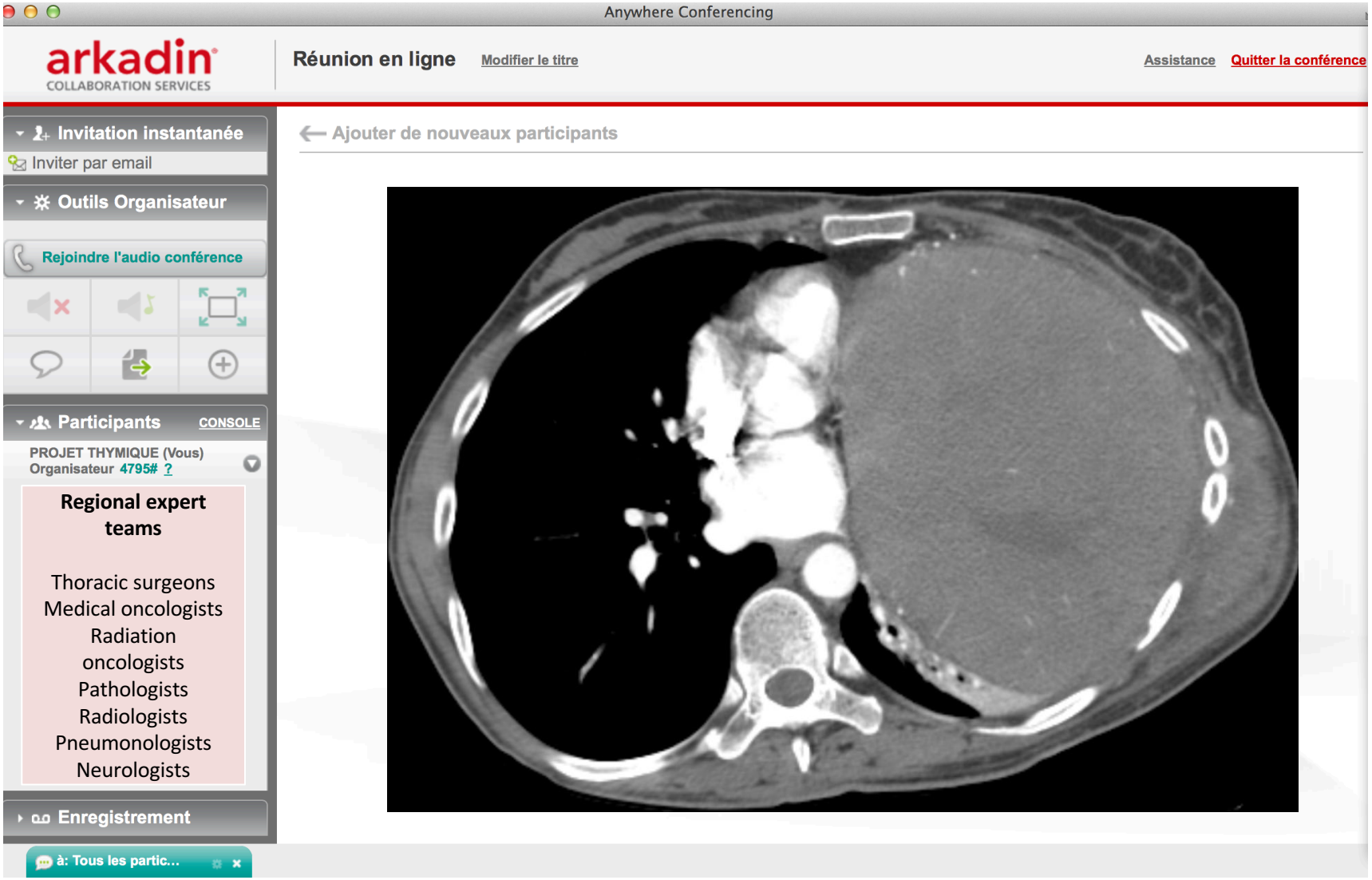
10 ANS D'ACTIONS CONTRE LES CANCERS
INSTITUT NATIONAL DU CANCER

RYTHMIC: notre réseau pour les tumeurs thymiques



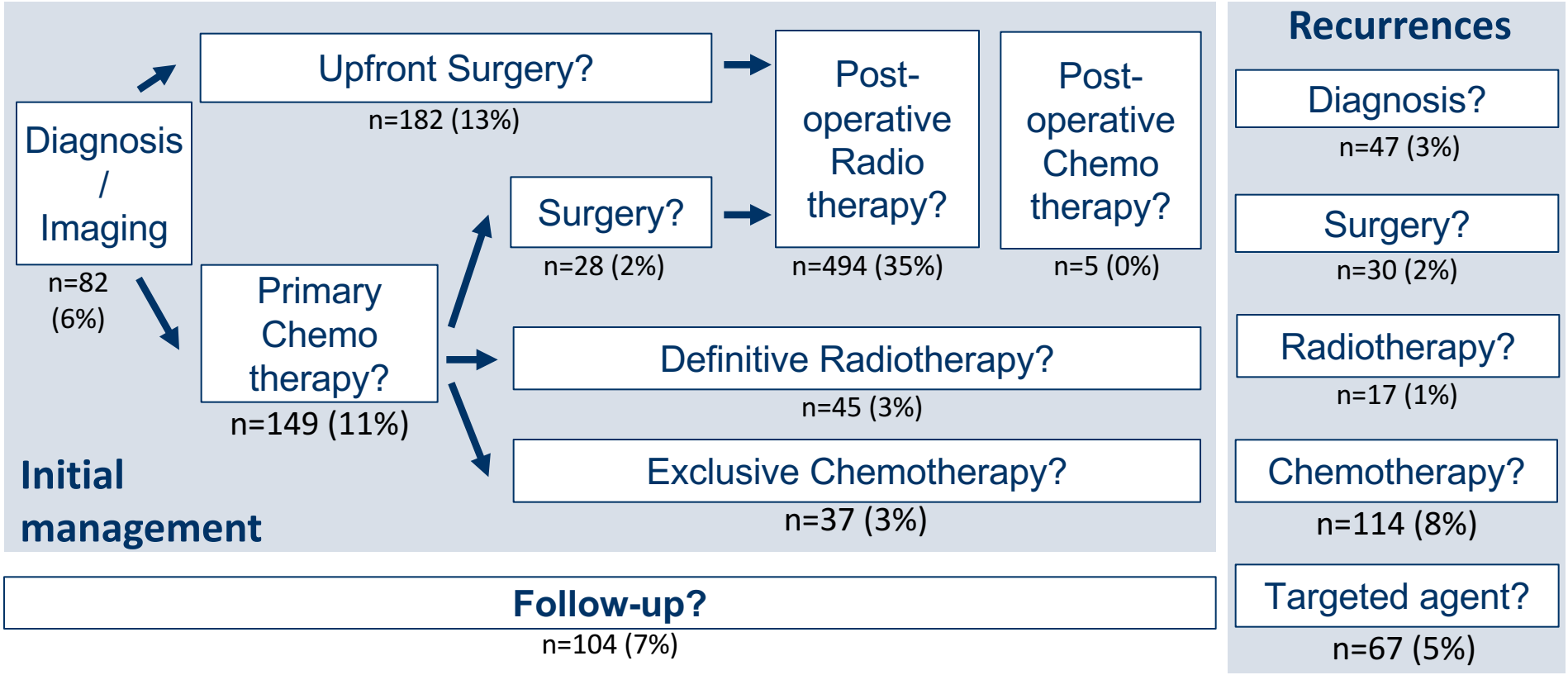
www.rythmic.org

RYTHMIC: notre réseau pour les tumeurs thymiques



RYTHMIC: des discussions à tous les stades de la prise en charge

- 1000 patients: 1401 questions posées en RCP



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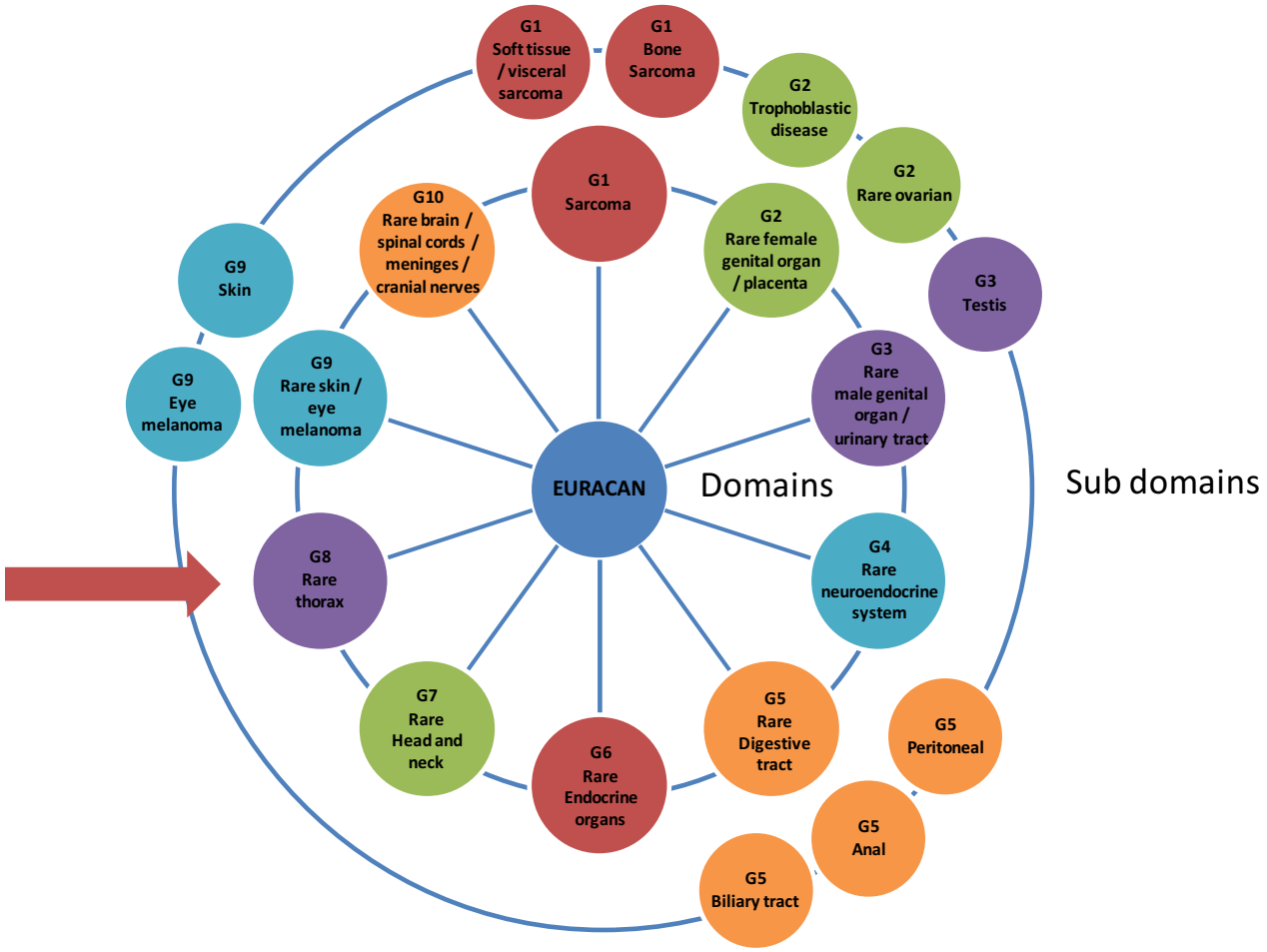
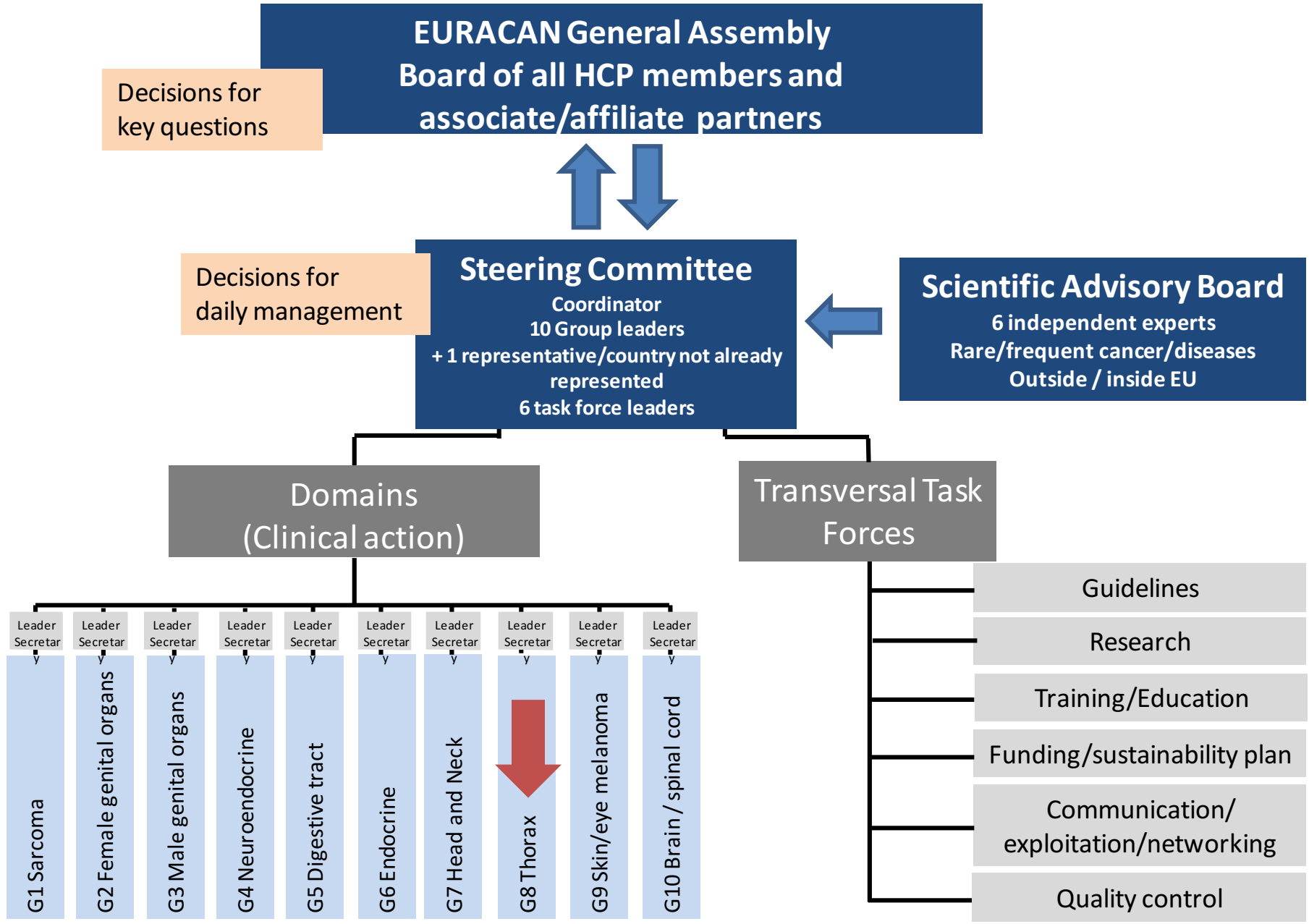
EURACAN: European Reference Network



EURACAN: European Reference Network

Member state Flag	Member state code	EURACAN HCP Number	HCP Town	HCP Acronym	HCP Name	HCP DOMAIN Representative Name
	BE	2	Antwerp	AUH (UZA)	Antwerp University Hospital (Universitair Ziekenhuis Antwerpen)	Paul VAN SCHIL
	BE	4	Brussels	IJB	Institut Jules Bordet	Thierry BERGHMANS
	BE	5	Leuven	LCI (LKI)	Leuven Cancer Institut (Leuvens kankerinstituut)	Dirk Van Raemdonck
	DE	12	Mannheim	UMM	Mannheim University Medical Center (UniversitatsMedizin Mannheim)	Prof. Dr. Peter Hohenberger
	DE	13	Essen	UK-Essen	University Hospital Essen (UniversitätsKlinikum Essen)	Clemens Aigner
	FR	22	Lyon	HCL	Hospices Civils de Lyon	Nicoals GIRARD
	FR	23	Villejuif	IGR	Institut Gustave Roussy	Prof Benjamin Besse
	IT	28	Torino	Cita della Salute	Azienda Ospedaliero - Universitaria Cita della Salute e della Scienza di Torino	Dr Enrico Ruffini
	IT	29	Siena	AOUS	Azienda Ospedaliera Universitaria Senese	Piero PALADINI
	IT	31	Aviano	CRO	Centro di Riferimento Oncologico di Aviano	Bearz Alessandra
	IT	32	Naples	CRTR	CRTR-AOU Federico II	MD, Giovannella Palmieri
	IT	38	Milano	INT	Fondazione IRCCS Istituto Nazionale dei Tumori	Dr Marina Garassino/Dr Martina Imbimbo
	IT	39	Meldola	IRST	Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori	Angelo Delmonte
	IT	42	Genoa	IST	IRCCS San Martino - IST	Francesco Grossi

EURACAN: structure



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- Essais cliniques

Immunothérapie et tumeurs rares
Essais dédiés à un type tumoral

EORTC-ETOP NIVOTHYM

Primary objective:

To detect activity of nivolumab as single agent as second line treatment for **type B3 thymoma and thymic carcinoma**

Eligible patients → Nivolumab 240 mg IV q2 weeks

Primary endpoint: PFS rate at 6 months

PIs: N. Girard, S. Peters

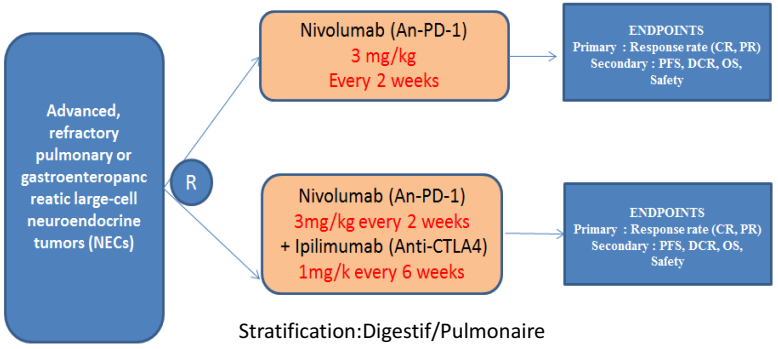
Secondary endpoints:

- ORR and DCR, Duration of response
- OS
- QOL
- Safety

Biomarkers: SPECTA

PD-L1
Cytokines
Molecular profiling

IFCT-FFCD-GERCOR-GCO-001 NIPINEC



Stratification:Digestif/Pulmonaire

Step 1
N=41 per cohort
The cohort will be terminated following Step 1 if≤ 5 response (CR +PR) are observed

Step 2
N=40 per cohort

IFCT

GCO
Groupes Coopérateurs en Oncologie

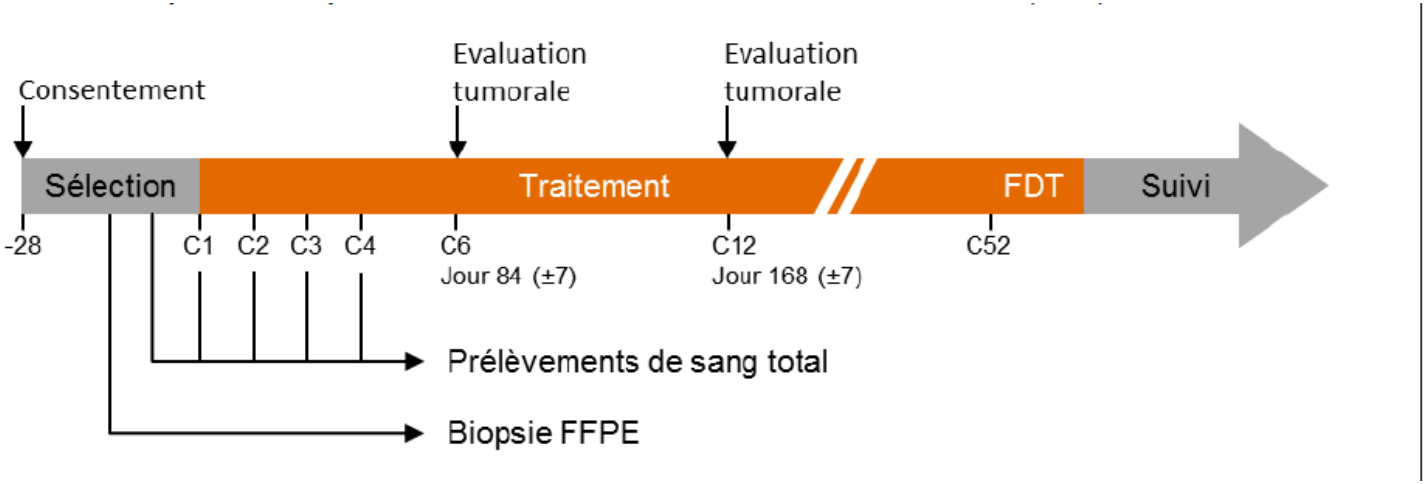
Immunothérapie et tumeurs rares
Essais de type Basket

Acsé Nivolumab

- Cohorte 1: Carcinome non à cellules claires du rein
- Cohorte 2: Cancer rare de la tête et du cou
- Cohorte 3: Cancer rare de la peau
- Cohorte 4: Cancer avec MSI autres que cancer colorectal
- Cohorte 5: Cancer du pénis

Acsé Pembrolizumab

- Cohorte 1: Sarcome rare
- Cohorte 2: Cancer rare des ovaires
- Cohorte 3: Lymphome primitif du système nerveux central
- Cohorte 4: Cancer rare de la tyroïde
- Cohorte 5: Cancer neuroendocrinien rare
- Cohorte 6: Cancer des cellules germinales



Les tumeurs rares intra-thoraciques

Définitions

- Localisation
- Histo
- Fréqu
- Molé

Traitement

Diagnostic incident

e

Sign

- Aspec
- Aspec
- Sous-

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rhansienne
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Diagnostic

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Merci!

nicolas.girard2@curie.fr