Tumores Pulmonares

Dra. Mónica Carrera Alvarez

Tumores Pulmonares

- BENIGNOS
  - Adenomas
  - Leiomiomas
- MALIGNOS
  - Carcinomas
  - Neuroendócrinos
  - Otros
  - Metástasis

Malignant epithelial tumours	
Squamous cell carcinoma	8070/3
Papillary	8052/3
Clear cell	8084/3
Small cell	8073/3
Basaloid	8083/3
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Adenocarcinoma	8140/3
Adenocarcinoma, mixed subtype	8255/3
Acinar adenocarcinoma	8550/3
Papillary adenocarcinoma	8260/3
Bronchioloalveolar carcinoma	8250/3
Nonmucinous	8252/3
Mucinous	8253/3
Mixed nonmucinous and mucinous or indeterminate	8254/3
Solid adenocarcinoma with mucin production	8230/3
Fetal adenocarcinoma	8333/3
Mucinous ("colloid") carcinoma	8480/3
Mucinous cystadenocarcinoma	8470/3
Signet ring adenocarcinoma	8490/3
Clear cell adenocarcinoma	8310/3
Large cell carcinoma	8012/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3
Basaloid carcinoma	8123/3
Lymphoepithelioma-like carcinoma	8082/3
Clear cell carcinoma	8310/3
Large cell carcinoma with rhabdoid phenotype	8014/3
Adenosquamous carcinoma	8560/3
Sarcomatoid carcinoma	8033/3
Pleomorphic carcinoma	8022/3
Spindle cell carcinoma	8032/3
Giant cell carcinoma	8031/3
Carcinosarcoma	8980/3
Pulmonary blastoma	8972/3
Carcinoid tumour	8240/3
Typical carcinoid	8240/3
Atypical carcinoid	8249/3
Salivary gland tumours	
Mucoepidermoid carcinoma	8430/3
Adenoid cystic carcinoma	8200/3
Epithelial-myoepithelial carcinoma	8562/3
Preinvasive lesions	
Squamous carcinoma *in situ*	8070/2
Atypical adenomatous hyperplasia	
Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia	
Mesenchymal tumours	
Epithelioid haemangioendothelioma	9133/1
Angiosarcoma	9120/3
Pleuropulmonary blastoma	8973/3
Chondroma	9220/0
Congenital peribronchial myofibroblastic tumour	8827/1
Diffuse pulmonary lymphangiomatosis	
Inflammatory myofibroblastic tumour	8825/1
Lymphangioleiomyomatosis	9174/1
Synovial sarcoma	9040/3
Monophasic	9041/3
Biphasic	9043/3
Pulmonary artery sarcoma	8800/3
Pulmonary vein sarcoma	8800/3
Benign epithelial tumours	
Papillomas	
Squamous cell papilloma	8052/0
Exophytic	8052/0
Inverted	8053/0
Glandular papilloma	8260/0
Mixed squamous cell and glandular papilloma	8560/0
Adenomas	
Alveolar adenoma	8251/0
Papillary adenoma	8260/0
Adenomas of the salivary gland type	
Mucous gland adenoma	8140/0
Pleomorphic adenoma	8940/0
Others	
Mucinous cystadenoma	8470/0
Lymphoproliferative tumours	
Marginal zone B-cell lymphoma of the MALT type	9699/3
Diffuse large B-cell lymphoma	9680/3
Lymphomatoid granulomatosis	9766/1
Langerhans cell histiocytosis	9751/1
Miscellaneous tumours	
Hamartoma	
Sclerosing hemangioma	8832/0
Clear cell tumour	8005/0
Germ cell tumours	
Teratoma, mature	9080/0
Immature	9080/3
Other germ cell tumours	
Intrapulmonary thymoma	8580/1
Melanoma	8720/3
Metastatic tumours	

Tumores Pulmonares

- 90-95% Carcinomas
- 1ª Causa de mortalidad a nivel mundial
- 215,000 casos nuevos por año
- 40-70 años
- Solo 2% menores de 40 años
- 41% de sobrevida a un año al momento del dx Cambio
- SV a 5 años 16% Cambio por Terapias dirigidas

Tumores Pulmonares

- Tabaquismo 87% en los pacientes con Ca de pulmón
- Relación con consumo, duración y tendencia
  - Fumadores pasivos 3000 muertes al año
  - Mutaciones de p53 secundaria a benzopirenos
  - Radiaciones ionizantes
  - Uranio
  - Amianto
  - Radón
- Genética
  - Oncogenes: c-MYC, RAS, EGFR, c-MET, c_KIT
  - Antioncogenes: p53, RB1, p16

Tumores Pulmonares

- CARCINOMAS
  - CELULAS PEQUEÑAS
  - CELULAS NO PEQUEÑAS
    - ADENOCARCINOMA
    - CARCINOMA EPIDERMOIDE
    - TUMORES NEUROENDOCRINOS
- SARCOMAS (CUALQUIERA)
- METASTASIS

-CON DIFERENCIACIÓN ESCAMOSA
-ADENOESCAMOSO
-CON DIFERENCIACIÓN GLANDULAR

- CON DIFERENCIACIÓN NEUROENDOCRINA

- CON DIFERENCIACIÓN SARCOMATOIDE

HISTOLOGIA

The conflicting features of some published histological classifications of lung cancer are briefly reviewed. The view that the tumours are so pleomorphic that classification serves no purpose has not been confirmed. A consecutive series of 207 resected lung cancers has been divided into five distinct types:

Oat-cell carcinoma	15·9%
Squamous-cell carcinoma	60·4%
Adenocarcinoma	15·5%
Polygonal-cell carcinoma	7·7%
Malignant " adenoma "	0·5%

WHO histological classification of tumours of the lung

Malignant epithelial tumours	
Squamous cell carcinoma	8070/3
Papillary	8052/3
Clear cell	8084/3
Small cell	8073/3
Basaloid	8083/3
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Adenocarcinoma	8140/3
Adenocarcinoma, mixed subtype	8255/3
Acinar adenocarcinoma	8550/3
Papillary adenocarcinoma	8260/3
Bronchioloalveolar carcinoma	8250/3
Nonmucinous	8252/3
Mucinous	8253/3
Mixed nonmucinous and mucinous or indeterminate	8254/3
Solid adenocarcinoma with mucin production	8230/3
Fetal adenocarcinoma	8333/3
Mucinous ("colloid") carcinoma	8480/3
Mucinous cystadenocarcinoma	8470/3
Signet ring adenocarcinoma	8490/3
Clear cell adenocarcinoma	8310/3
Large cell carcinoma	8012/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3
Basaloid carcinoma	8123/3
Lymphoepithelioma-like carcinoma	8082/3
Clear cell carcinoma	8310/3
Large cell carcinoma with rhabdoid phenotype	8014/3
Adenosquamous carcinoma	8560/3
Sarcomatoid carcinoma	8033/3
Pleomorphic carcinoma	8022/3
Spindle cell carcinoma	8032/3
Giant cell carcinoma	8031/3
Carcinosarcoma	8980/3
Pulmonary blastoma	8972/3
Carcinoid tumour	8240/3
Typical carcinoid	8240/3
Atypical carcinoid	8249/3
Mesenchymal tumours	
Epithelioid haemangioendothelioma	9133/1
Angiosarcoma	9120/3
Pleuropulmonary blastoma	8973/3
Chondroma	9220/0
Congenial peribronchial myofibroblastic tumour	8827/1
Diffuse pulmonary lymphangiomatosis	
Inflammatory myofibroblastic tumour	8825/1
Lymphangioleiomyomatosis	9174/1
Synovial sarcoma	9040/3
Monophasic	9041/3
Biphasic	9043/3
Pulmonary artery sarcoma	8800/3
Pulmonary vein sarcoma	8800/3
Benign epithelial tumours	
Papillomas	
Squamous cell papilloma	8052/0
Exophytic	8052/0
Inverted	8053/0
Glandular papilloma	8260/0
Mixed squamous cell and glandular papilloma	8560/0
Adenomas	
Alveolar adenoma	8251/0
Papillary adenoma	8260/0
Adenomas of the salivary gland type	
Mucous gland adenoma	8140/0
Pleomorphic adenoma	8940/0
Others	
Mucinous cystadenoma	8470/0
Lymphoproliferative tumours	
Marginal zone B-cell lymphoma of the MALT type	9699/3
Diffuse large B-cell lymphoma	9680/3
Lymphomatoid granulomatosis	9766/1
Langerhans cell histiocytosis	9751/1
Miscellaneous tumours	
Harmatoma	
Sclerosing hemangioma	8832/0
Clear cell tumour	8005/0
Germ cell tumours	
Teratoma, mature	9080/0
Immature	9080/3
Other germ cell tumours	
Intrapulmonary thymoma	8580/1

Thorax (1955), 10, 107

HISTOLOGIA

CLASIFICACIÓN WHO 2004	
SUBTIPO MIXTO	
ACINAR	
PAPILAR	
CARCINOMA BRONQUIOLOALVEOLAR	
	NO MUCINOSO
	MUCINOSO
	MIXTO
ADENOCARCINOMA SOLIDO	
	COLOIDECOLIOIDE
	FETAL
	CISTADENOCARCINOMA MUCINOSO
	CÉLULAS EN ANILLO DE SELLO
	CELULAS CLARAS

GRANDES CAMBIOS EN LA NUEVA CLASIFICACIÓN DE IASLC/ATC/ETS

- Término BAC descontinuado
- Término subtipo mixto descontinuado
- Dominancia de subtipos patológicos en incrementos de 5% de acuerdo a la clasificación de los adenocarcinomas según el subtipo dominante.
- Introducción de los términos AIS y MIA como nuevas entidades
- Introducción de adenocarcinoma predominantemente lepídico y crecimiento lepídico como nuevas terminologías
- Exclusión de adenocarcinoma de células en anillo de sello y células claras

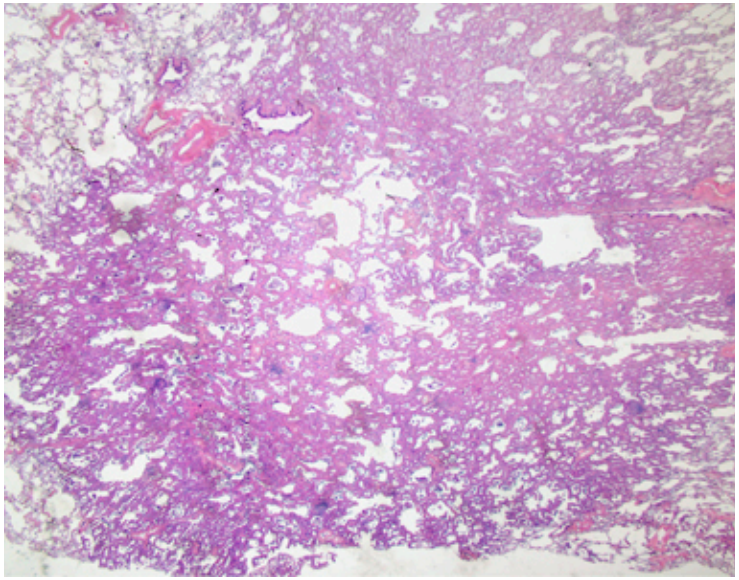
CLASIFICACION IASLC / ATS/ERS		
LESIONES PREINVAORAS		
	HIPERPLASIA ADENOMATOSA ATIPICA	
	ADENOCARCINOMA IN SITU	
		NO MUCINOSO
		MUCINOSO
		MIXTO
ADENOCARCINOMA MINIMAMENTE INVASIVO (MIA)		
	NO MUCINOSO	
	MUCINOSO	
	MIXTO	
ADENOCARCINOMA INVASOR		
	PREDOMINANTEMENTE LEPIDICO	
	PREDOMINANTEMENTE ACINAR	
	PREDOMINANTEMENTE PAPILAR	
	PREDOMINANTEMENTE MICROPAPILAR	
	PREDOMINENTEMENTE SOLIDO CON PRODUCCION DE MUCINA	
VARIANTES DE ADENOCARCINOMA INVASOR		
	IMA (ADENOCA MUCINOSO INVASOR)	
	COLOIDE	
	FETAL	
	ENTERICO	

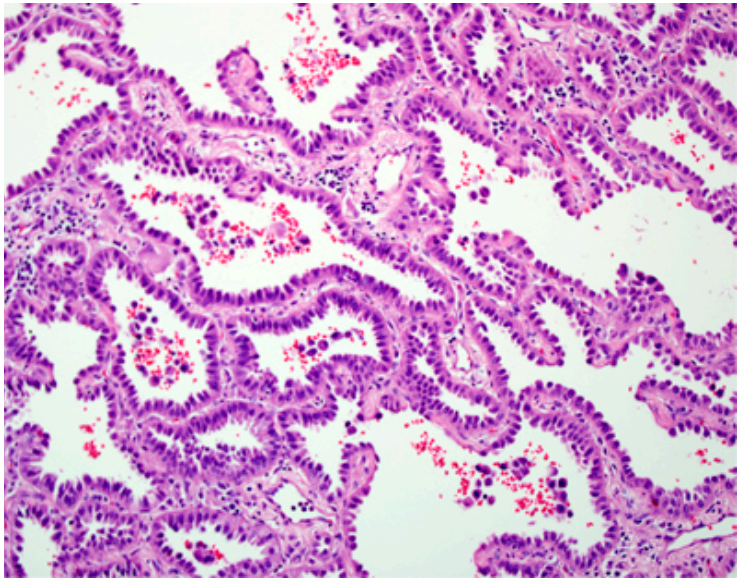
Panel central internacional de expertos IASLC, ATS y ERS con oncólogos / neumólogos, radiólogos, patólogos, biólogos moleculares, y cirujanos torácicos.

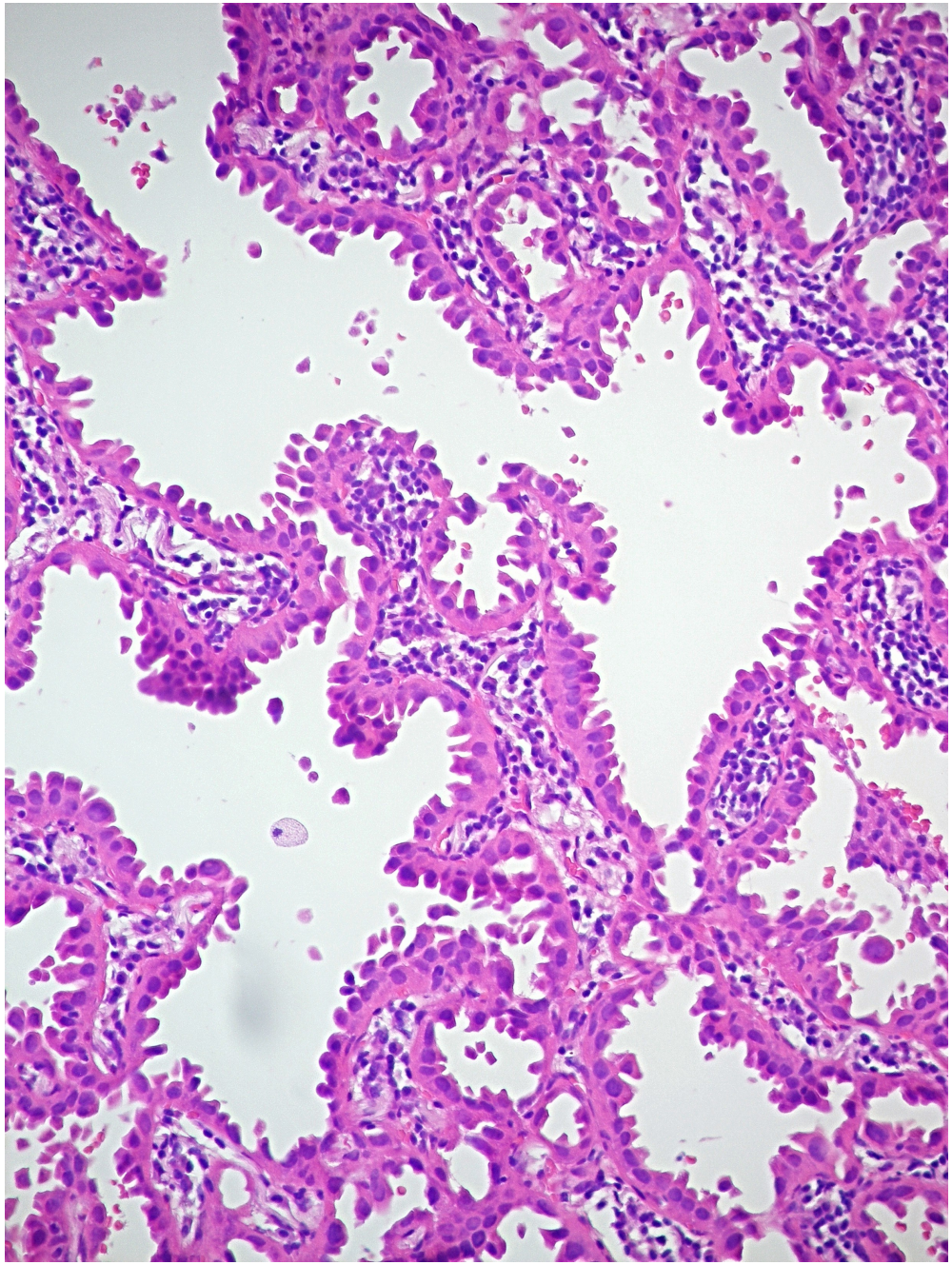
J Thorac Dis 2014;6(S5):S526-S536

HISTOLOGIA

ADENOCARCINOMA IN SITU (AIS)

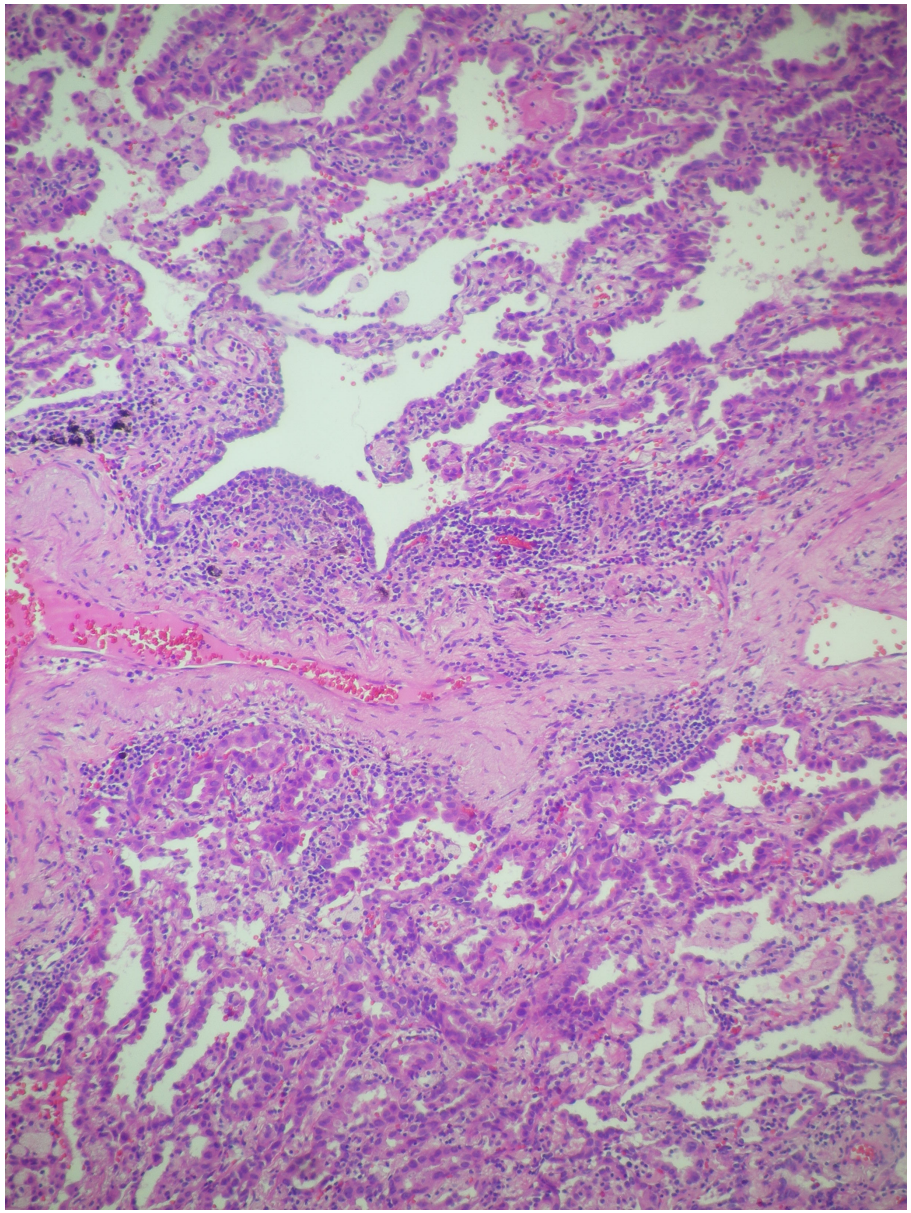


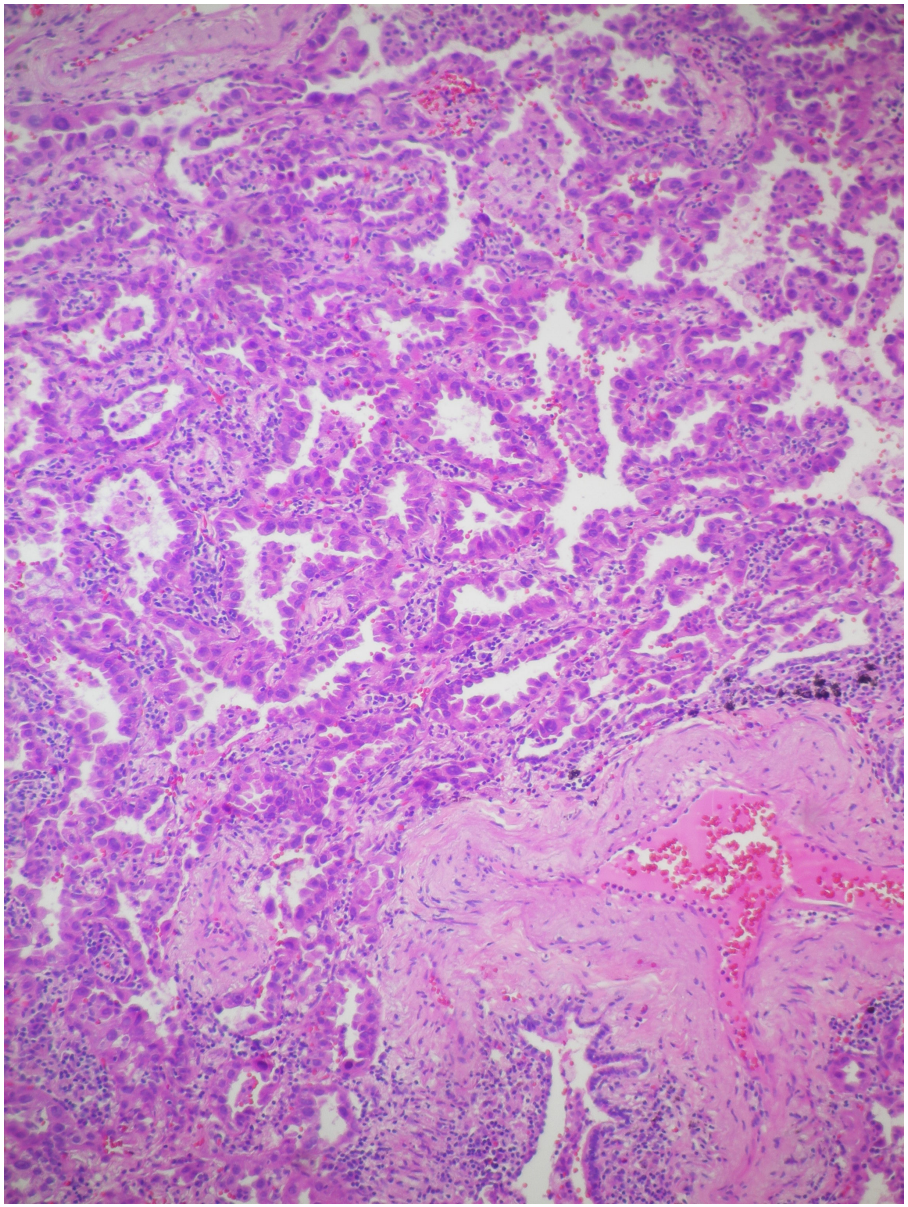




HISTOLOGIA

ADENOCARCINOMA MINIMAMENTE INVASIVO (MIA)

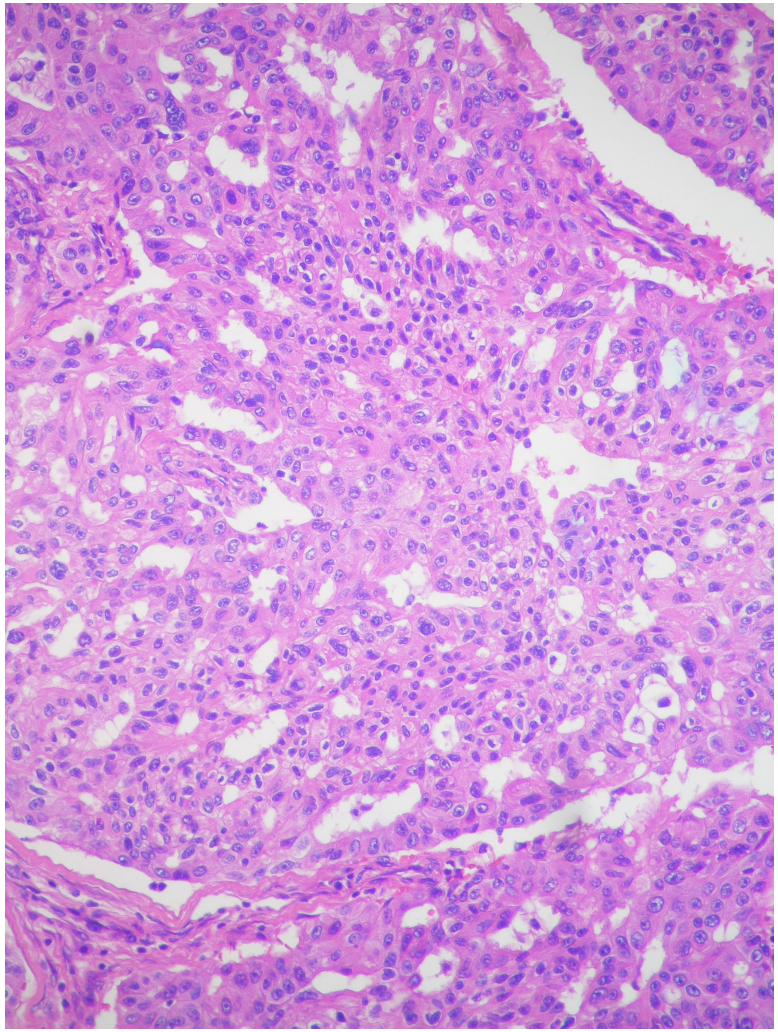


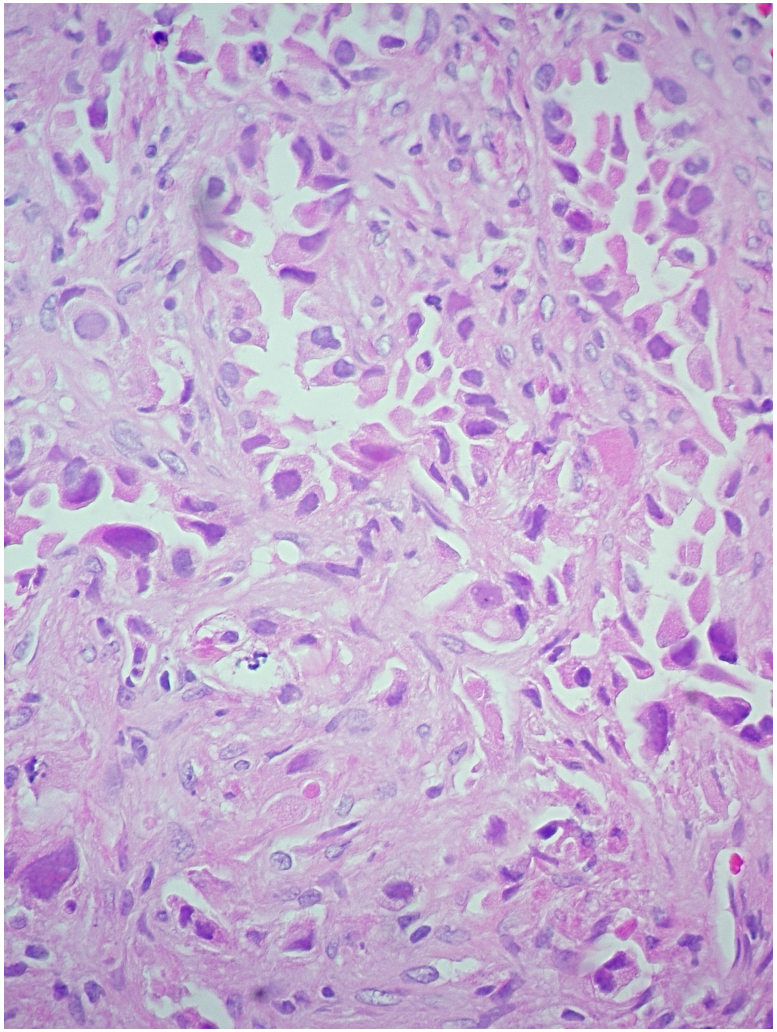


HISTOLOGIA

ADENOCARCINOMAS INVASORES

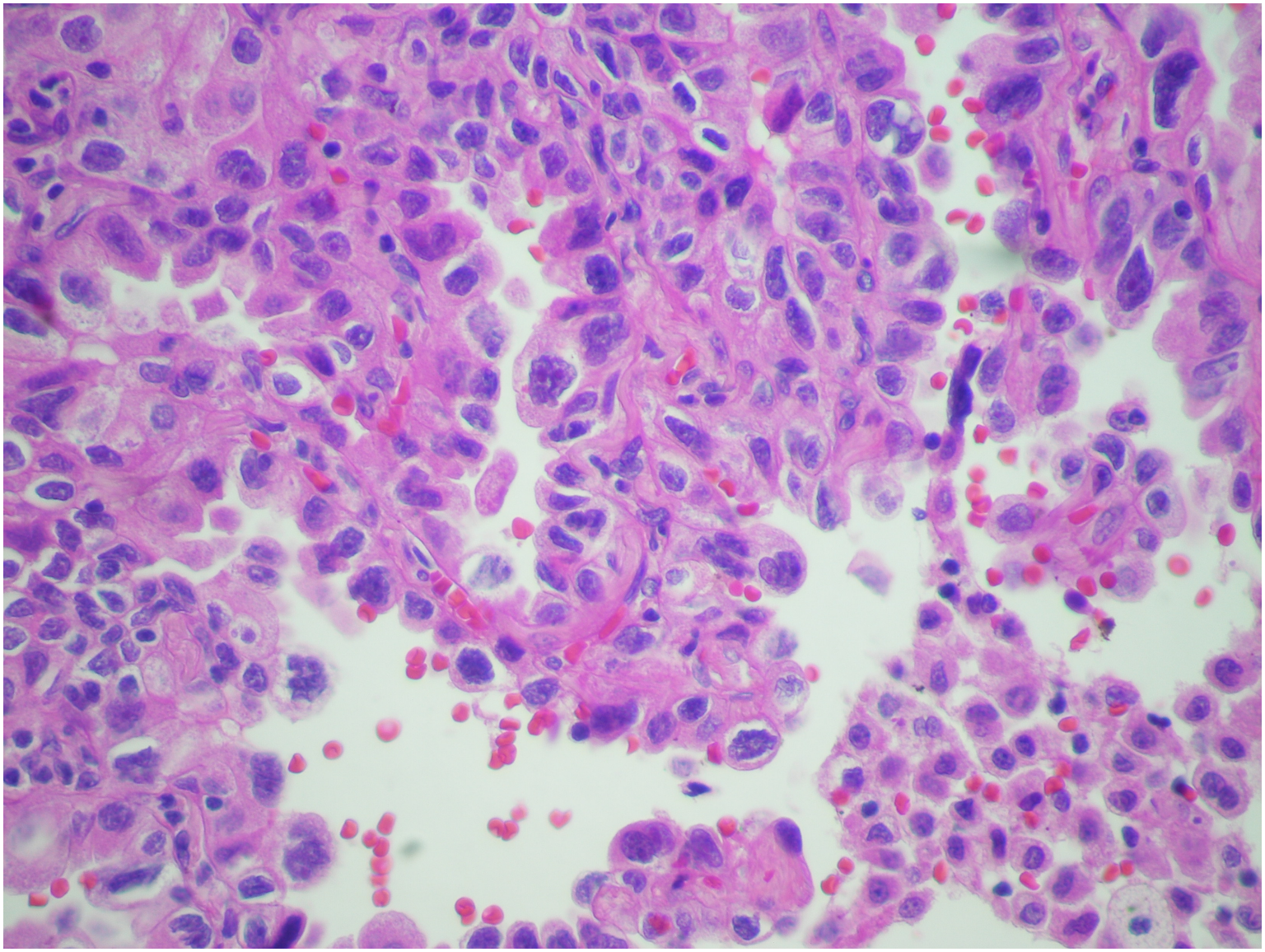
Recomendaciones de los expertos sugieren que el porcentaje de los patrones no predominantes también se debe describir en los informes patológicos.





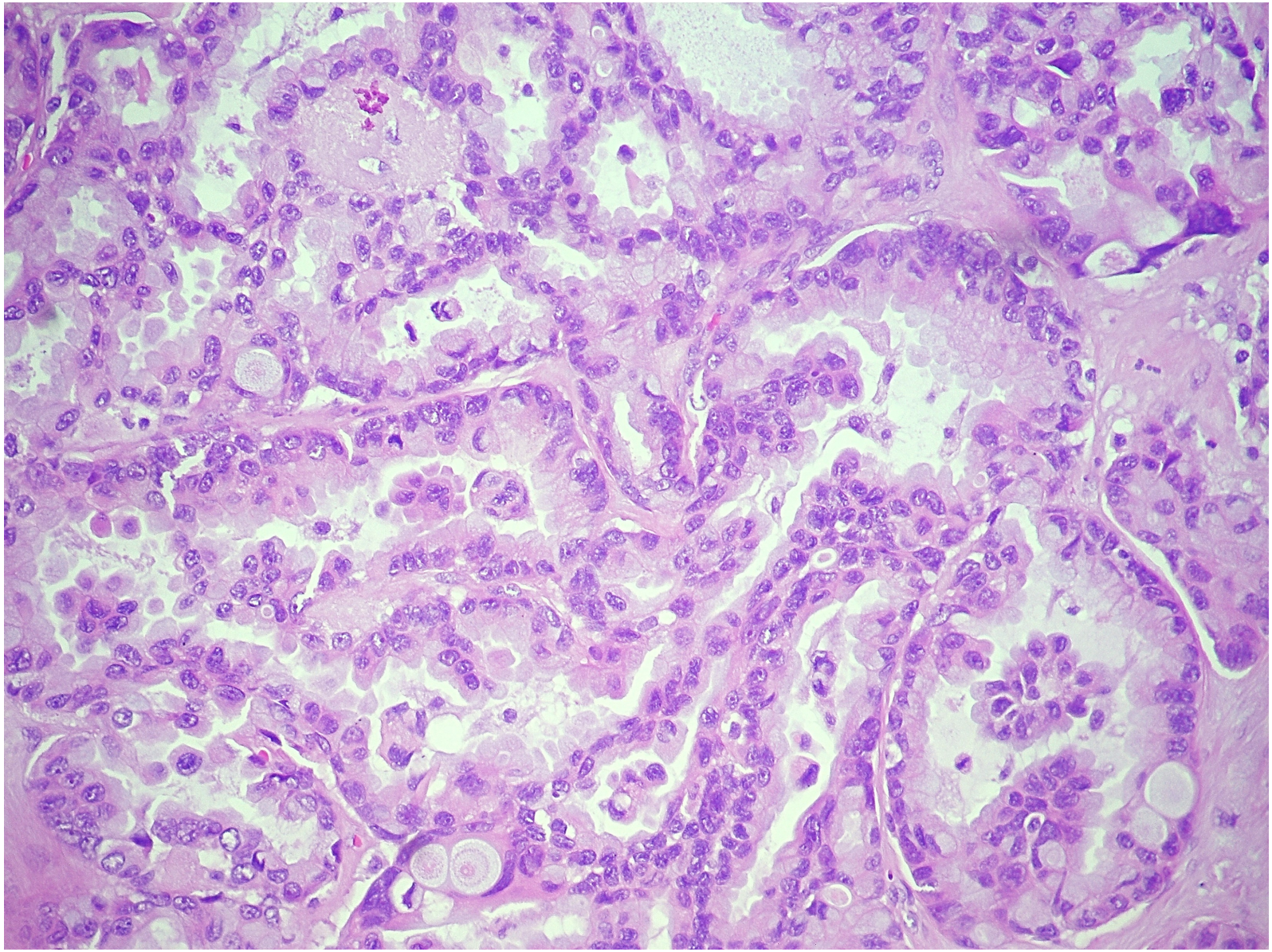
INVASORES

ADENOCARCINOMA PREDOMINANTEMENTE LEPIDICO



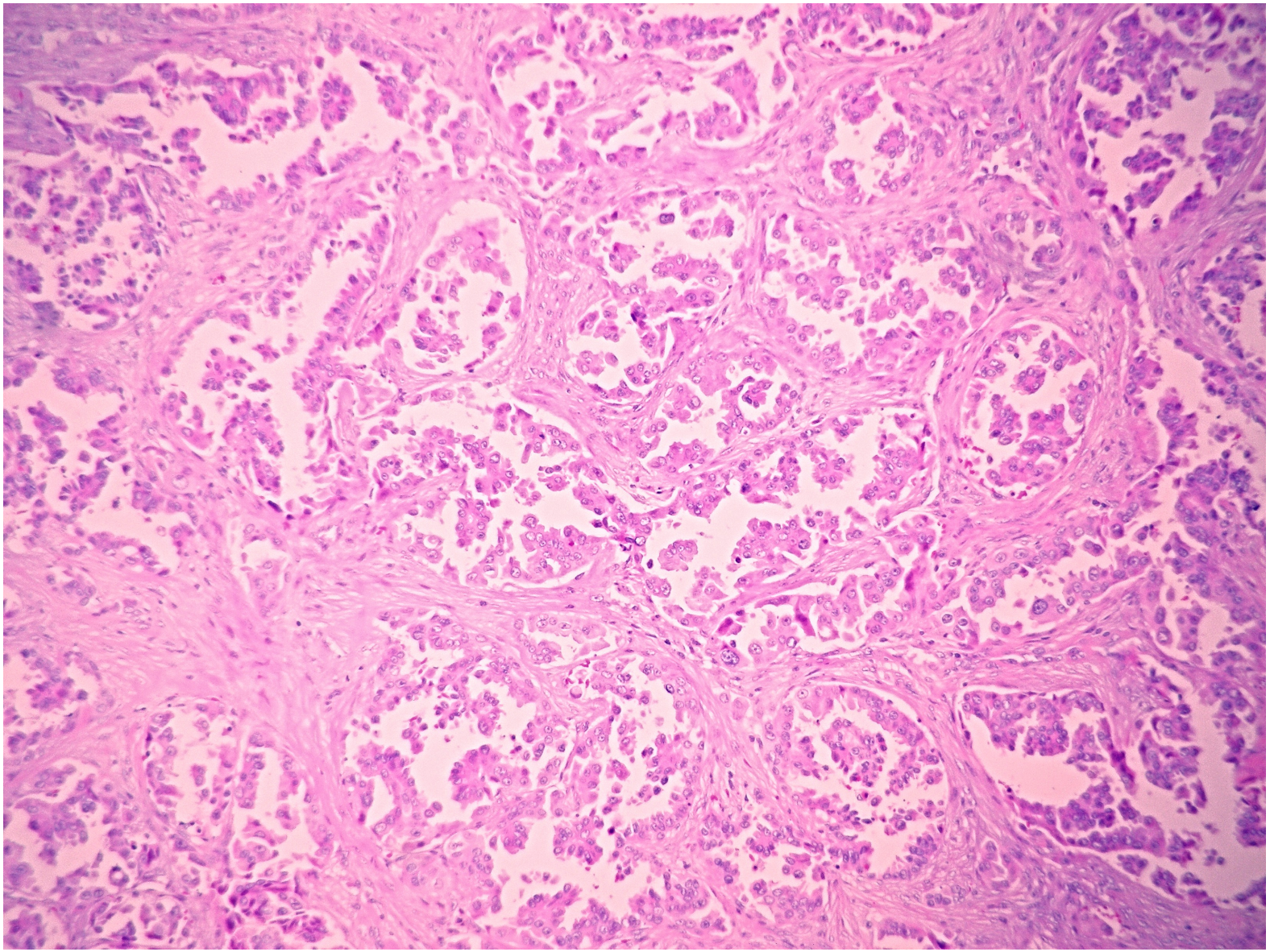
INVASORES

ADENOCARCINOMA PREDOMINANTEMENTE ACINAR



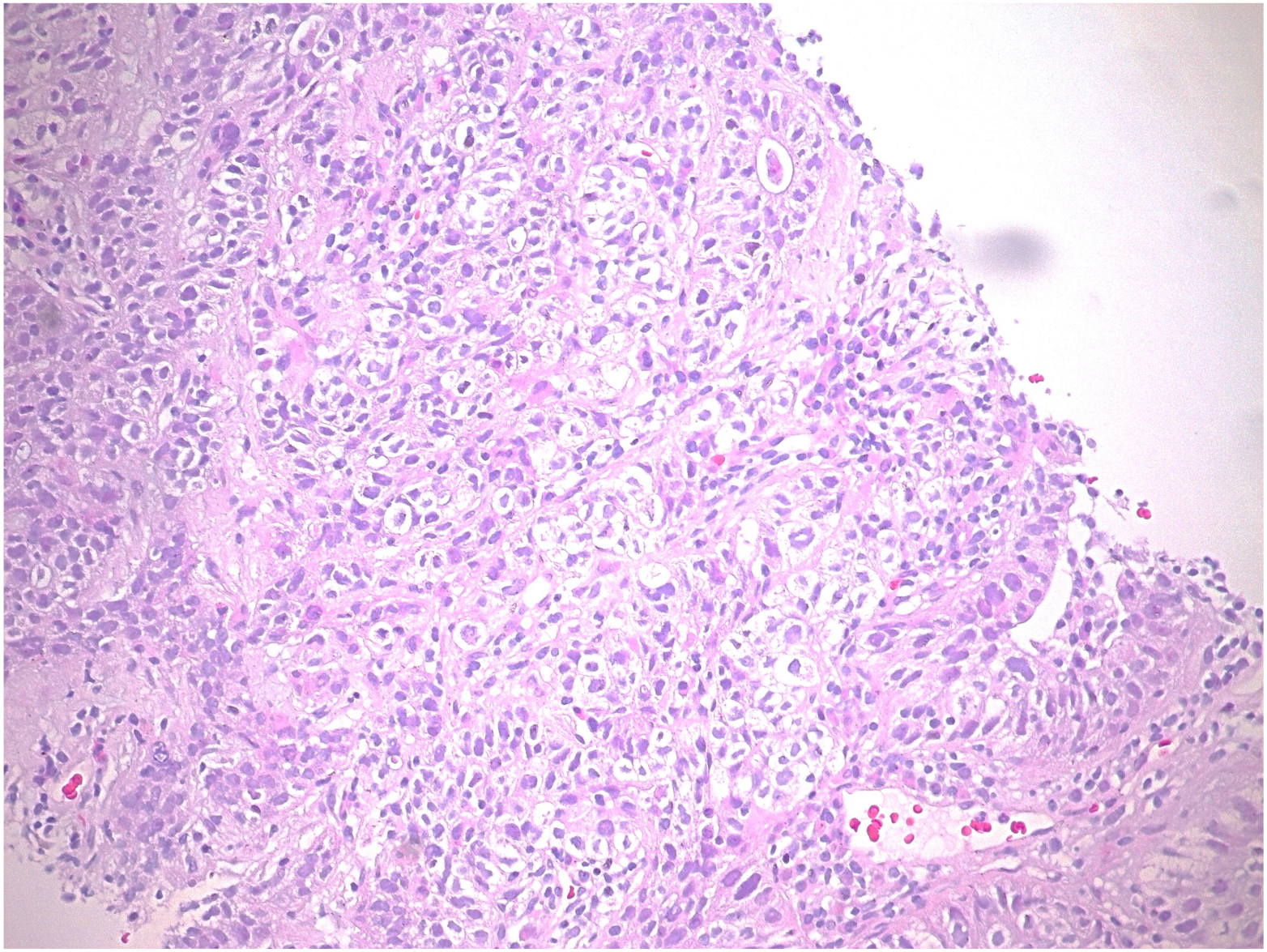
INVASORES

ADENOCARCINOMA PREDOMINANTEMENTE PAPILAR



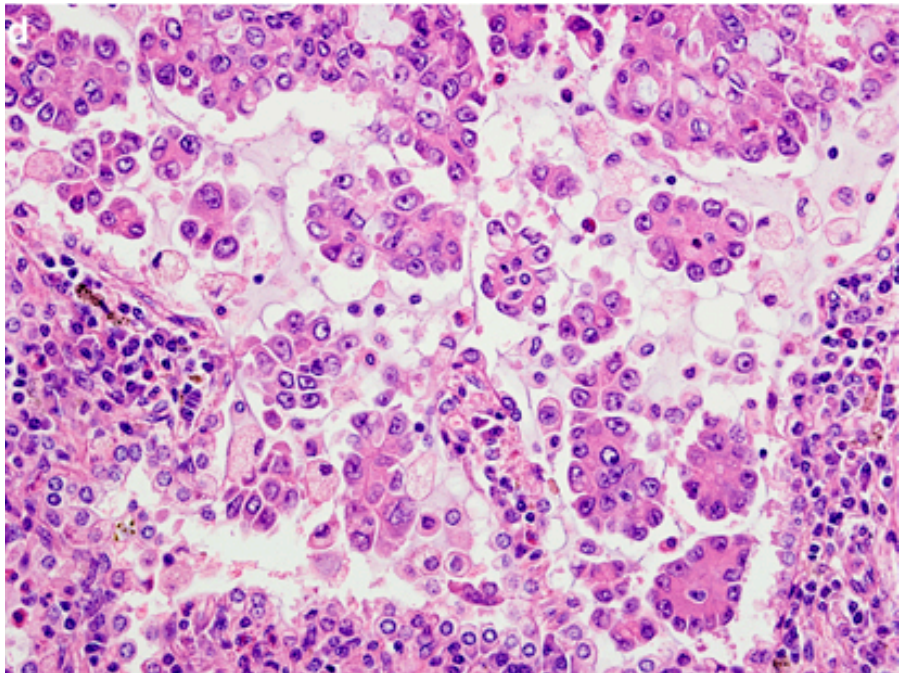
INVASORES

ADENOCARCINOMA PREDOMINANTEMENTE SOLIDO



INVASORES

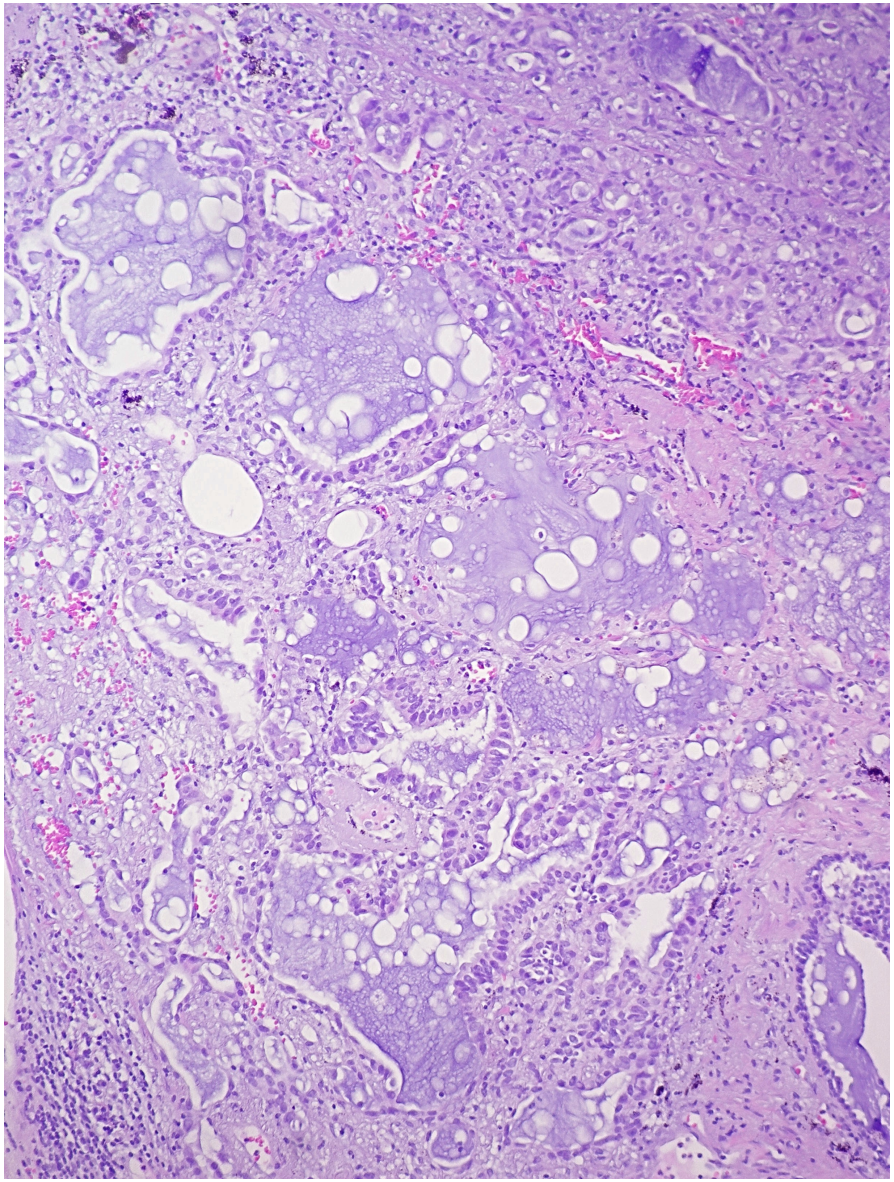
ADENOCARCINOMA PREDOMINANTEMENTE MICROPAPILAR

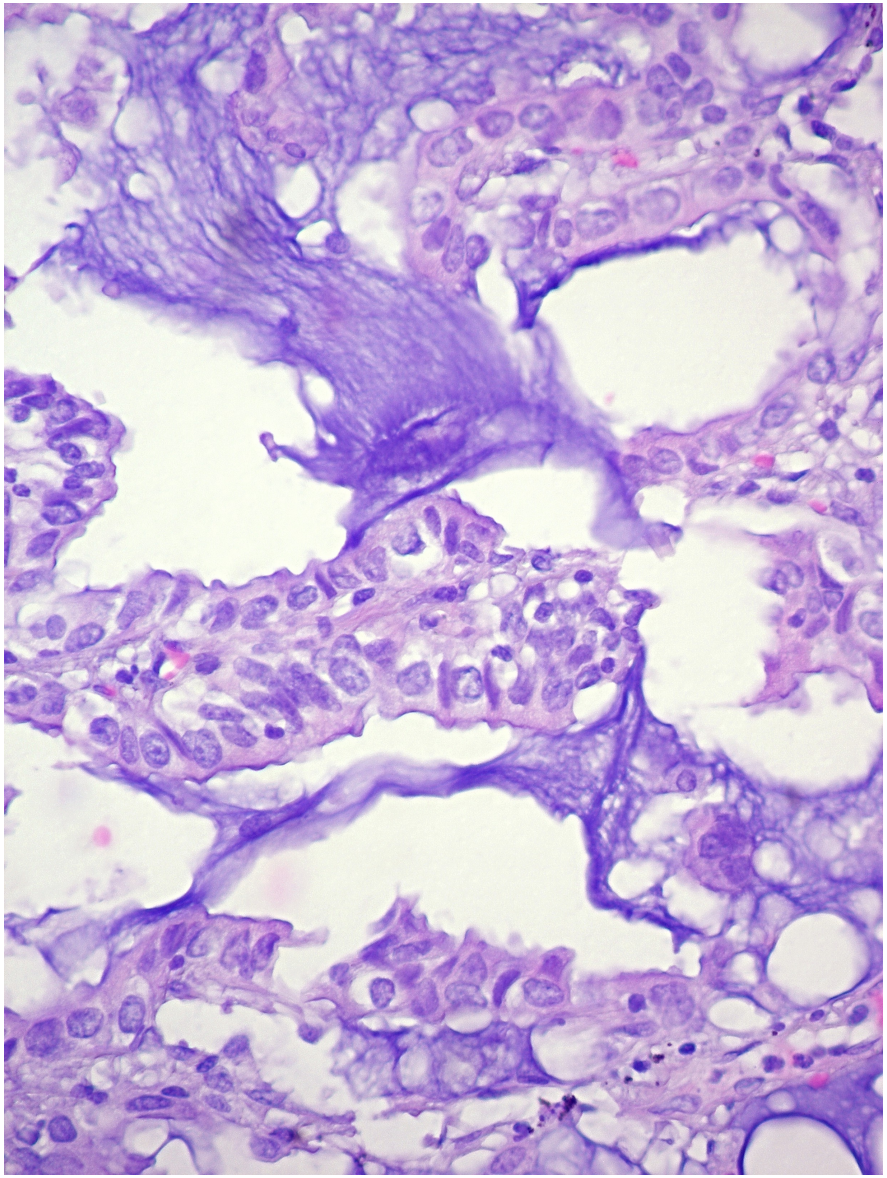


INVASORES

VARIANTES

ADENOCARCINOMA MUCINOSO INVASOR

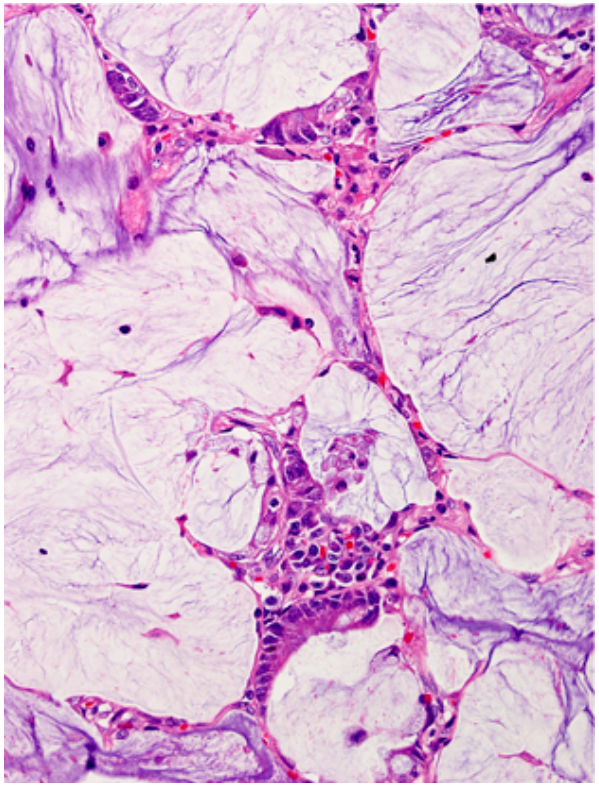


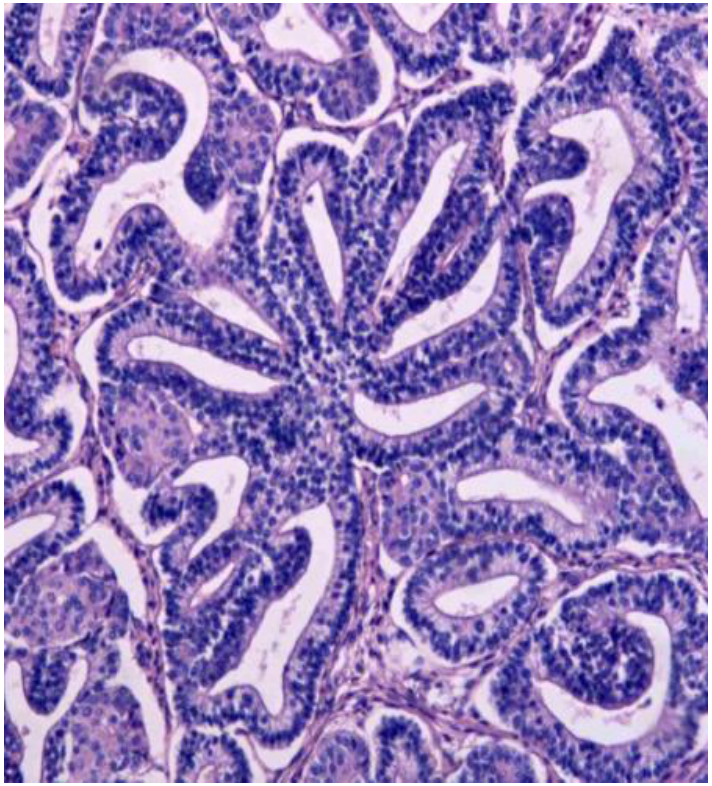


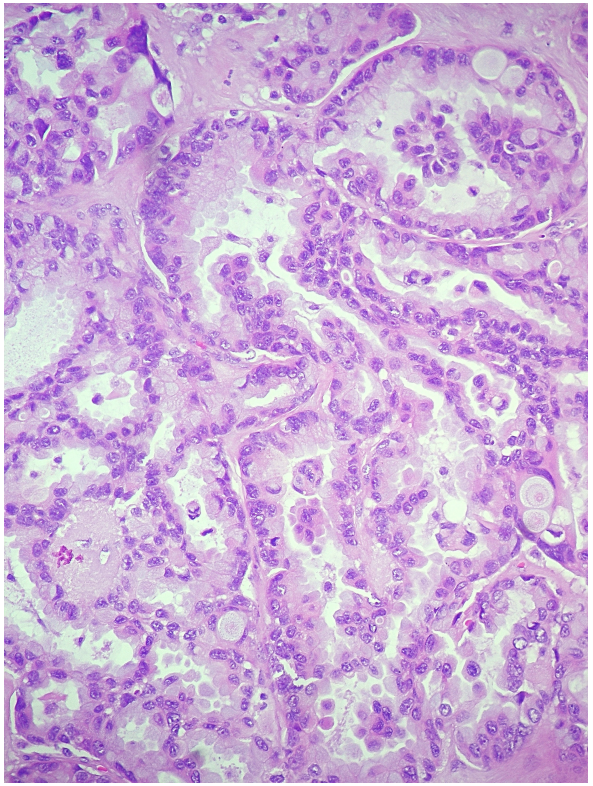
INVASORES

VARIANTES

ADENOCARCINOMA COLOIDE, FETAL Y ENTÉRICO



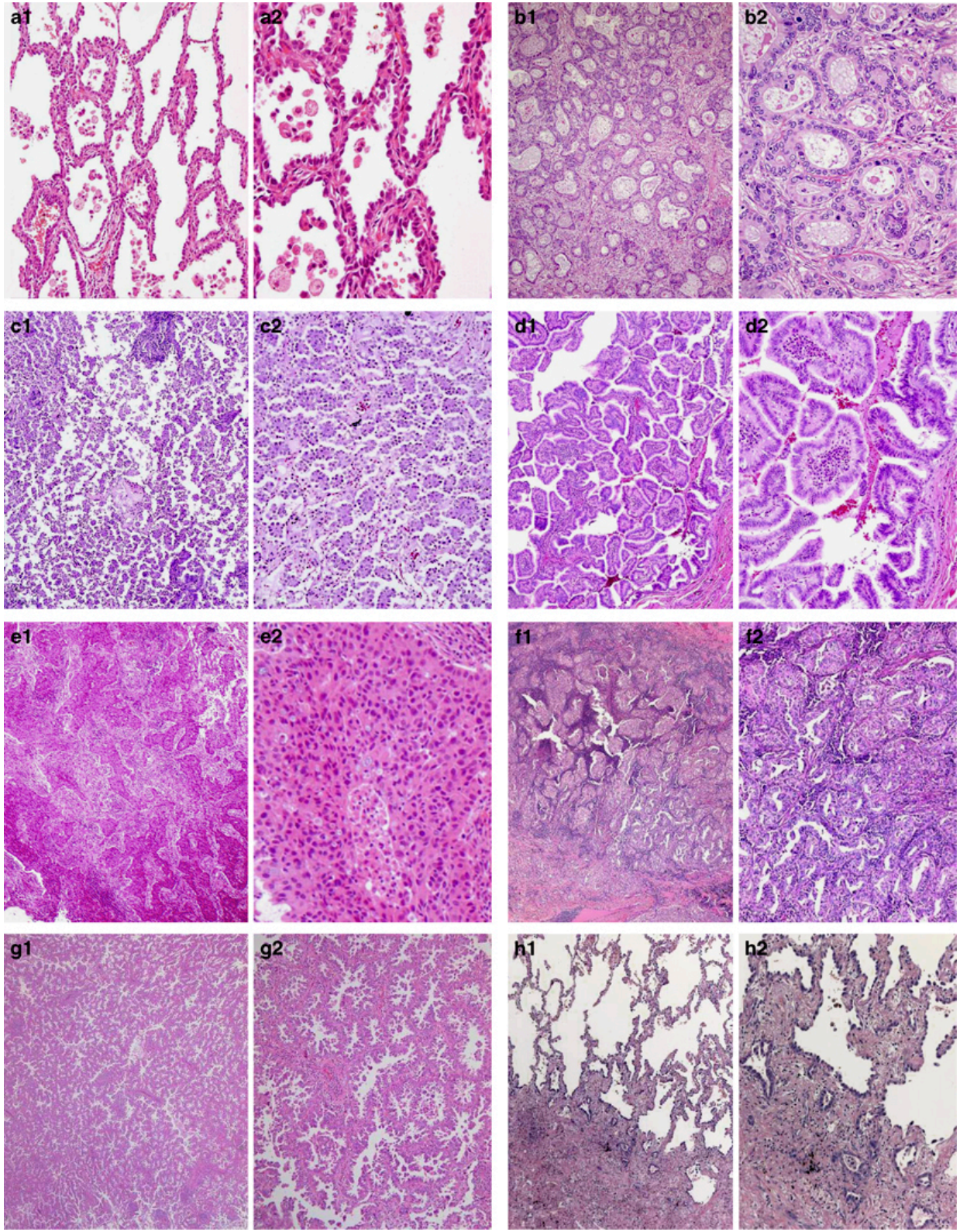




HISTOLOGIA

REPRODUCIBILIDAD:

- Alto para especialistas en patología pulmonar
- Bajo para inexpertos
- Entrenamiento reduce variabilidad interobservador
- Patrones mas difíciles de evaluar
- Actual clasificacion reproducible pero se requiere entrenaniento



Mod Pathol 2012;25:1574-83.

HISTOLOGIA

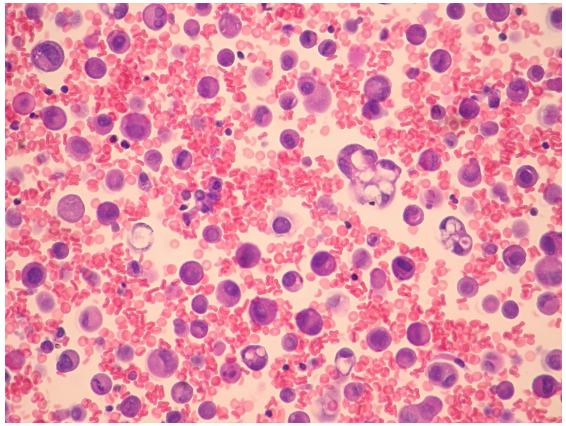
IMPLICACIONES CLINICAS DE SUBTIPIFICAR:

CLASIFICACION IASLC / ATS/ERS			
LESIONES PREINVAORAS			
	HIPERPLASIA ADENOMATOSA ATIPICA		
	ADENOCARCINOMA IN SITU		GRADO BAJO
		NO MUCINOSO	
		MUCINOSO	
		MIXTO	
ADENOCARCINOMA MINIMAMENTE INVASIVO (MIA)			
	NO MUCINOSO		
	MUCINOSO		
	MIXTO		
ADENOCARCINOMA INVASOR			
	PREDOMINANTEMENTE LEPIDICO		GRADO INTERMEDIO
	PREDOMINANTEMENTE ACINAR		
	PREDOMINANTEMENTE PAPILAR		
	PREDOMINANTEMENTE MICROPAPILAR		ALTO GRADO
	PREDOMINENTEMENTE SOLIDO CON PRODUCCION DE MUCINA		
VARIANTES DE ADENOCARCINOMA INVASOR			
	IMA (ADENOCA MUCINOSO INVASOR)		
	COLOIDE		
	FETAL		
	ENTERICO		

Mod Pathol 2011;24:653-64.

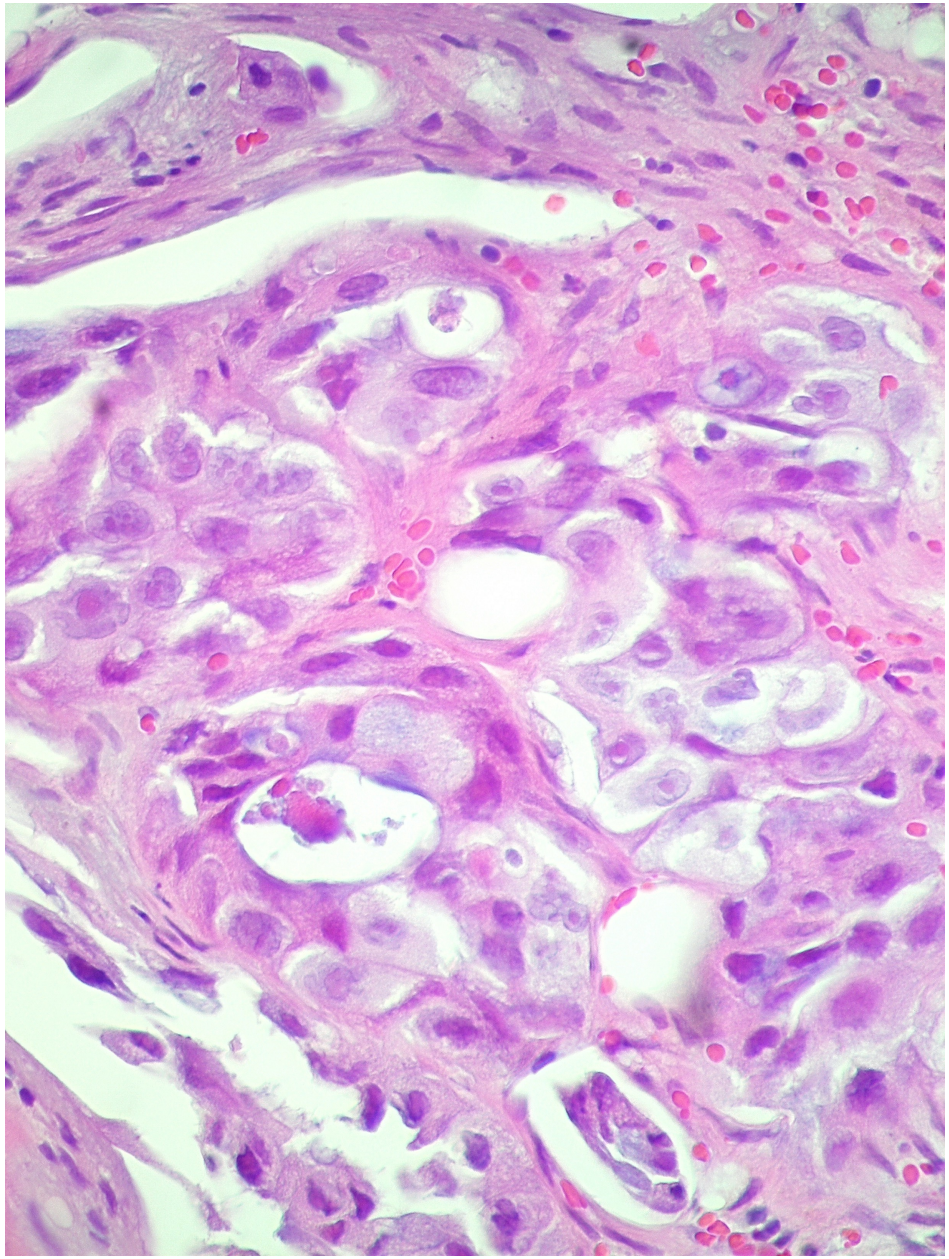
HISTOLOGIA

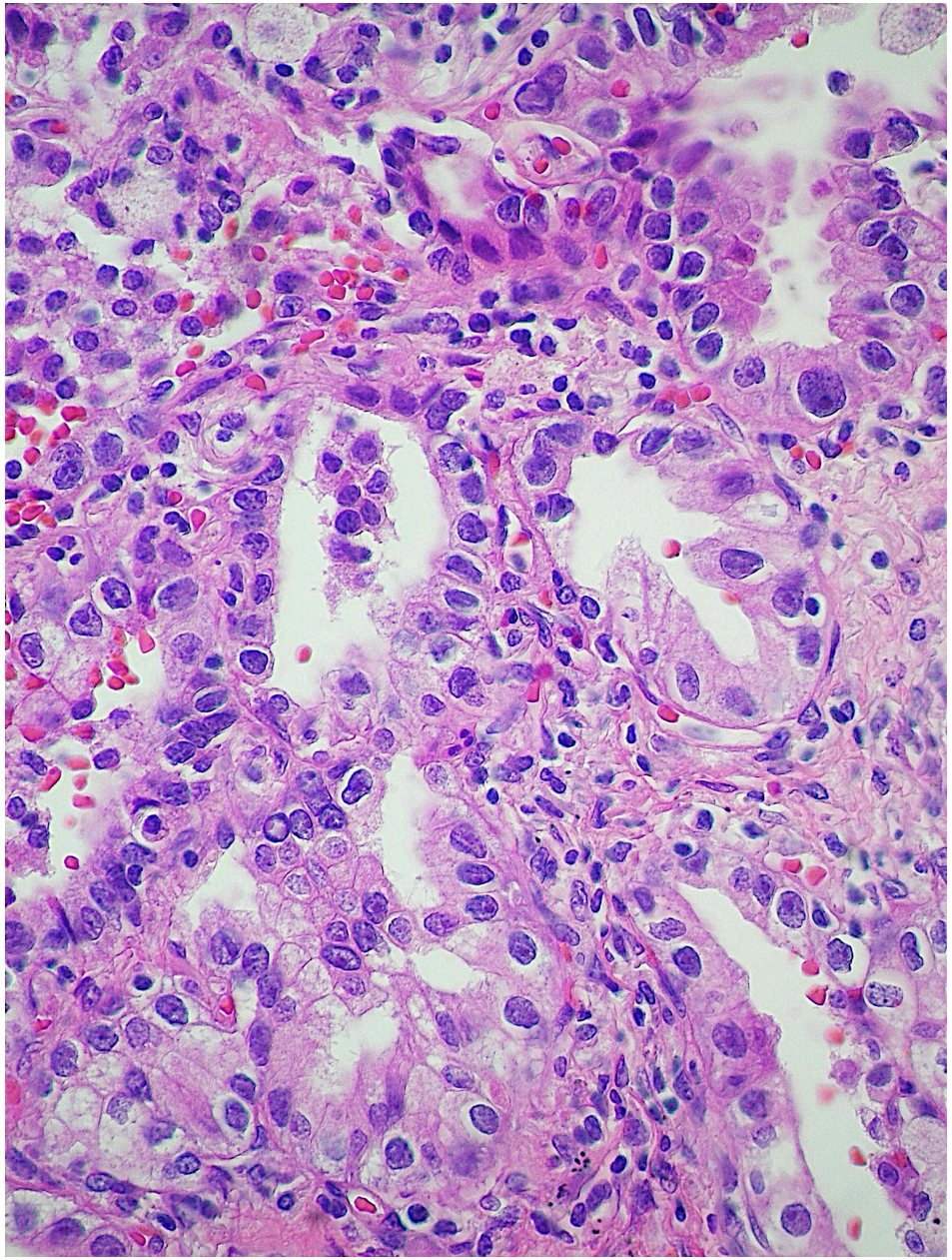
TOMAR EN CUENTA EN QUE TEJIDO SE HACE EL DIAGNÓSTICO:



HISTOLOGIA

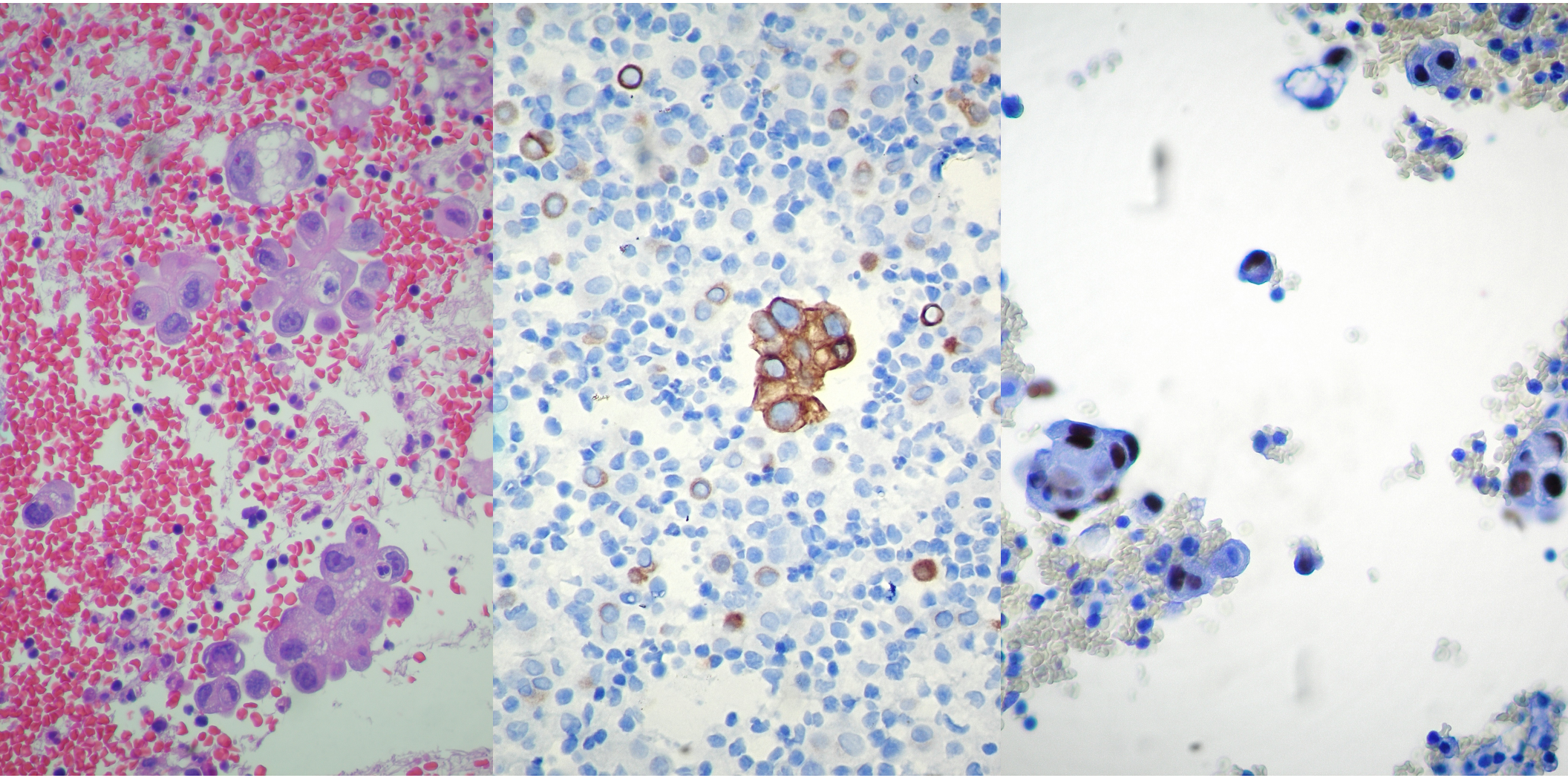
HACER DIAGNOSTICO:





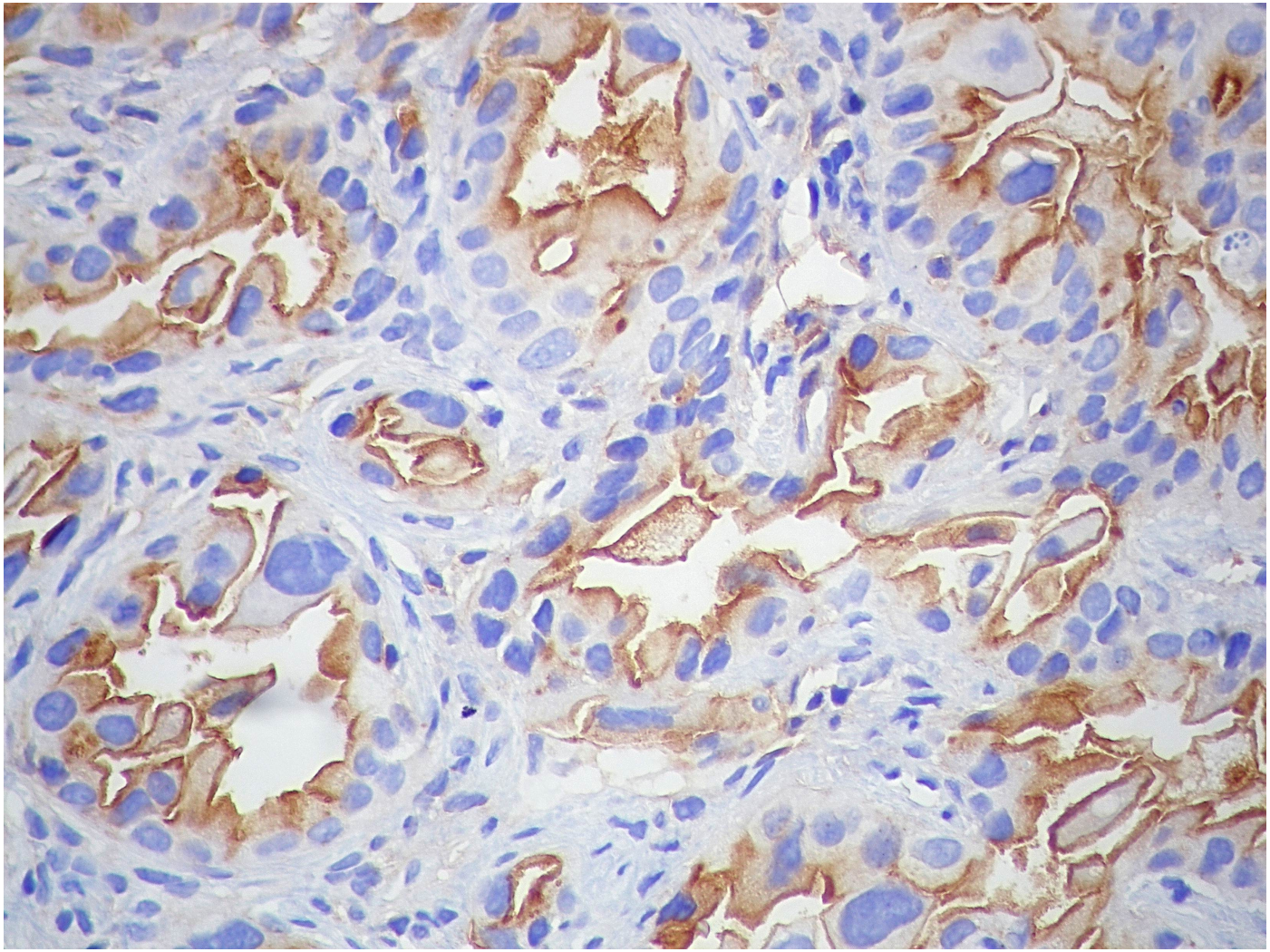
INMUNOHISTOQUIMICA

HACER DIAGNOSTICO:



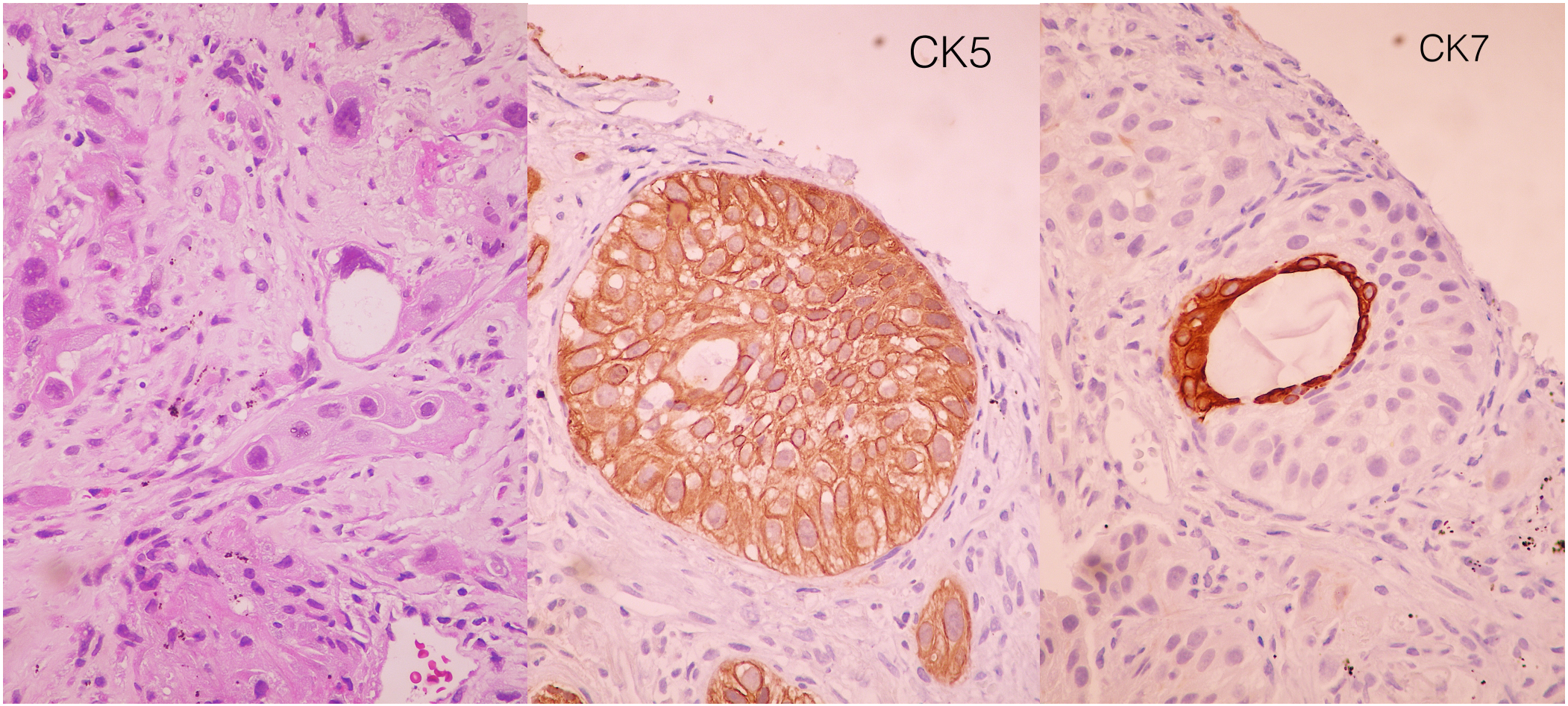
INMUNOHISTOQUIMICA

NO DIAGNOSTICABLES:



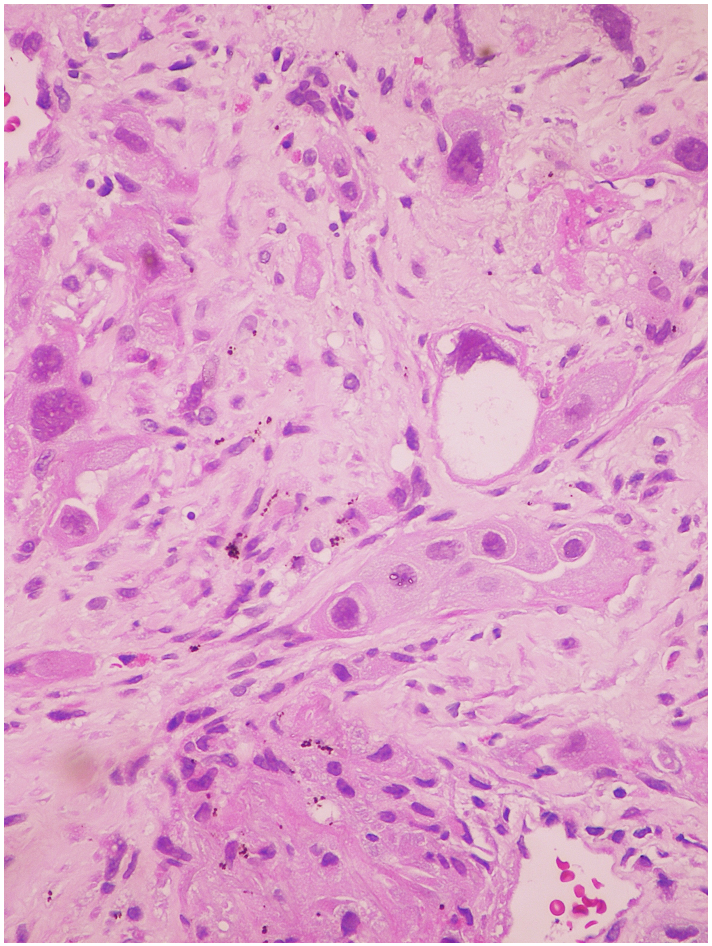
INMUNOHISTOQUIMICA

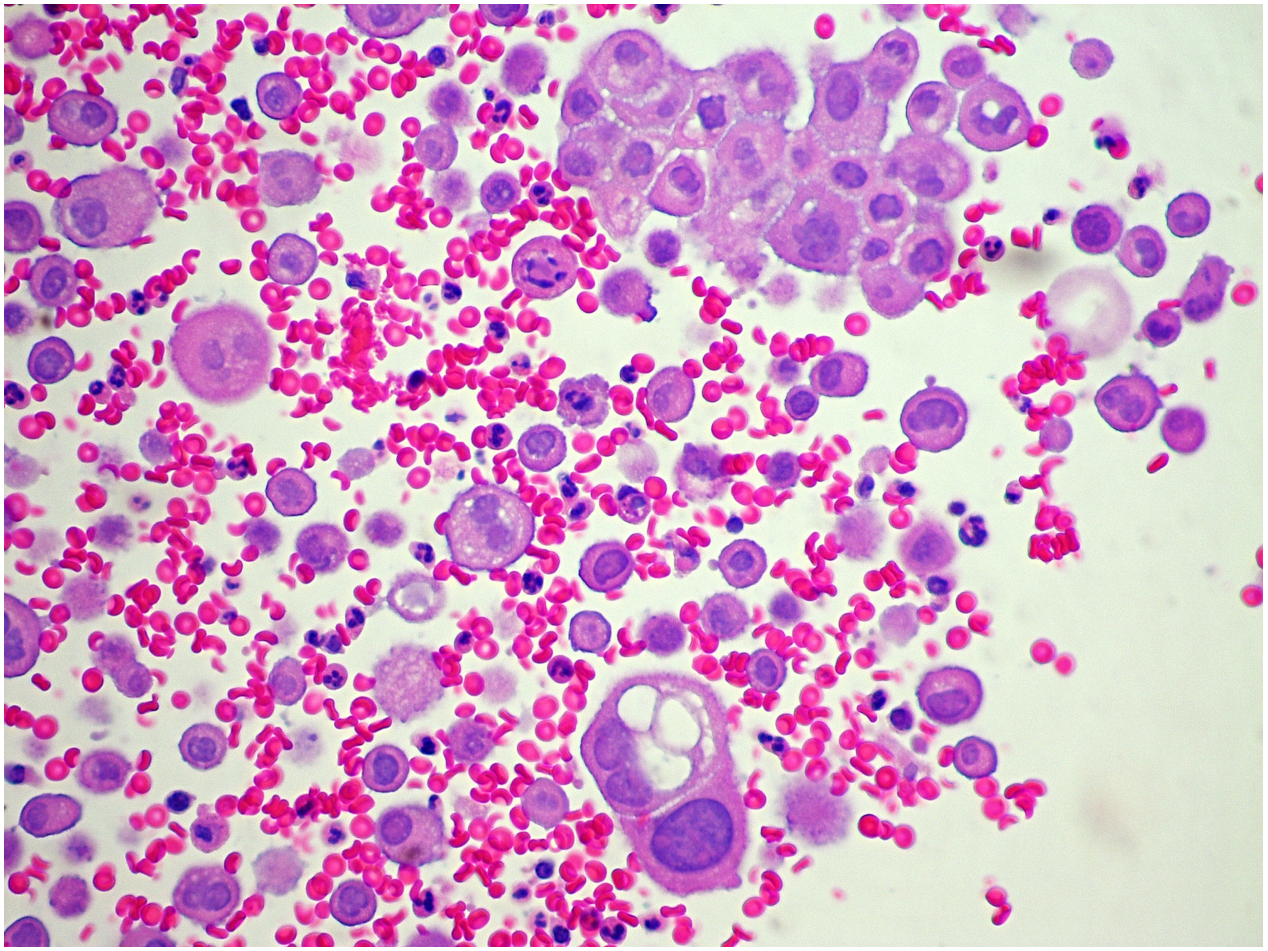
ADENOESCAMOSO



BIOLOGIA MOLECULAR

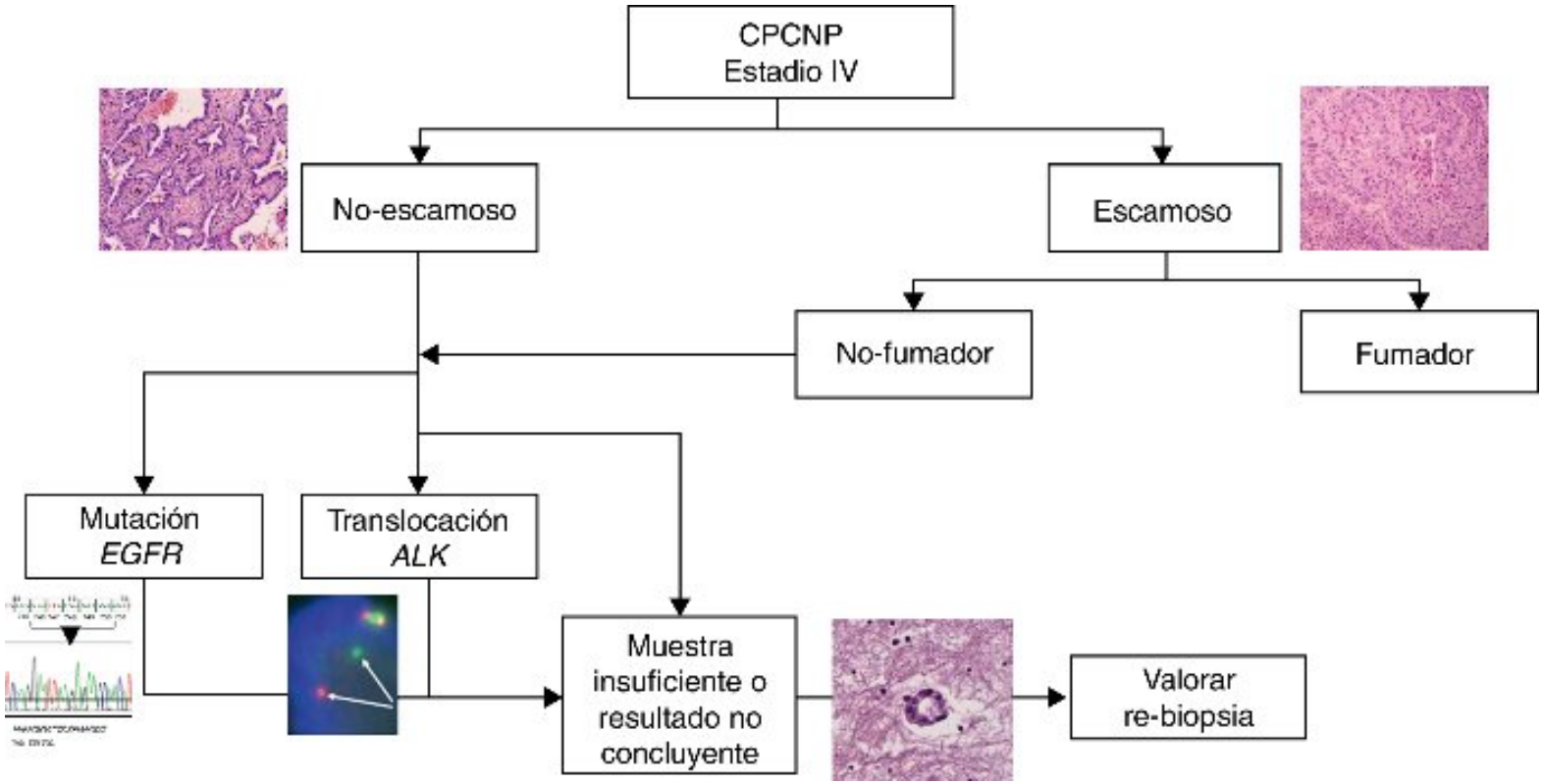
PRIMERO DEFINIR ADENOCARCINOMA O EPIDERMOIDE





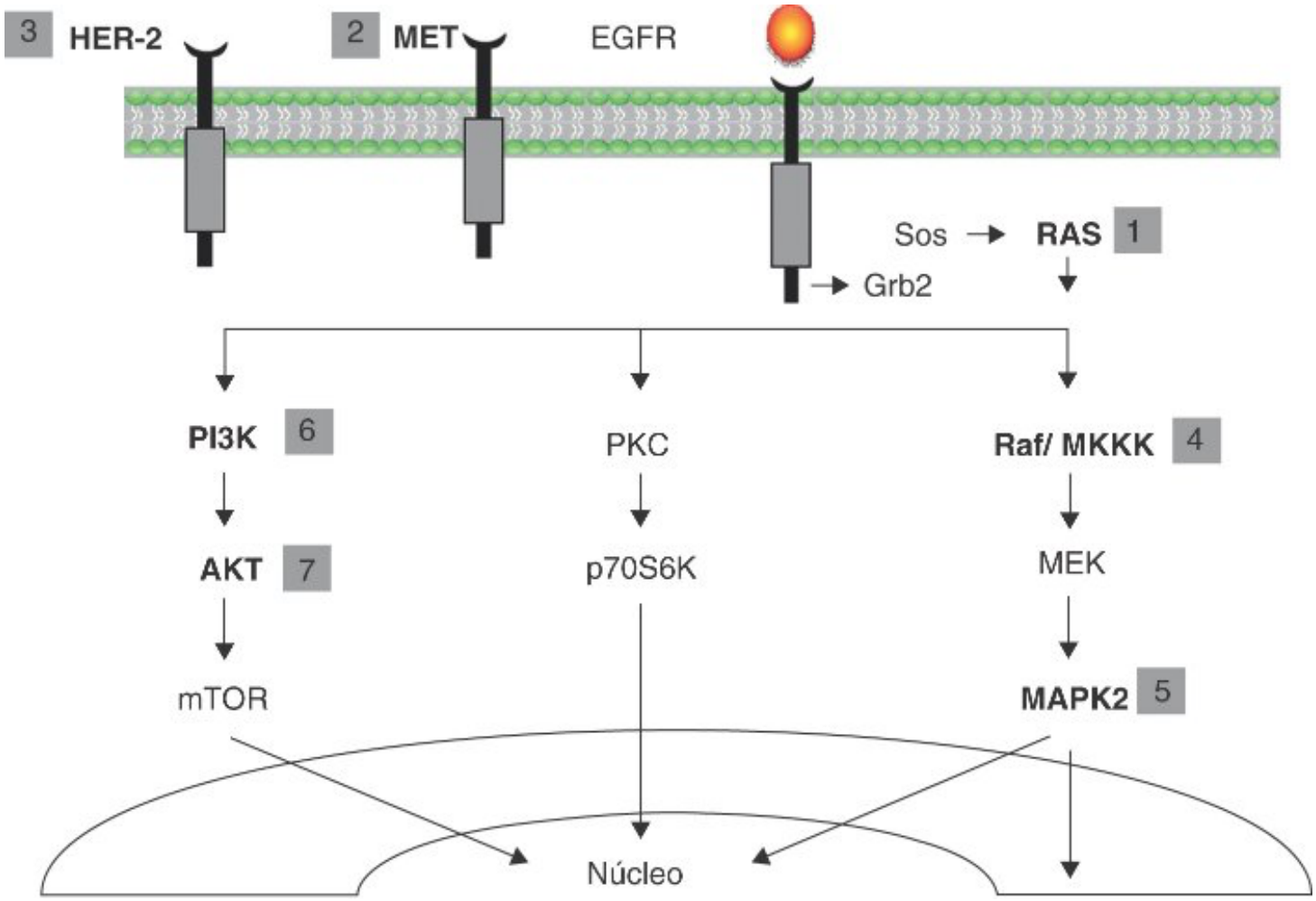
BIOLOGIA MOLECULAR

CARACTERISTICAS MOLECULARES PARA TRATAMIENTO DIRIGIDO



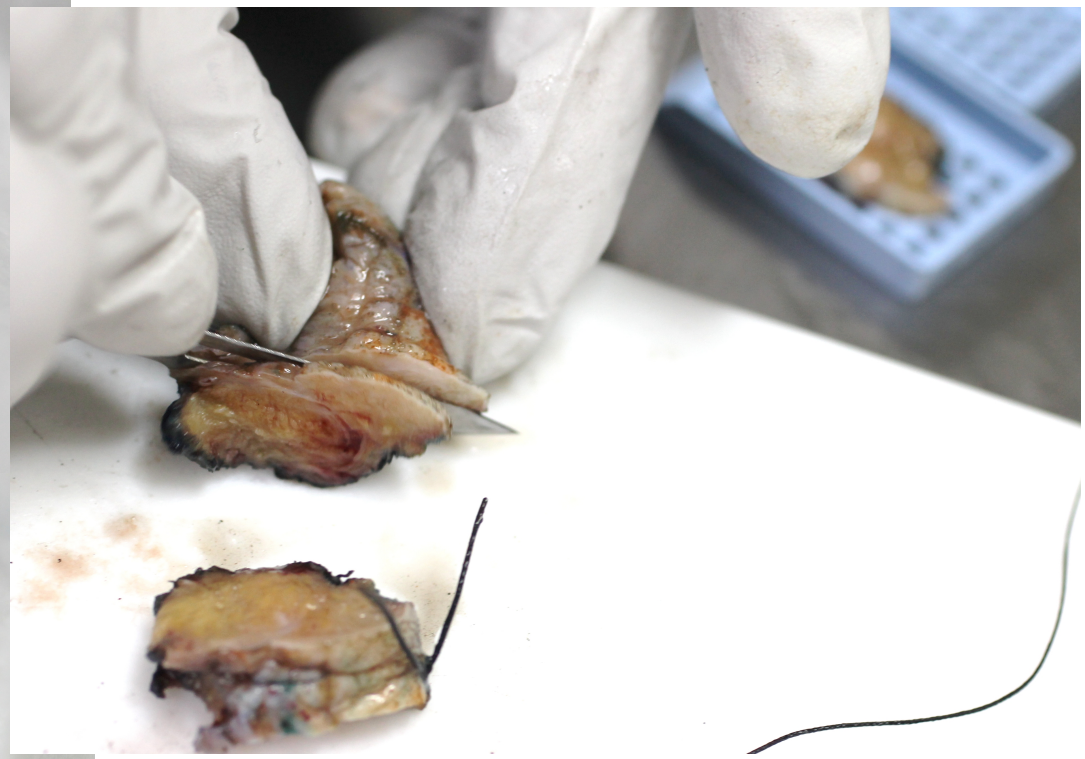
BIOLOGIA MOLECULAR

CARACTERISTICAS MOLECULARES COMO RELEVANCIA CLINICA PRONOSTICA



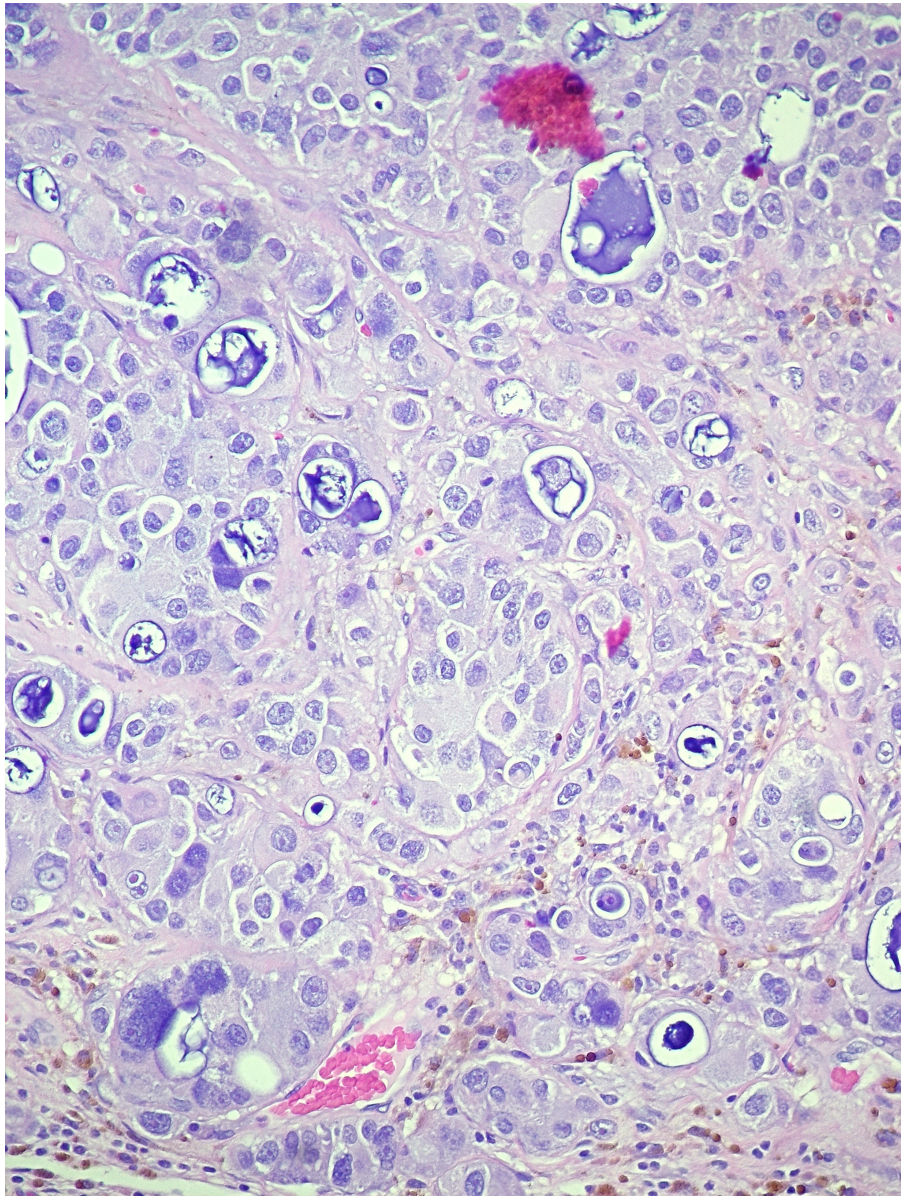
BIOLOGIA MOLECULAR

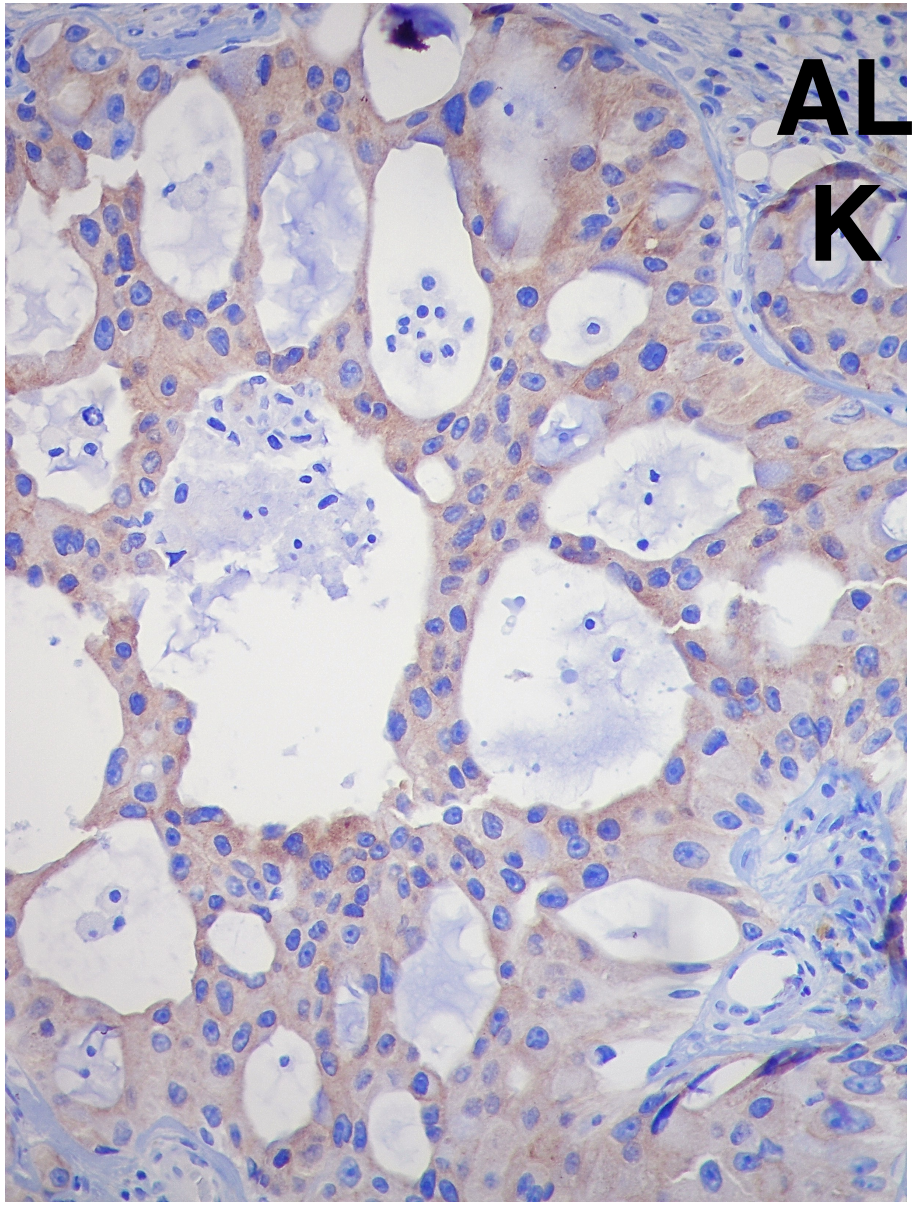
DIAGNOSTICO PARA SELECTIVDAD



BIOLOGIA MOLECULAR

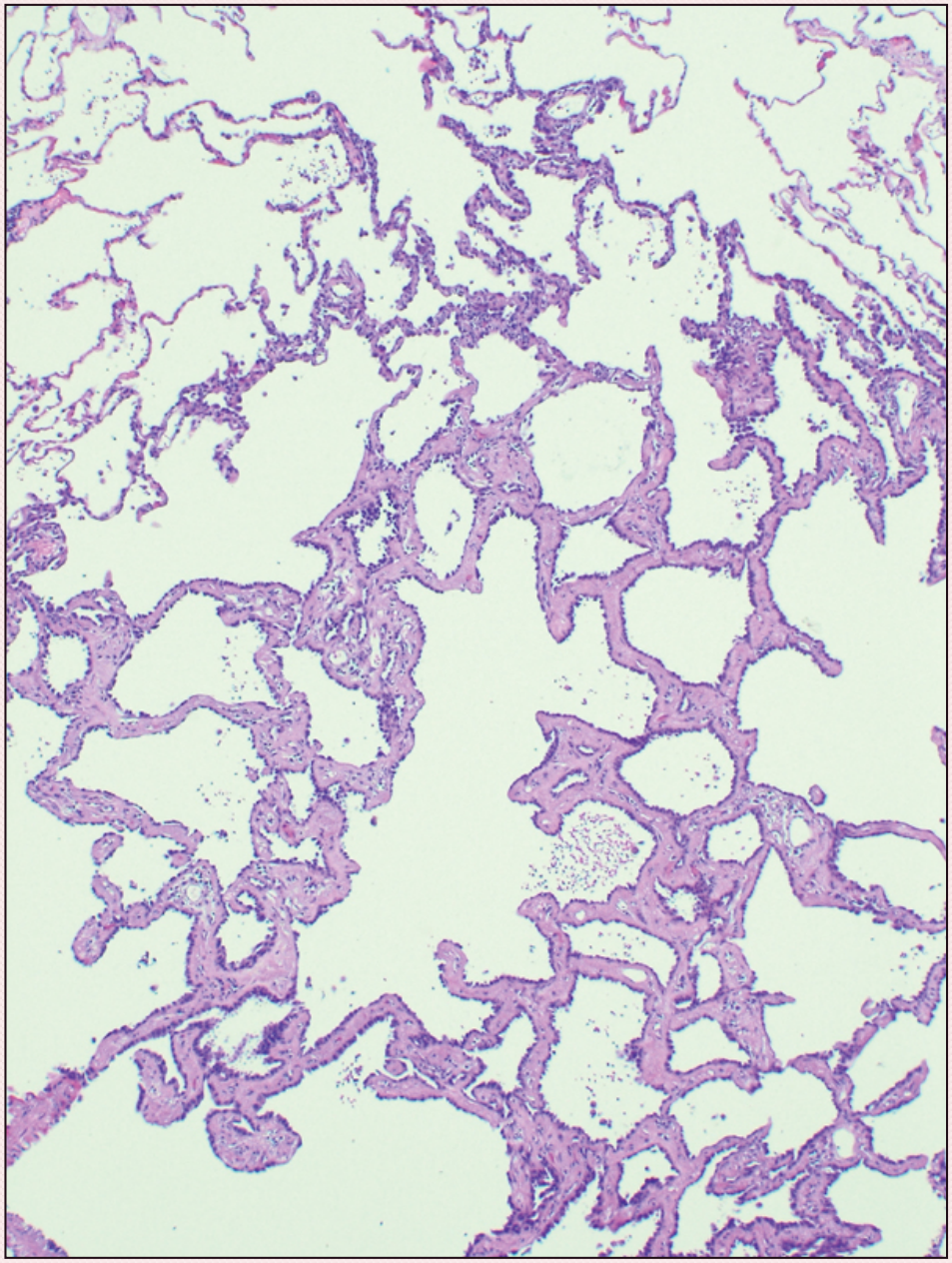
PREDICCION DE AGENTES GENETICOS





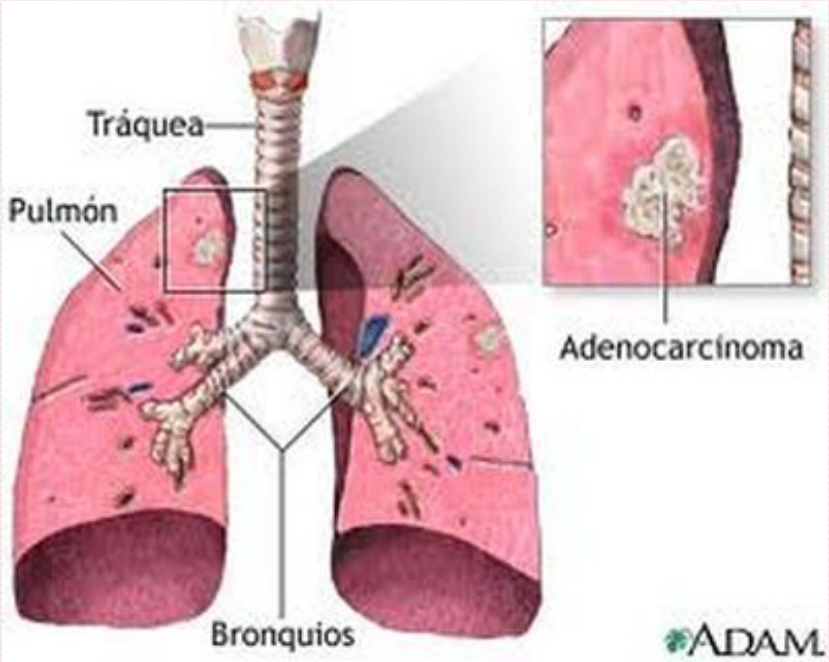
Lesiones Precursoras

- Displasia de epitelios y carcinoma in situ
- Hiperplasia adenomatosa atípica
- Hiperplasia idiopática difusa de las células neuroendócrinas



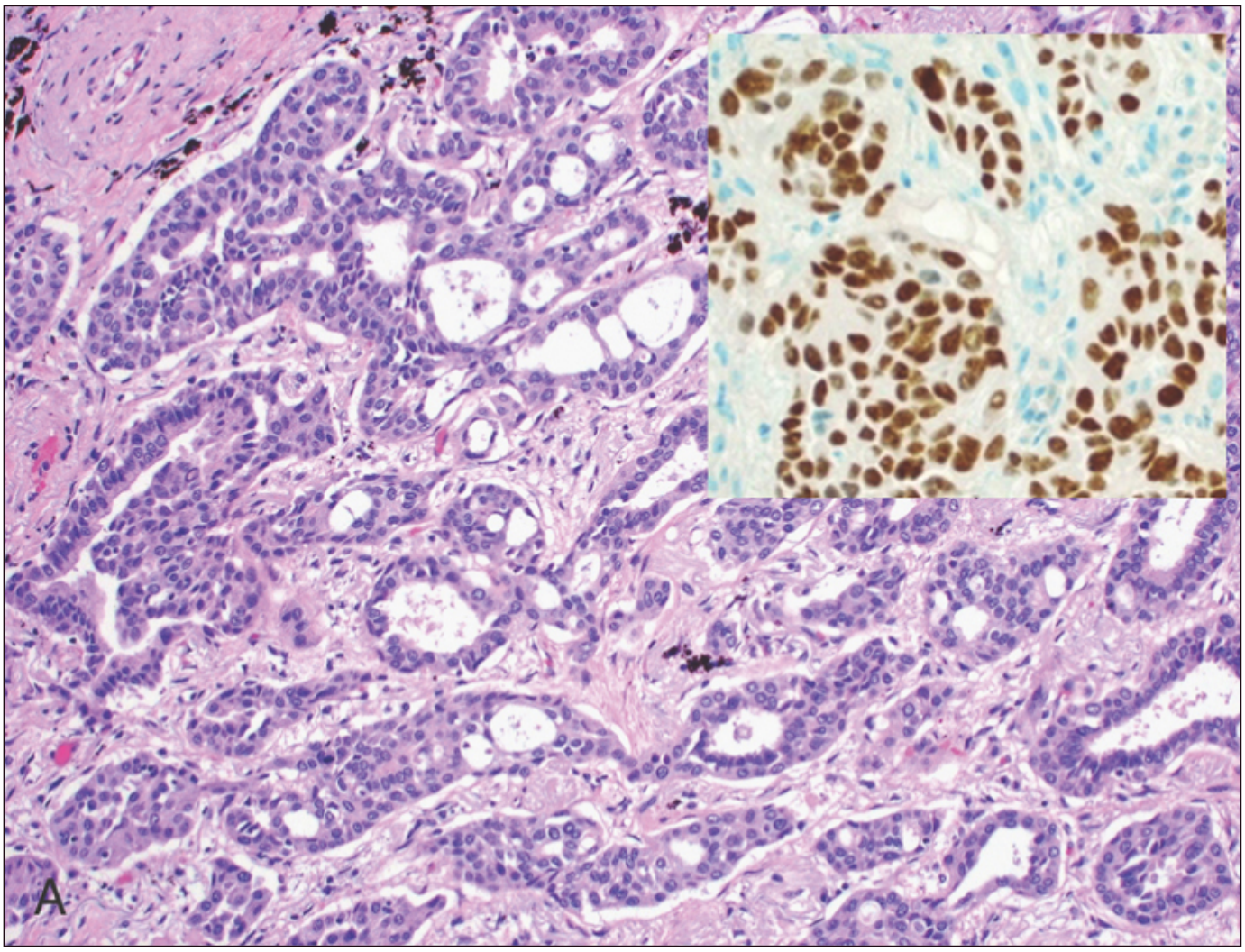
Adenocarcinoma

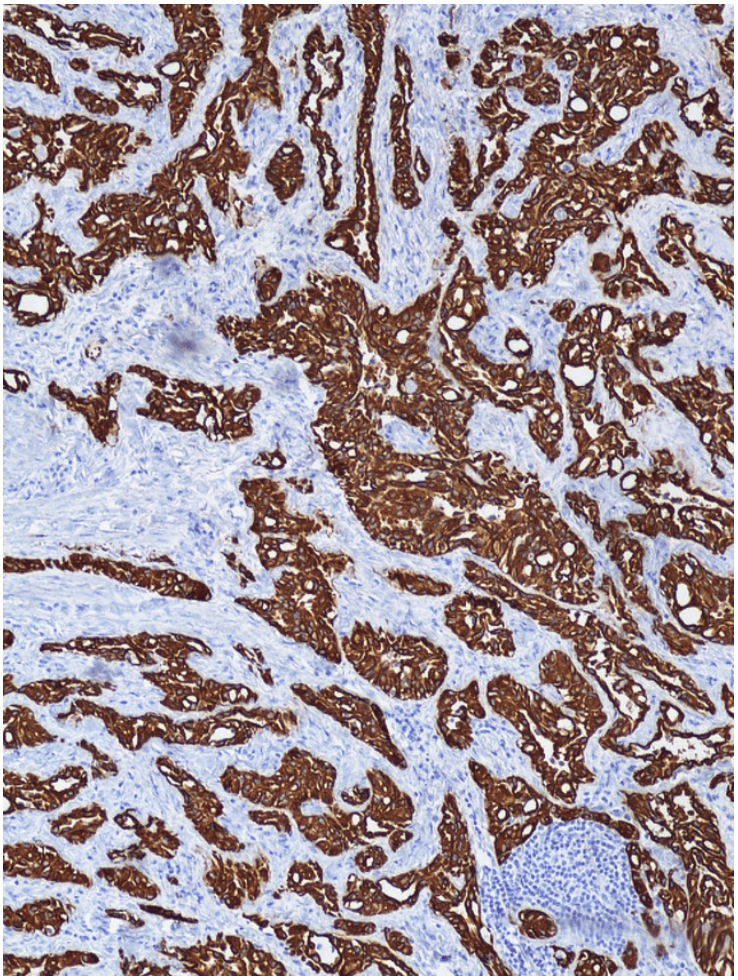
- Diferenciación glandular (producción de mucina)
- Predilección mujeres no fumadoras
- Lesiones periféricas
- FENOTIPO:
  - TTF1
  - NapsinA
  - CK7
- Crecimiento menor a epidermoide pero mas agresivos.

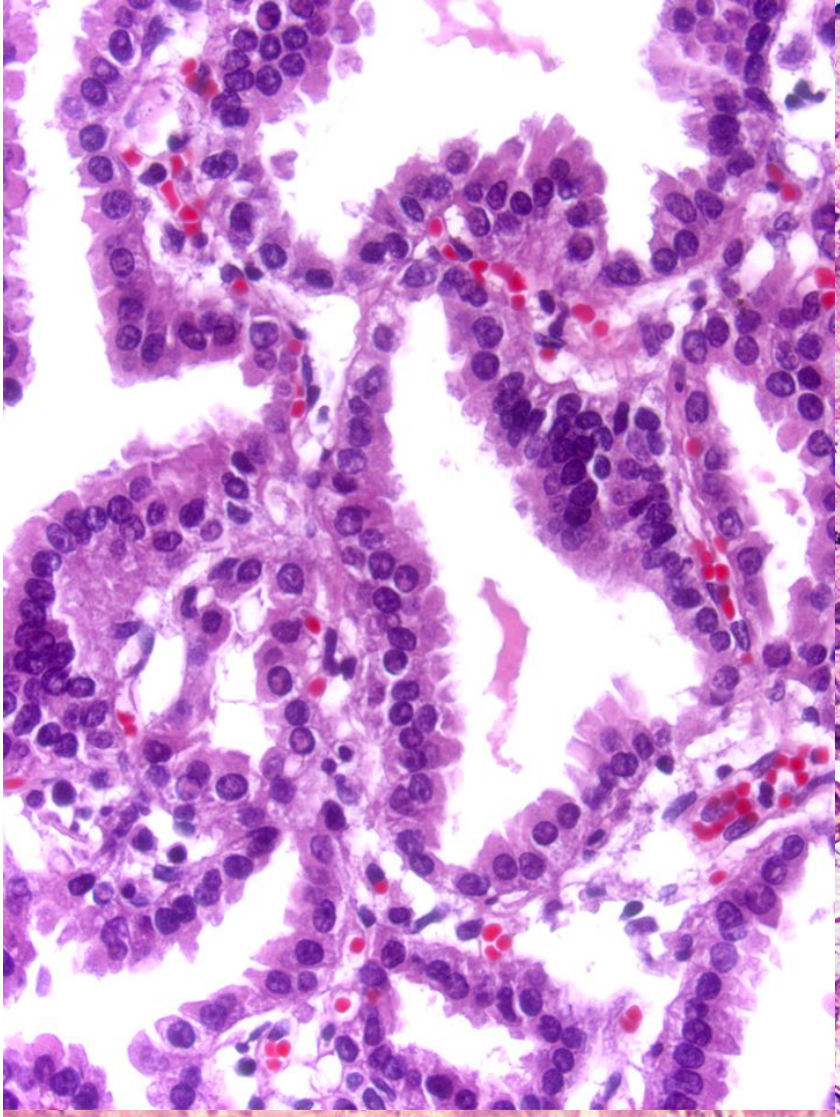


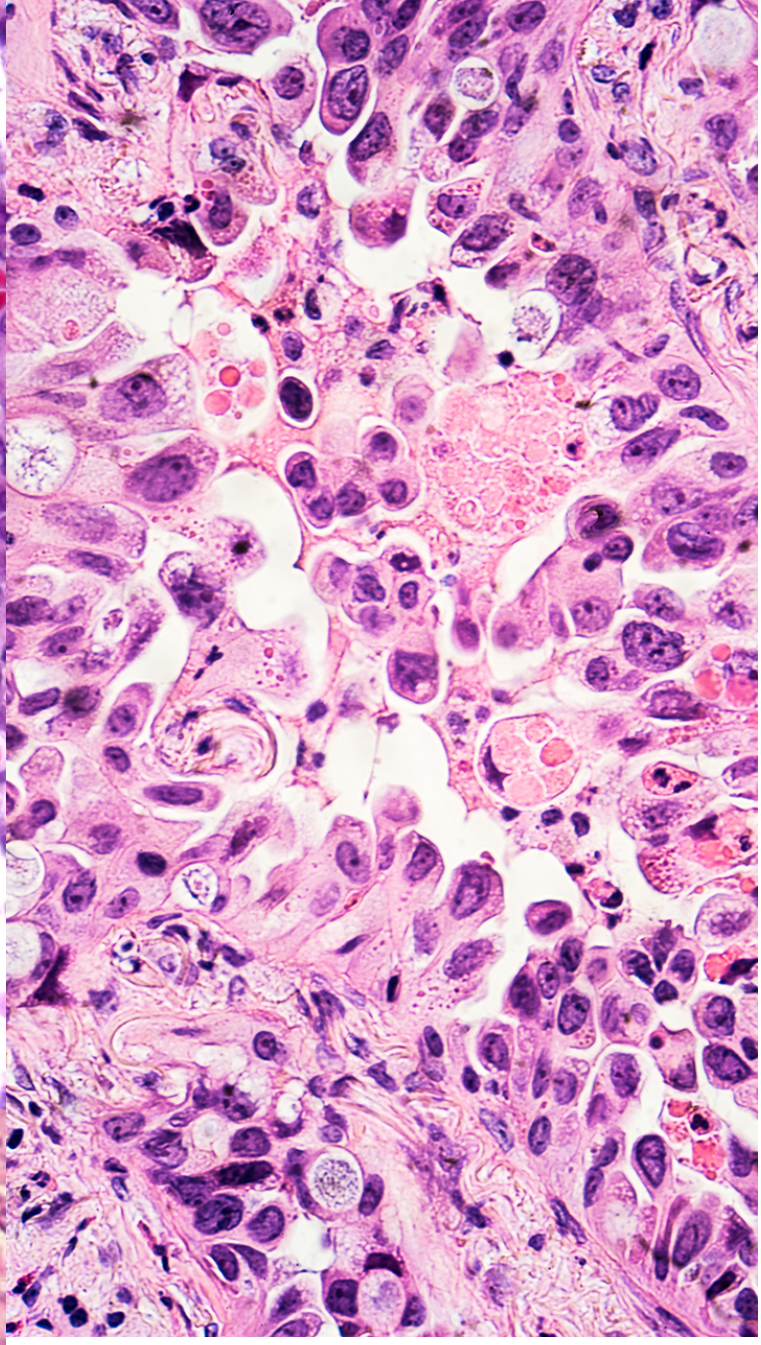
Hombre 45 años, no fumador, atleta.
Ingresa por urosepsis y en su tratamiento =
Nodulo pulmonar sup izq.

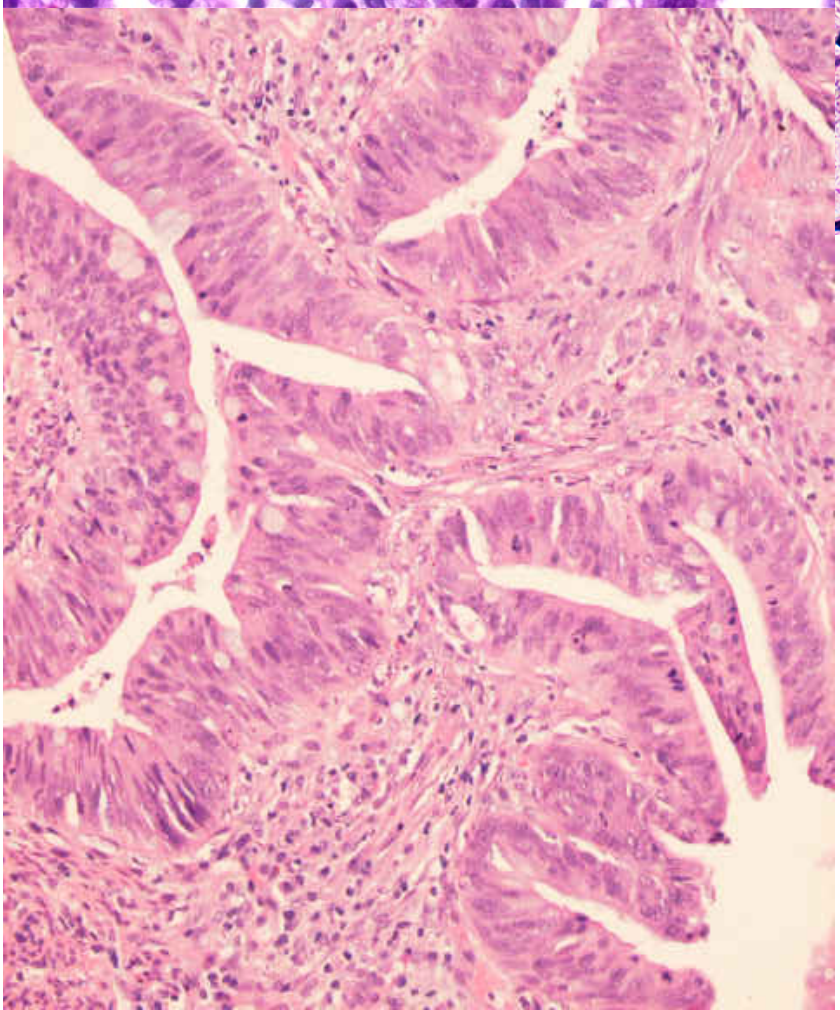
Mujer 52 años, no fumadora, ama de casa, valoración prequirurgica
por cirugía ocular, rx nódulo pulmonar

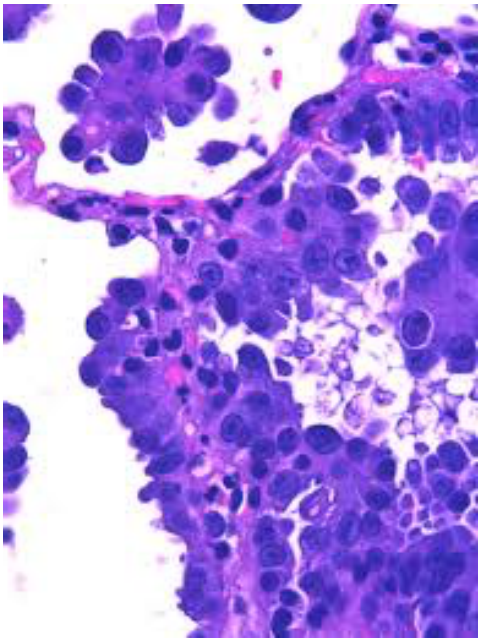

A

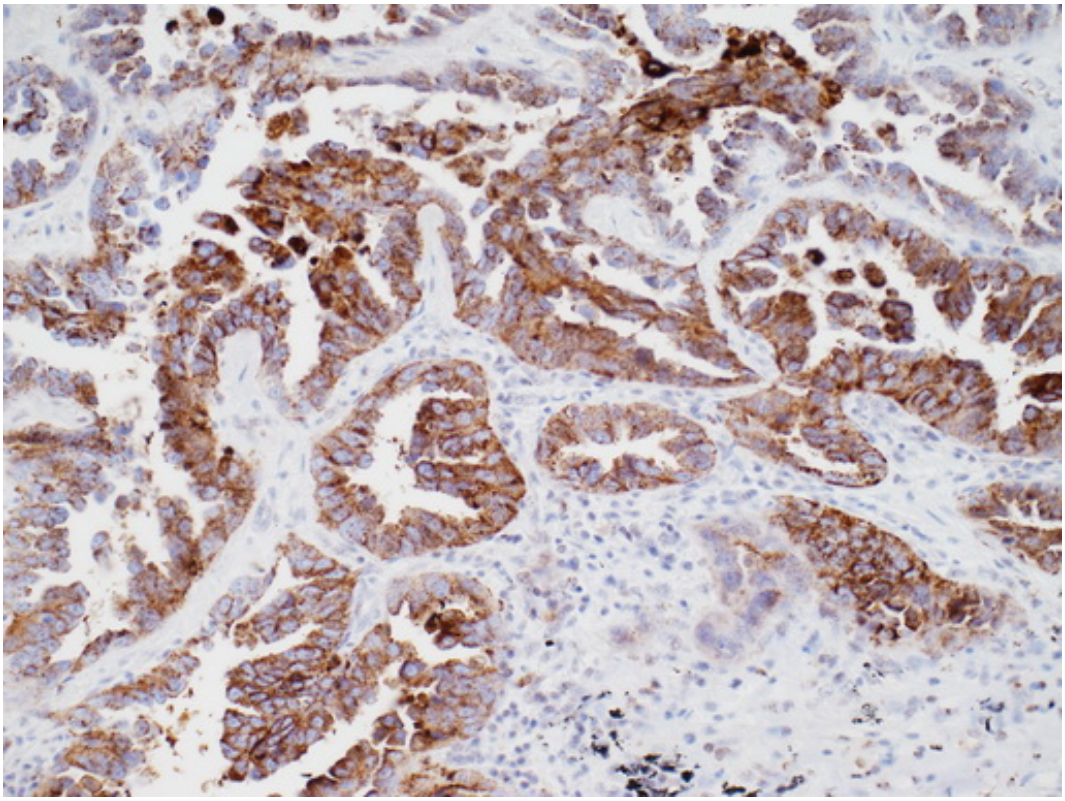


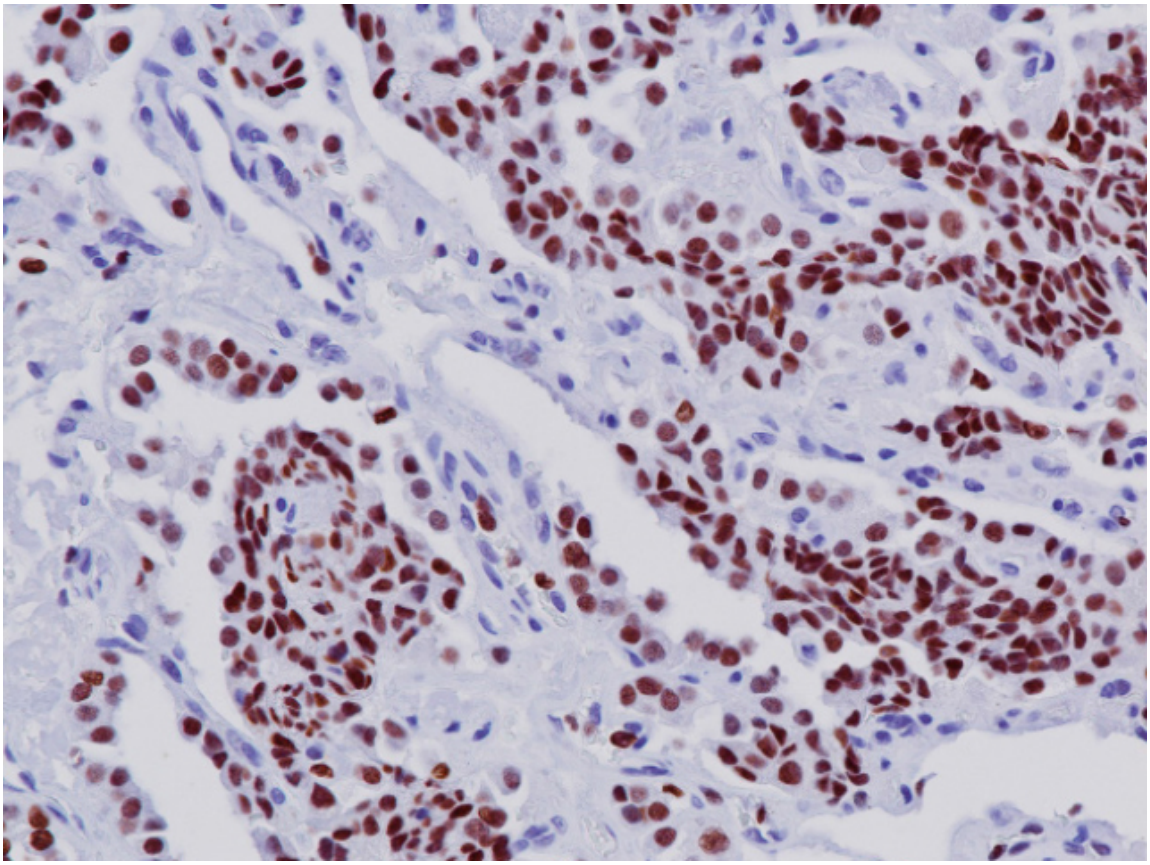






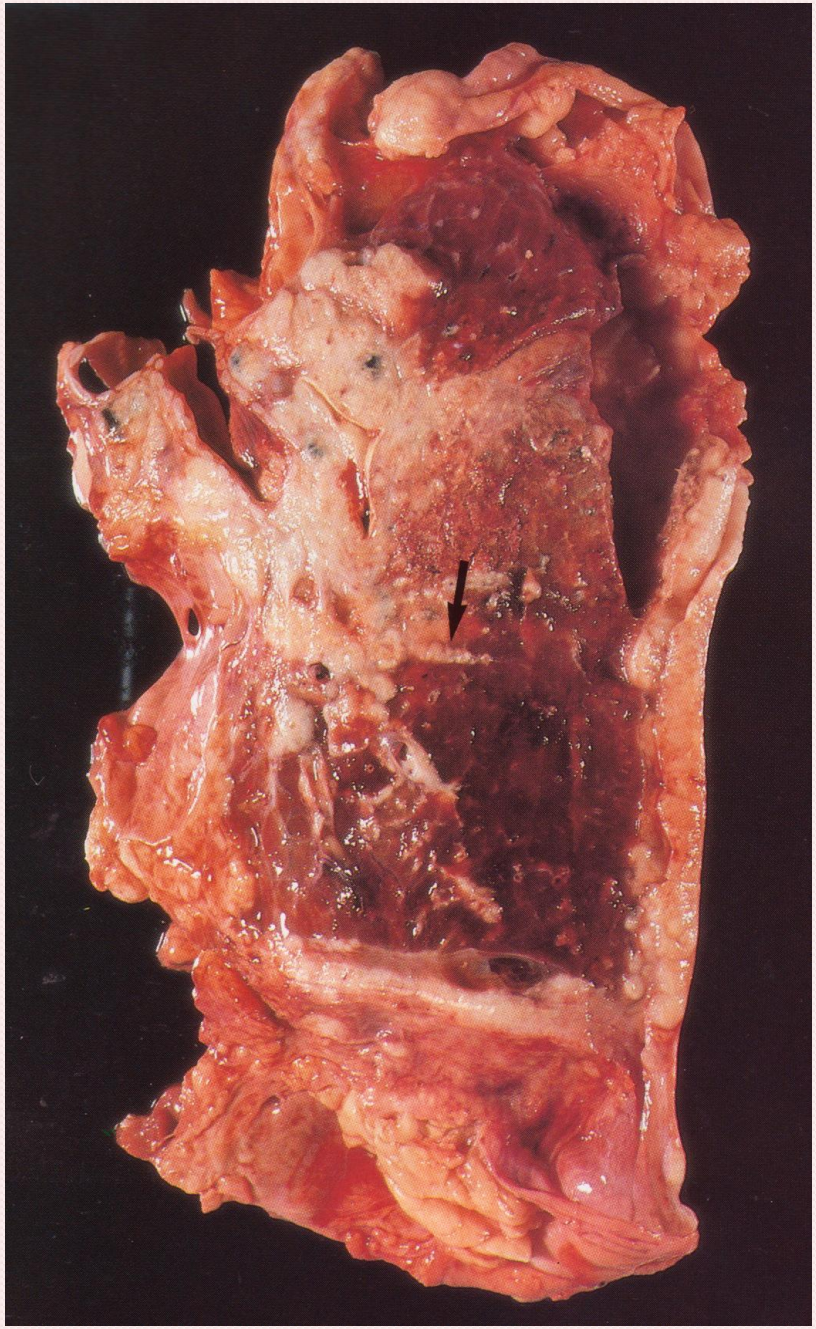




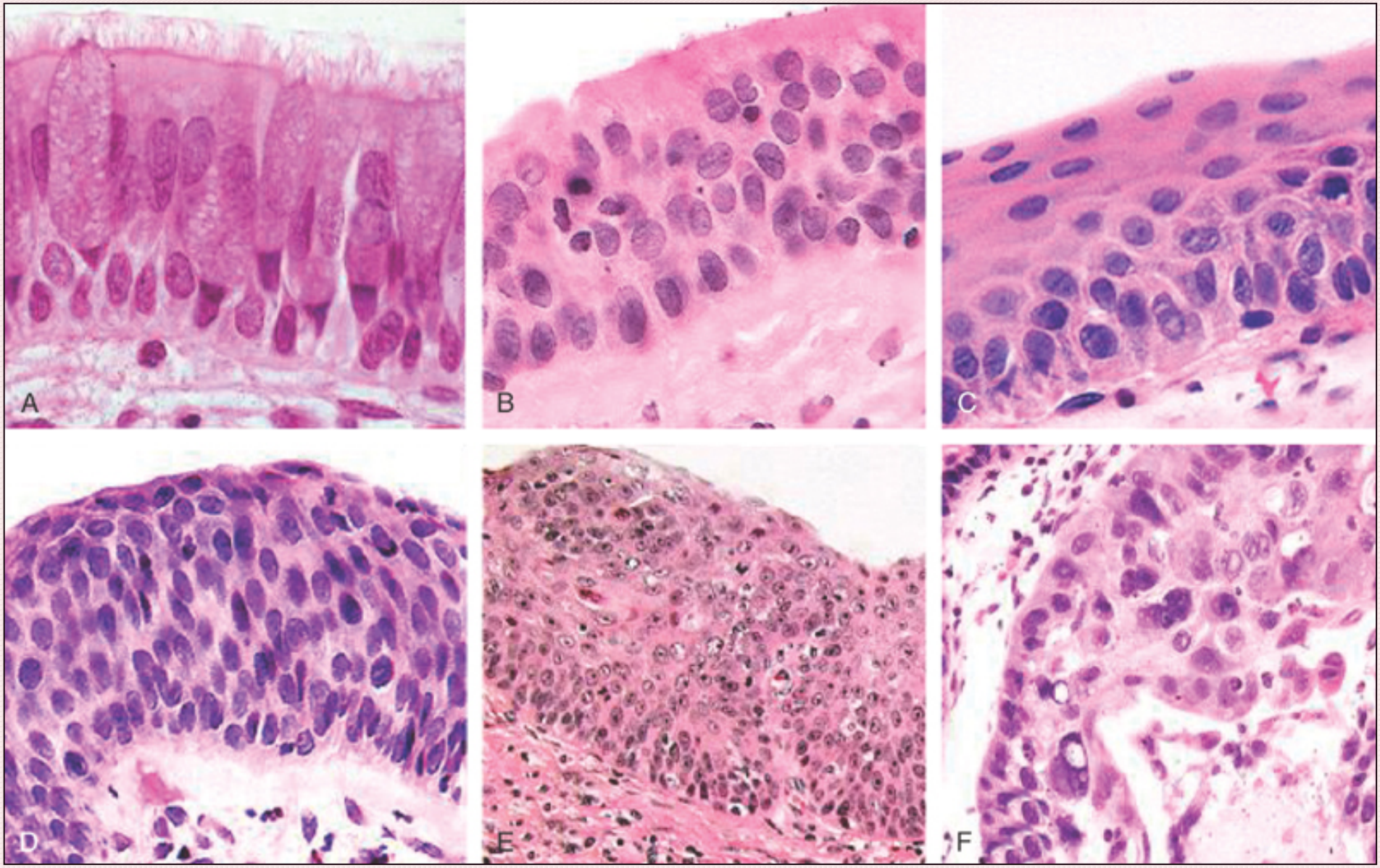


Carcinoma epidermoide

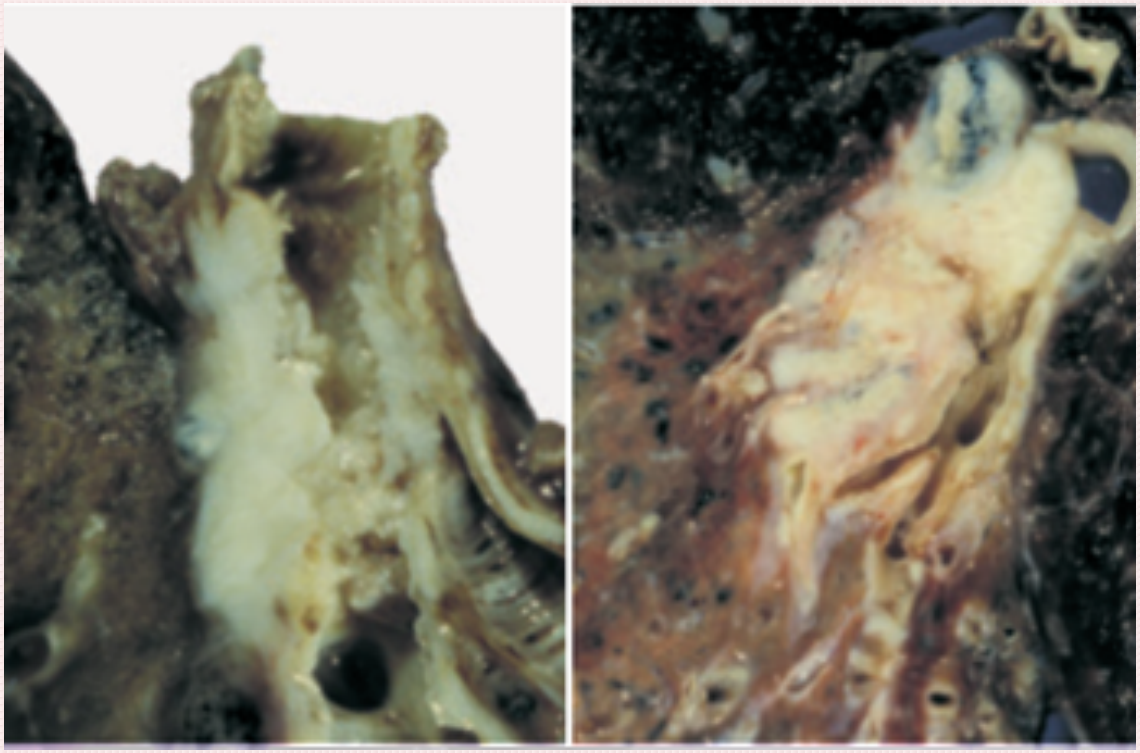
- Hombres +
- Estrechamente relacionado tabaco
- Puentes intercelulares
- Formación de queratina (bien dif)
- Alta tasa mitósica
- Centrales
- Epitelio bronquial metaplásico adyacente.
- p53 frecuentemente mutado sobreexpresado 60-90%
- Pérdida de expresión del RB1 10-50%
- p16 inactivo 65%
- Hiperexpresión de EGFR 80% (no mutado)
- Fenotipo: CK5, p40, p63

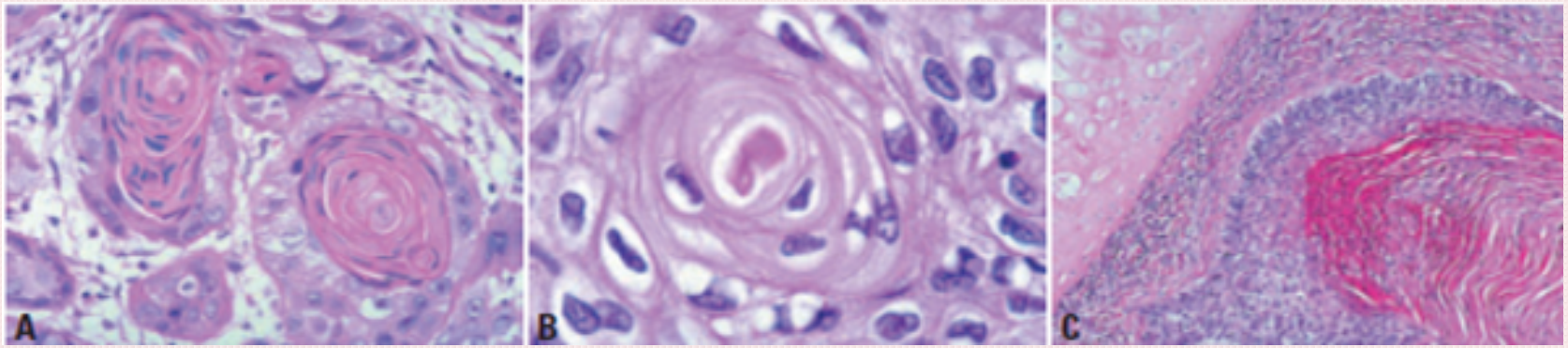


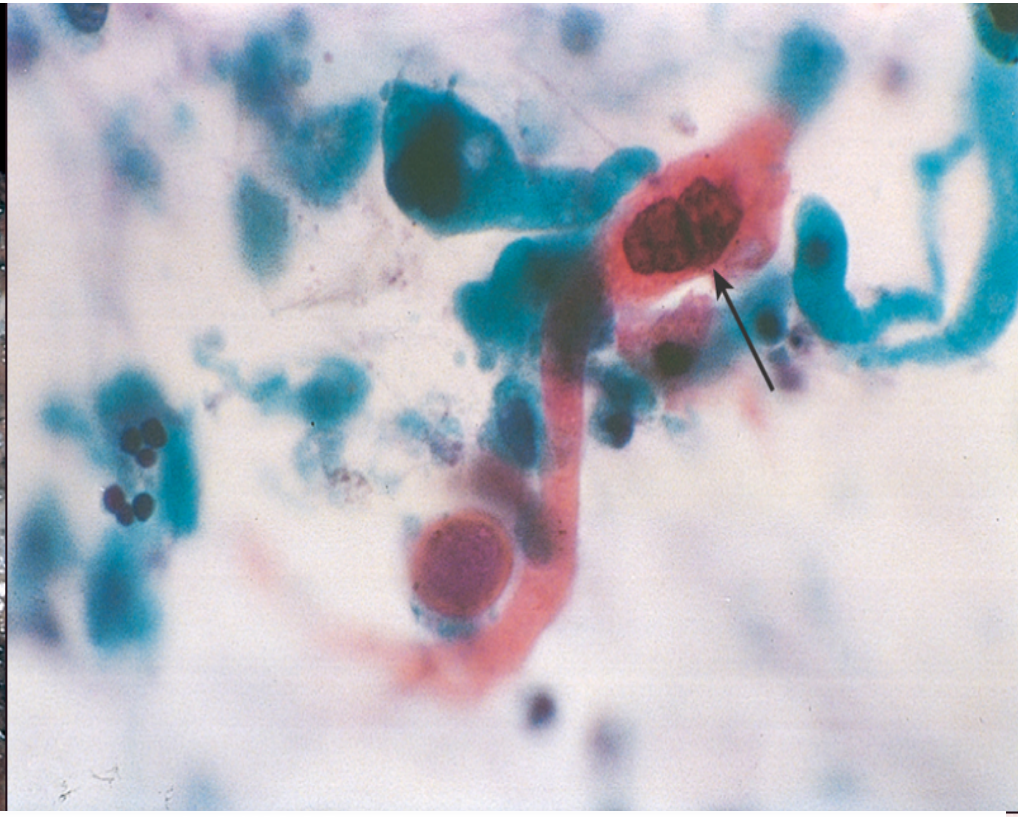
Lesiones Precursoras

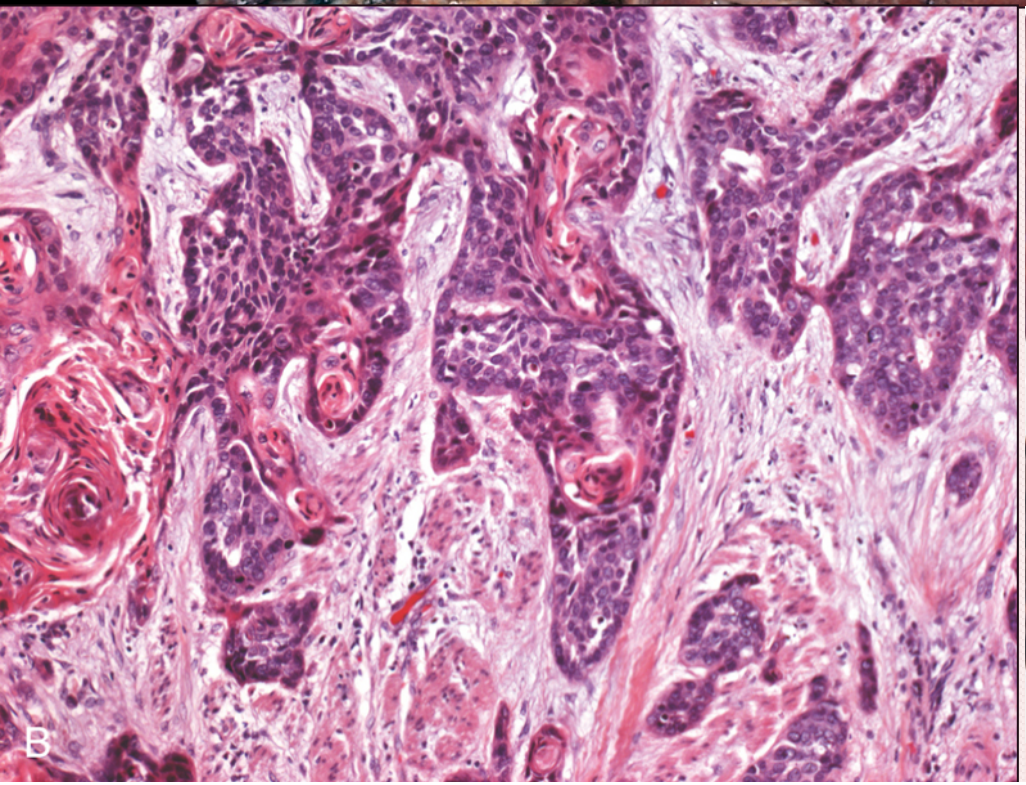


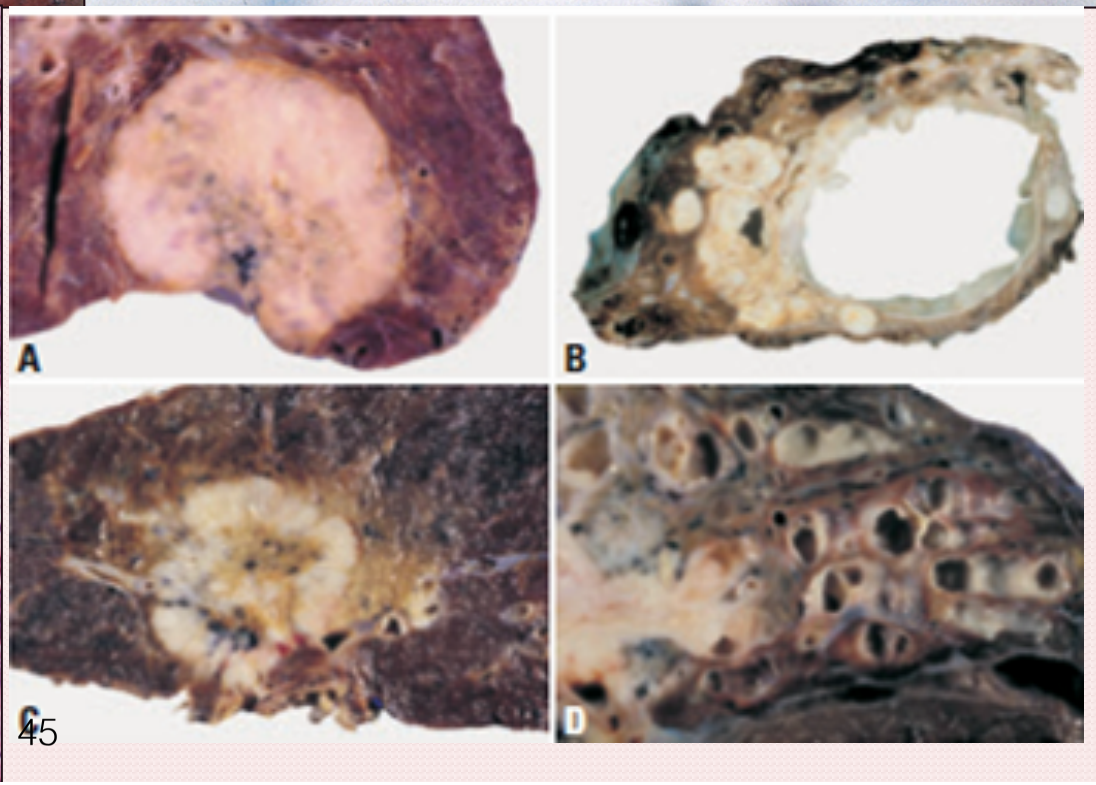
Cracinoma epidermoide





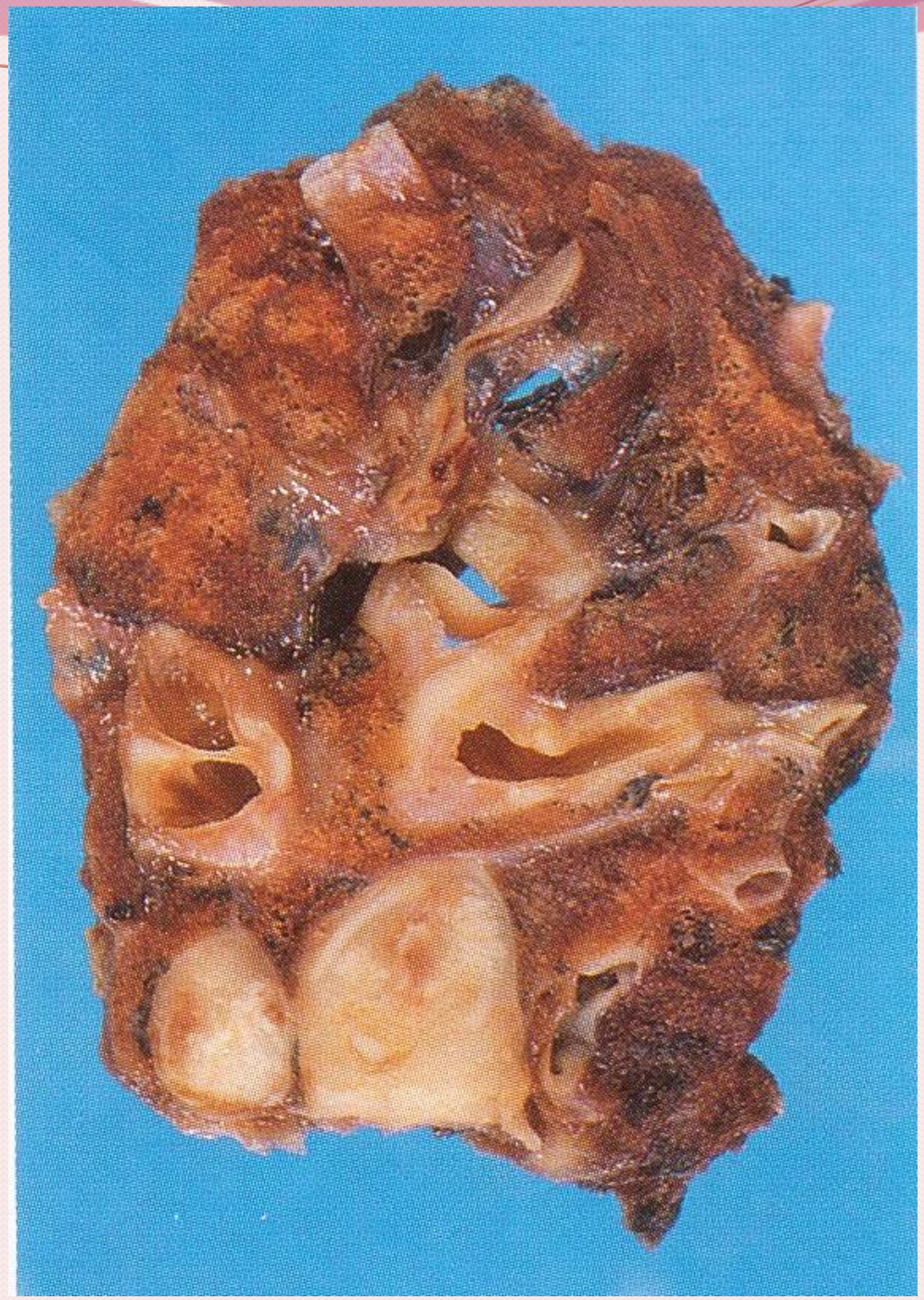



B


A
B
C
D

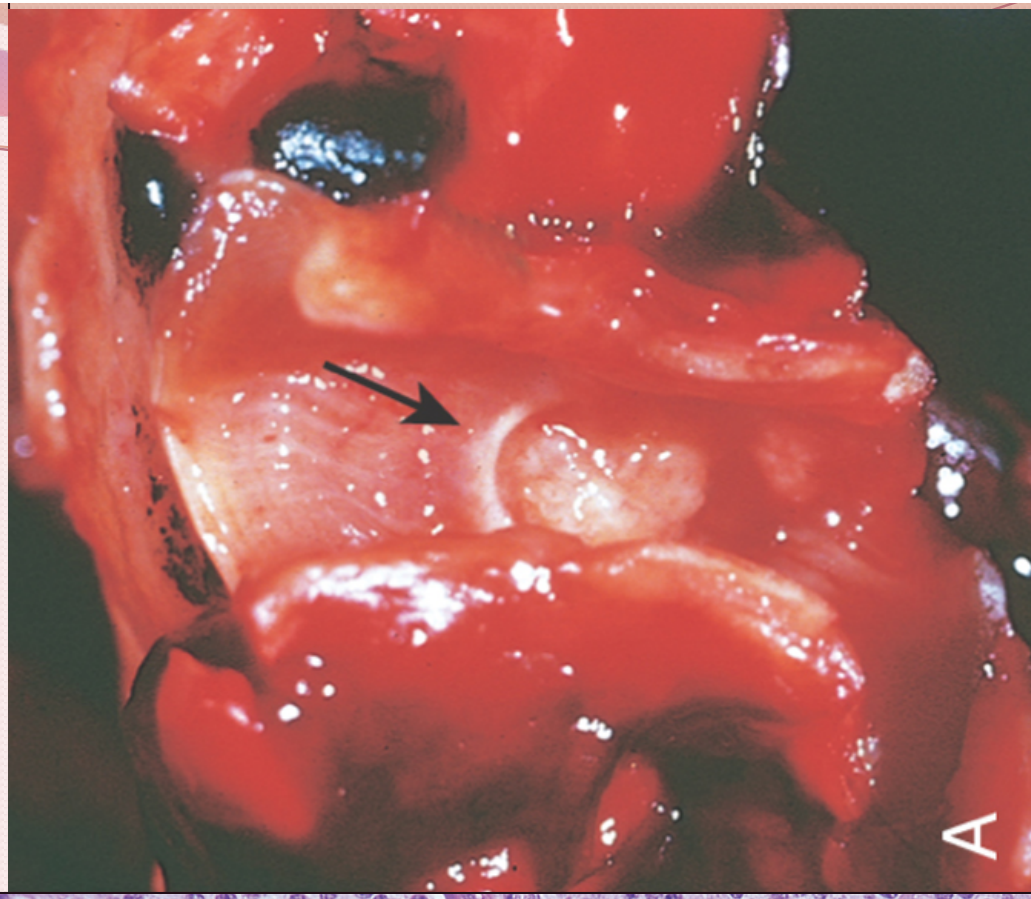
Tumores NE

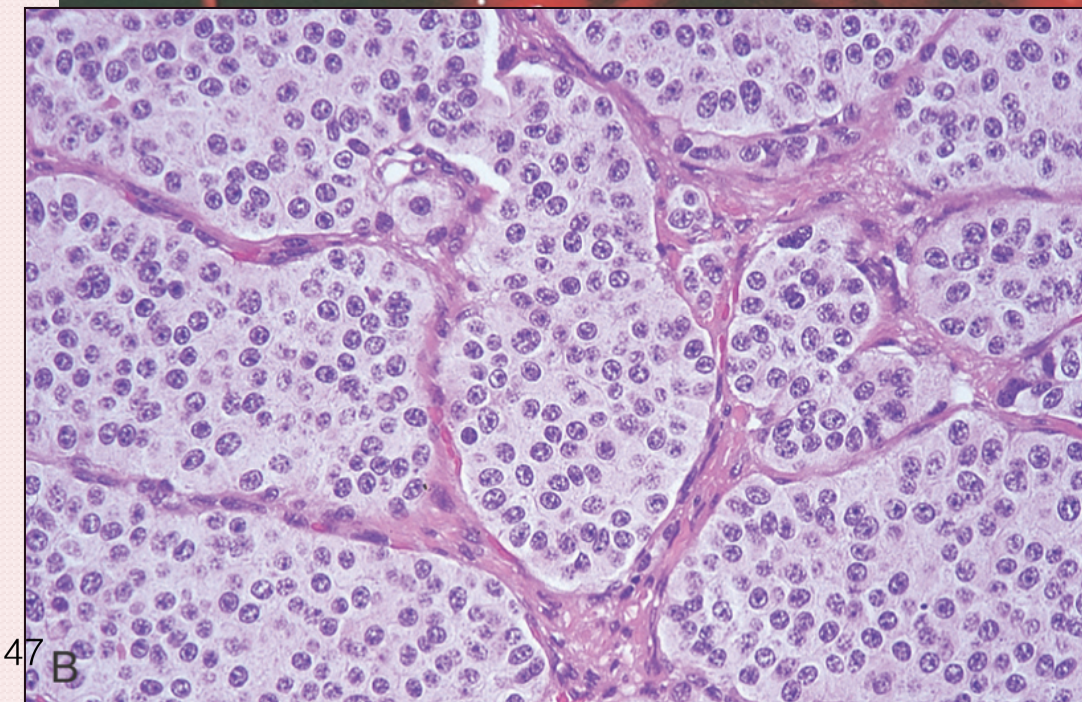
- Hiperplasia de células NE
- Asociado o no a NEM1
- Carcinoide
  - Típico (<2mitosis/10chp)
  - Atípico (2-10 mitosis)
- Ca Cel pequeñas
- Ca de cel no pequeñas
- Sd. Carcinoide (diarrea, rubicundez y cianosis)
- SV 5 años hasta 97%



Carcinoide

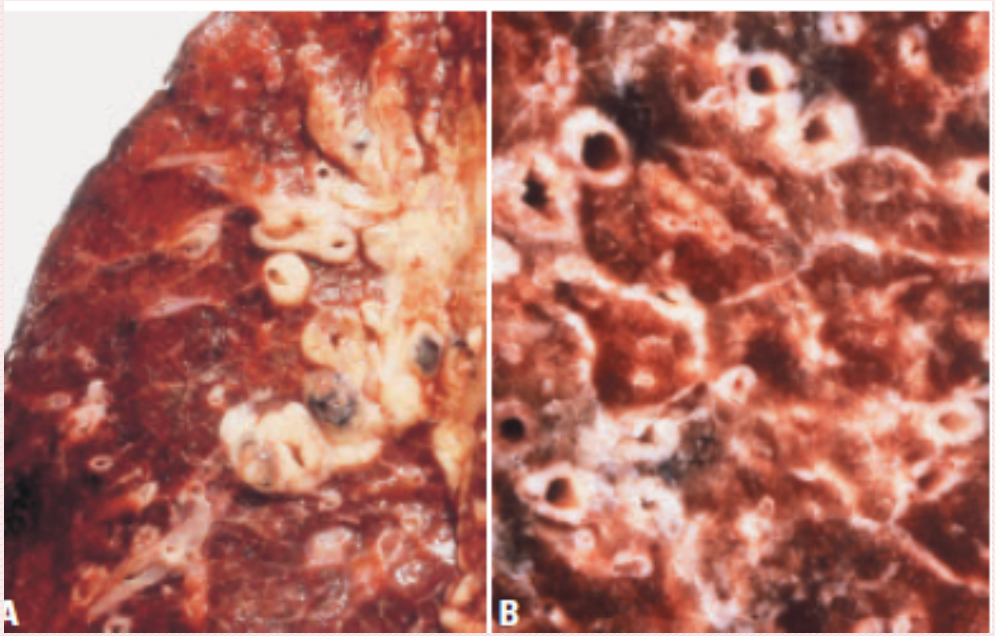
- 1-5% de T pulmón
- <40 años
- 20-40% no fumadores
- Central o periférico
- Neoplasias malignas de bajo grado
- Típicos sin mutaciones
- Atípicos: p53, Bcl2 y BAX.
- Pequeños (3-4cm)
- Diseminación según crecimiento
- Poca diseminación linfática

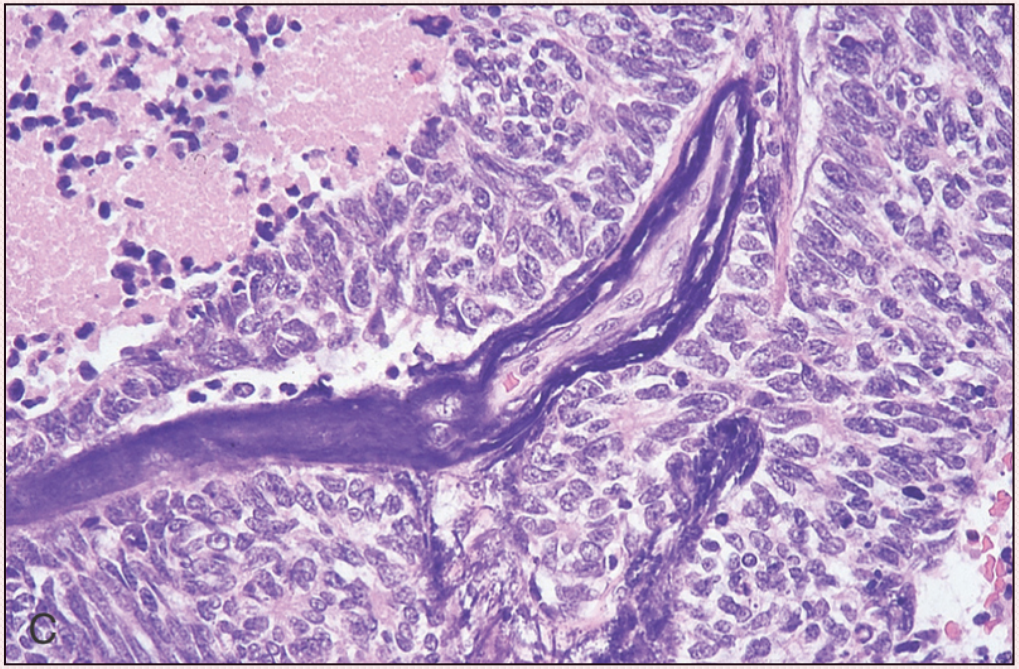


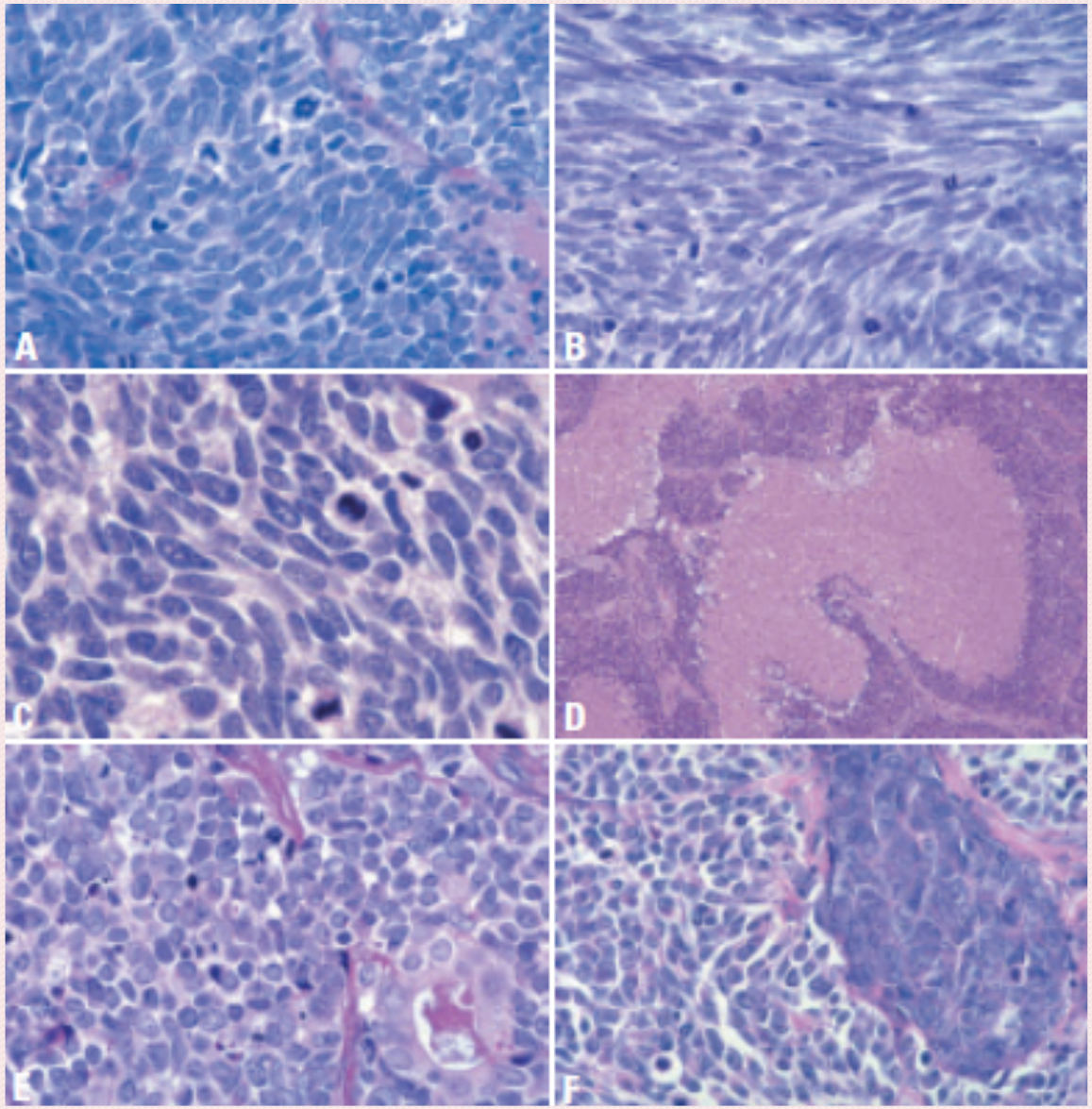


Cracinoma células pequeñas

- Muy agresivo
- Célula pequeña
- Núcleo en sal y pimienta
- Necrosis (Fenomeno de Azzopardi)
- Mitosis
- Gránulos NS (CD57, Cr, SYNP
- Origen en células NE
- Producción ectópica hormonas
- Fumadores
- Incurables
- p53 y RB1 mutados
- Altas [] proteína Bcl-2 (antiapoptosis)
- BAX bajo (pro apoptósica)

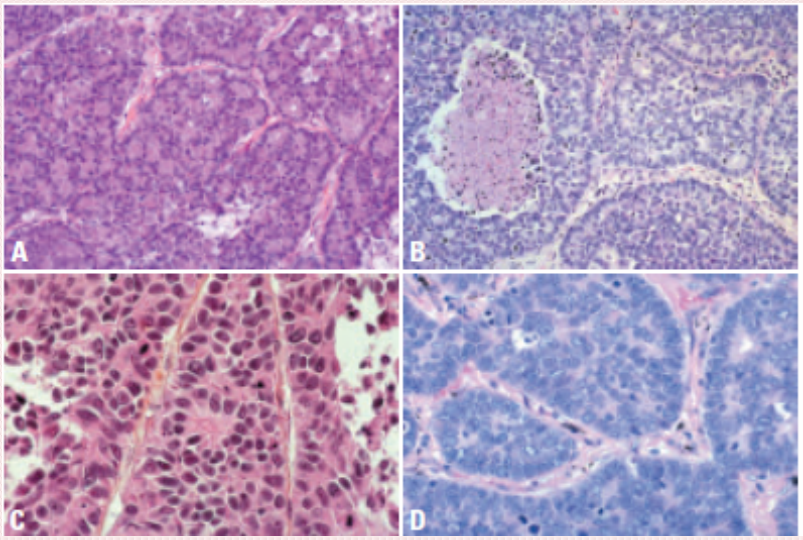


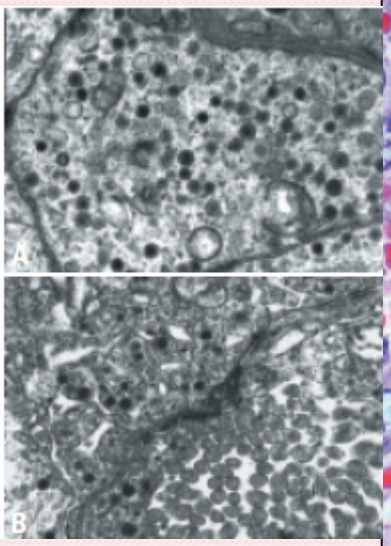


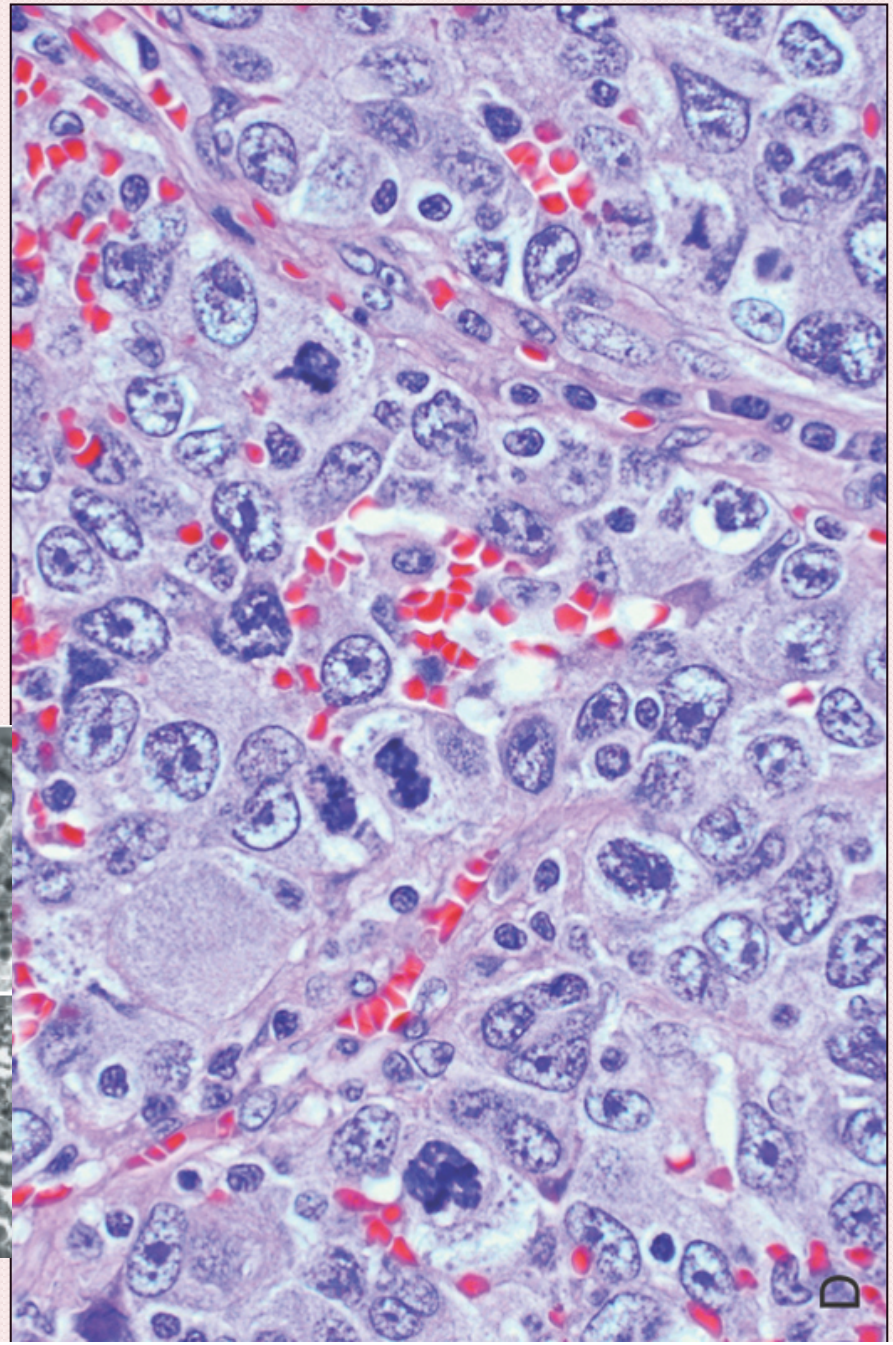

A
B
C
D
E
F

Cracinoma células grandes

- Epitelial maligno indiferenciado
- Citología (Nombre)
- ME (Glandular o escamosa)
  - Ca NE variante del mismo
- Mismos cambios moleculares que el carcinoma de células pequeñas.

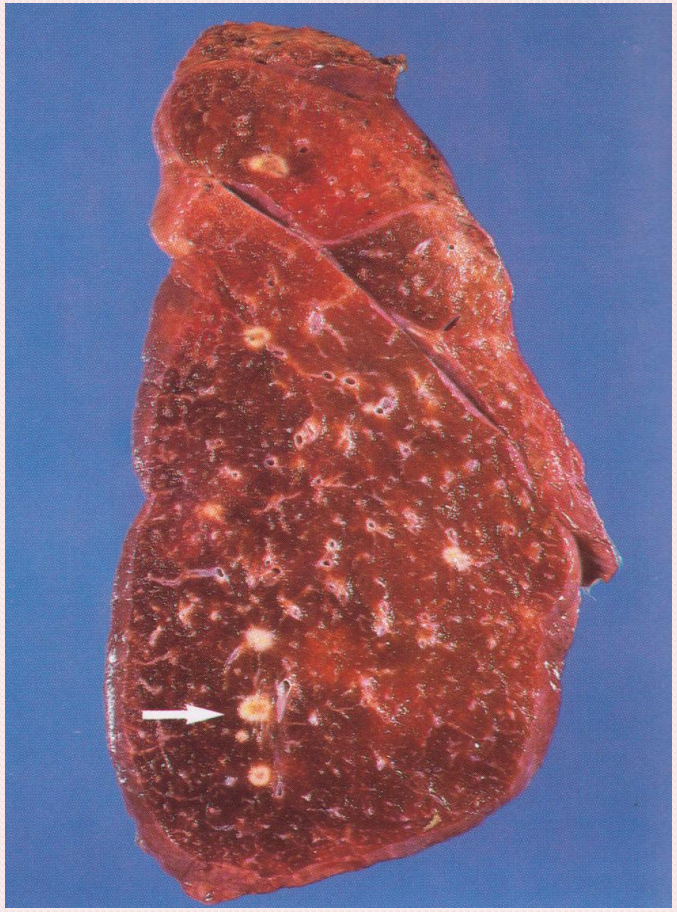




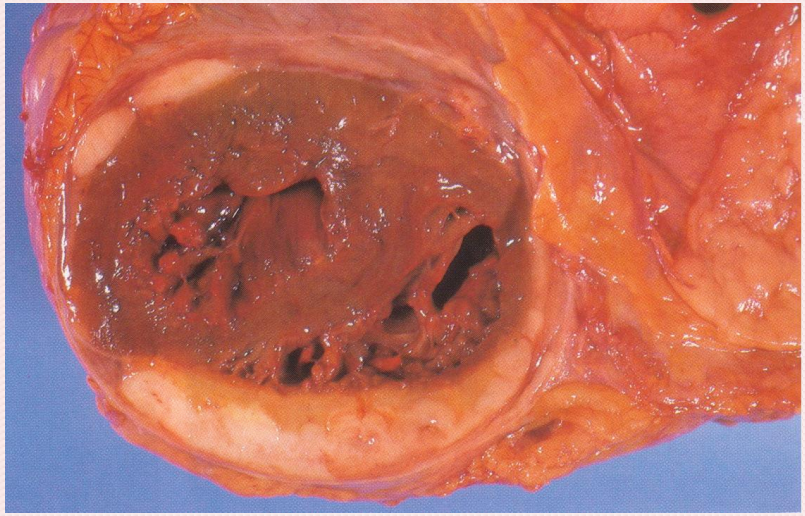


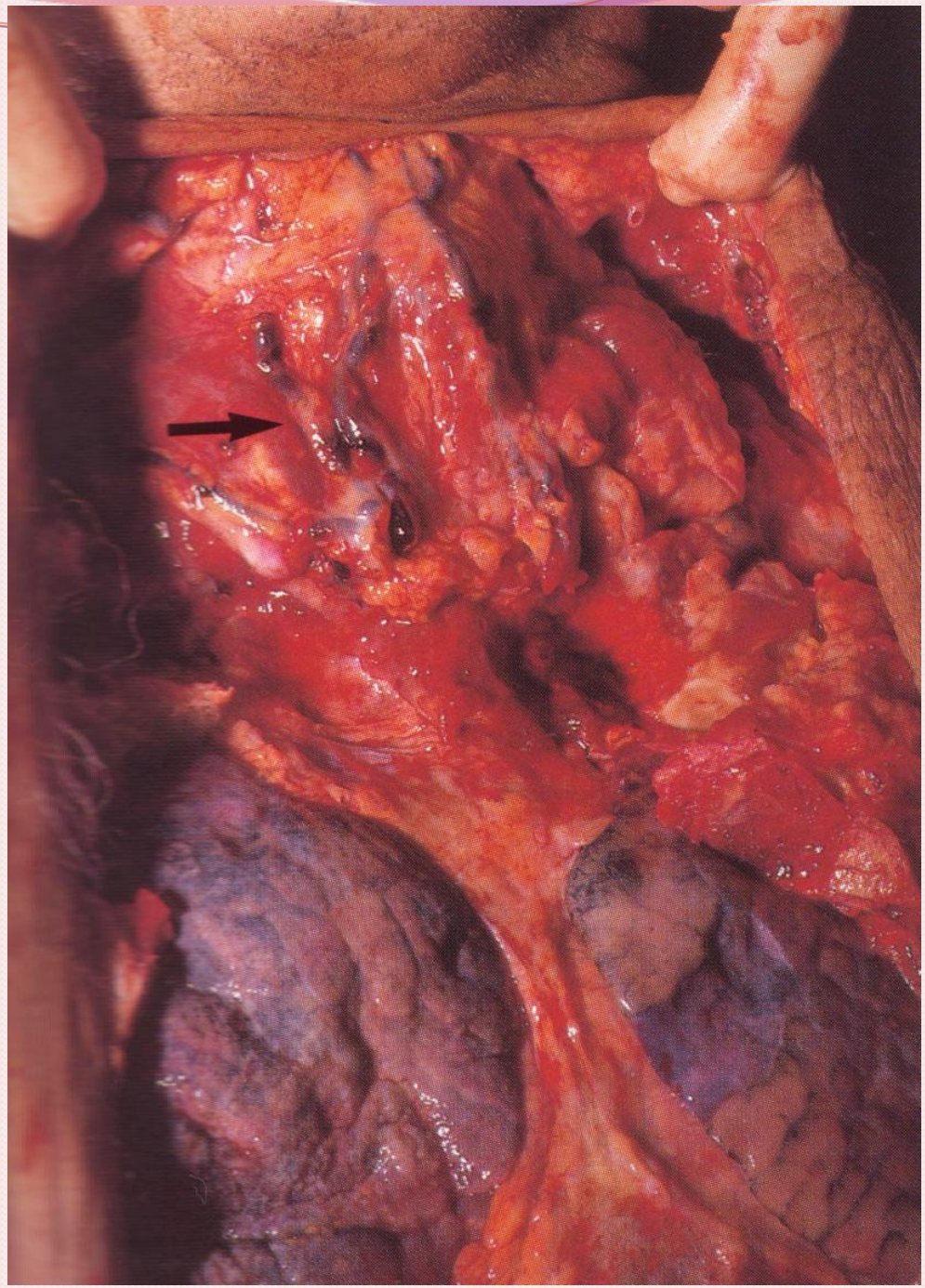
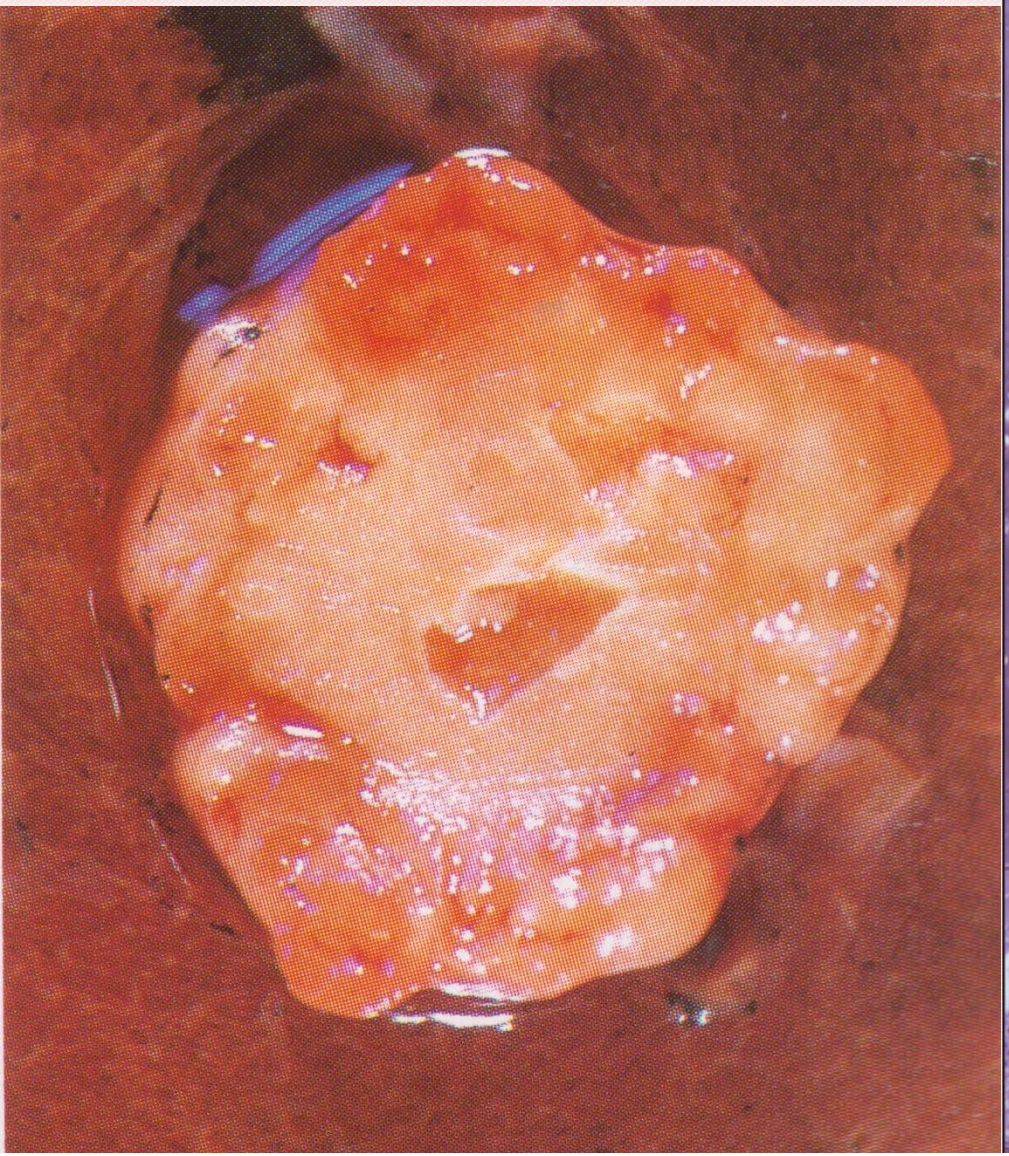
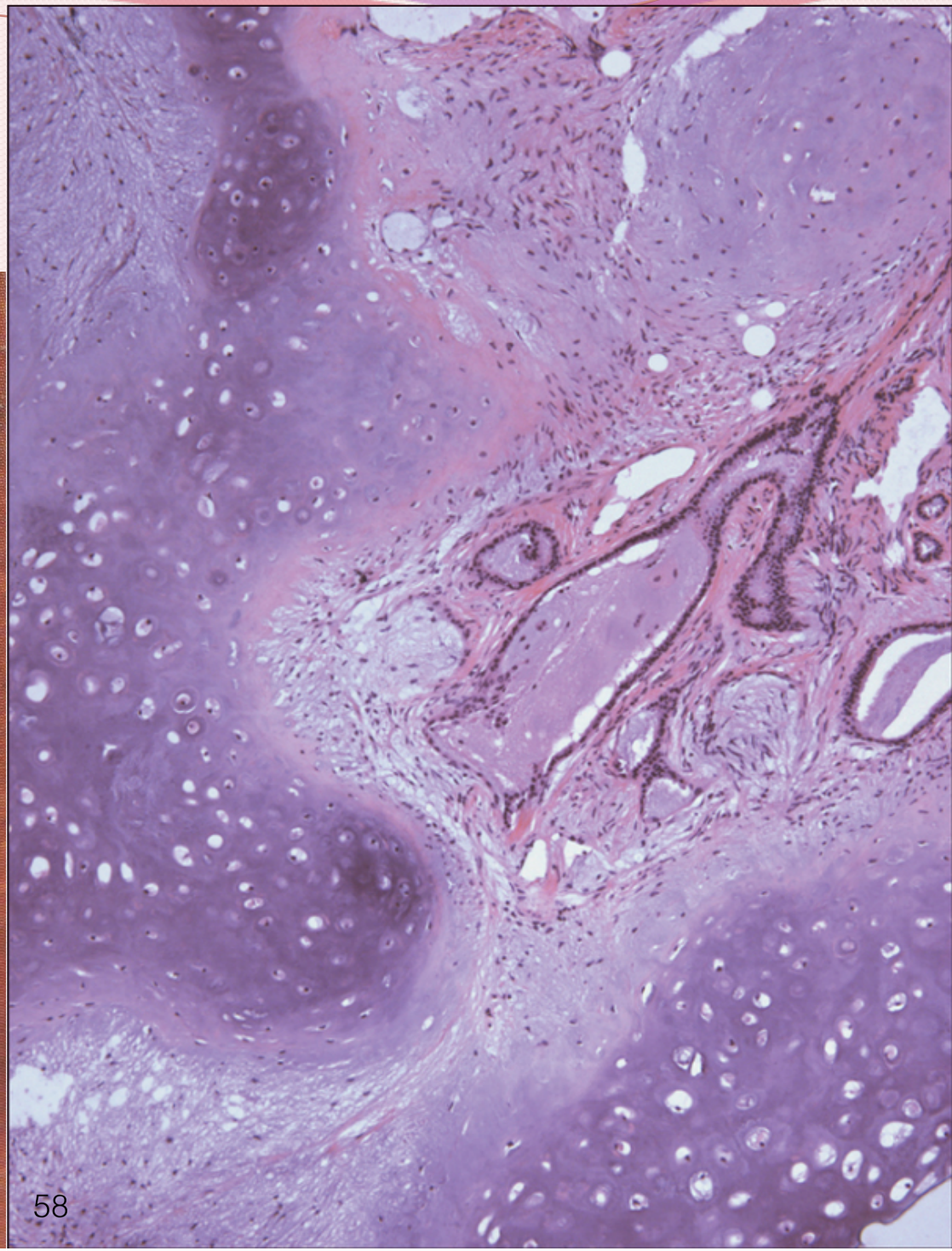
Tumores Metastásicos

- Vía sanguínea o linfática
- Carcinomas
- Sarcomas



- 10% de los Ca de pulmón muestran una histología combinada
- Según la localización será la dominancia de síntomas
- Obstrucción parcial, enfisema
- Obstrucción total atelectasia
- Obstrucción vías respiratorias bronquitis supurativa ulcerosa grave, bronquiectasias
- Abscesos pulmonares
- Compresión o invasión de VCS congestión y edema en cabeza y extremidad superior
- Extensión a sacos pericardicos, pleura con derrames abundantes





Hamartoma