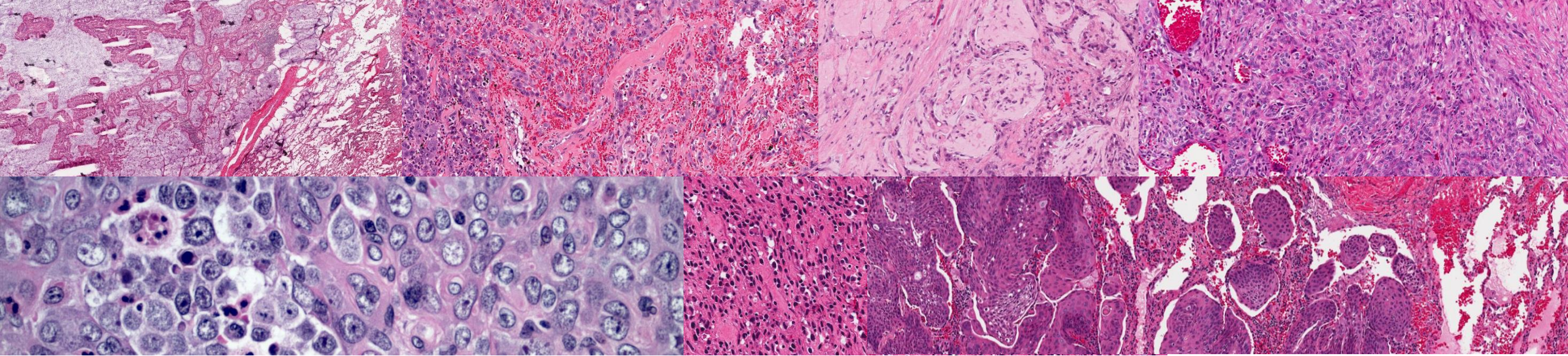
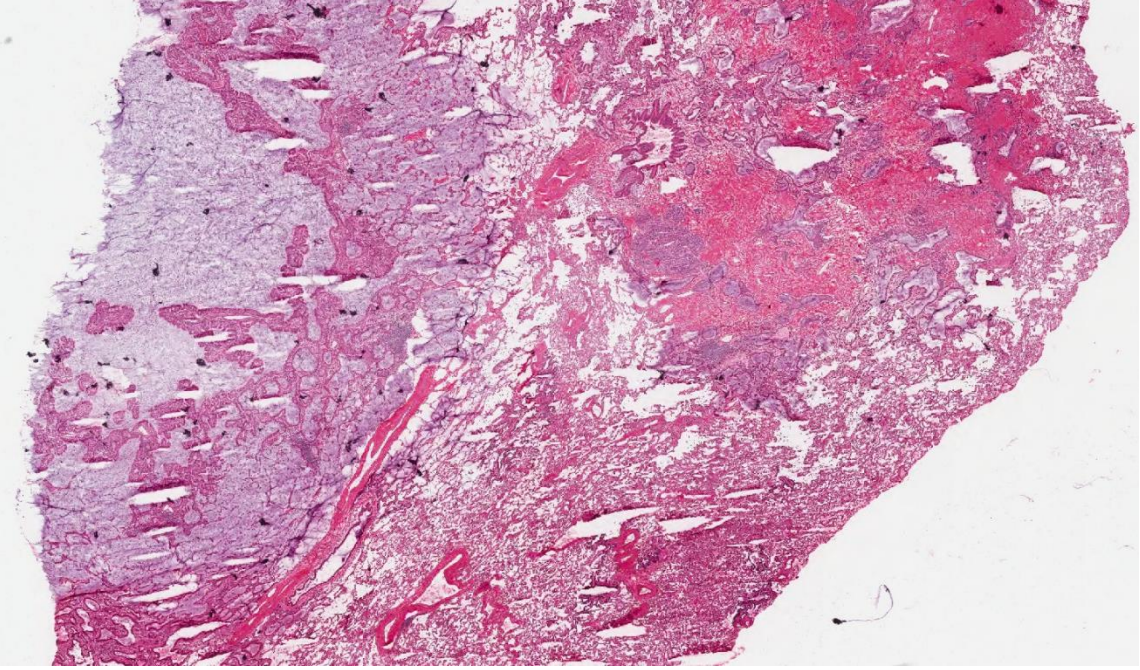
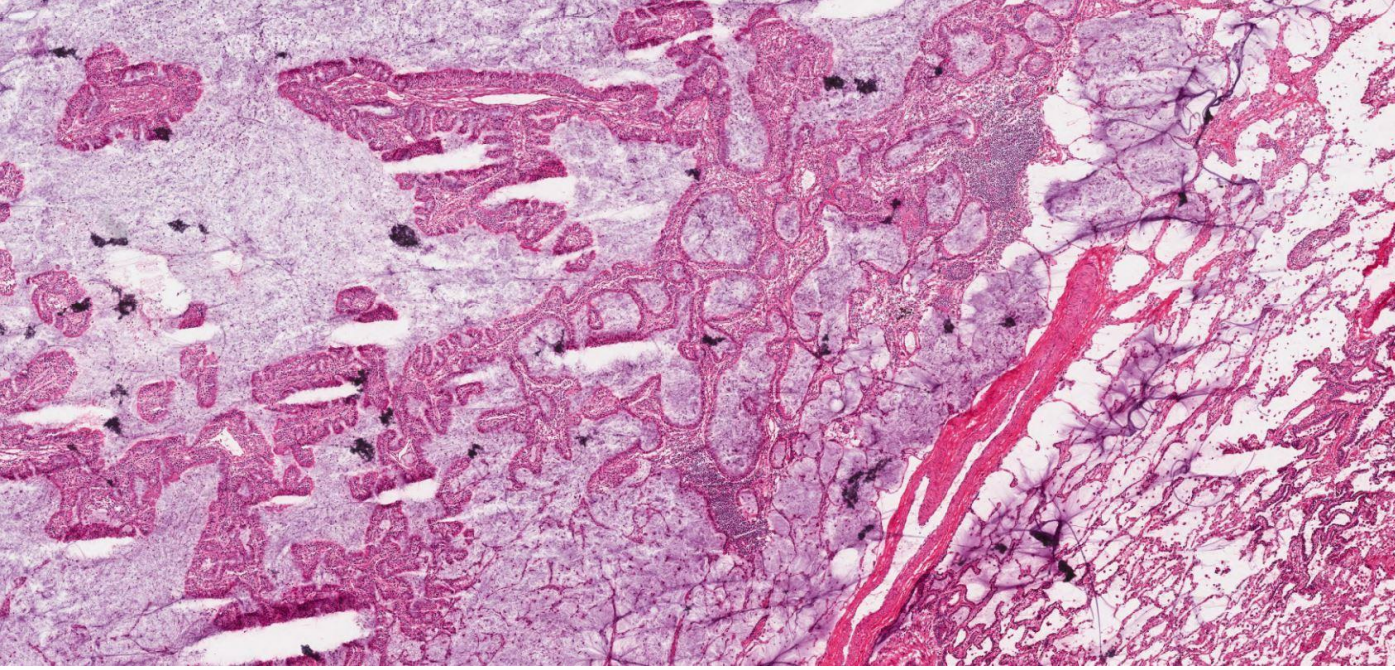




UPGRADE YOUR THORACIC PATHOLOGY SKILLS

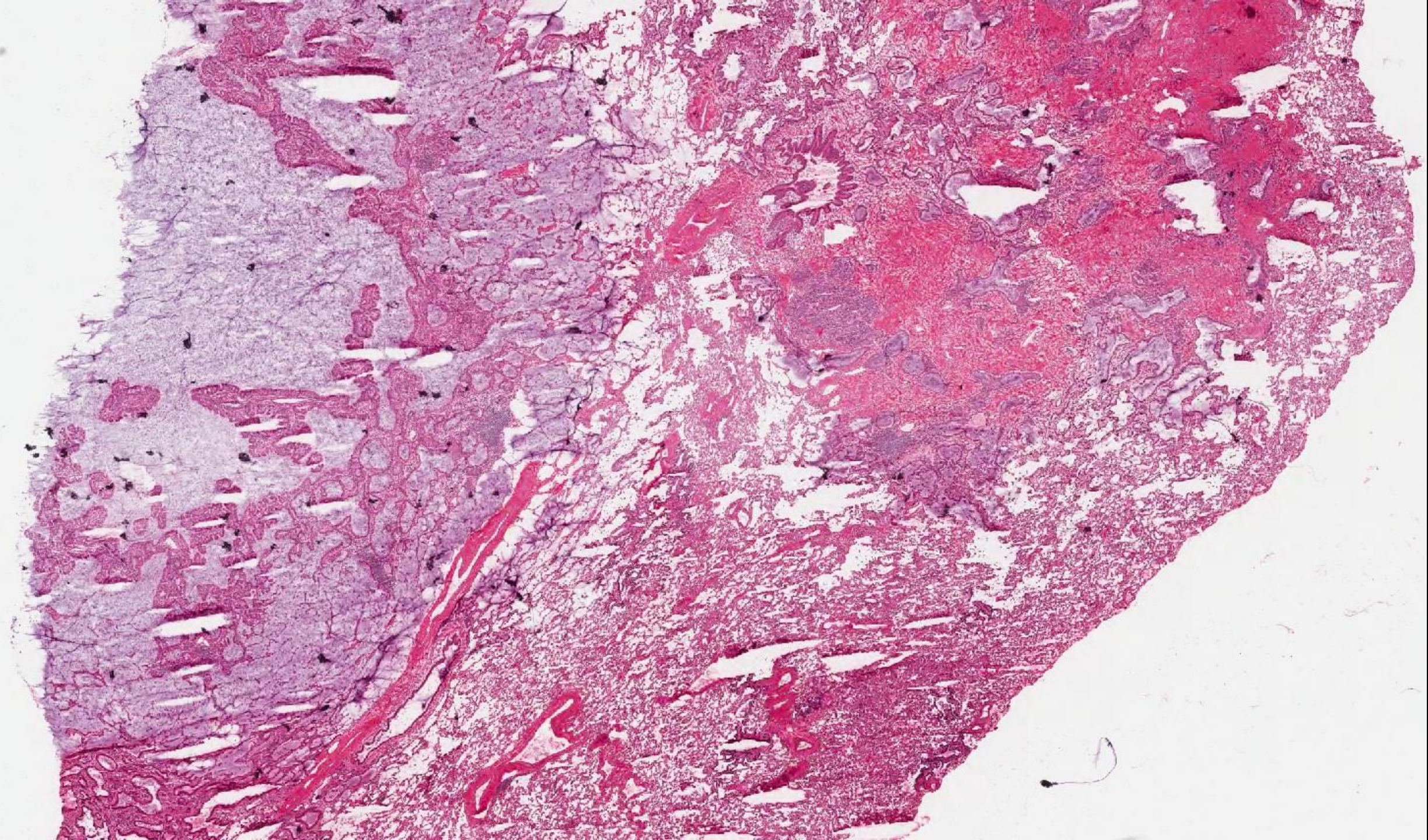
TEN TUMORS YOU MUST HAVE
IN YOUR **TOOLBOX**

SANJAY MUKHOPADHYAY, MD
[@smlungpathguy](https://twitter.com/smlungpathguy)

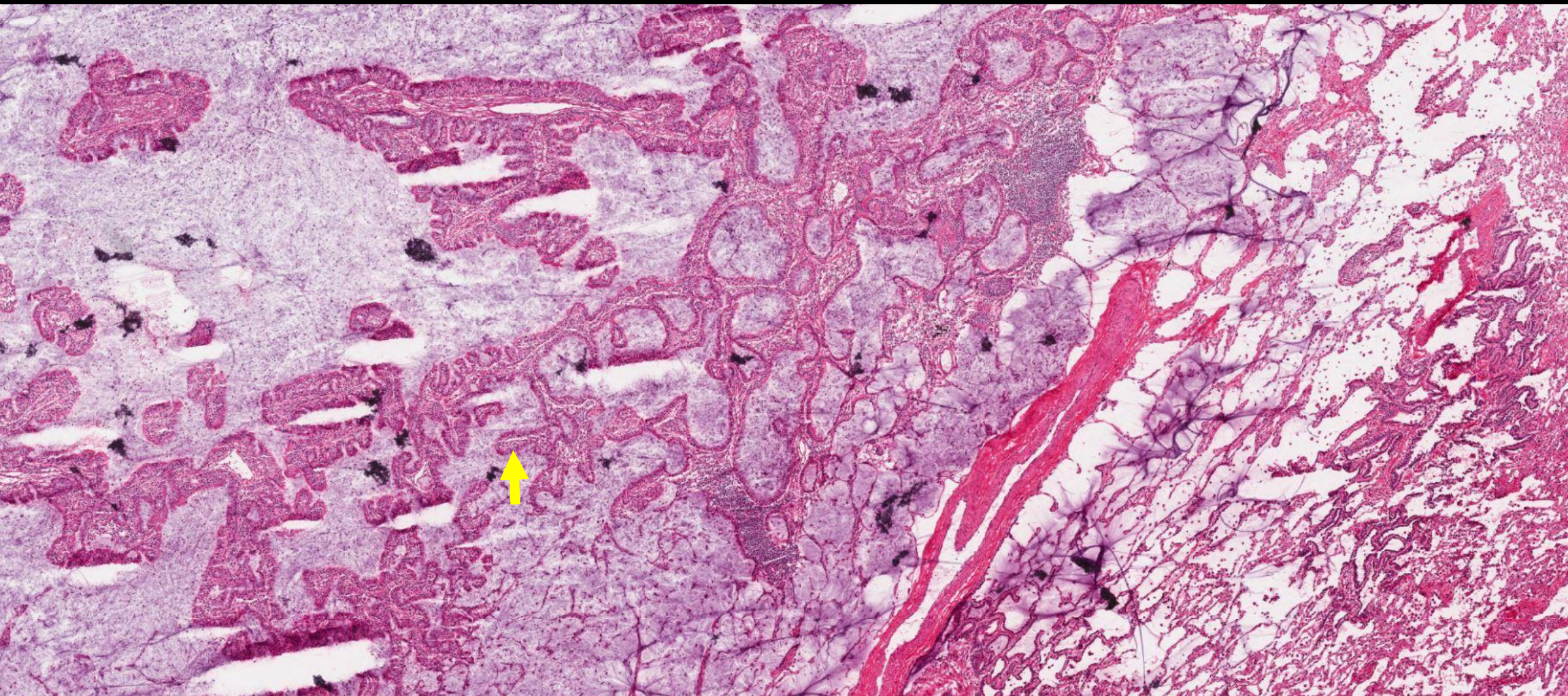


IS IT ADENOCARCINOMA?

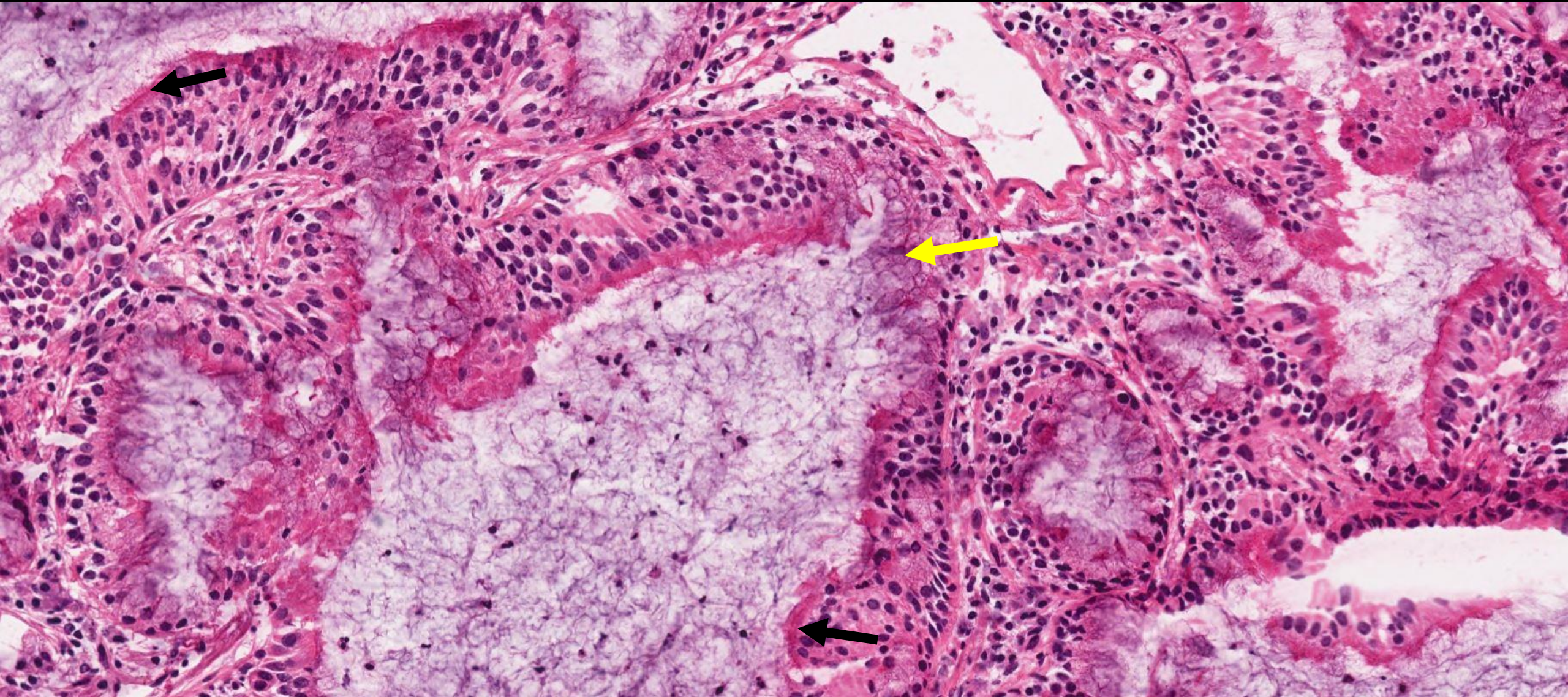
TUMOR 1



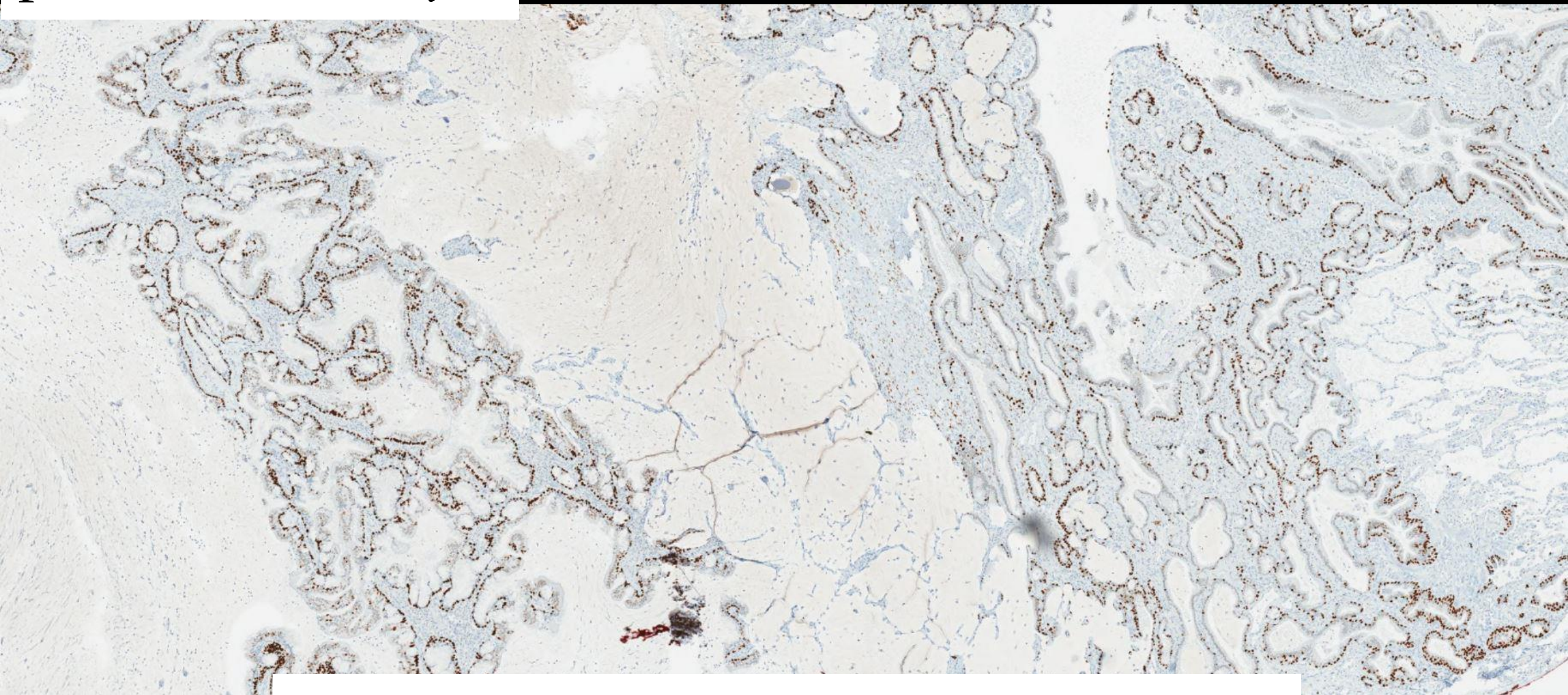
Papillary architecture



Cilia, mucinous cells, bilayered epithelium

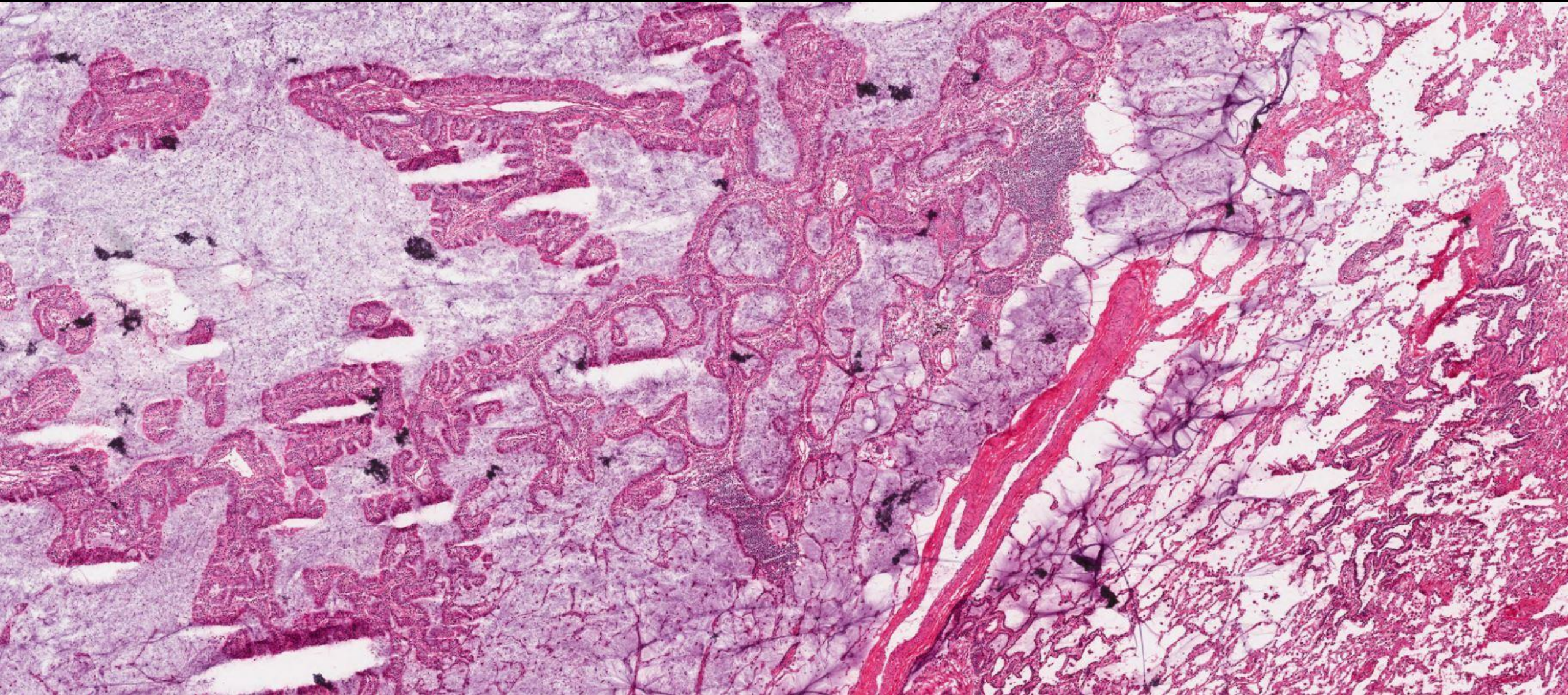


p63: basal cell layer

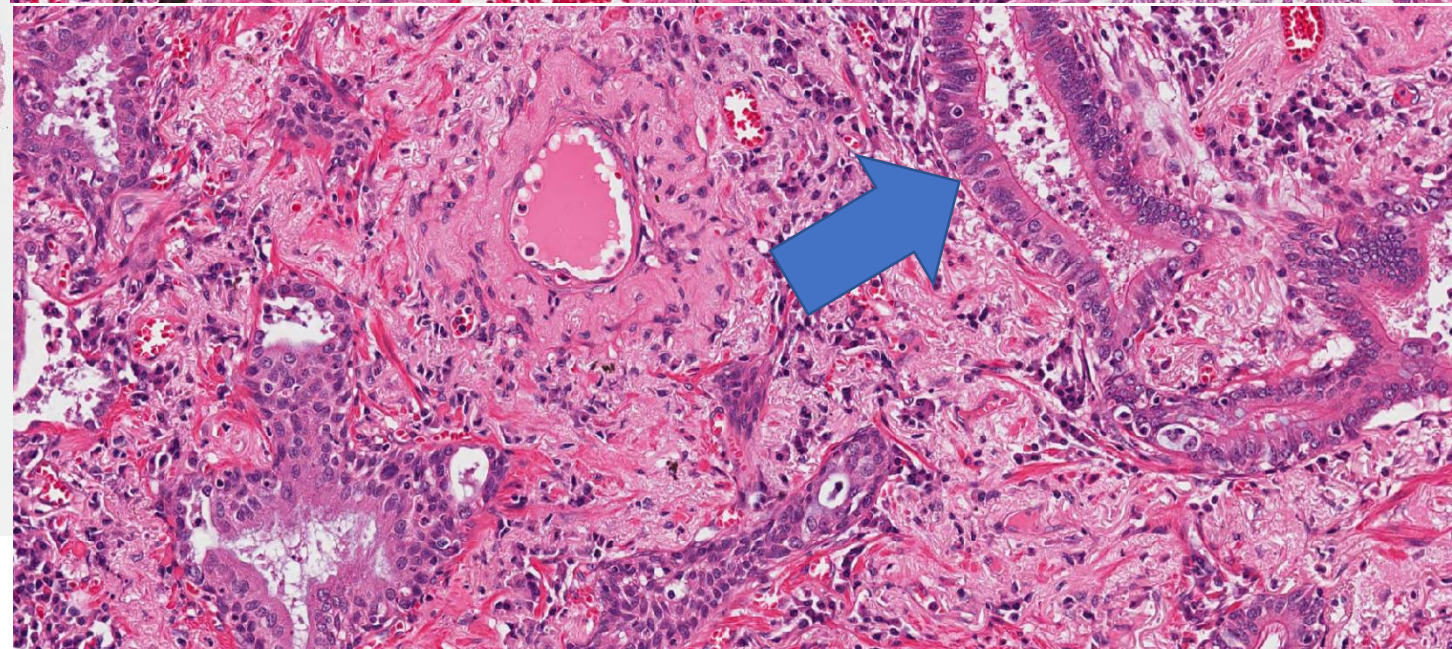
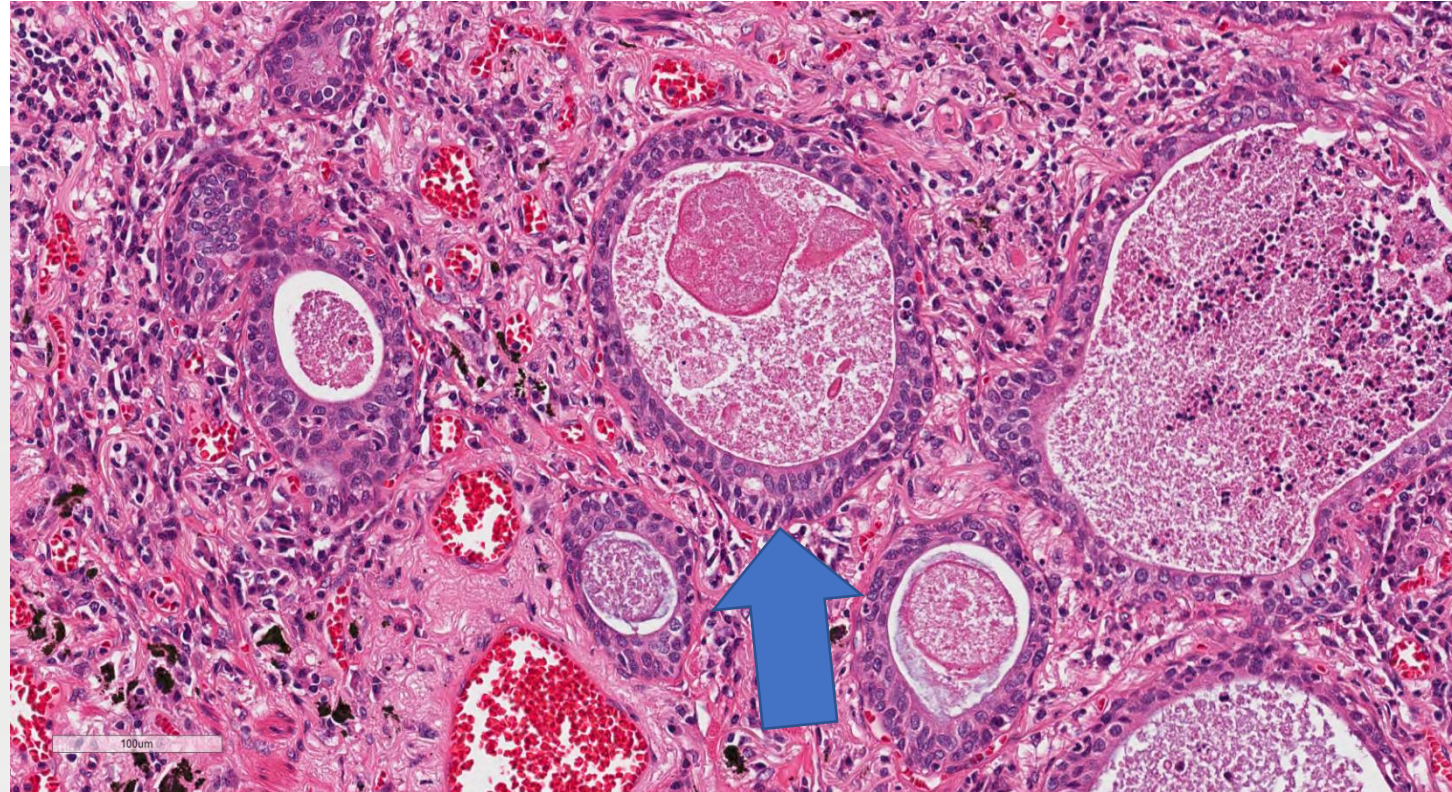
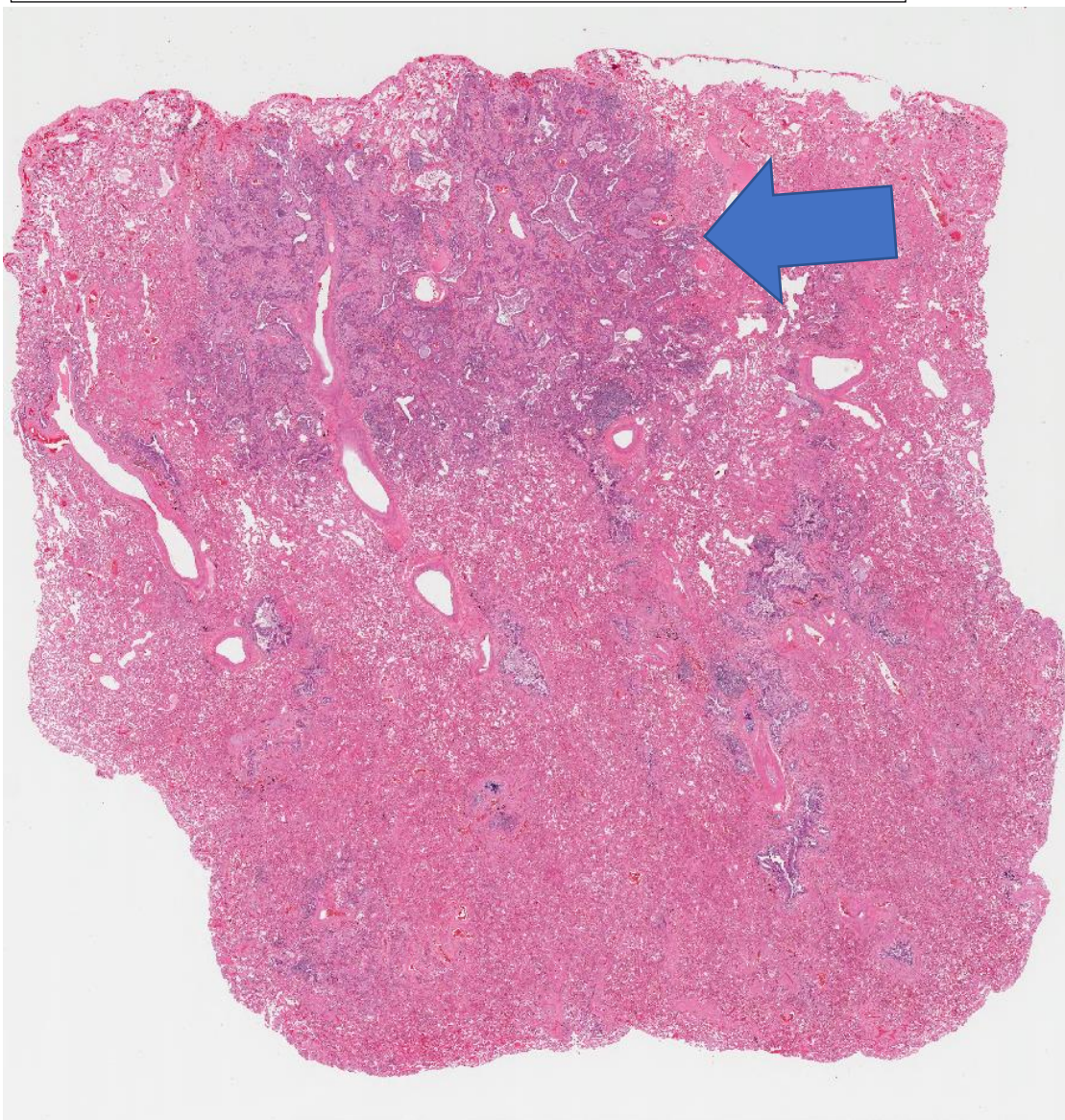


Ciliated muconodular papillary tumor

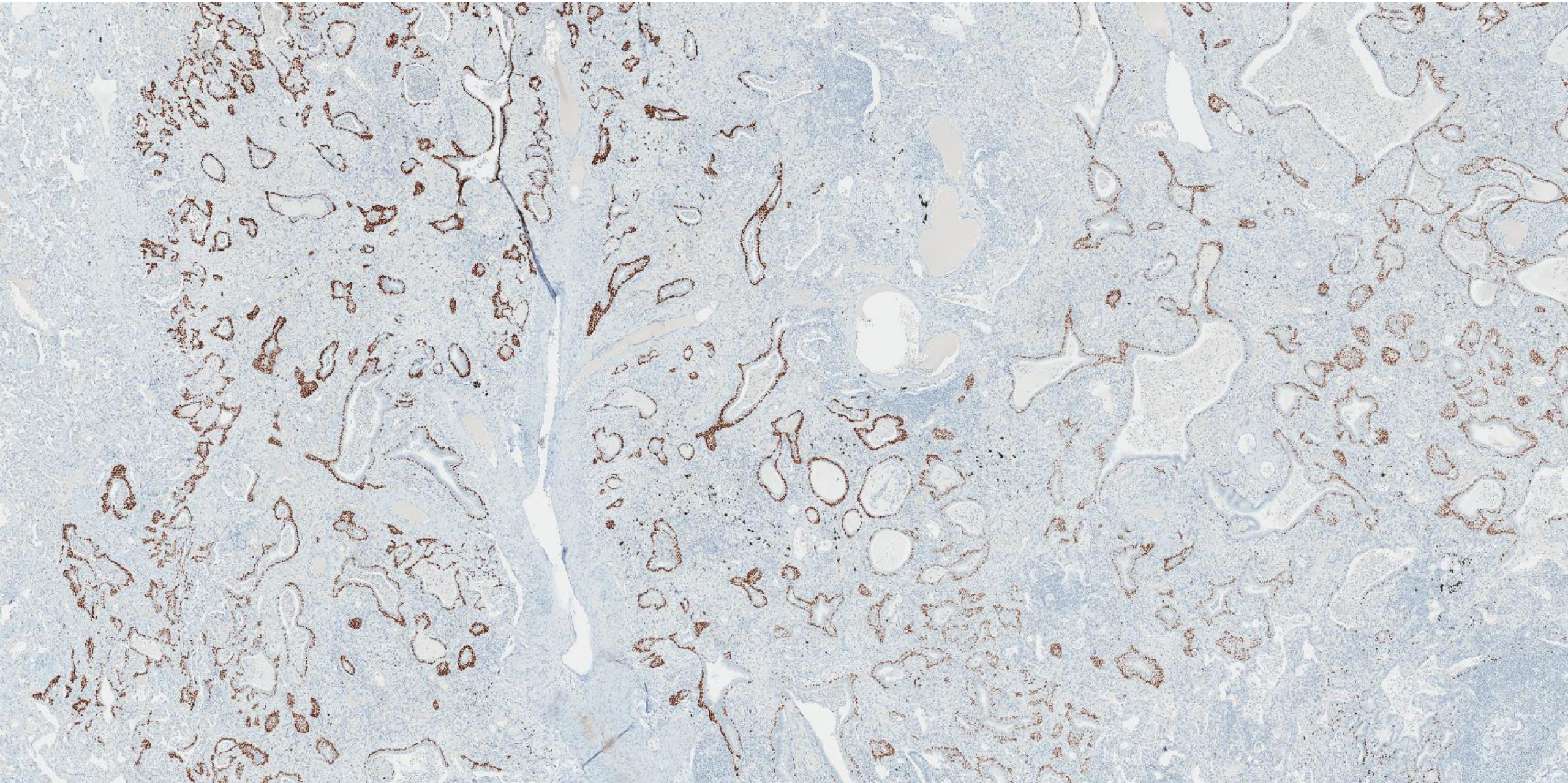
Beware of mucinous lesions on frozen section



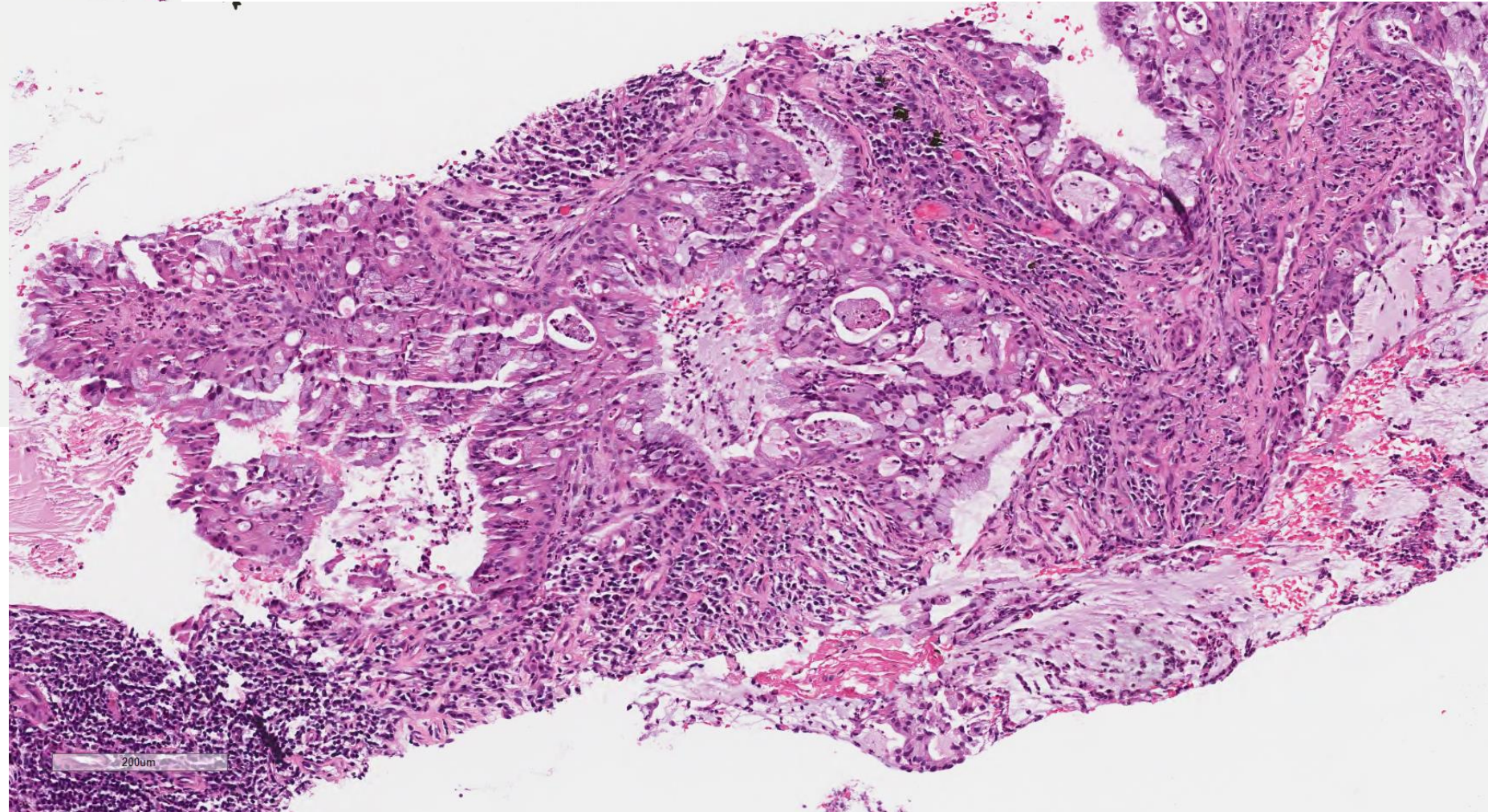
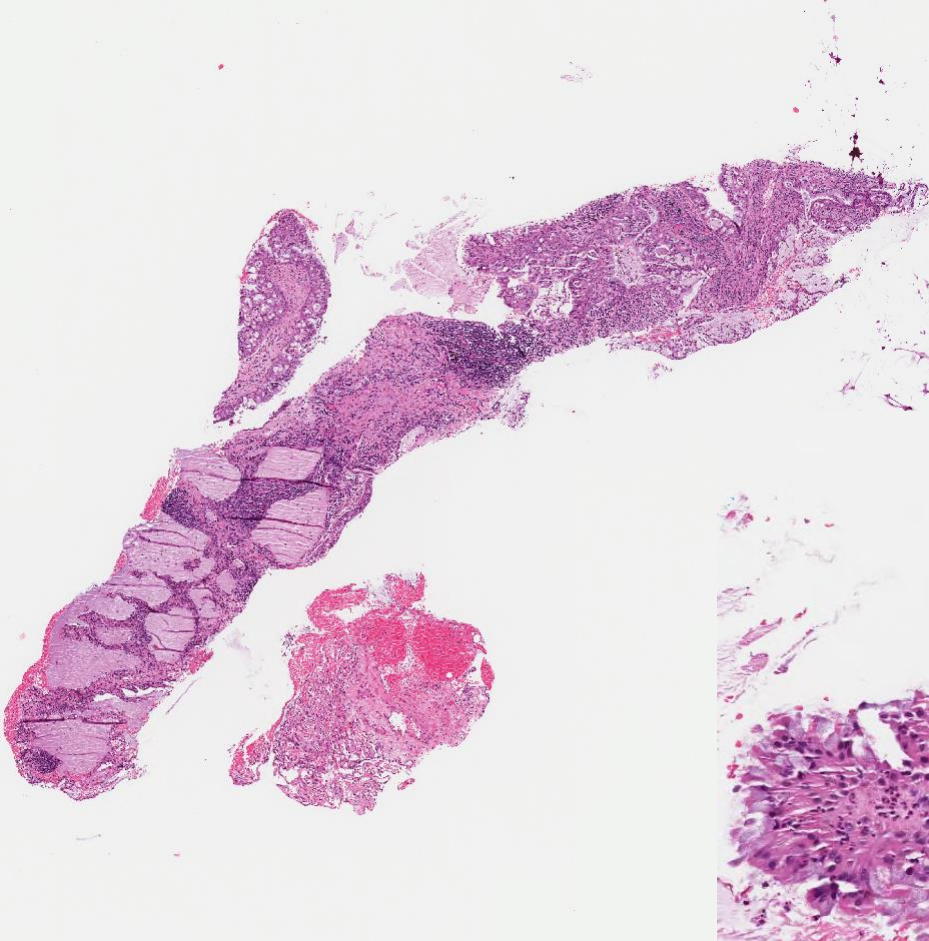
Bronchiolar adenoma



Bronchiolar adenoma: p40 highlights basal cell layer

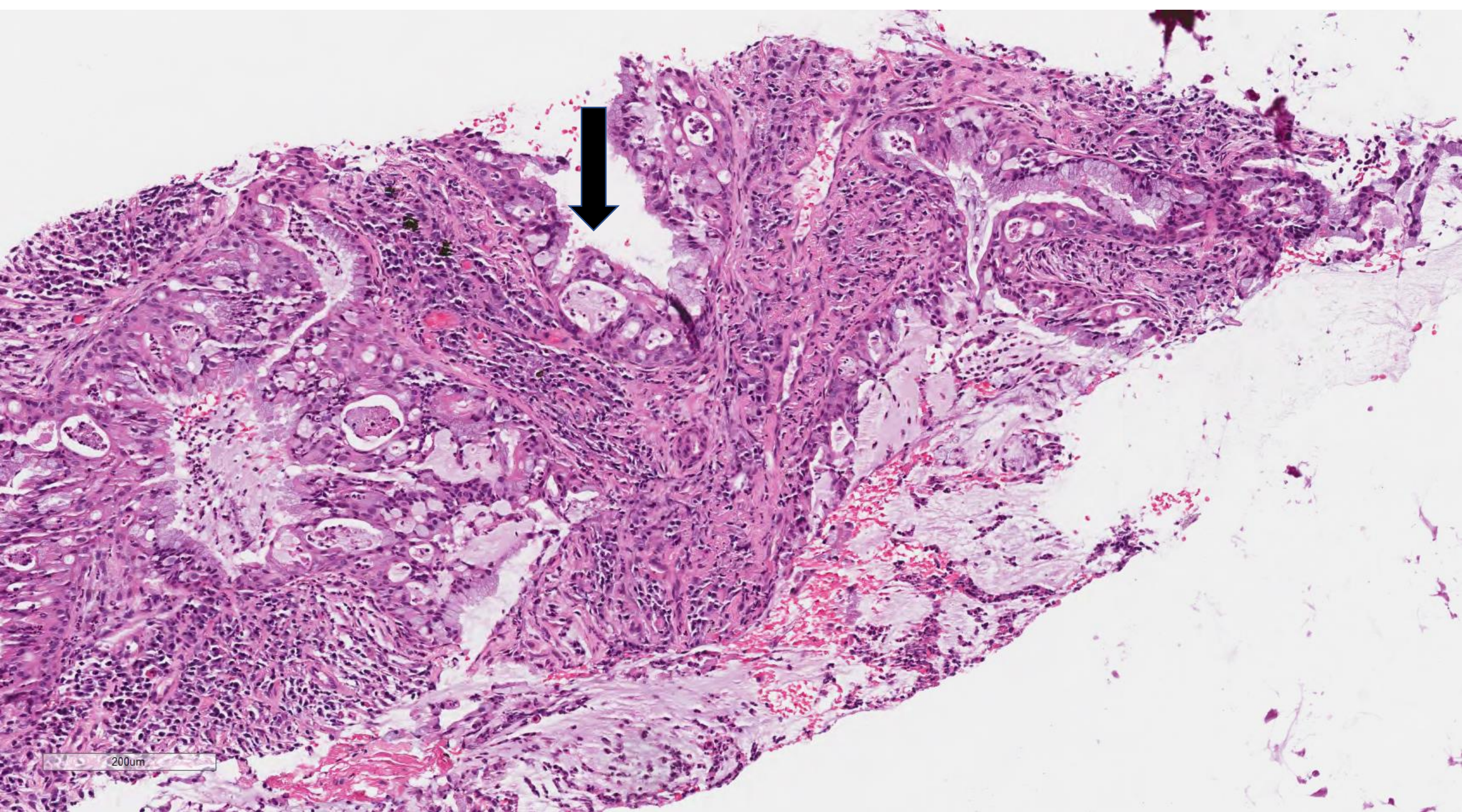


Ciliated muconodular papillary tumor (bronchiolar adenoma)

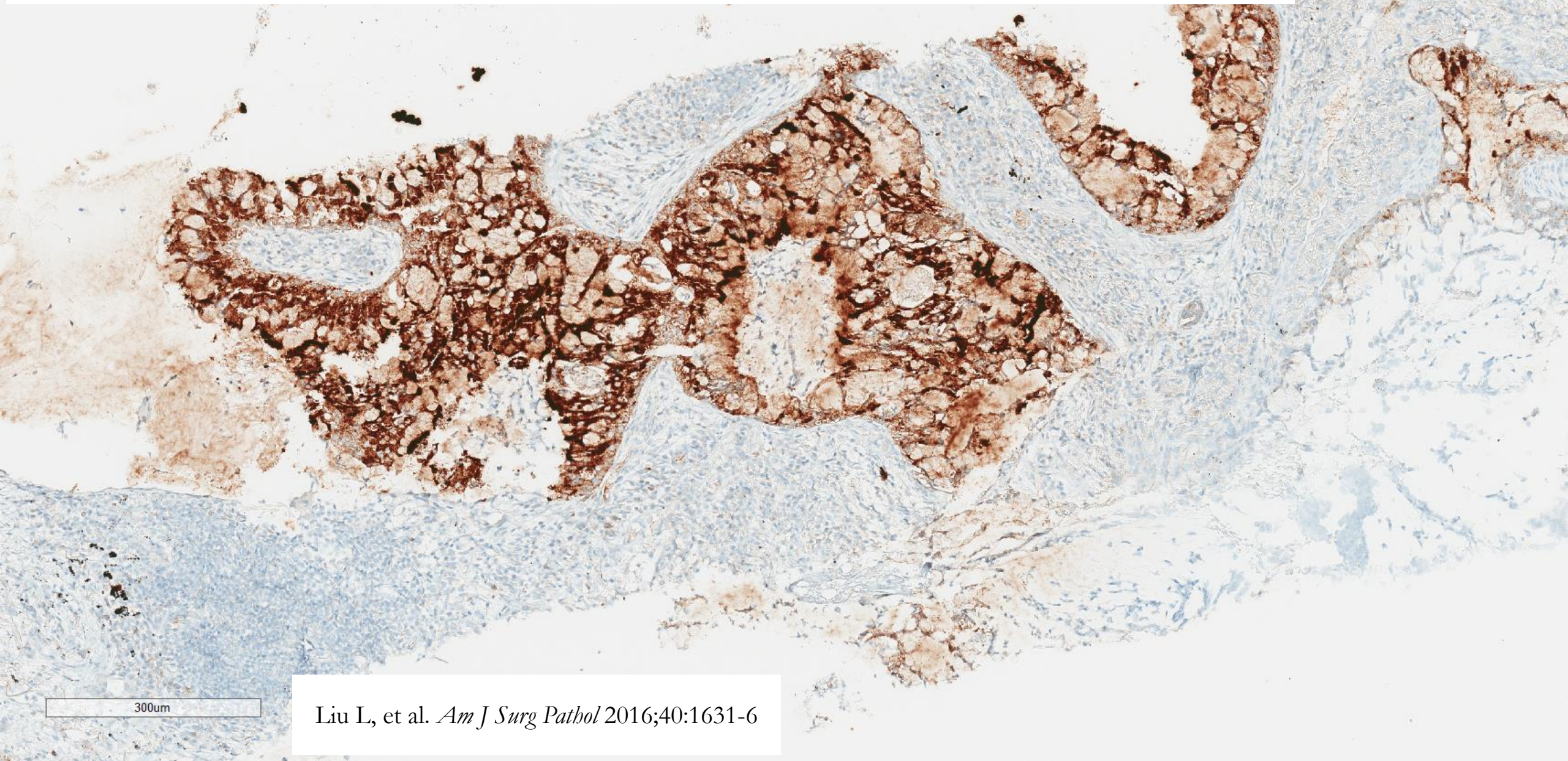


Sato S, et al. *Interact Cardiovasc Thorac Surg* 2010;5:685-7

Chang JC, et al. *Mod Pathol* 2018;42:1010-1026

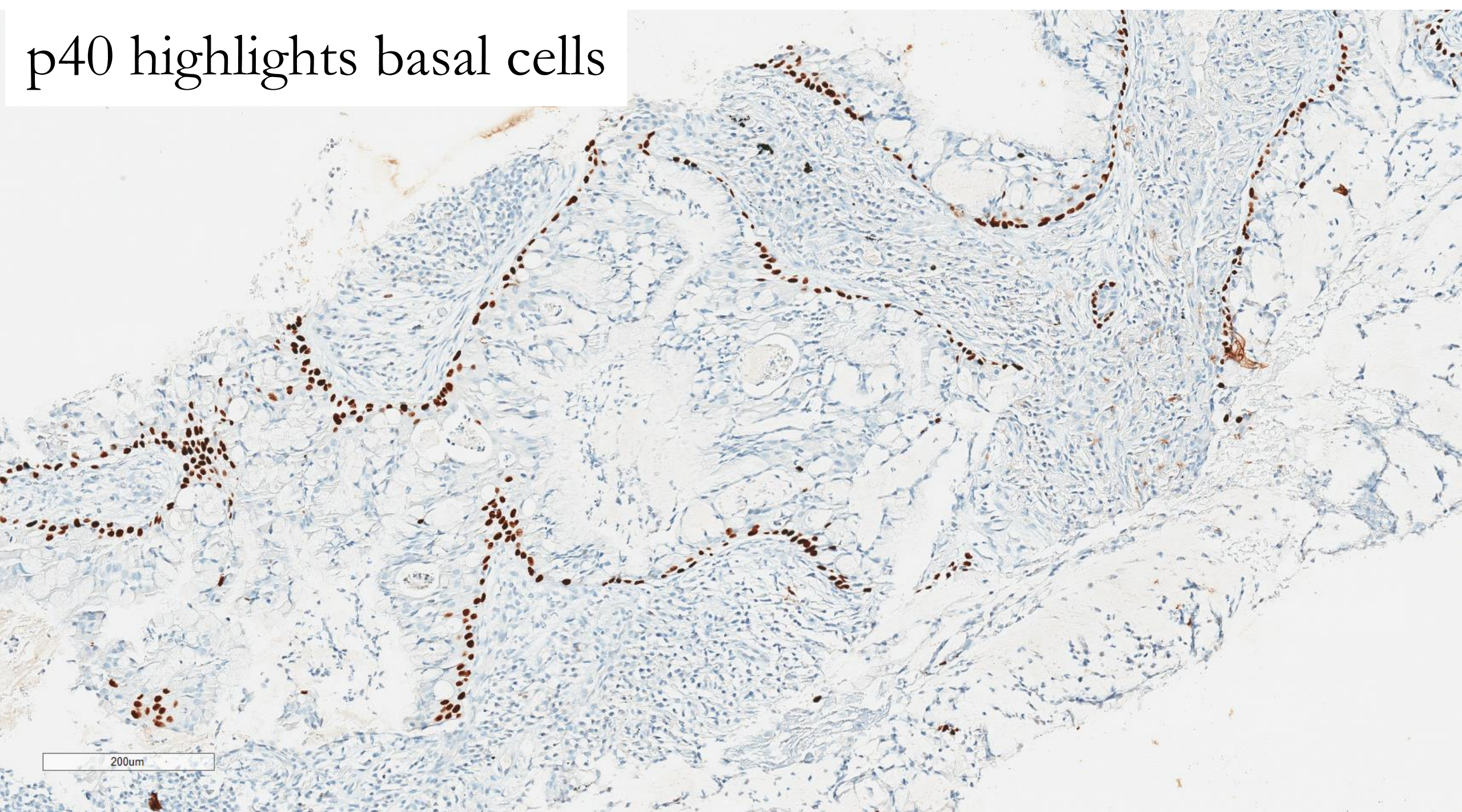


BRAF (40% of CMPT); BRAF V600E reported



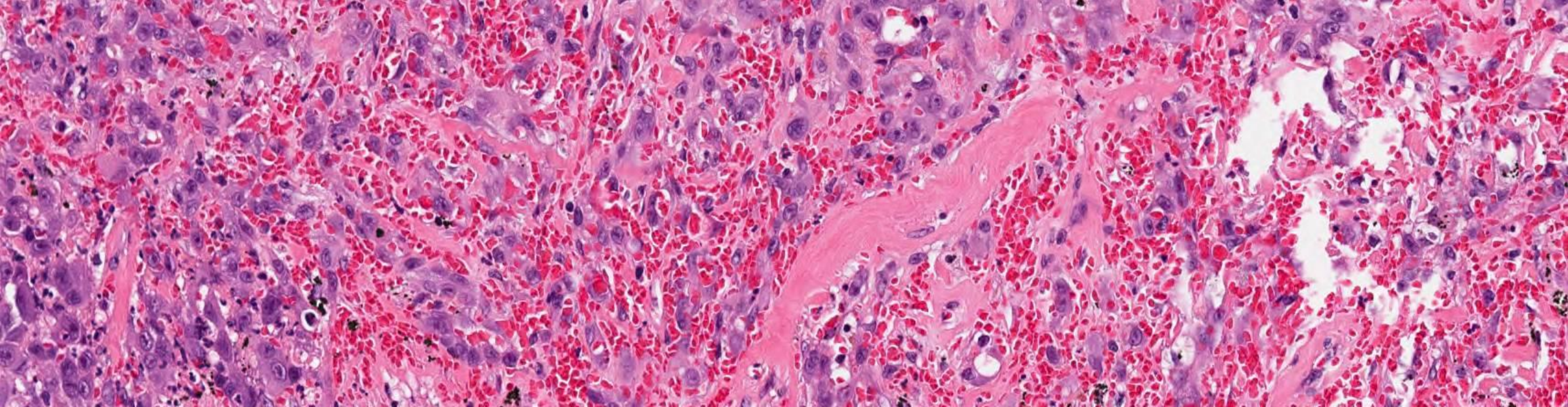
Liu L, et al. *Am J Surg Pathol* 2016;40:1631-6

p40 highlights basal cells



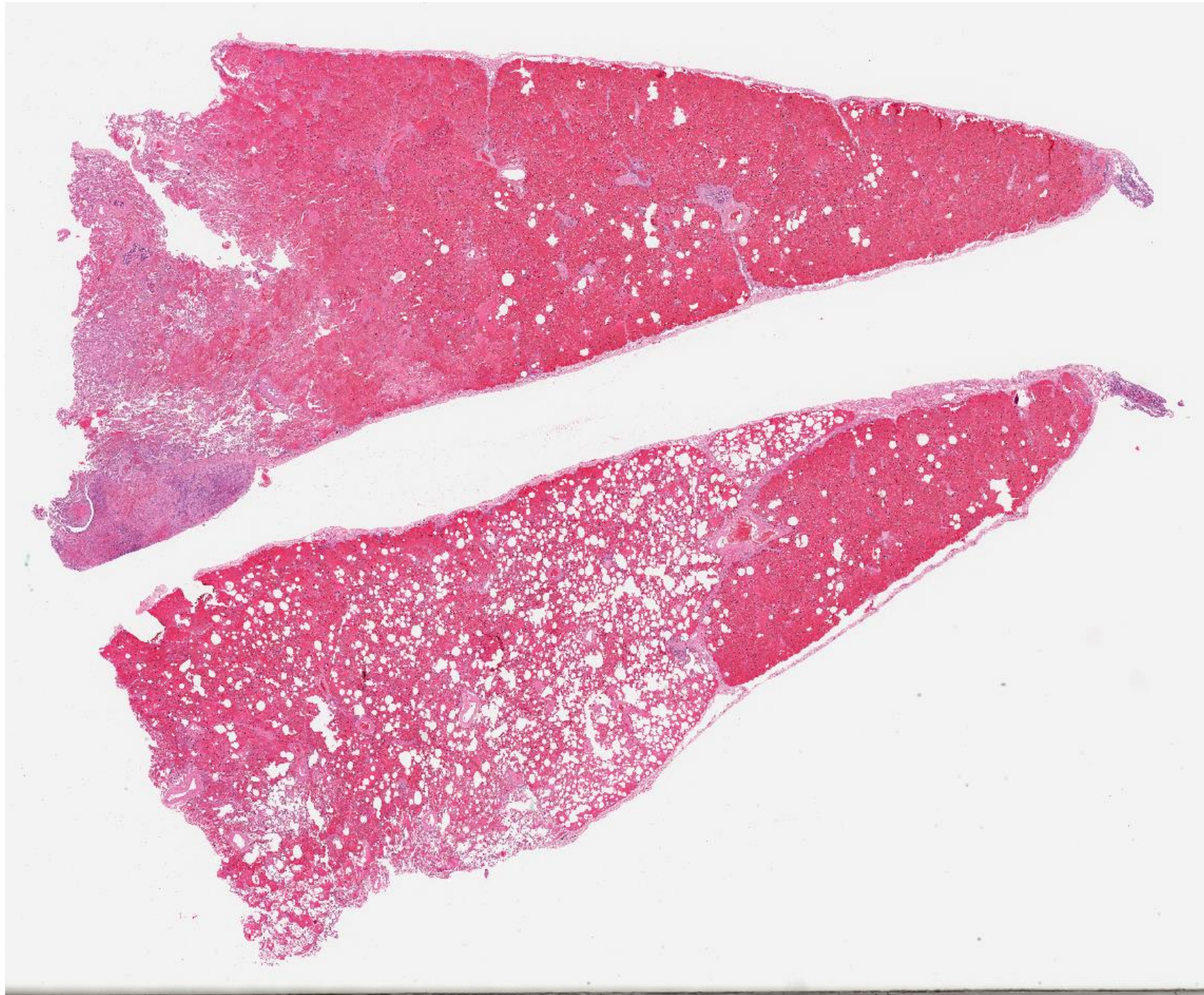
CILIATED MUCONODULAR PAPILLARY TUMOR (BRONCHIOLAR ADENOMA)

- Clinical: Small lung nodule
- H&E: Papillary + bilayered + mucinous cells + cilia
- Immunohistochemistry: basal cells (p63/p40/CK5/6)
- How to confirm? IHC + morphology



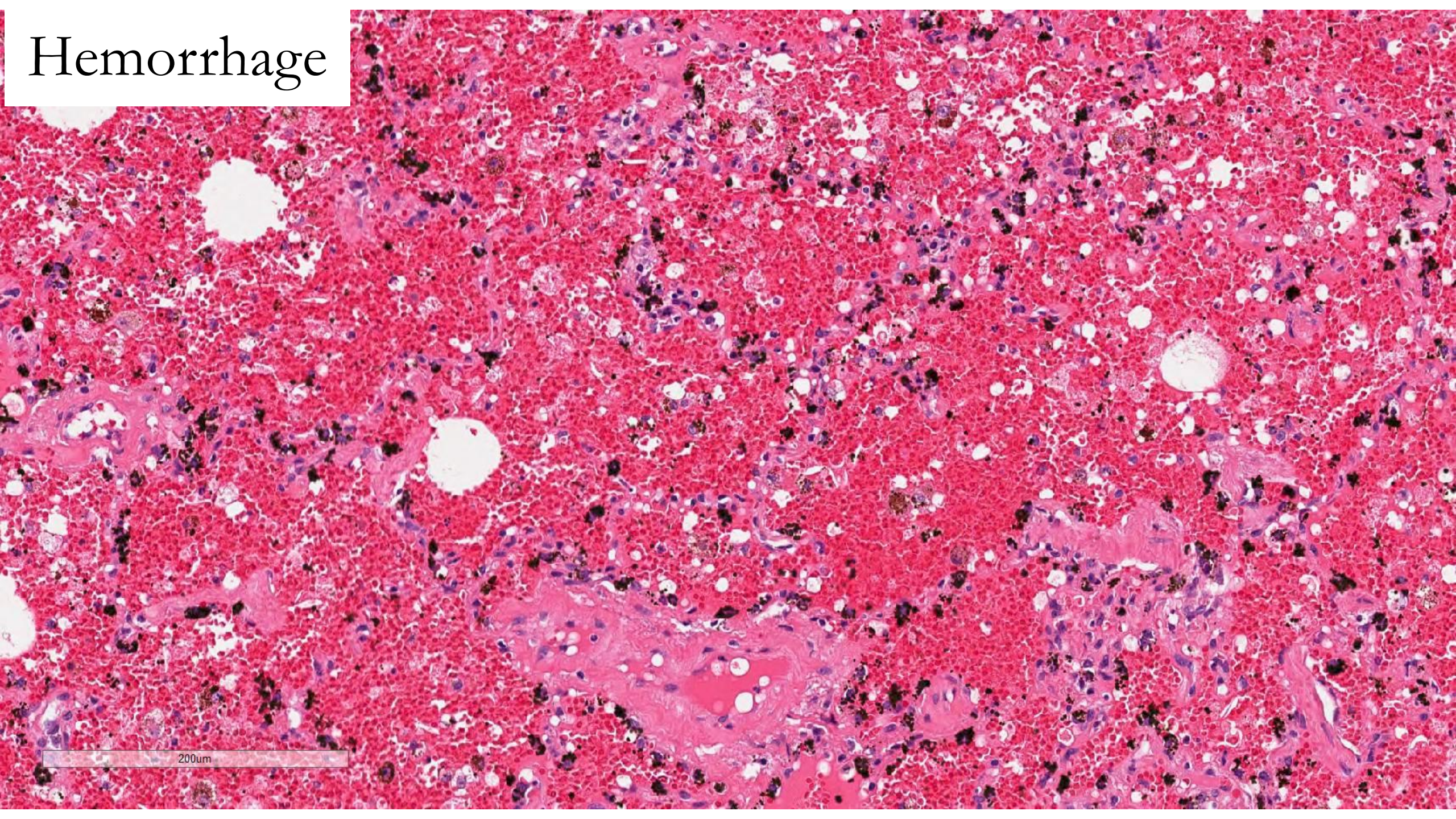
IS IT HEMORRHAGE WITH REACTIVE CELLS?

TUMOR 2



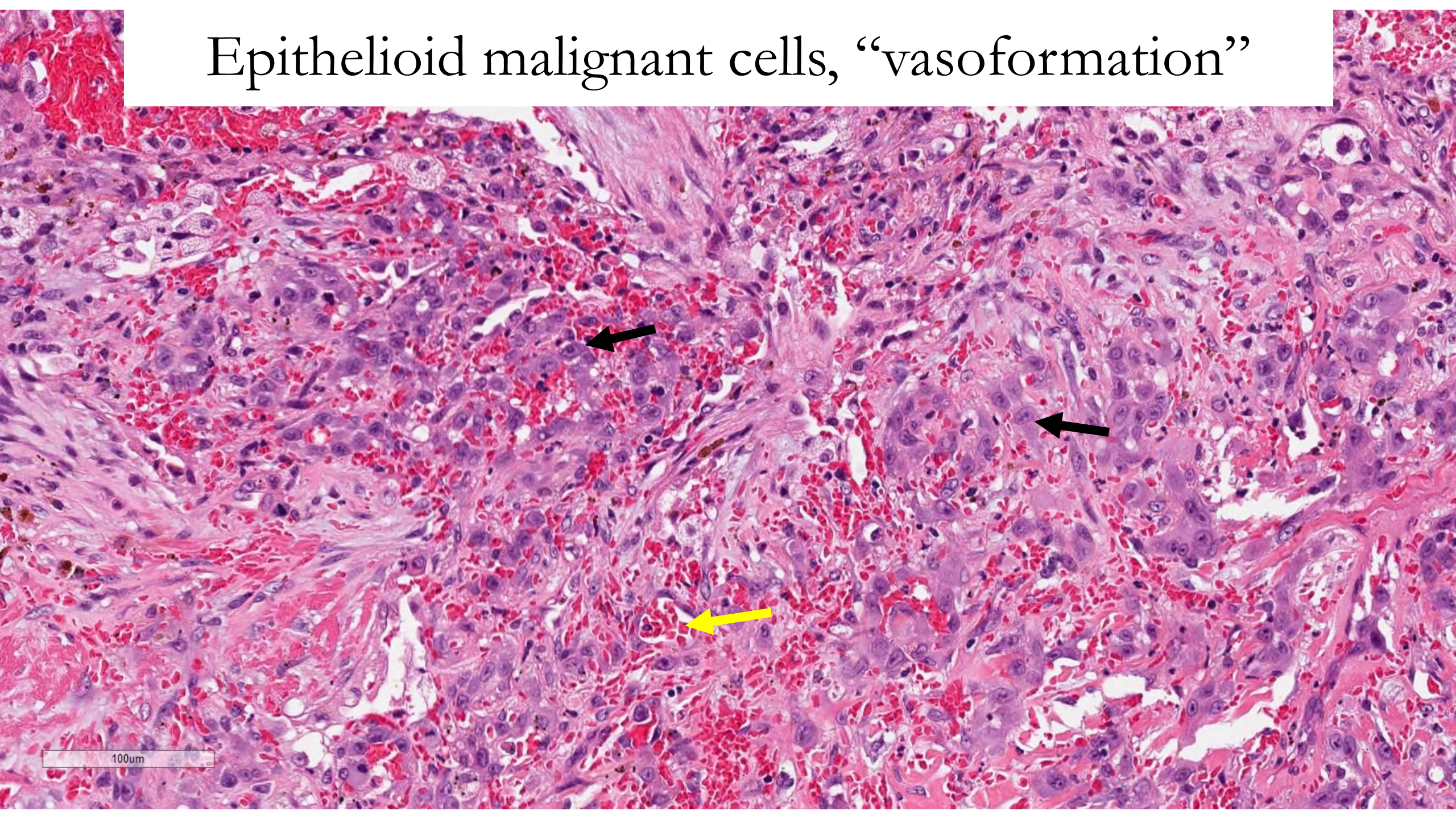
5mm

Hemorrhage



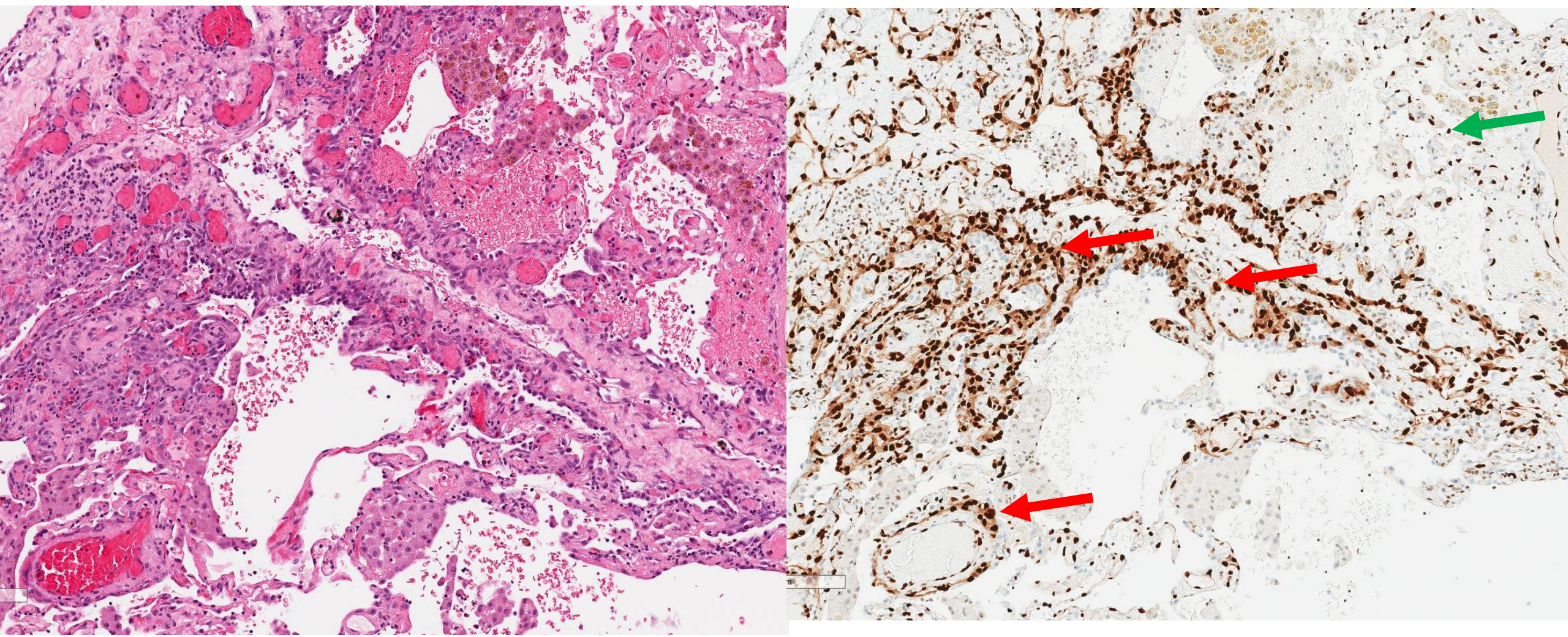
200um

Epithelioid malignant cells, “vasoformation”



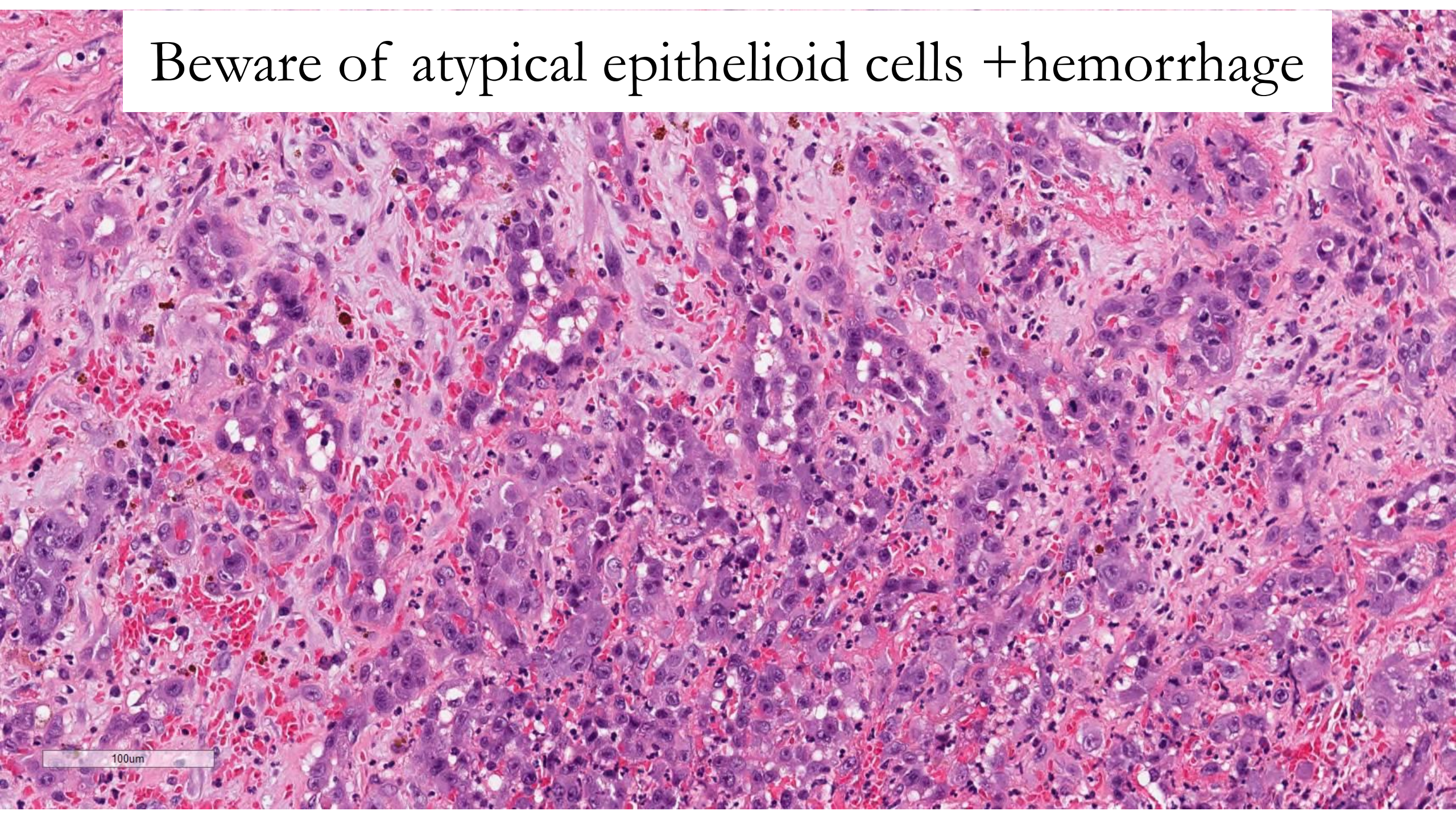
100um

ERG (nuclear endothelial marker)



Metastatic angiosarcoma

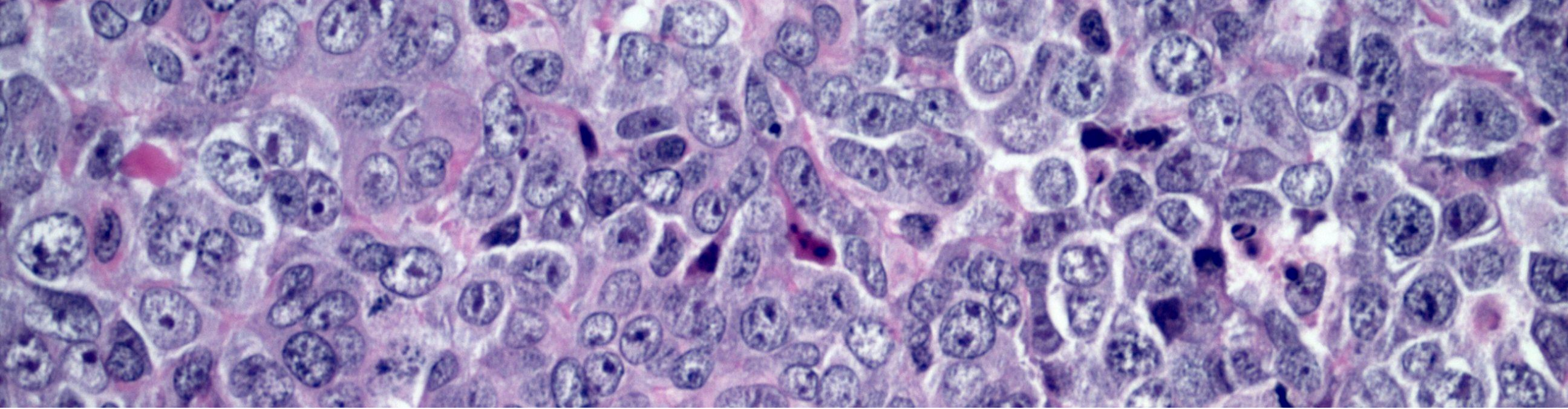
Beware of atypical epithelioid cells + hemorrhage



100um

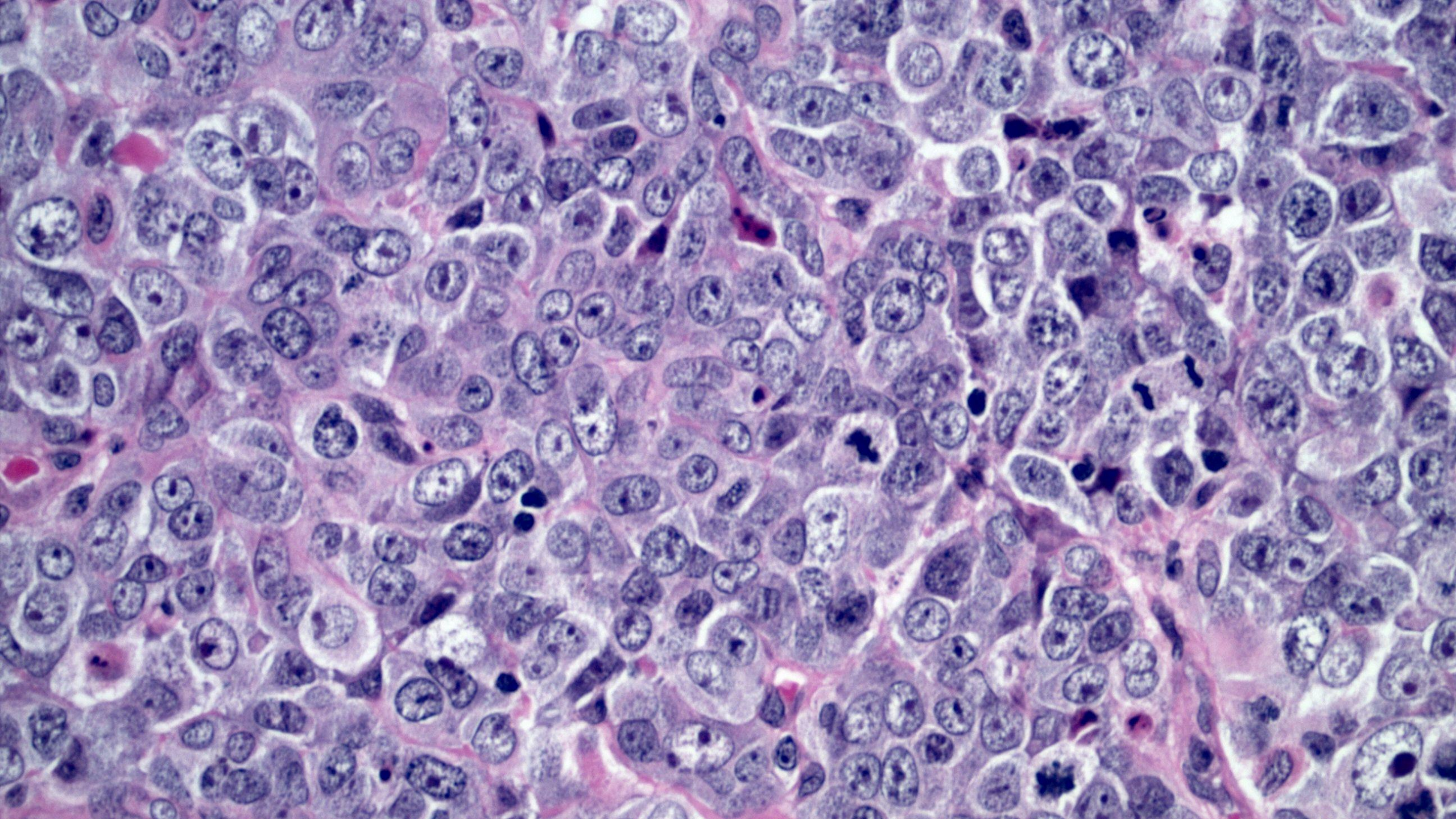
ANGIOSARCOMA

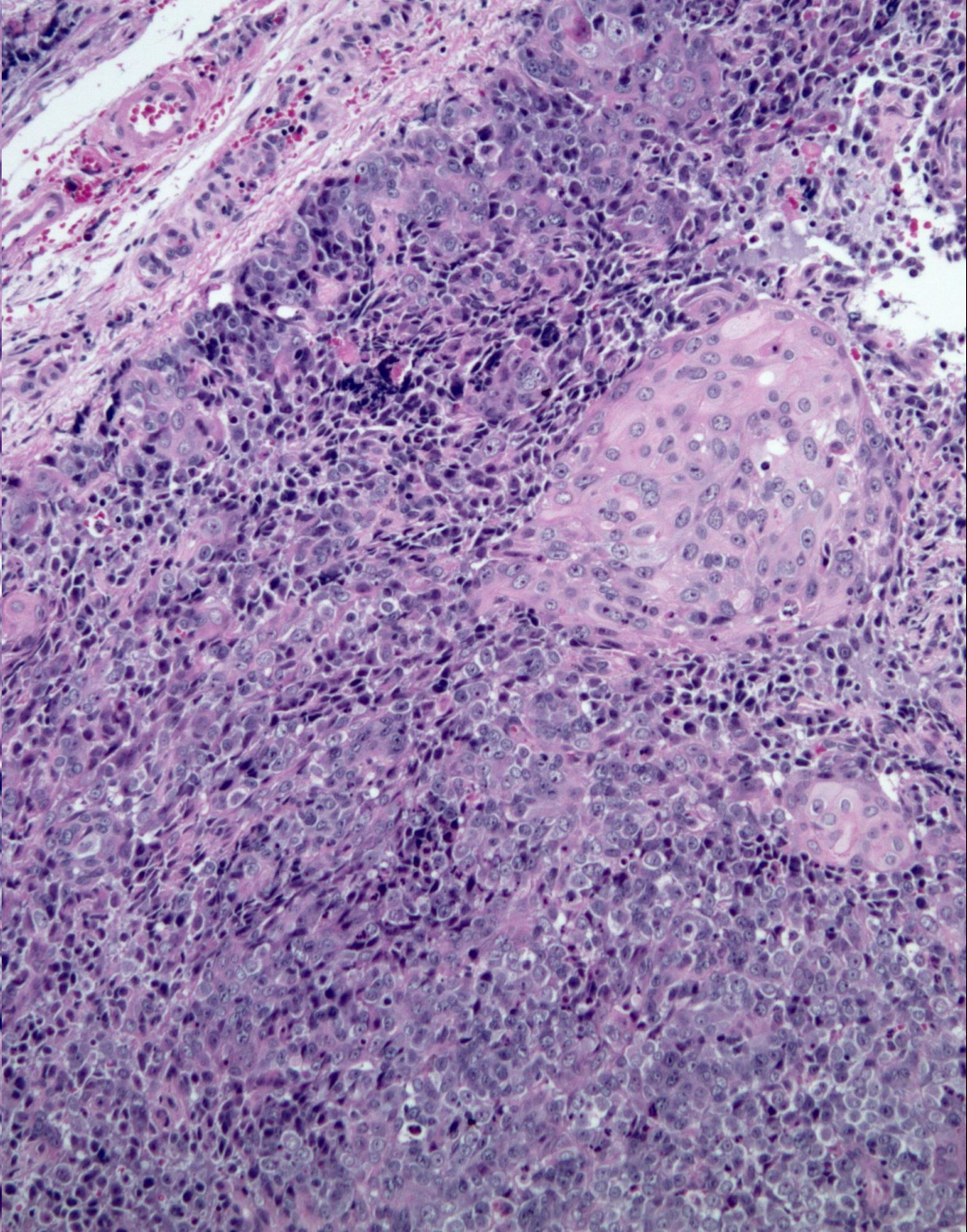
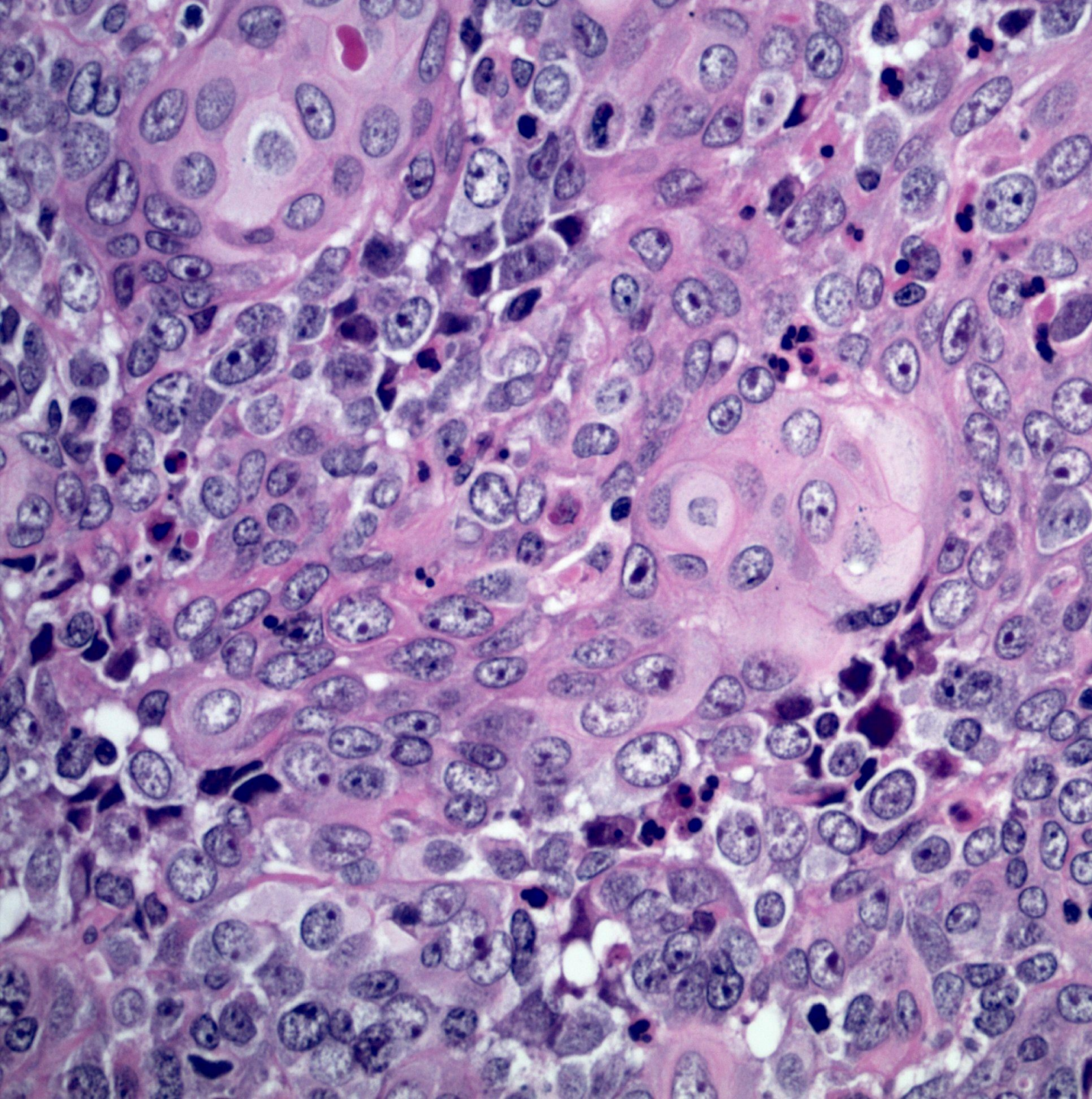
- Clinical: Bilateral infiltrates or nodules, patients can be young, history of angiosarcoma +/-
- H&E: Hemorrhage + malignant epithelioid cells along pleura or interlobular septa
- Immunohistochemistry: ERG, CD31 (macrophages are +)
- How to confirm? H&E + IHC



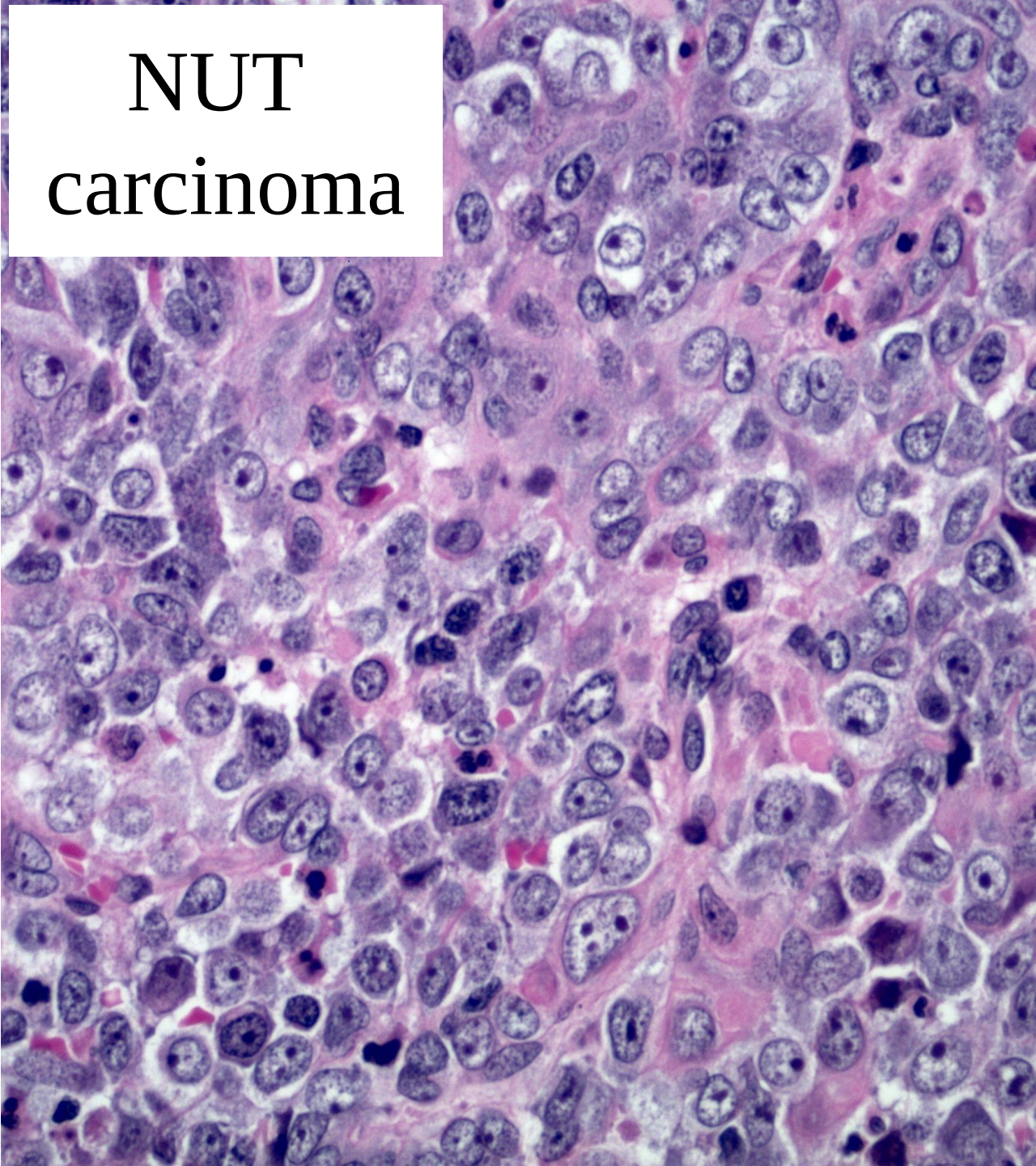
SQUAMOUS CELL CARCINOMA?

TUMOR 3

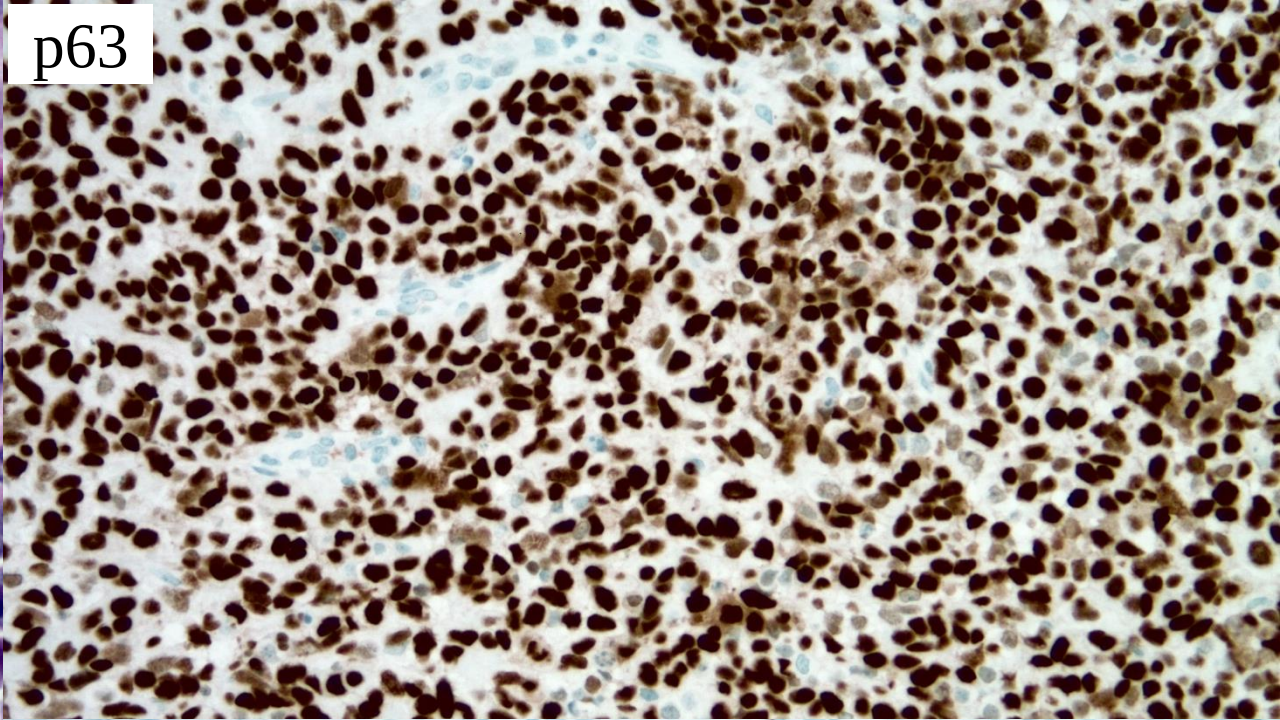




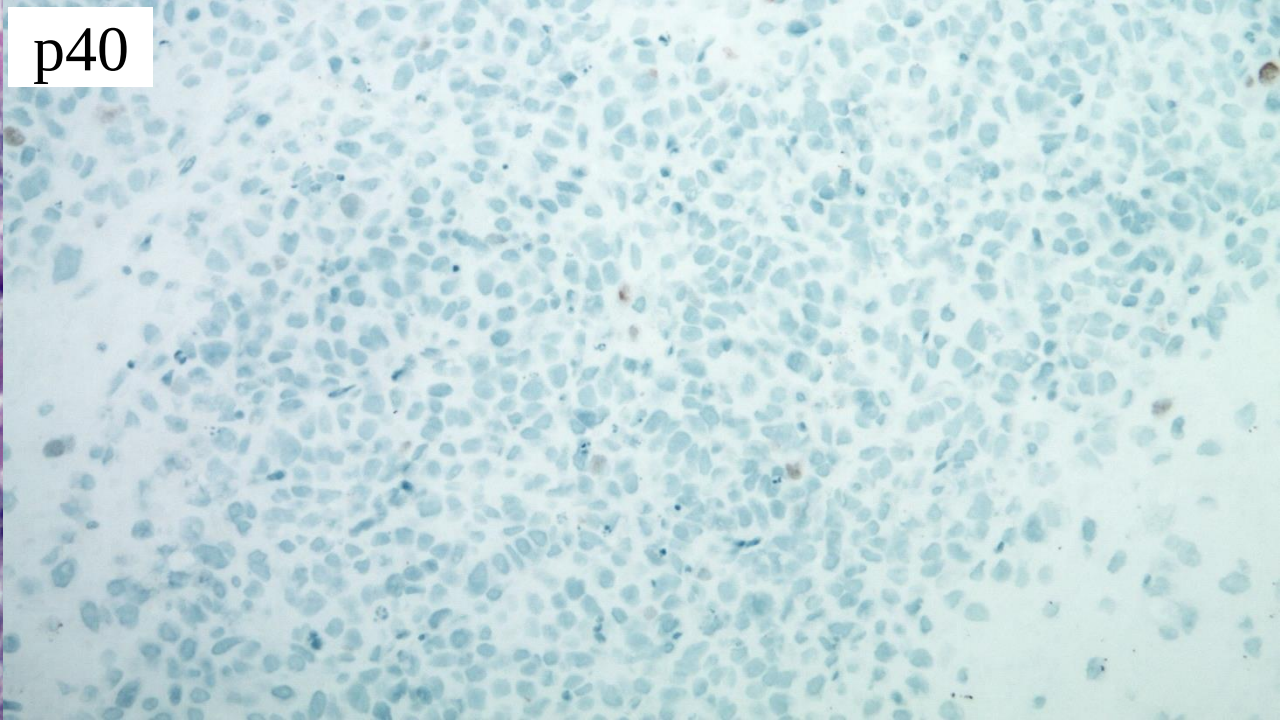
NUT carcinoma



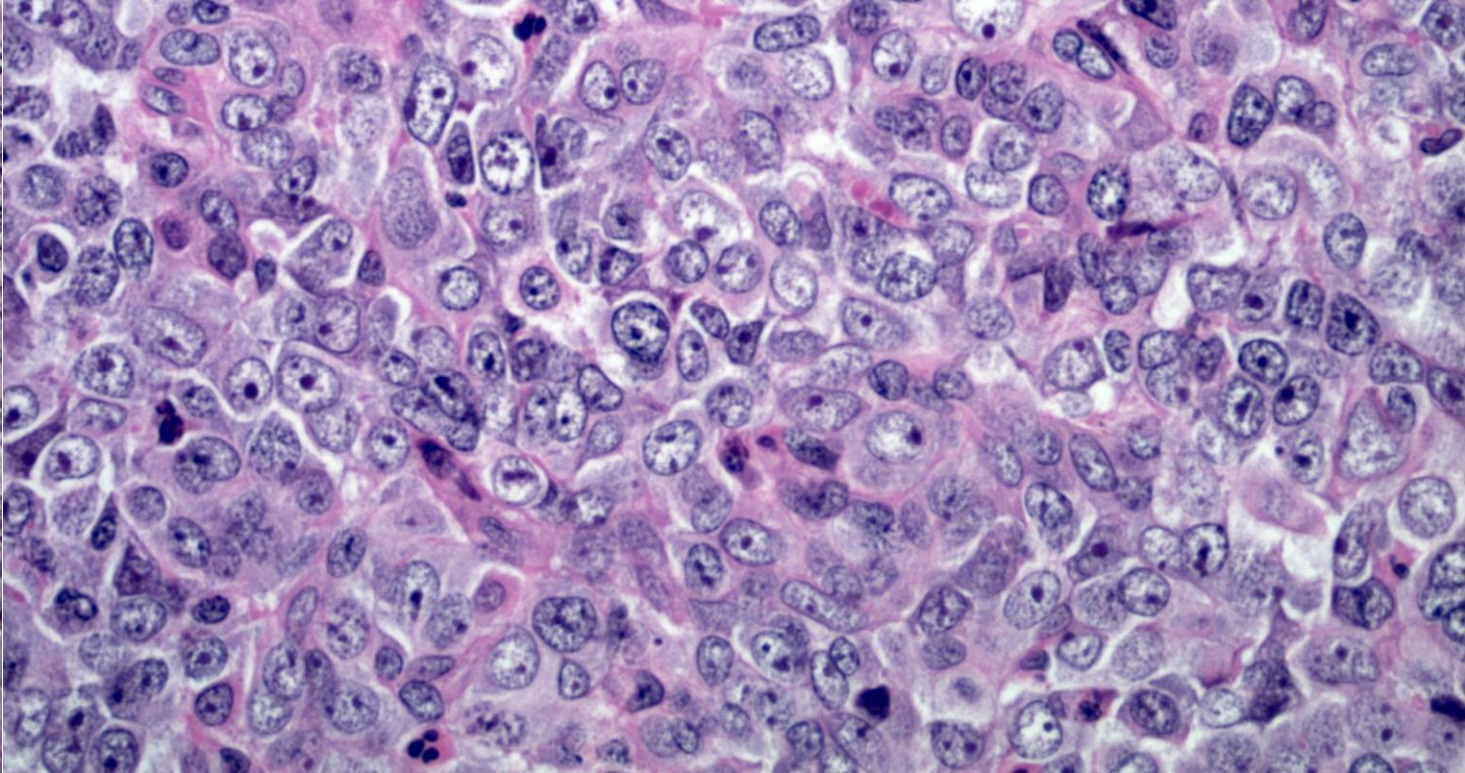
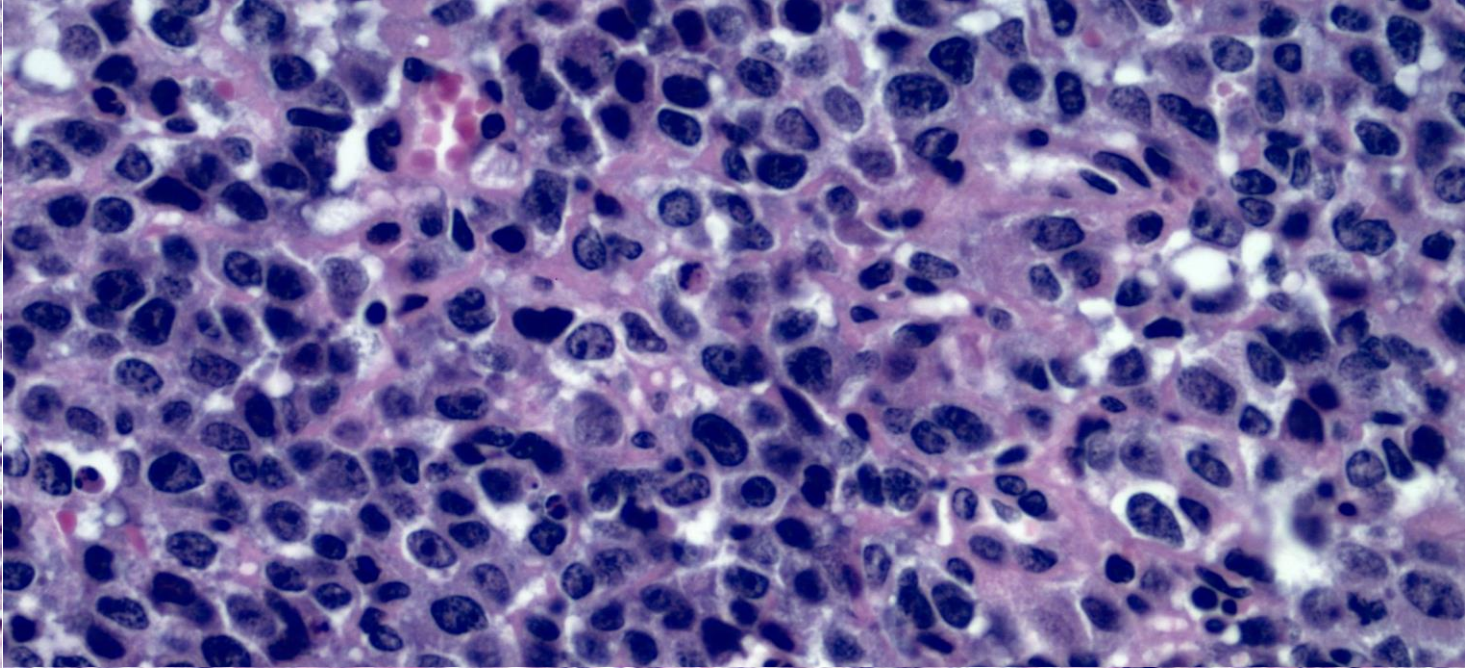
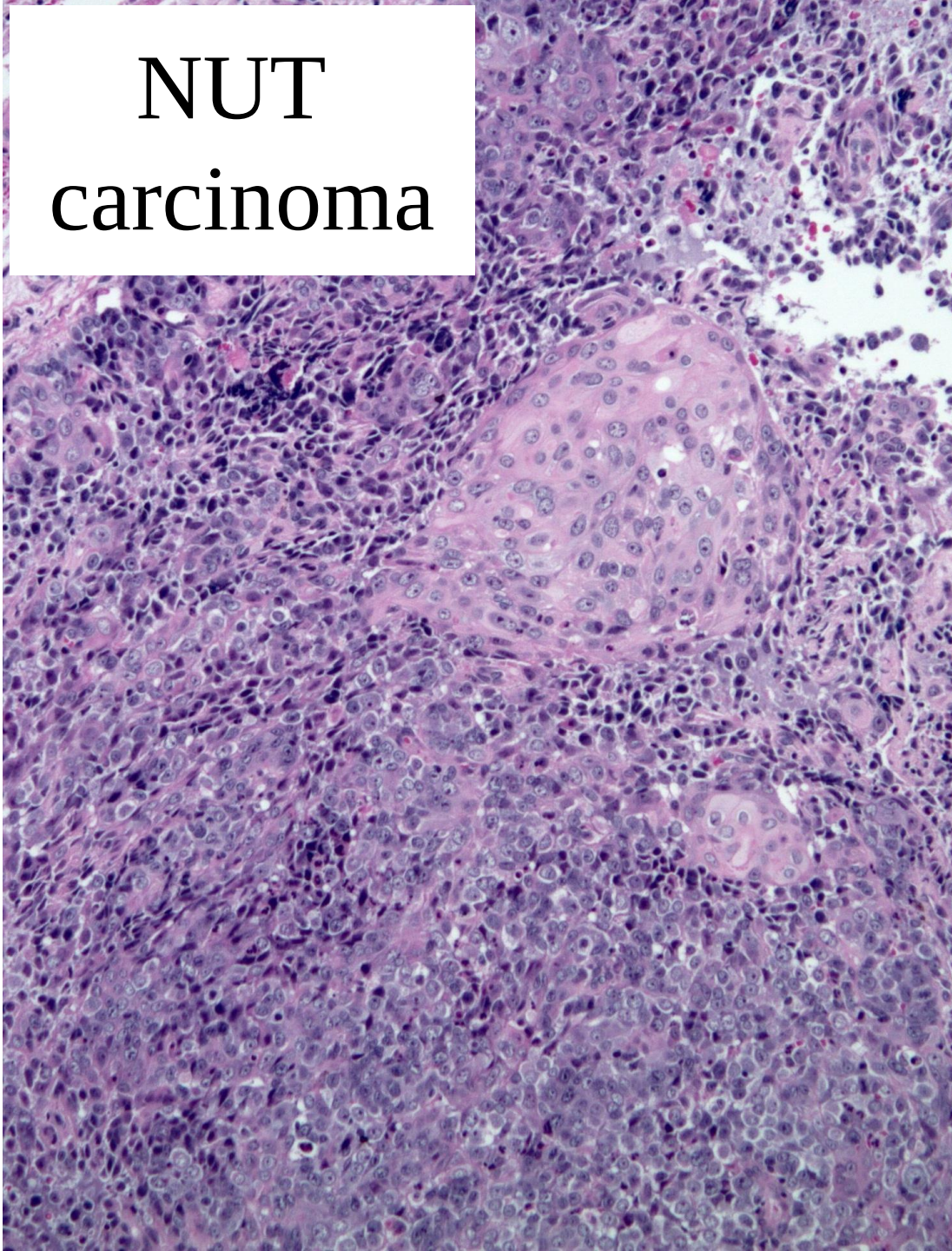
p63



p40



NUT carcinoma



The Isoform Matters in NUT Carcinoma: A Diagnostic Pitfall of p40 Immunohistochemistry

October 2020

Letters to the Editor

e177

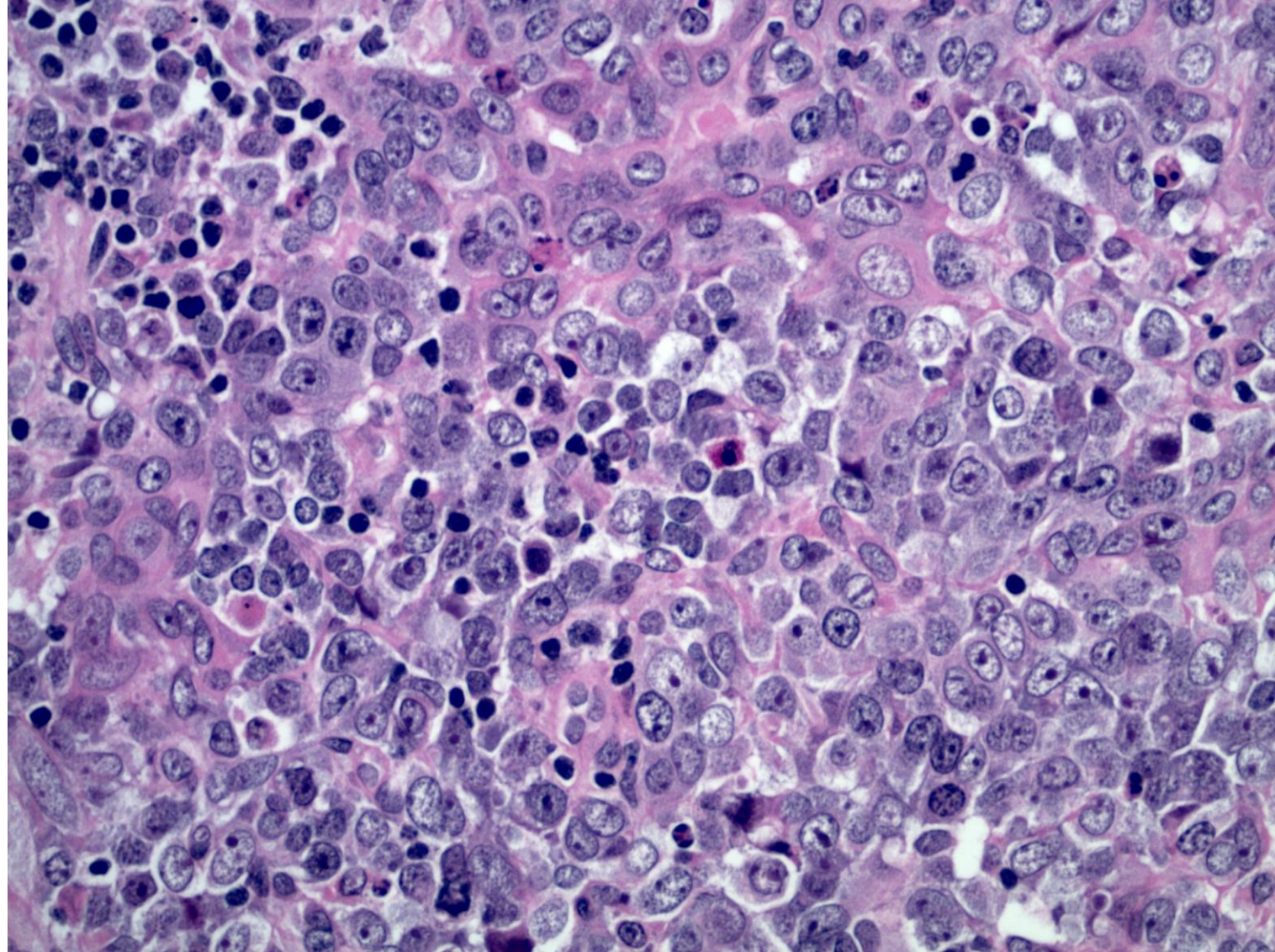
Table 1. Patient Characteristics and Immunohistochemical Results of NUT Carcinoma

No	Age, y	Sex	Organ	Specimen	IHC		NUT	FISH
					p63	p40		<i>NUTM1</i> Rearrangement
1	14	F	Lung	TBB	(+, diffuse)	(±, focal)	(+)	+
2	30	F	Lung	TBB	(+, rare)	(-)	(+)	+
3	35	M	Lung	TBB	(+, diffuse)	(-)	(+)	+
4	39	M	Lung	TBB	(+, focal)	(-)	(+)	NA
5	40	F	Lung	TBB	(+, diffuse)	(-)	(+)	+
6	41	M	Trachea	Operative specimen	(+, diffuse)	(±, focal)	(+)	+
7	18	F	Liver	Needle biopsy	(+, diffuse)	(±, patchy)	(+)	+

F, female; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; M, male; NA, not available owing to severe crush artifacts; NUT, nuclear protein in the testis; TBB, transbronchial biopsy.

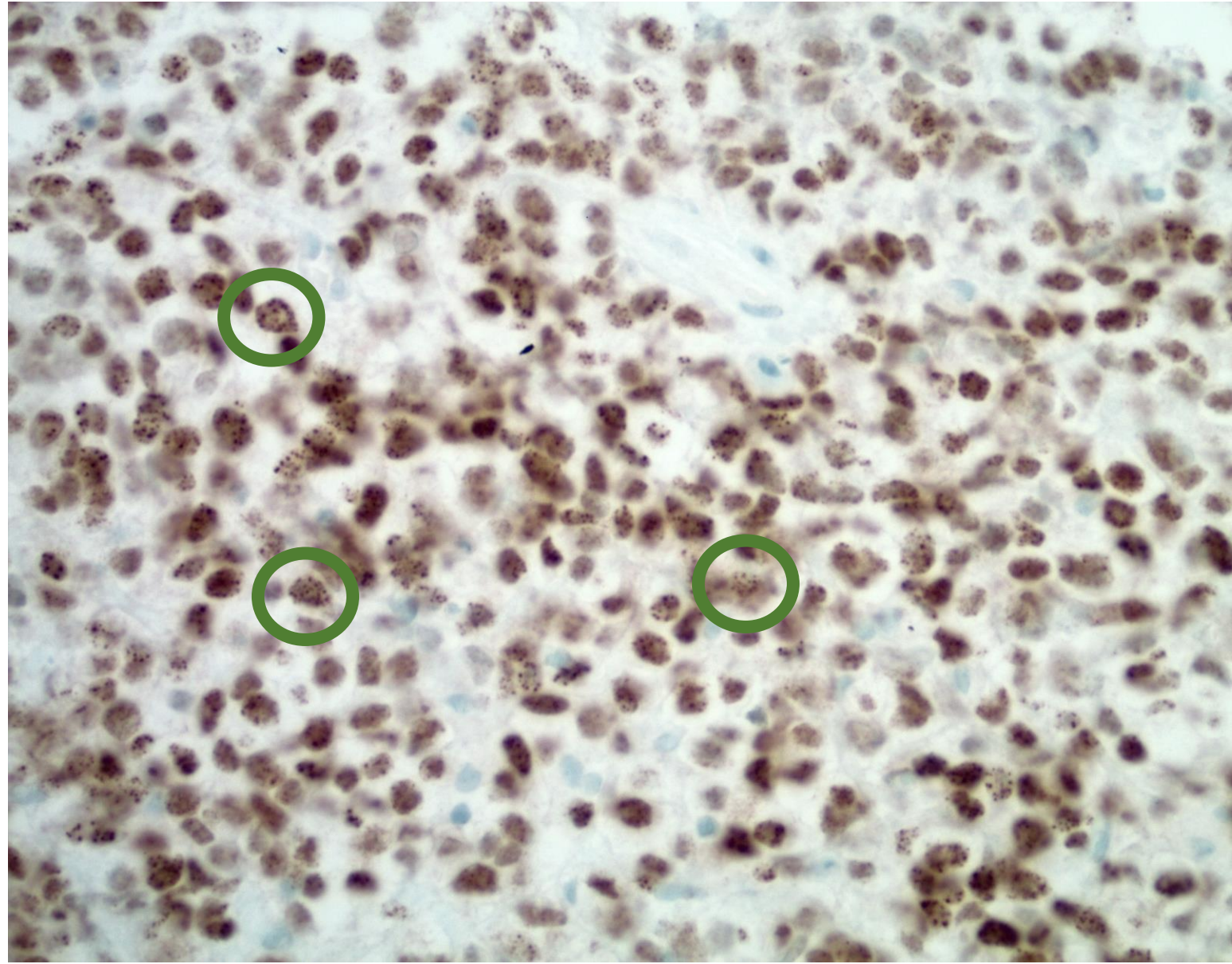
NUT carcinoma

- Very aggressive
- Median survival: 7.5-9 months



NUT carcinoma: how to confirm?

- NUT immunohistochemistry: speckled nuclear staining
- FISH
- NGS



We are seeing more cases

INTERNATIONAL
NUT MIDLINE CARCINOMA
REGISTRY

Home About Us Families Doctors Enroll Clinical Trials Donate Publications Contact

Clinical Trials

There is a clinical trial investigating the maximum tolerated dose and safety profile of a BET bromodomain inhibitor, BI 894999, in patients with advanced malignancies. Enrollment is **open** at the following US locations:

Dana-Farber Cancer Institute in Boston, MA
Memorial Sloan-Kettering Cancer Center in New York, NY
Cleveland Clinic in Cleveland, OH
The University of Texas MD Anderson Cancer Center in Houston, TX

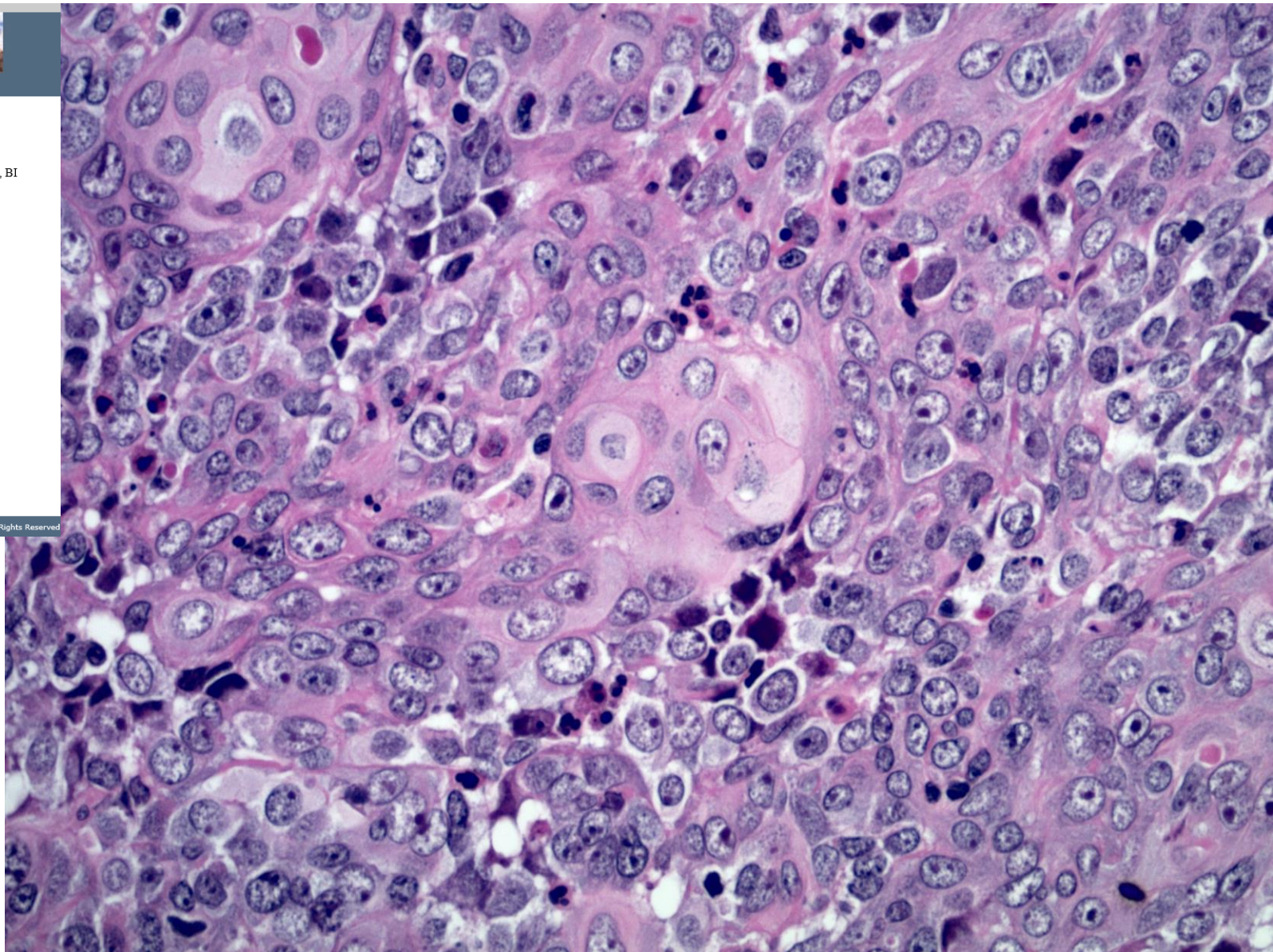
Additional information about this trial can be found at the following link:
<https://clinicaltrials.gov/ct2/show/NCT02516553?cond=BI+894999>

For inquiries regarding entry into these trials, please contact Dr. Chris French at cfrench@partners.org, tel 617 525-4415.

BRIGHAM AND WOMEN'S HOSPITAL DANA-FARBER CANCER INSTITUTE Children's Hospital Boston HARVARD MEDICAL SCHOOL

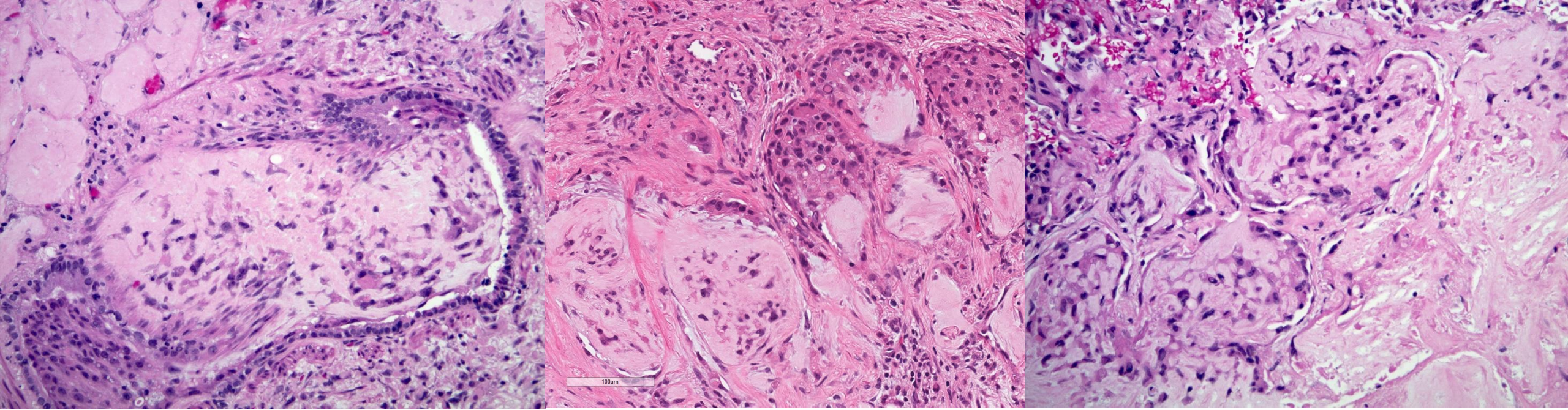
Copyright © 2011 International NUT Midline Carcinoma Registry. All Rights Reserved

- Phase 1 Clinical trial: BET bromodomain inhibitor BI 894999



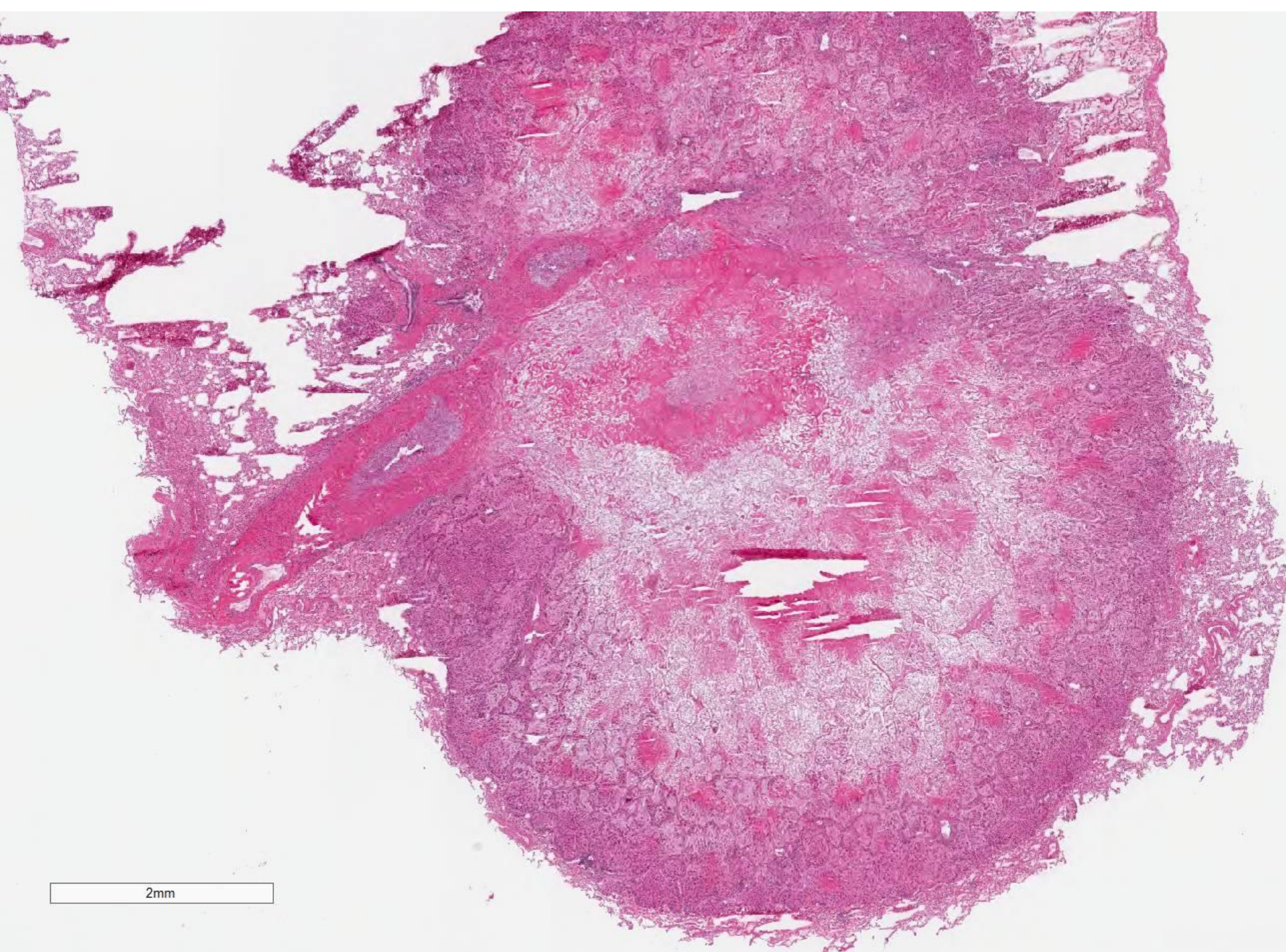
NUT CARCINOMA

- Clinical: young patient, mediastinal mass
- H&E: poorly differentiated carcinoma, abrupt keratinization
- Immunohistochemistry: Keratin +, TTF-1 neg (most), p63 + (most), p40+ (most, but some neg!), can be SALL4 +!!
- How to confirm? IHC (C52B1) or FISH/NGS: *NUTM1* rearrangement



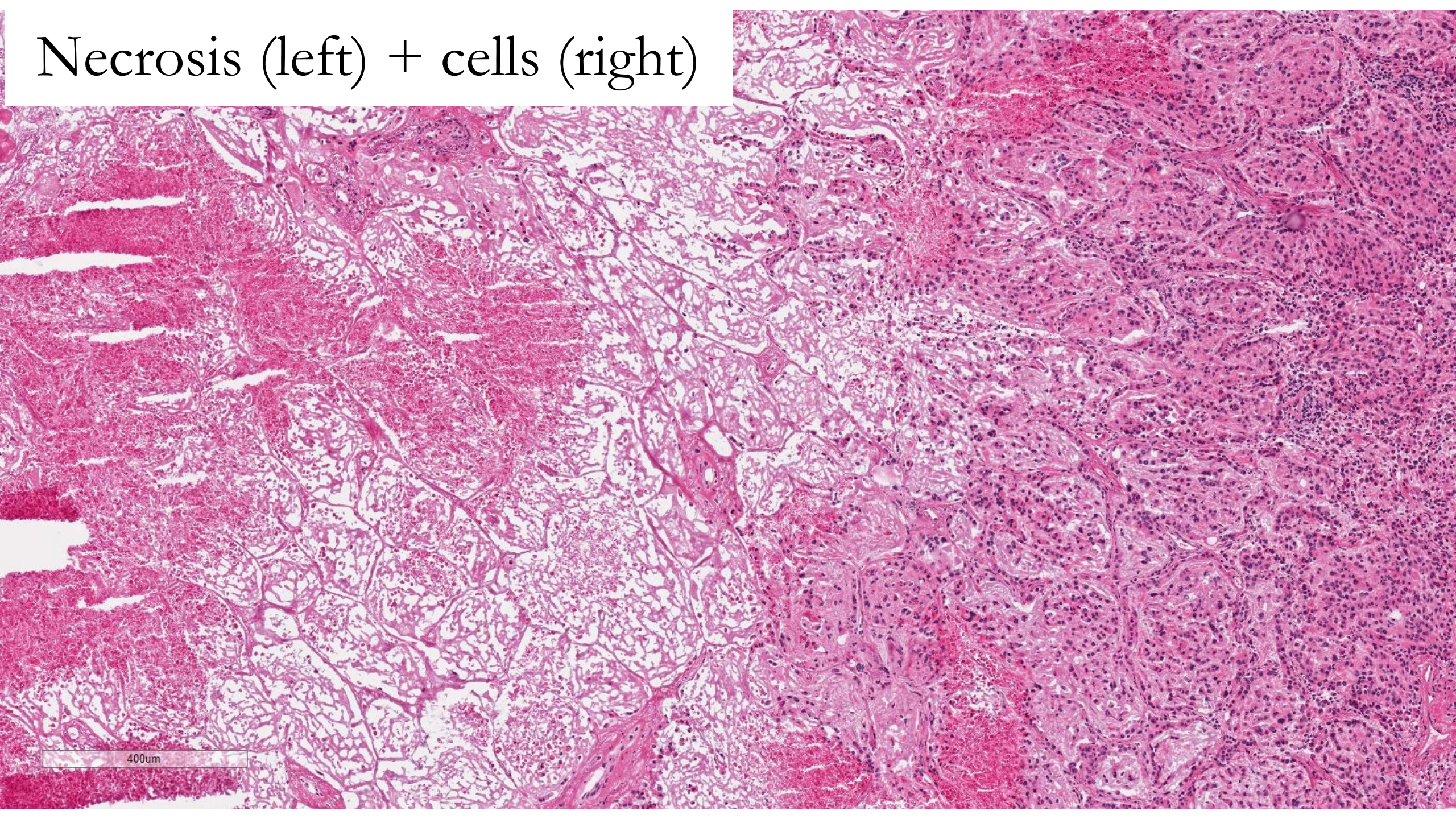
CARCINOMA OR GRANULOMA?

TUMOR 4

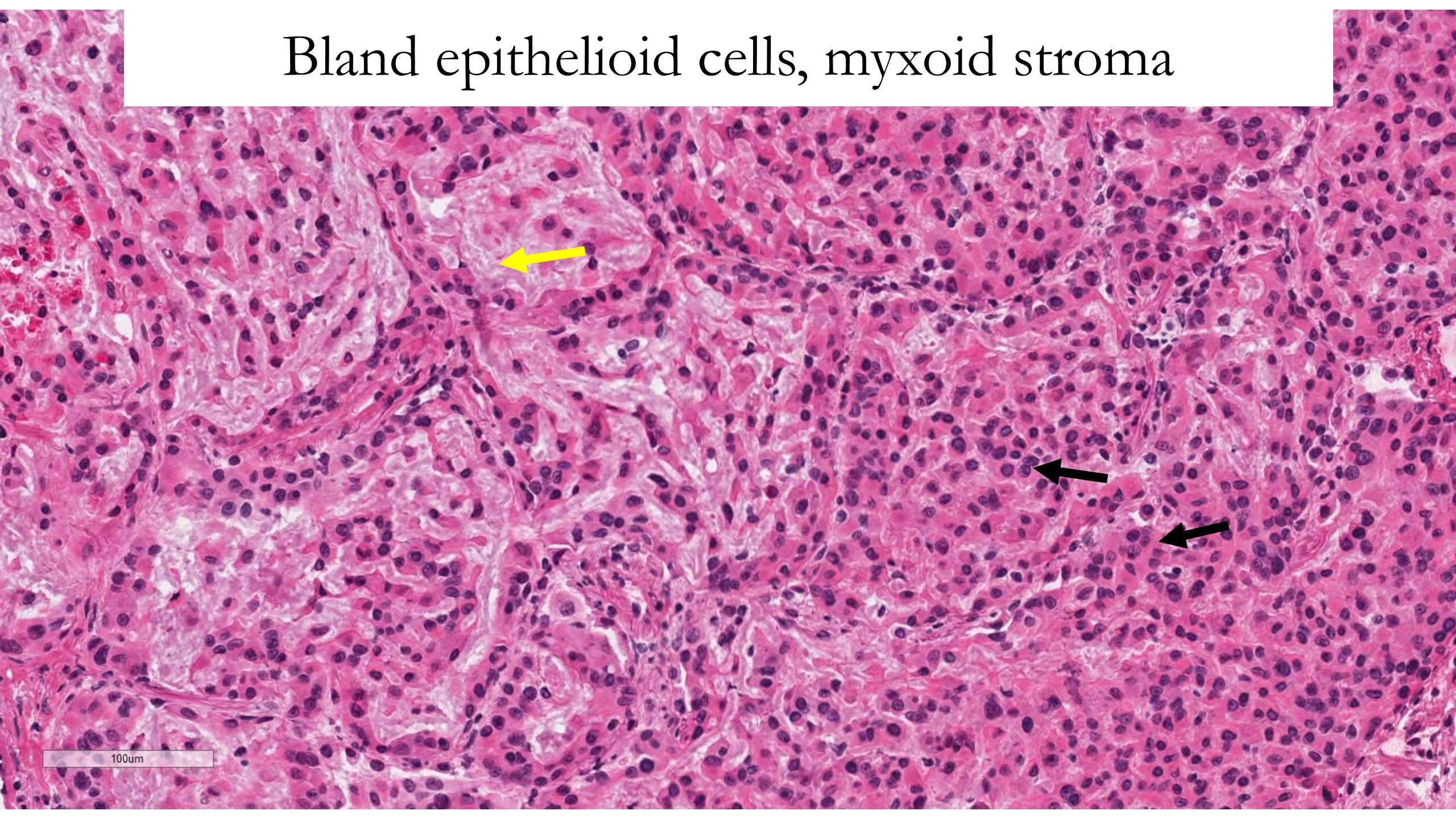


2mm

Necrosis (left) + cells (right)



Bland epithelioid cells, myxoid stroma



Typical pink center, myxohyaline stroma

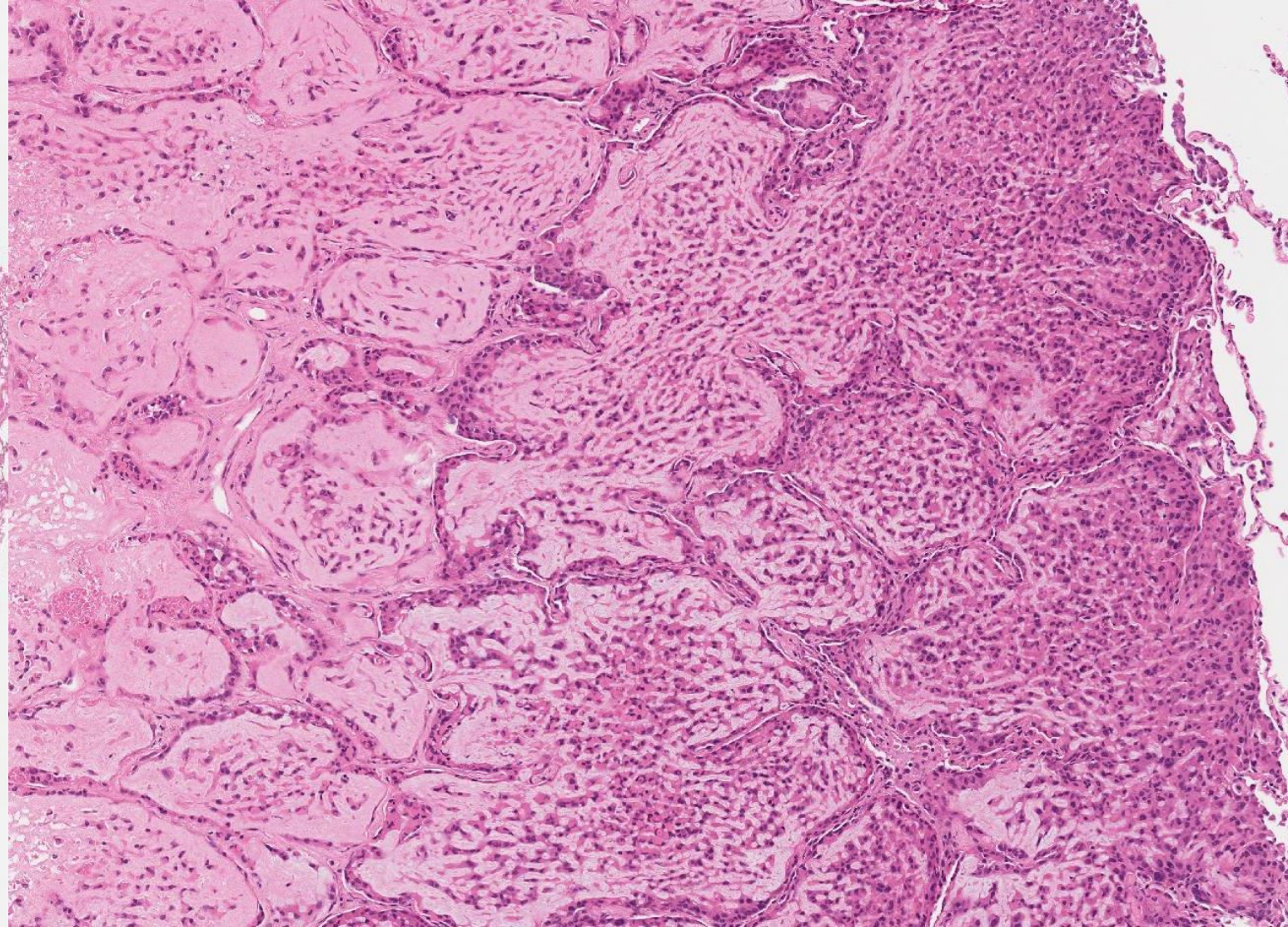
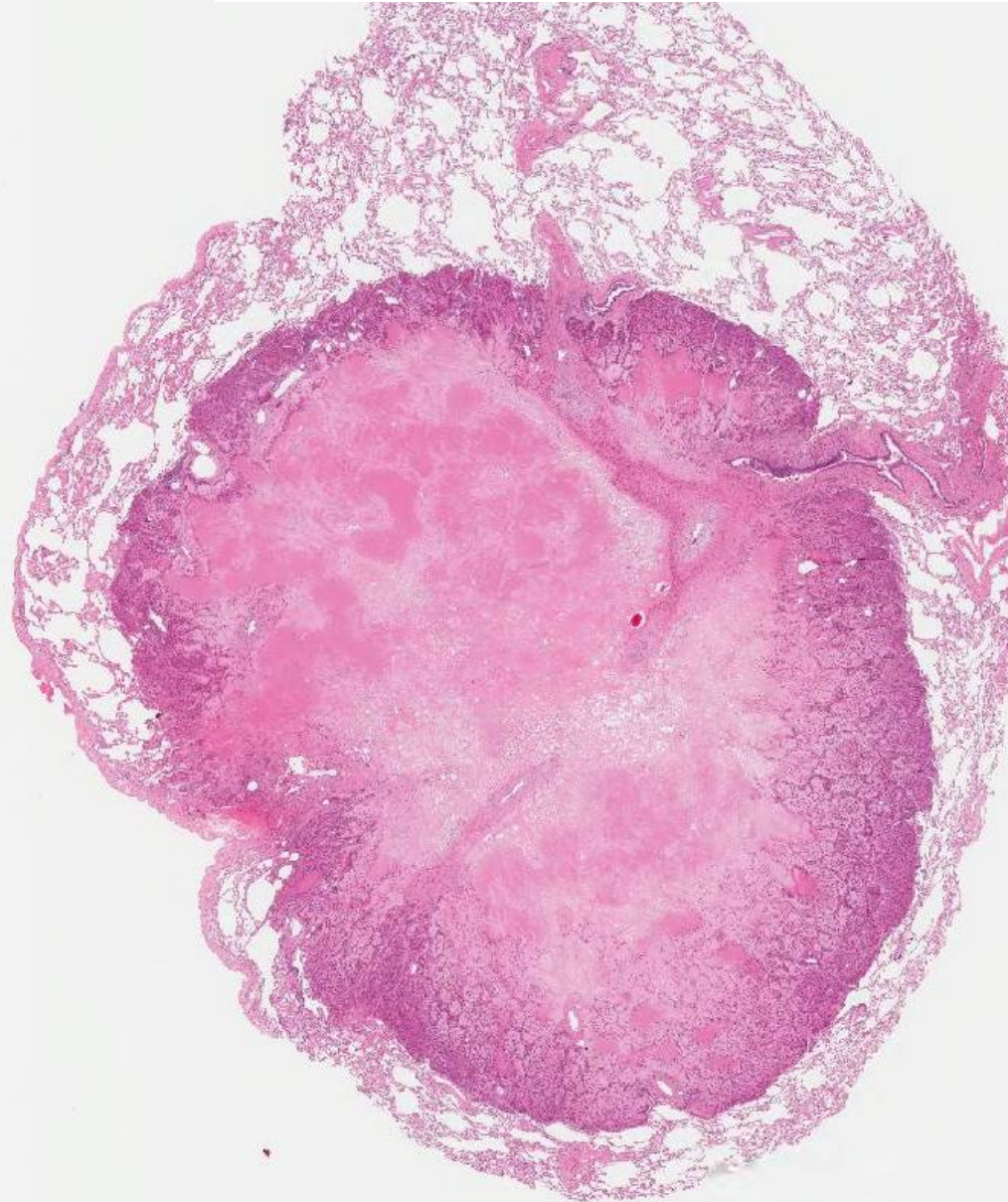




FIG. 2. A typical chest radiograph with multiple widespread bilateral small nodules in a 14-year-old girl (Case 3).

(In one more recent case not in this series, gross endobronchial tumor was noted by bronchoscopy.¹⁷)

Microscopic Pathologic Findings

Even when a limited number of nodules was documented by x-ray, many more nodules were generally present at open biopsy and on pathologic exam. Low power microscopic examination showed round to oval nodules with pale pink acellular centers surrounded by rims of viable tumor. The degree of cellularity at the

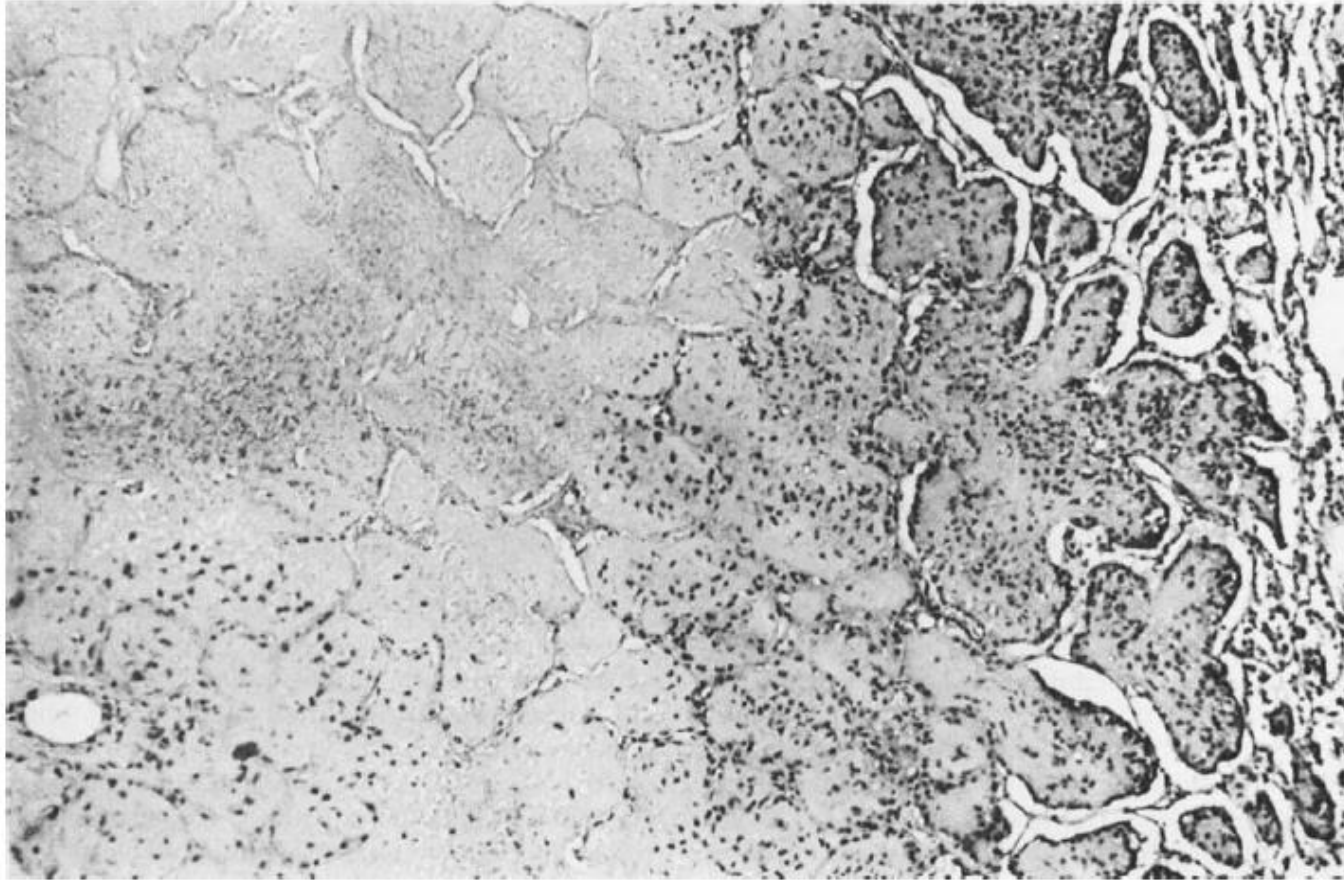
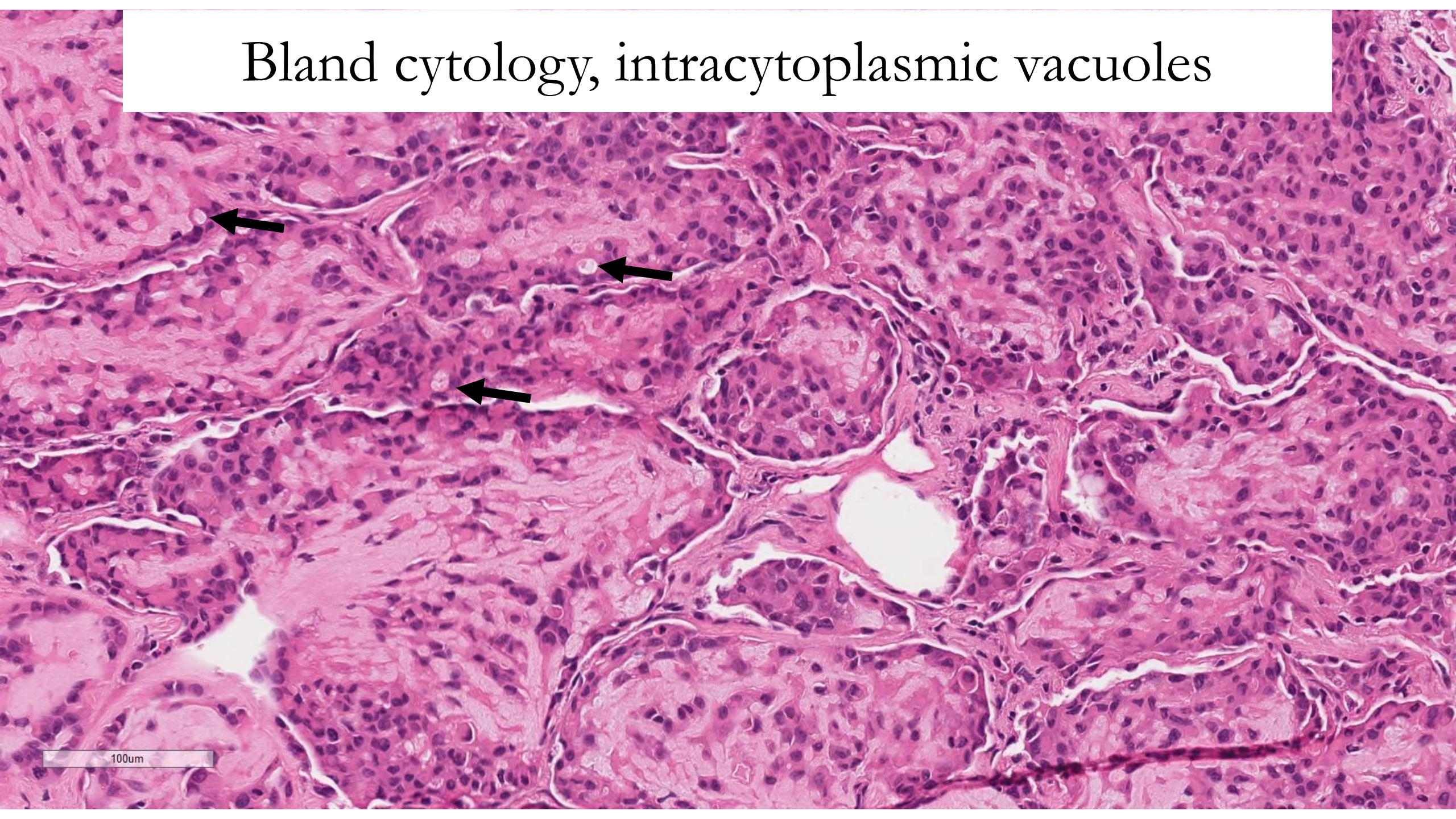
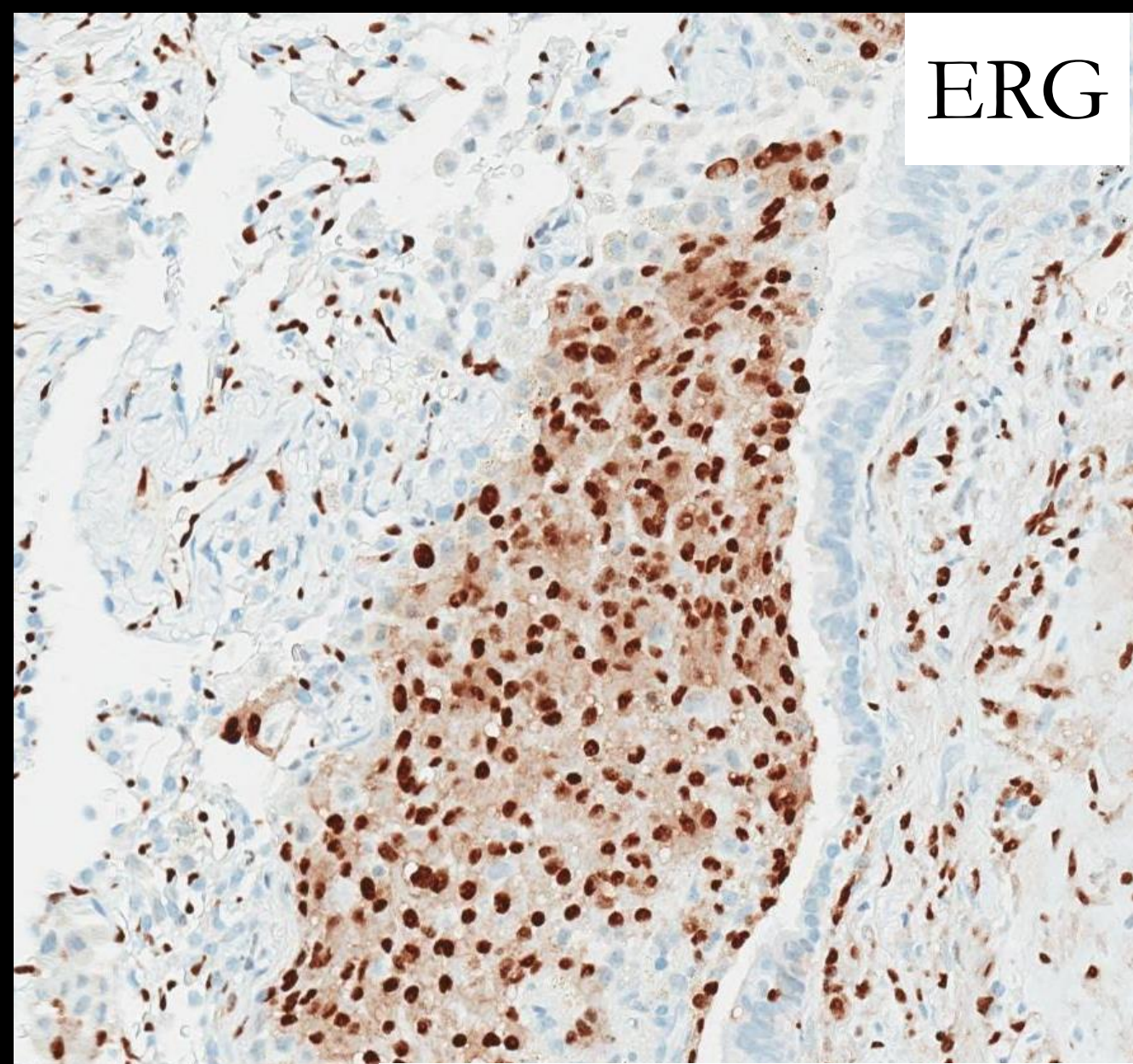


FIG. 3. Border of typical lung nodule shows the more active cellular growth zone extending in a micropolypoid fashion at right. Note retraction artifact. There is some preservation of viable cells around a small patent vessel in the left lower edge. The remaining tumor has undergone coagulative necrosis with remnant dense stroma, empty cellular or nuclear lacunae and ghosts of architecturally well preserved infarcted alveolar septa (Case 1, H & E, $\times 50$).

“pale pink acellular centers surrounded by rims of viable tumor”

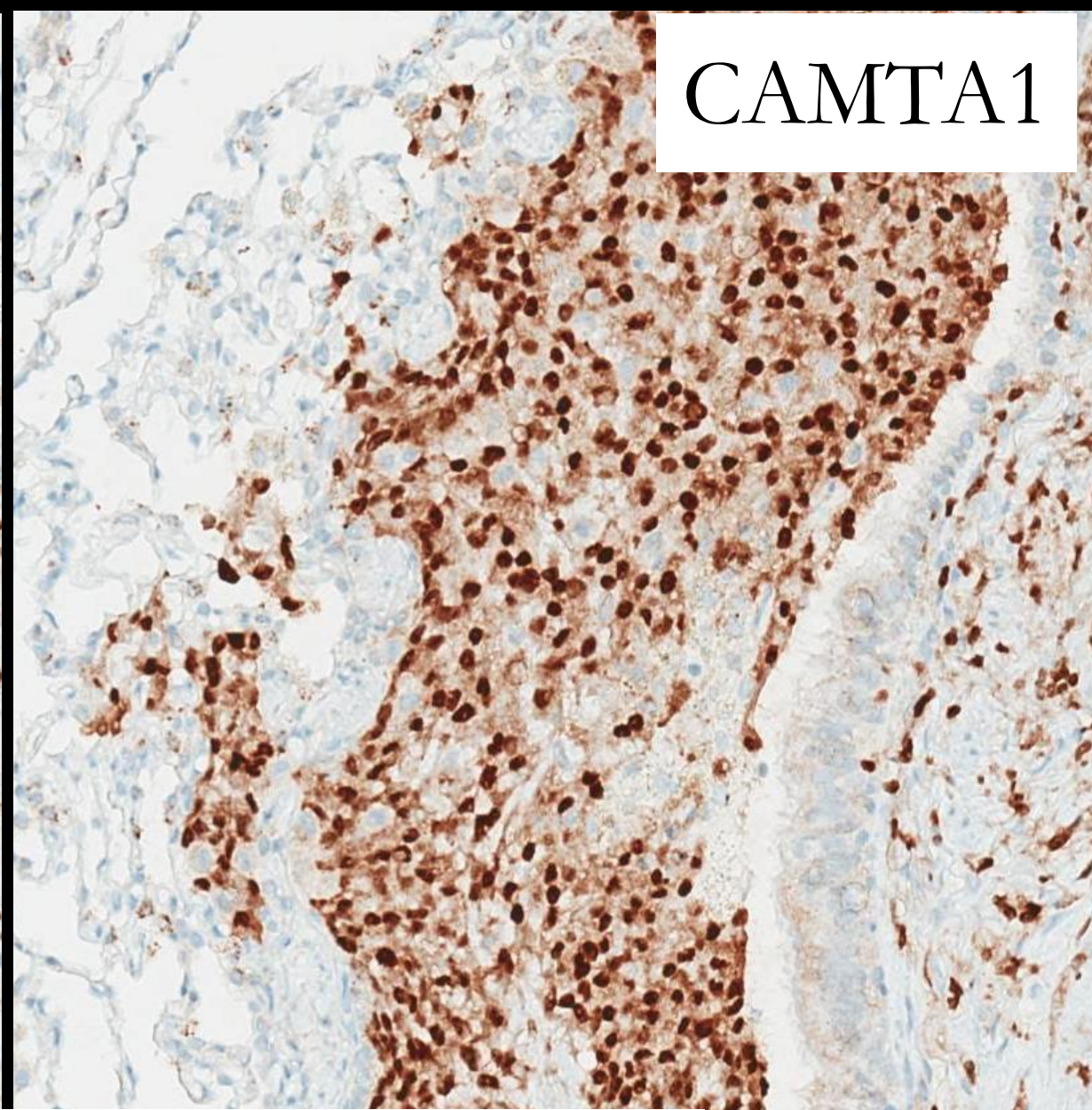
Bland cytology, intracytoplasmic vacuoles





ERG

This panel shows a histological section of a tissue sample stained for ERG. The tissue is composed of clusters of cells with brown, granular cytoplasmic staining, indicating a positive result for ERG. The surrounding stroma is stained blue with hematoxylin.



CAMTA1

This panel shows a histological section of the same tissue sample stained for CAMTA1. The cells show strong brown, granular cytoplasmic staining, indicating a positive result for CAMTA1. The surrounding stroma is stained blue with hematoxylin.

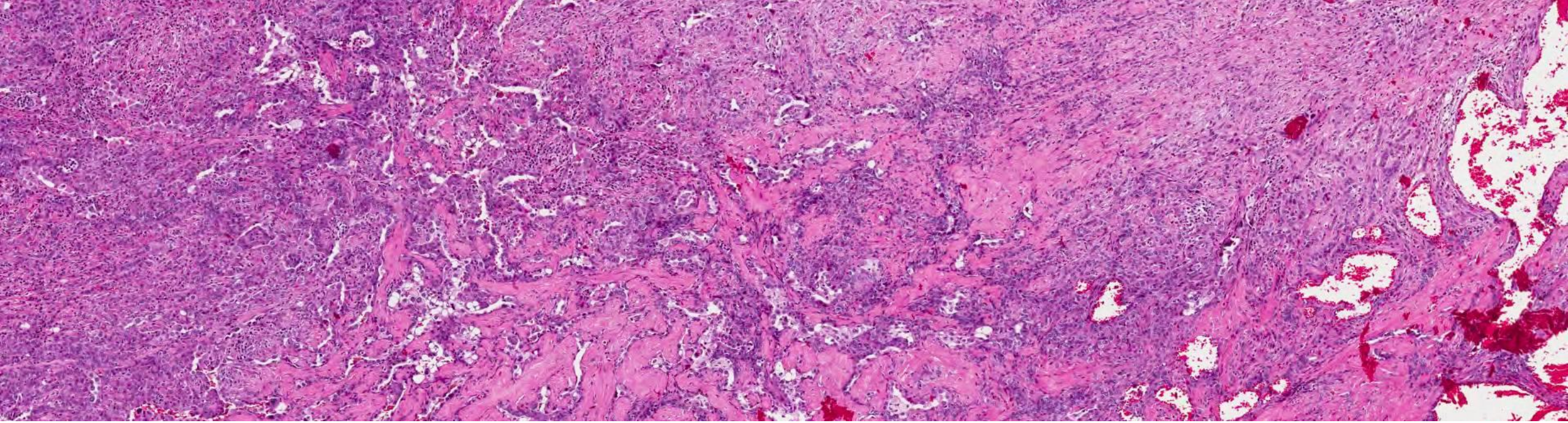
Epithelioid hemangioendothelioma

Not all that is epithelioid is carcinoma!



EPITHELIOID HEMANGIOENDOTHELIOMA

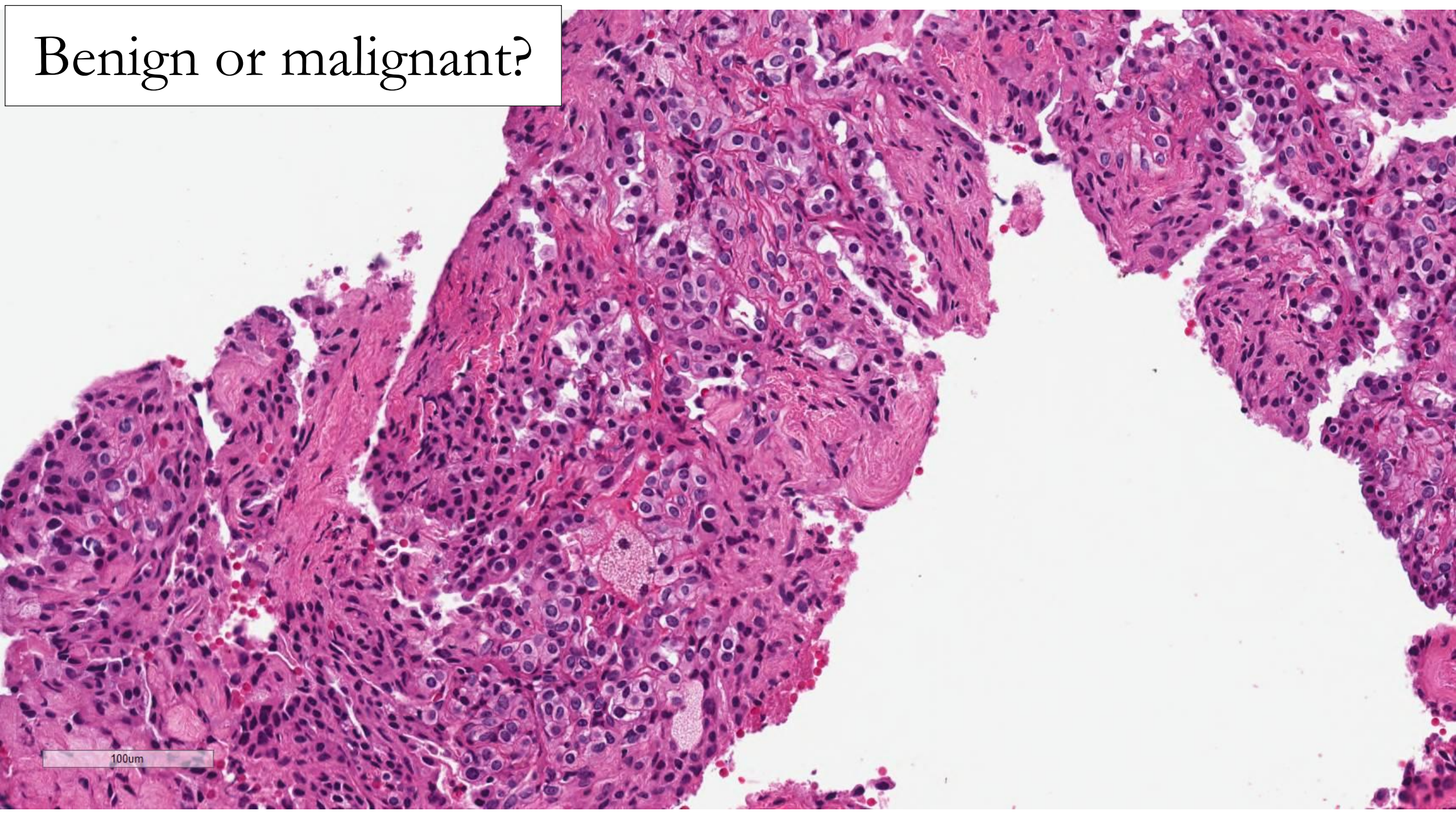
- Clinical: Lung nodule(s), pleural thickening, patients can be young (median age for pulm EHE = 38 y)
- H&E: Bland epithelioid cells, vacuoles, myxohyaline stroma
- Immunohistochemistry: ERG +, CAMTA1 + CD31/34 +
- How to confirm? FISH or NGS: *WWTR1-CAMTA1* or *YAP1-TFE3*



ADENOCARCINOMA?

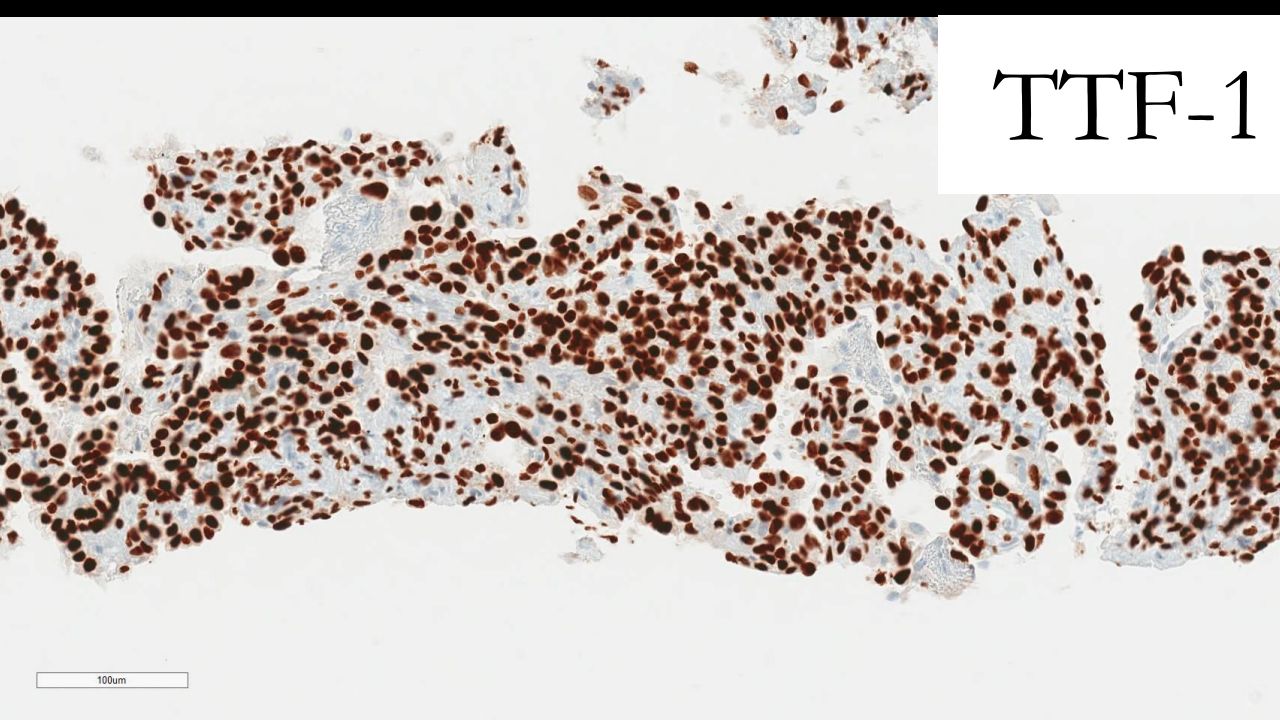
TUMOR 5

Benign or malignant?

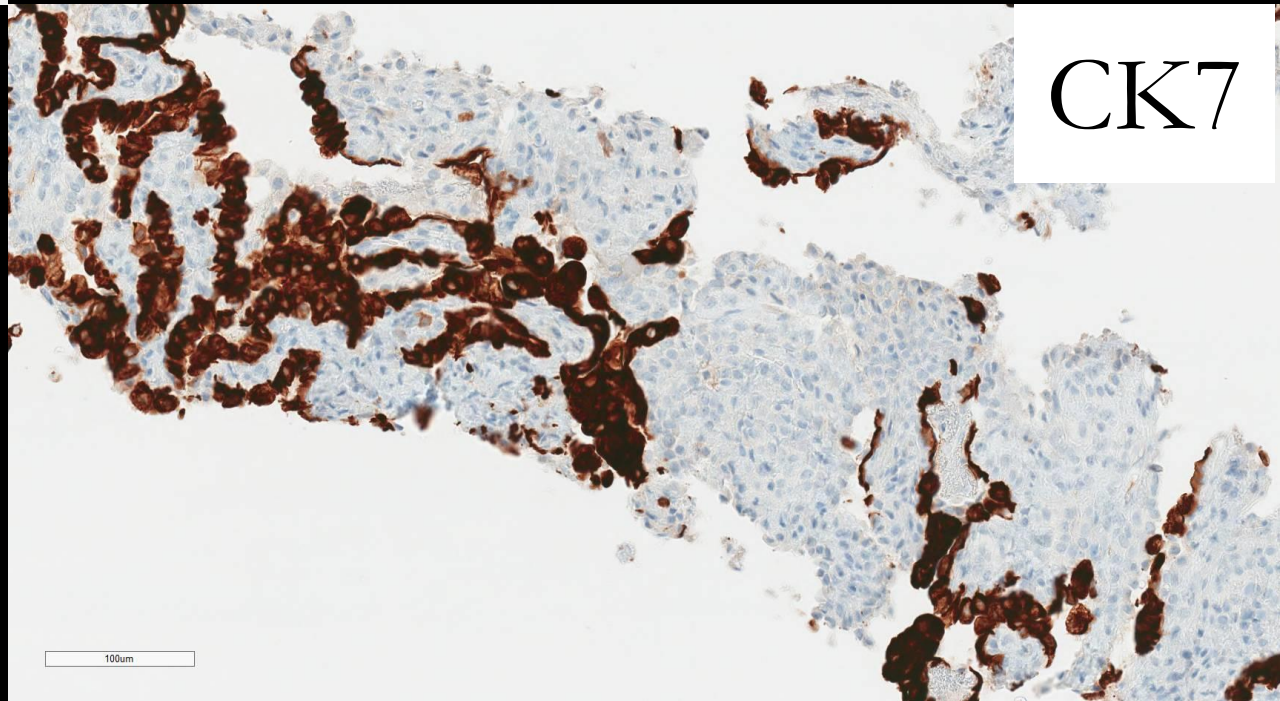


TTF-1

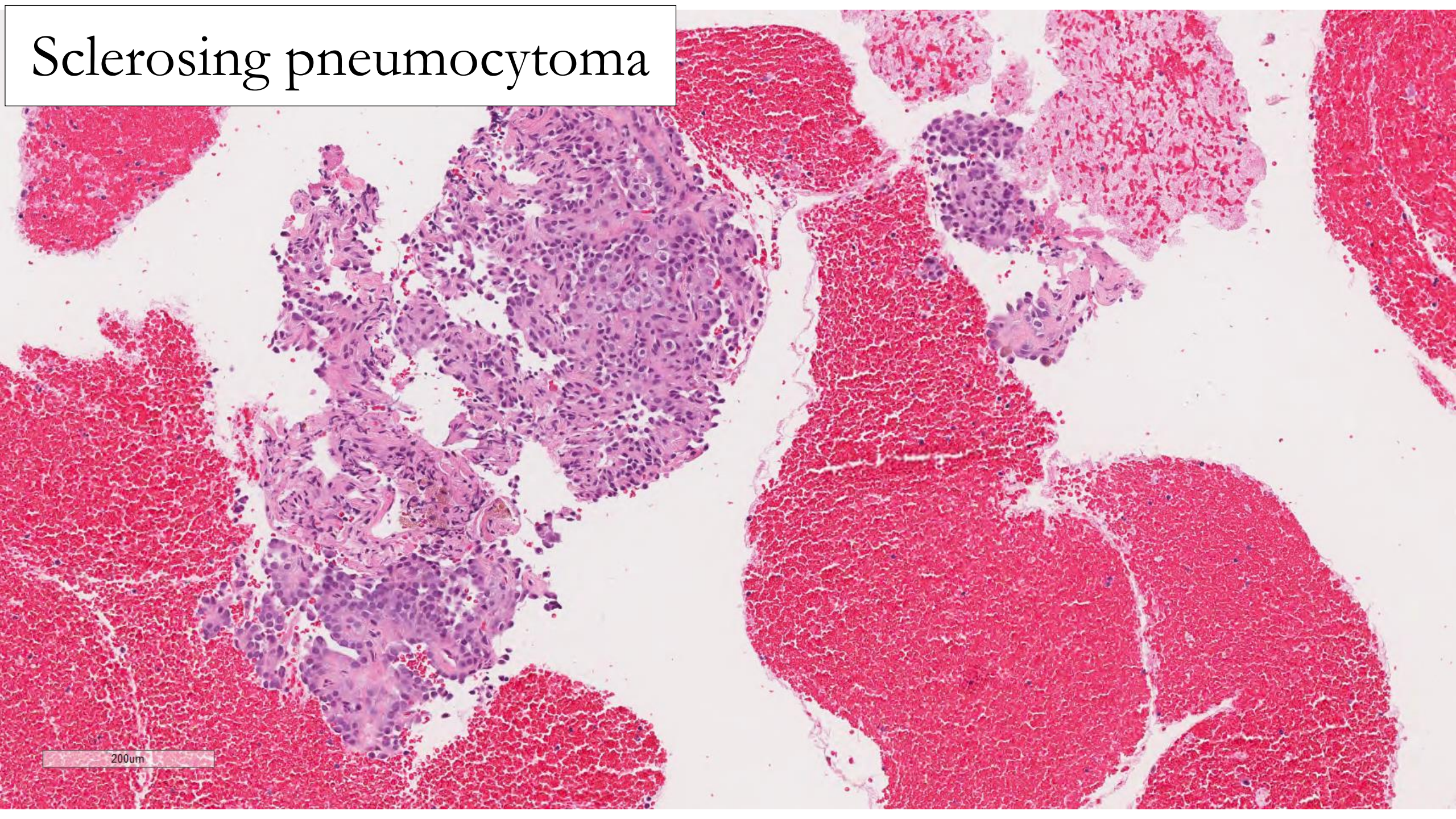
TTF-1 confirms
primary lung
adenocarcinoma?



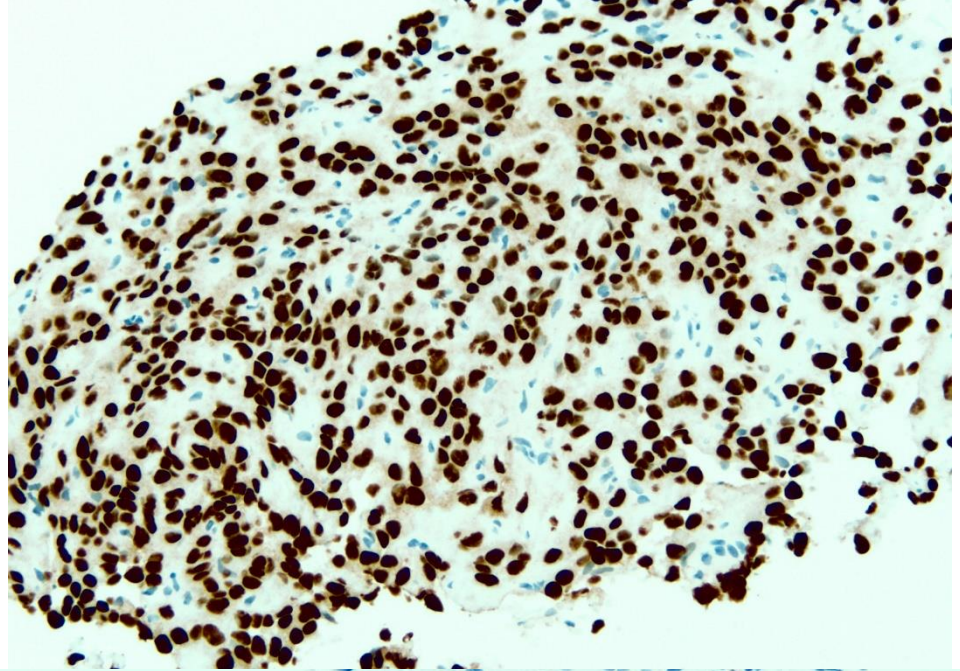
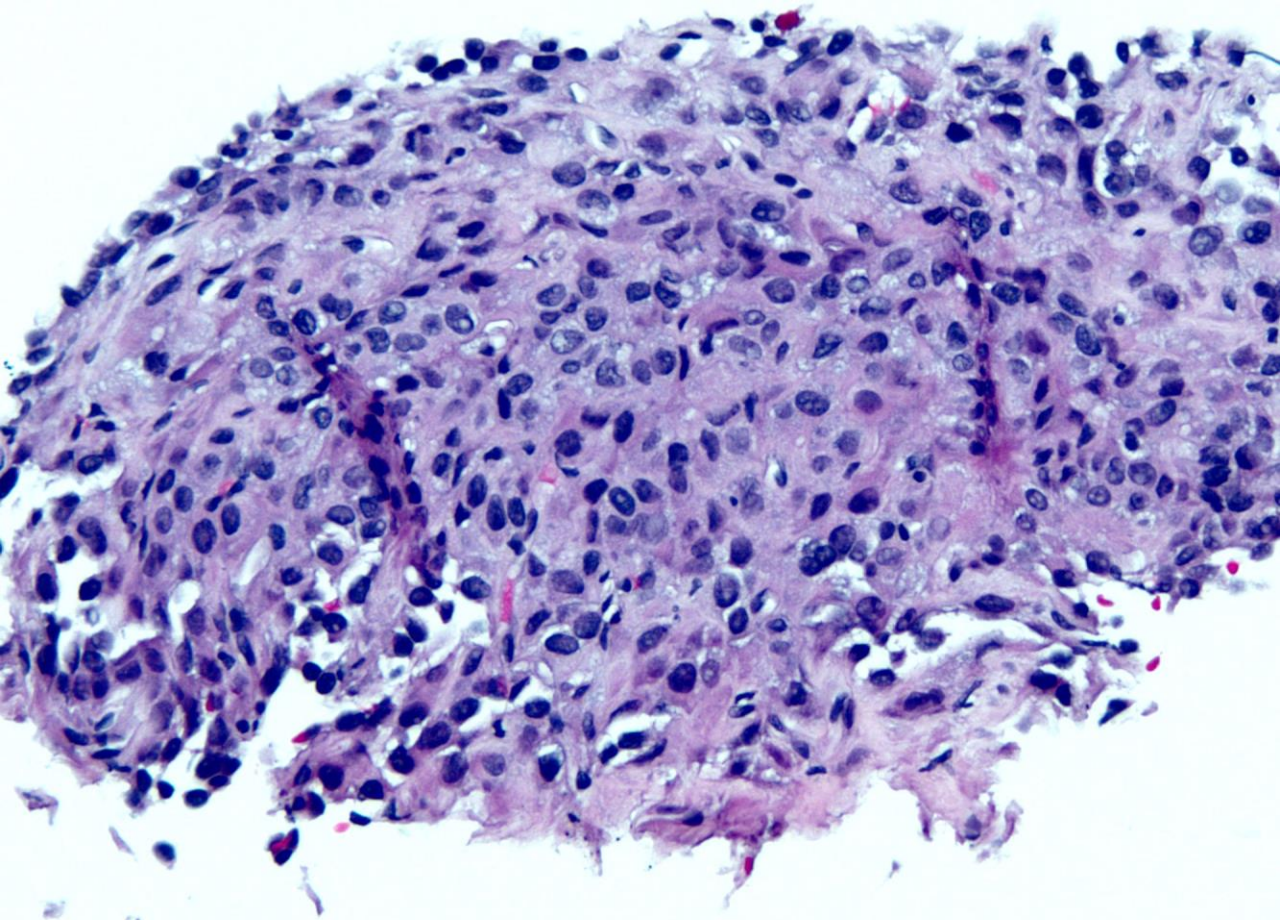
CK7



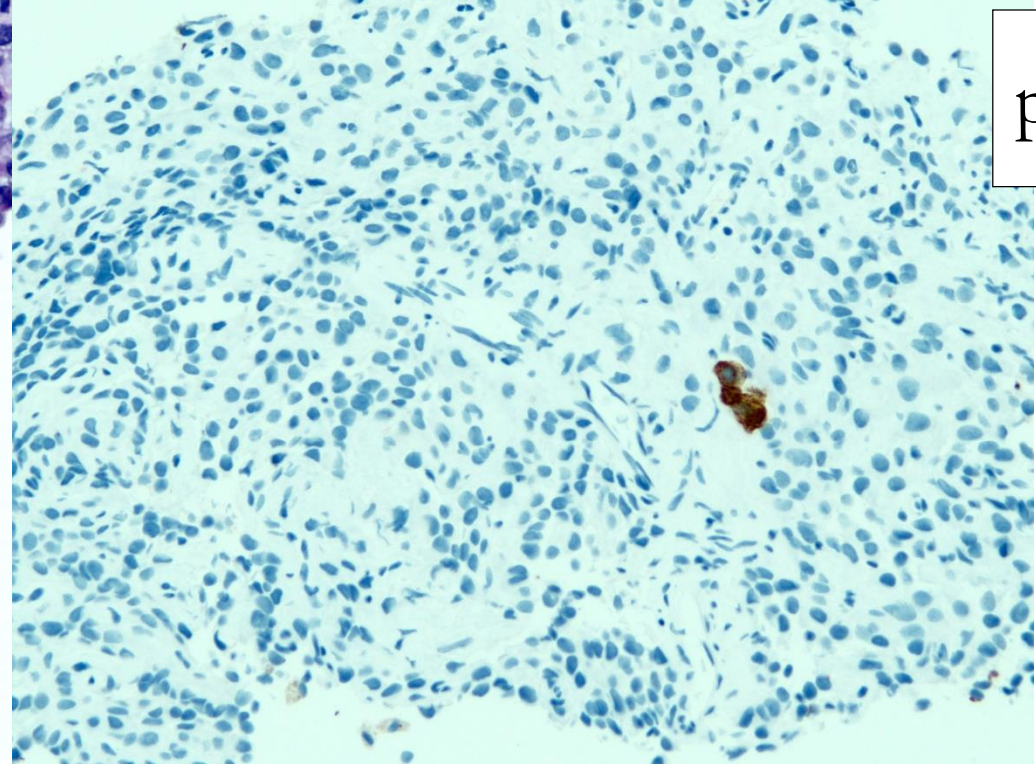
Sclerosing pneumocytoma



Sclerosing pneumocytoma

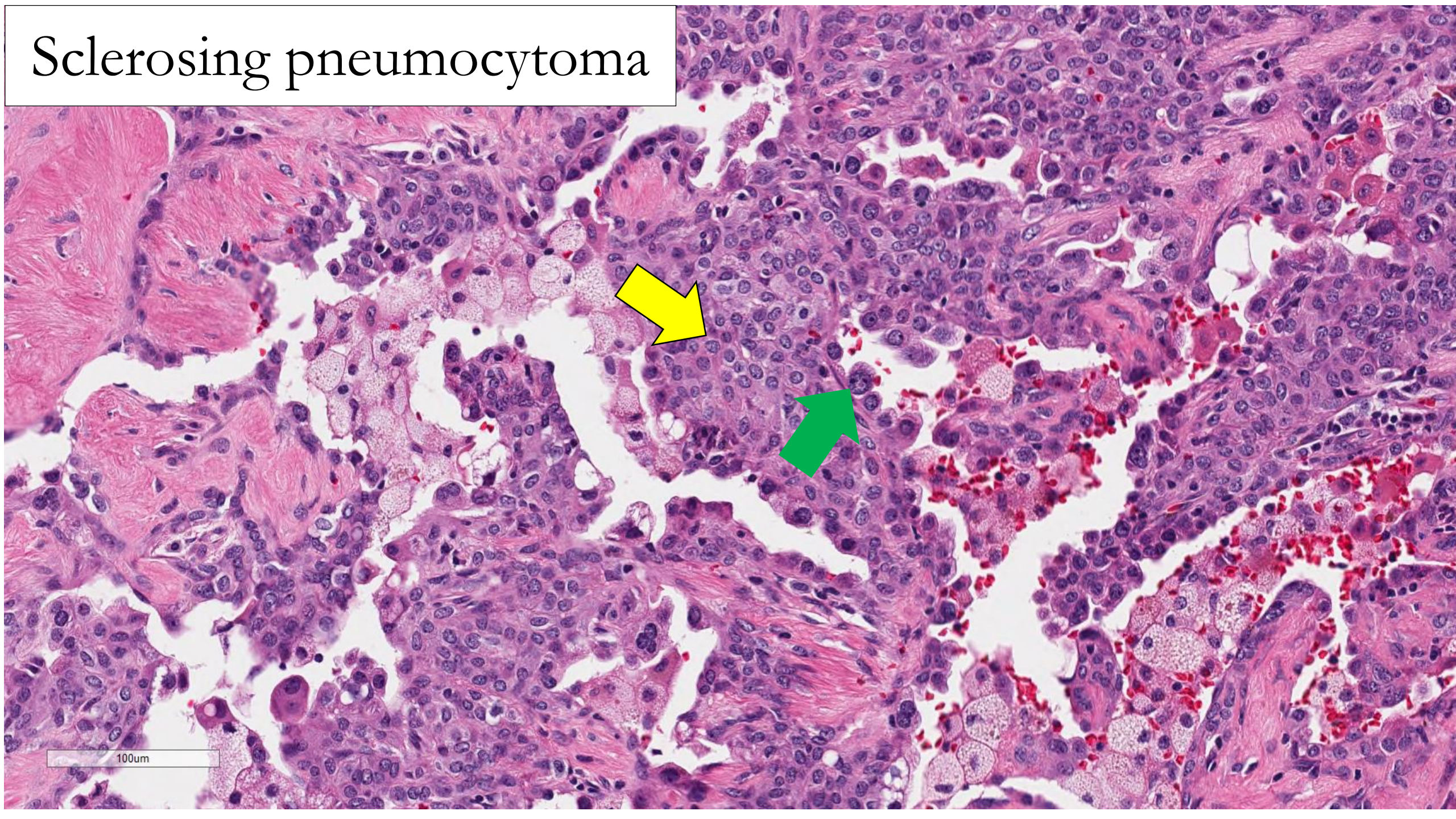


TTF-1

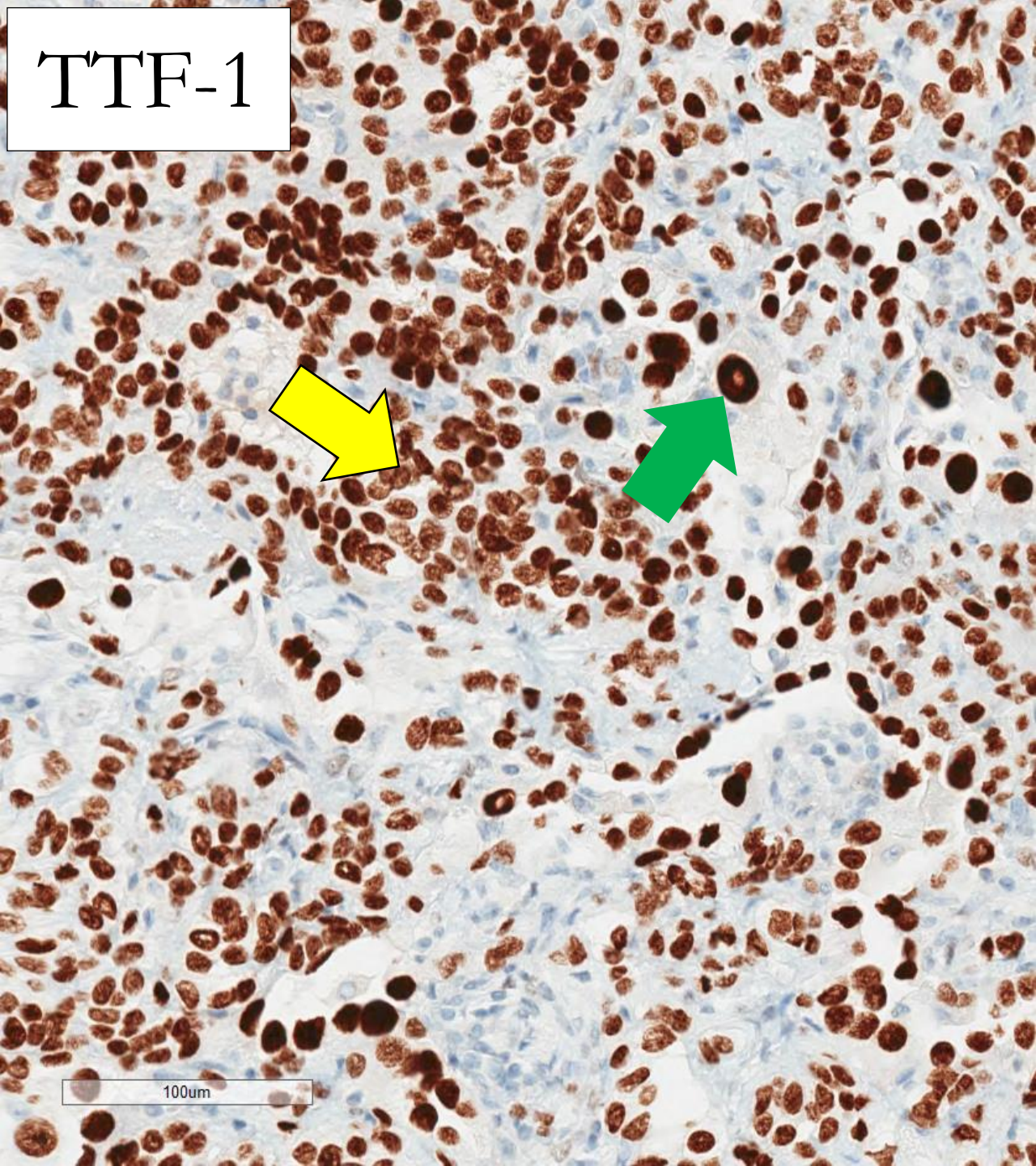


panCK

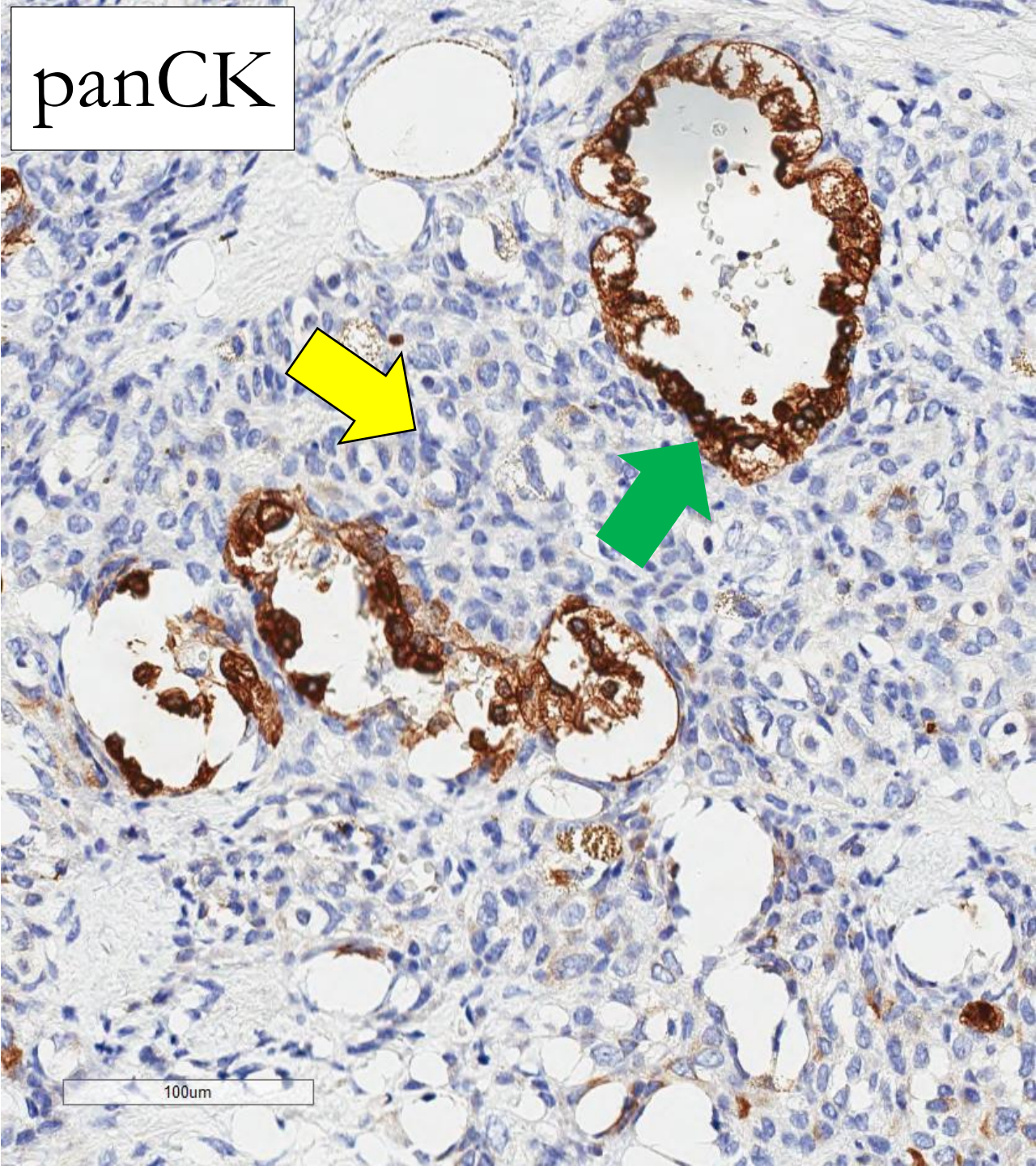
Sclerosing pneumocytoma



TTF-1

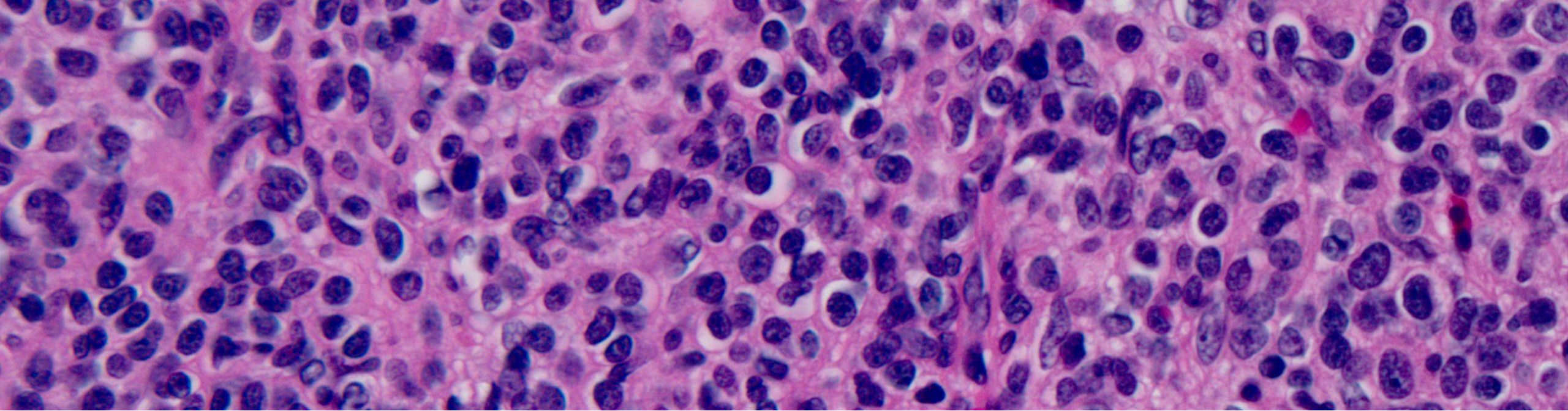


panCK



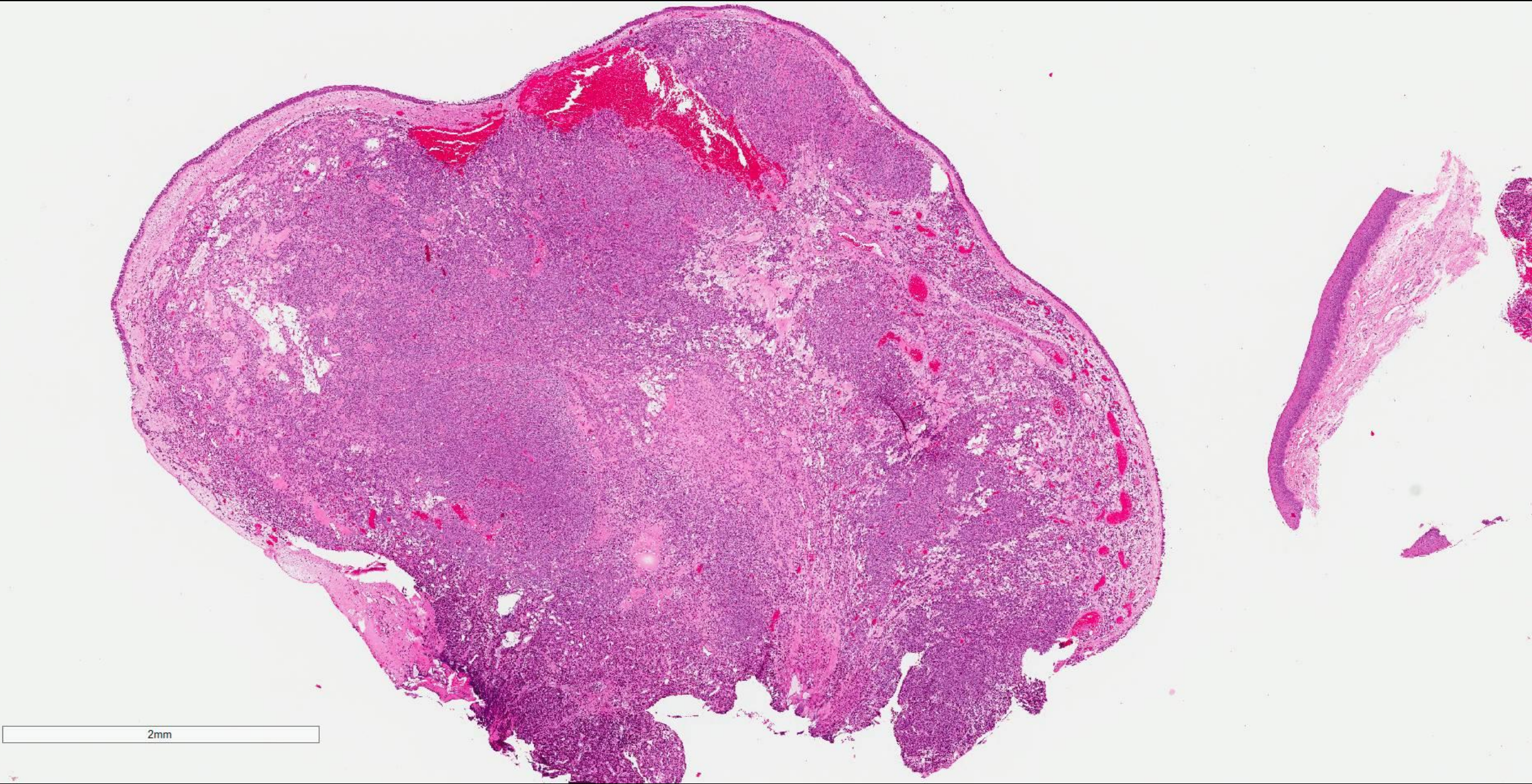
SCLEROSING PNEUMOCYTOMA

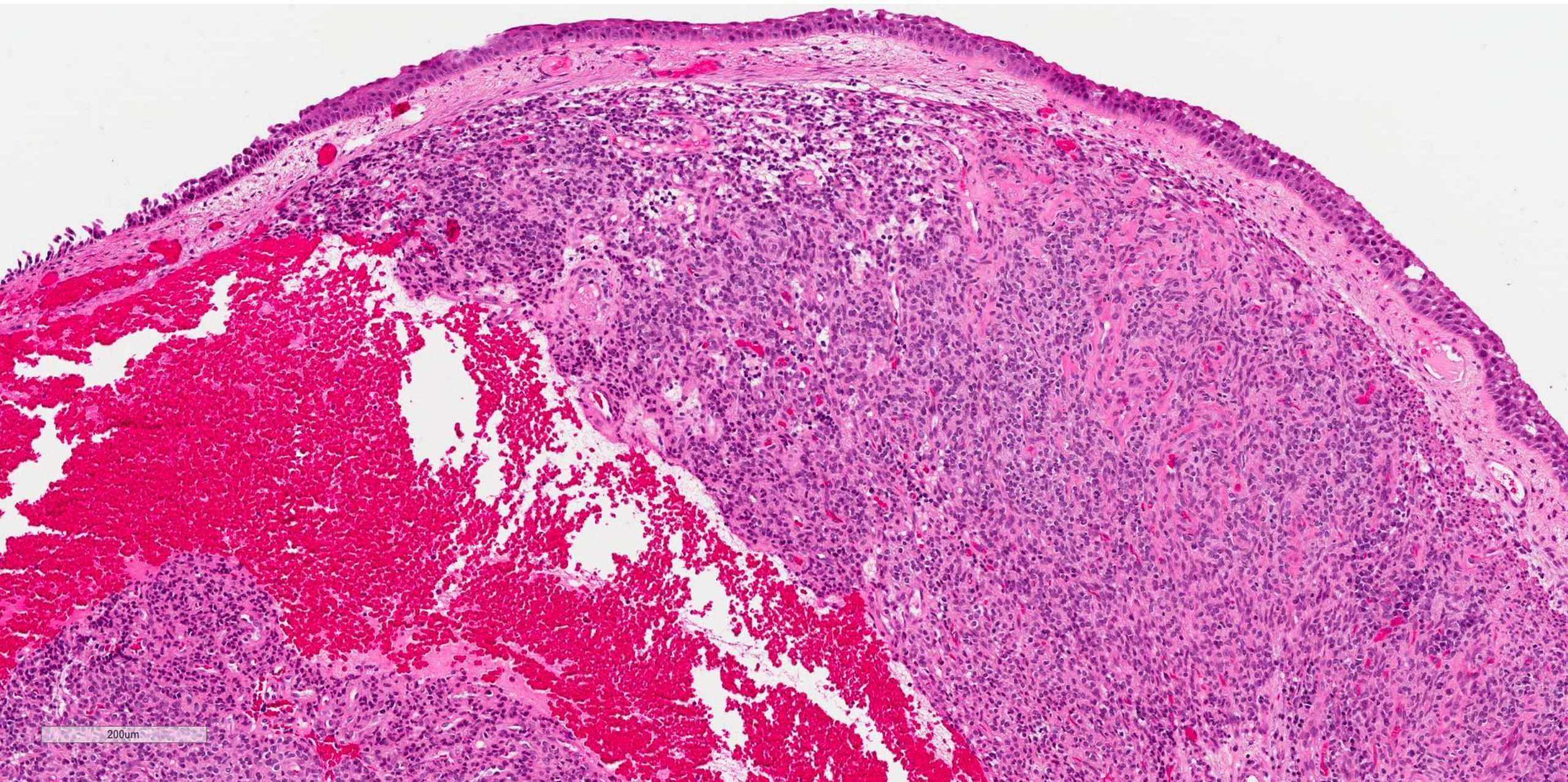
- Clinical: Lung nodule in a woman (often Asian)
- H&E: Bland stromal cells, plump surface epithelial cells, sclerosis, hemosiderin, foamy macrophages
- Immunohistochemistry: 2 cell population: TTF-1 +, keratin neg stromal cells, TTF-1 pos, keratin + surface cells
- How to confirm? H&E + IHC



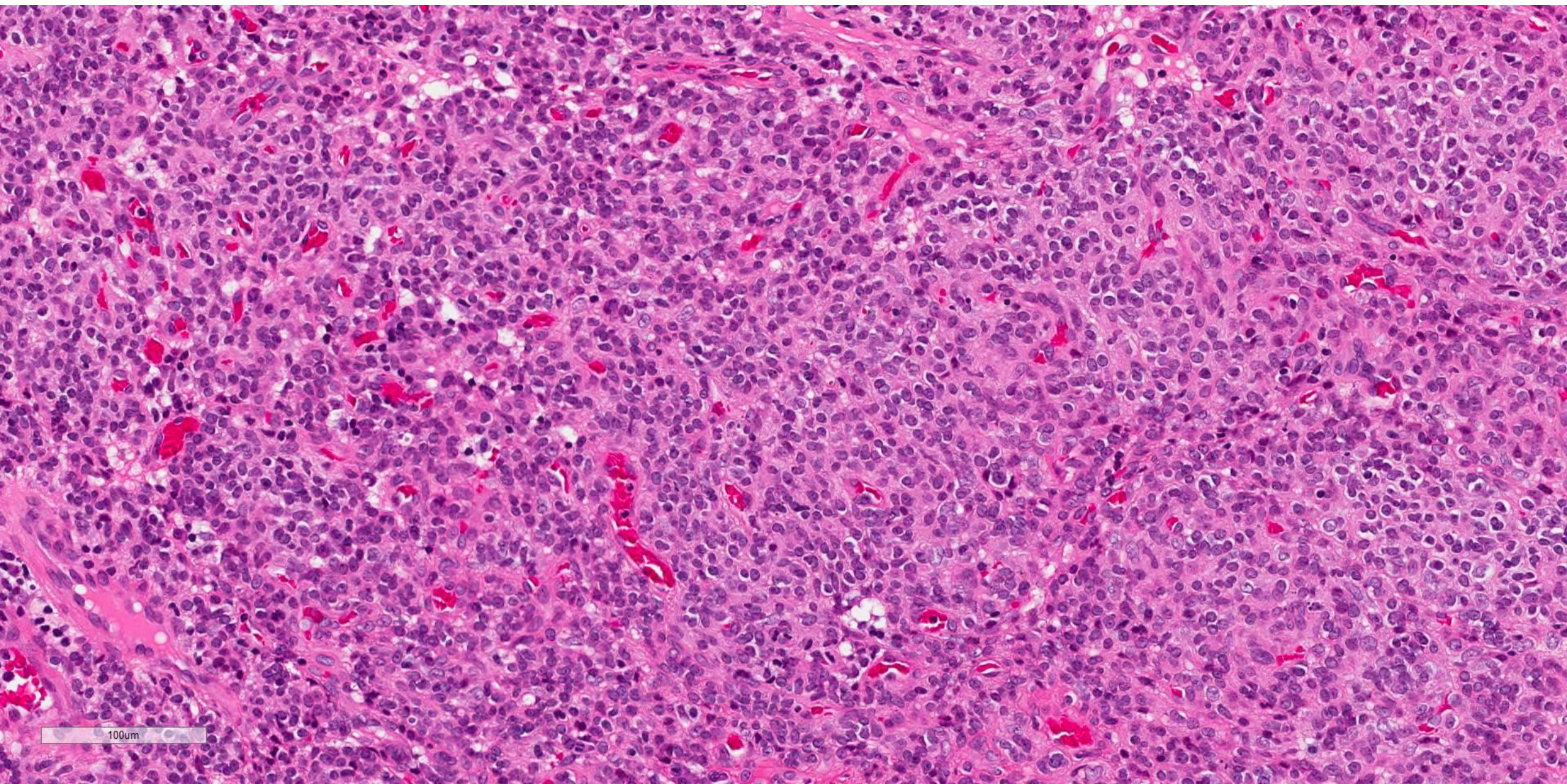
CARCINOID TUMOR?

TUMOR 6



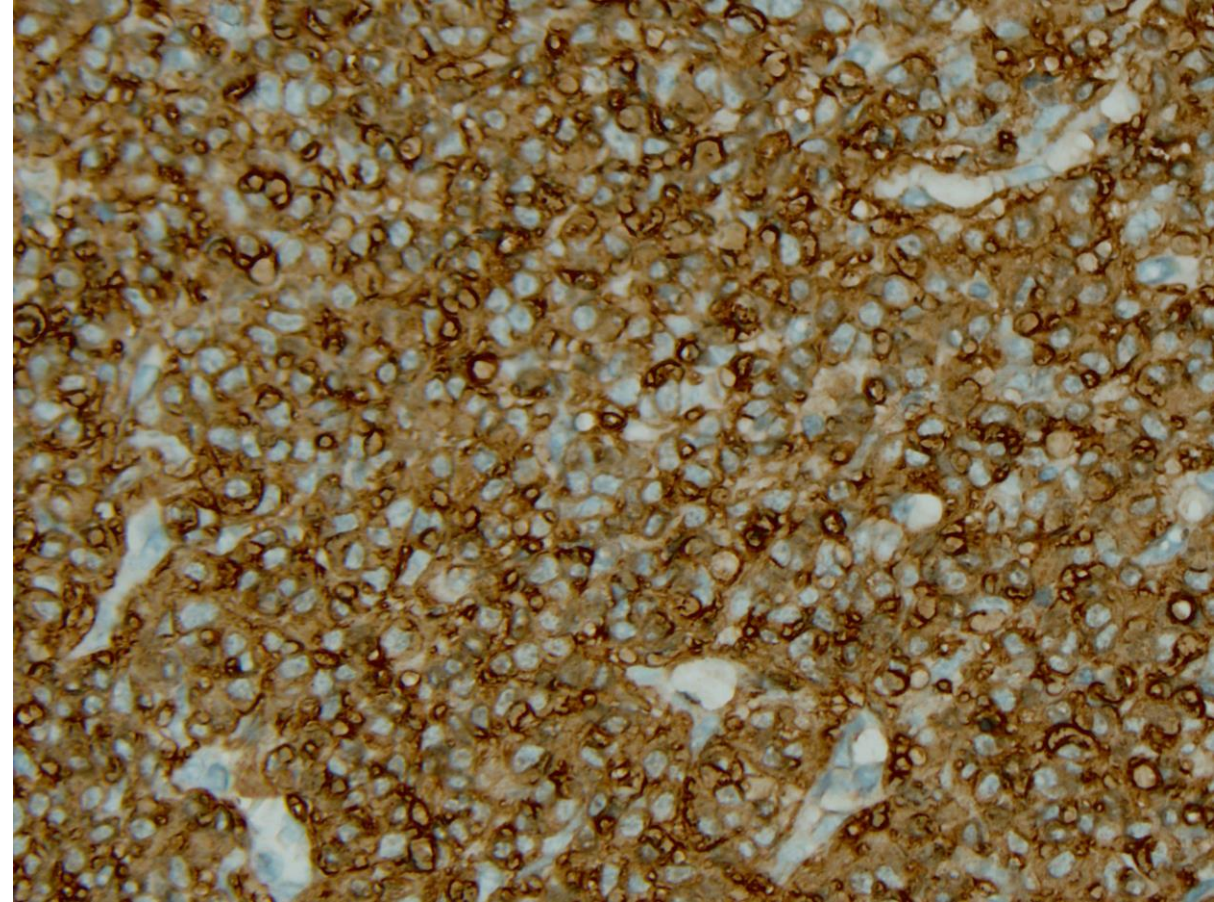
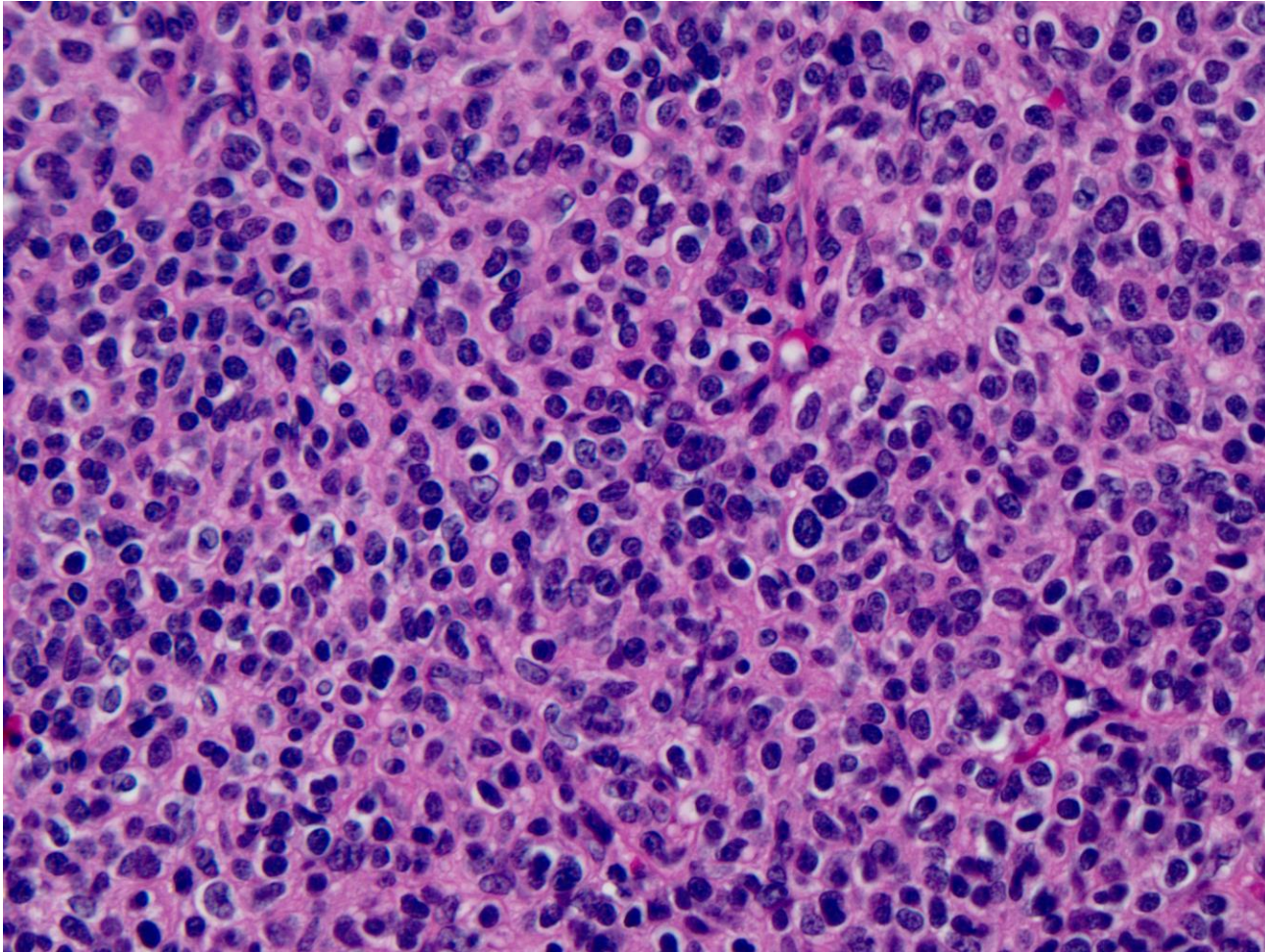


Carcinoid tumor?



100um

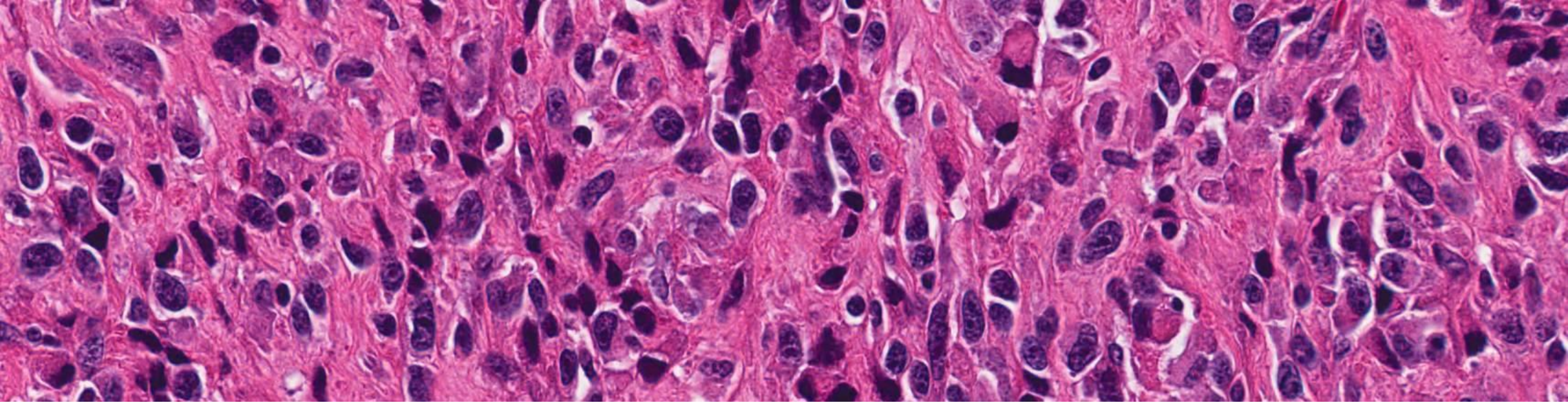
Smooth muscle actin +, neuroendocrine markers -



Glomus tumor

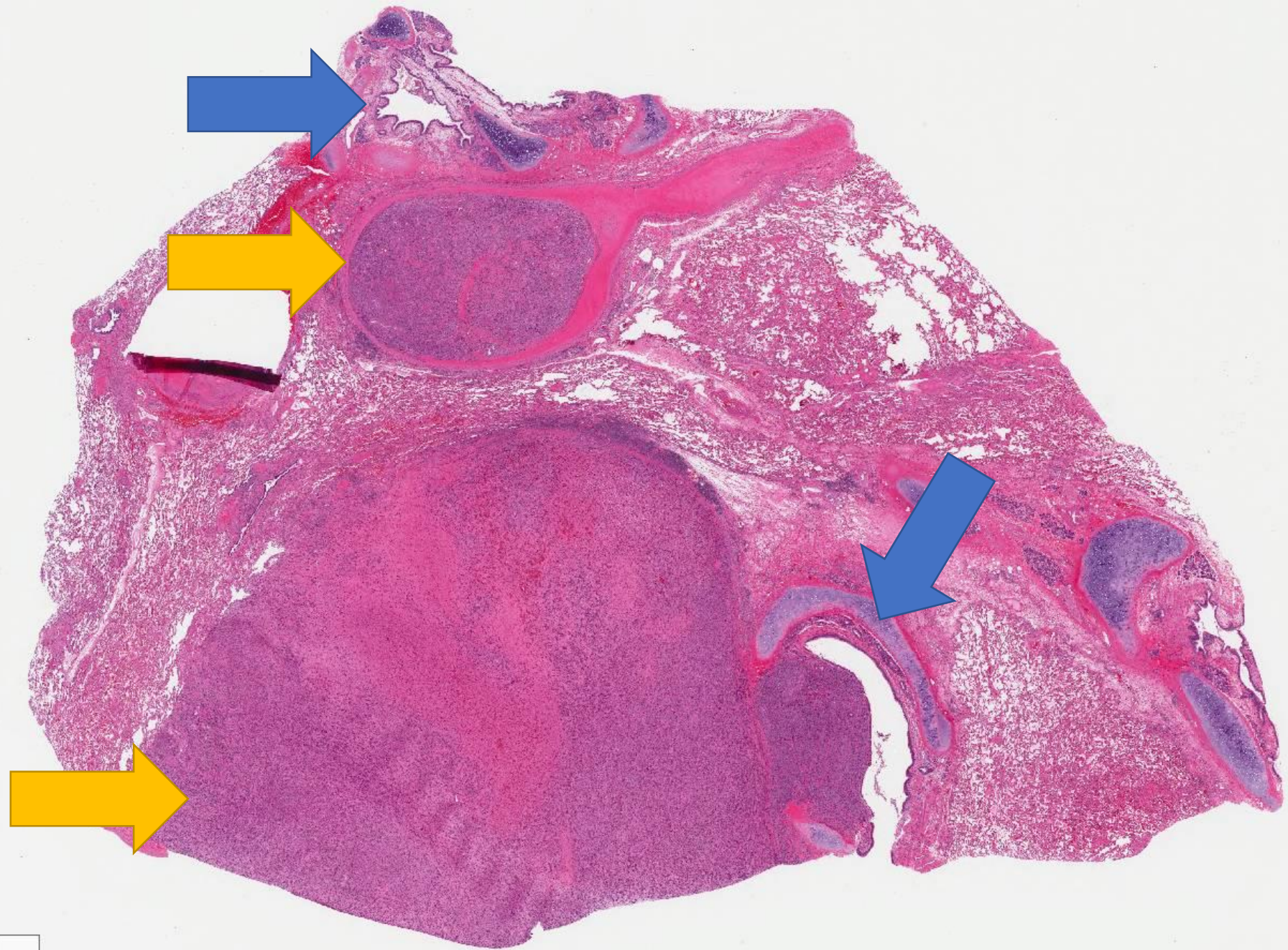
GLOMUS TUMOR

- Clinical: Rare tumor, seen in trachea or bronchus
- H&E: Bland cytology, like carcinoid
- Immunohistochemistry: SMA +, keratin neg, neuroendocrine marker neg, desmin neg
- How to confirm? H&E + IHC

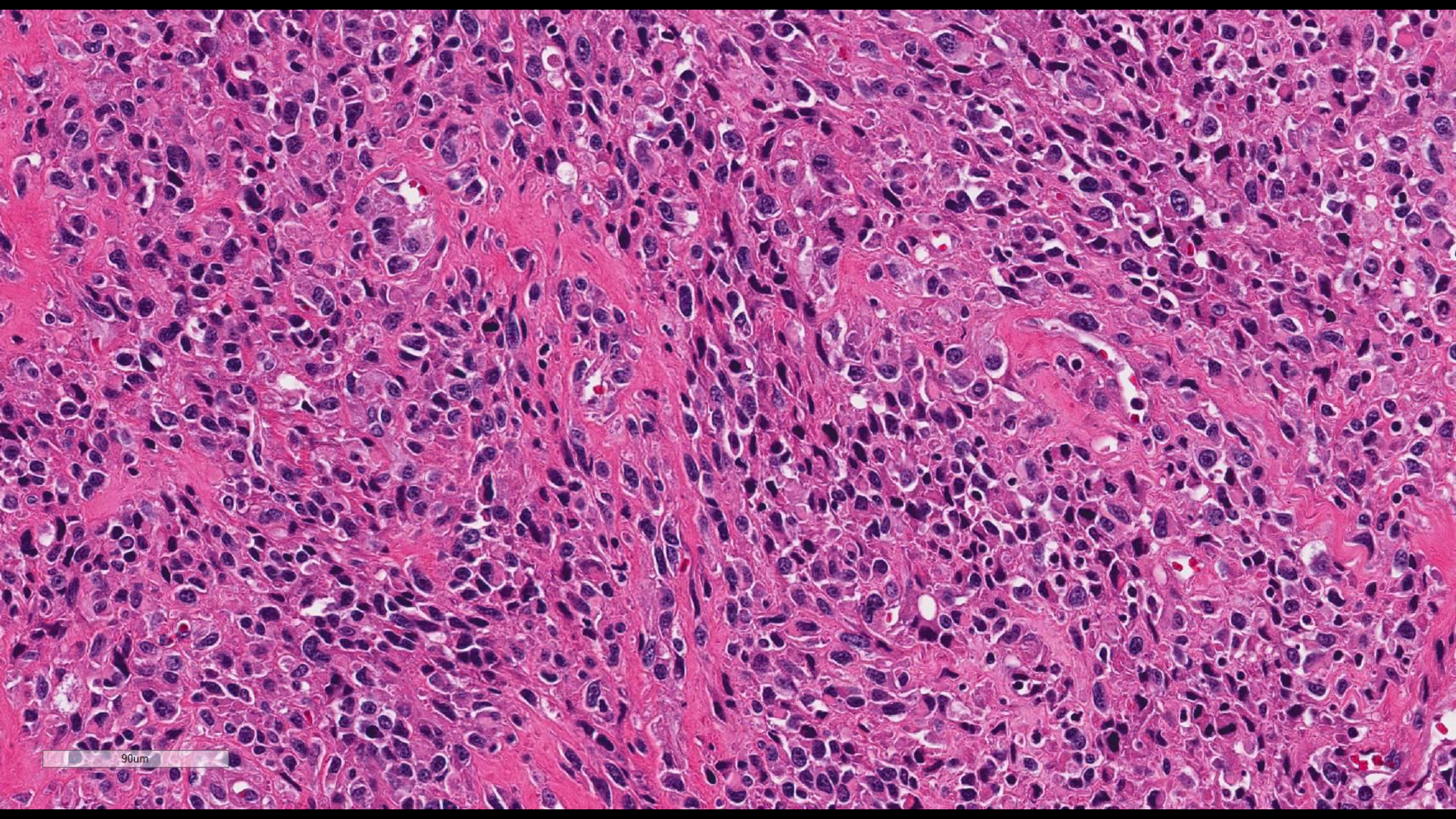


POORLY DIFFERENTIATED MALIGNANCY?

TUMOR 7



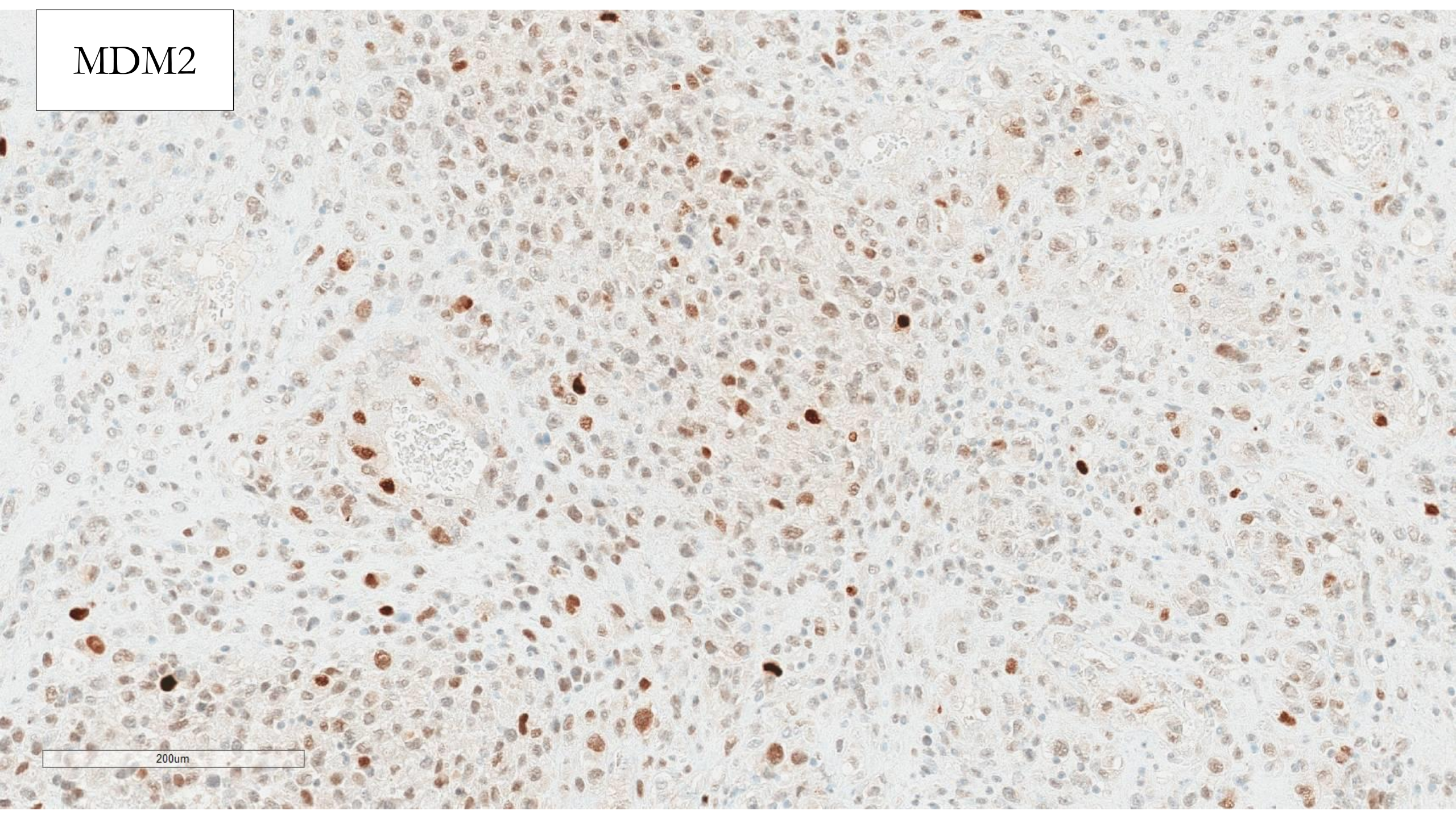
4mm



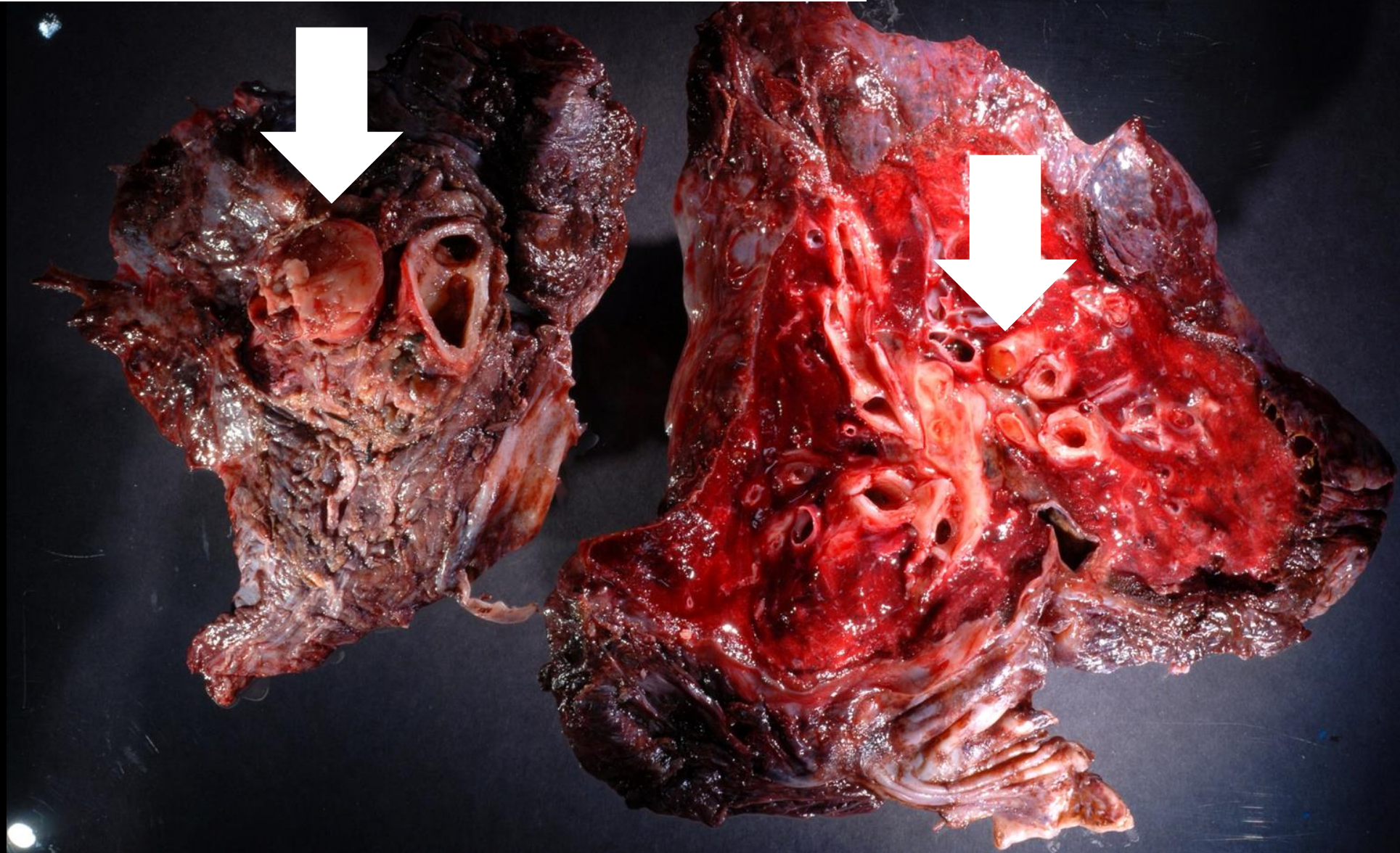
90um

MDM2

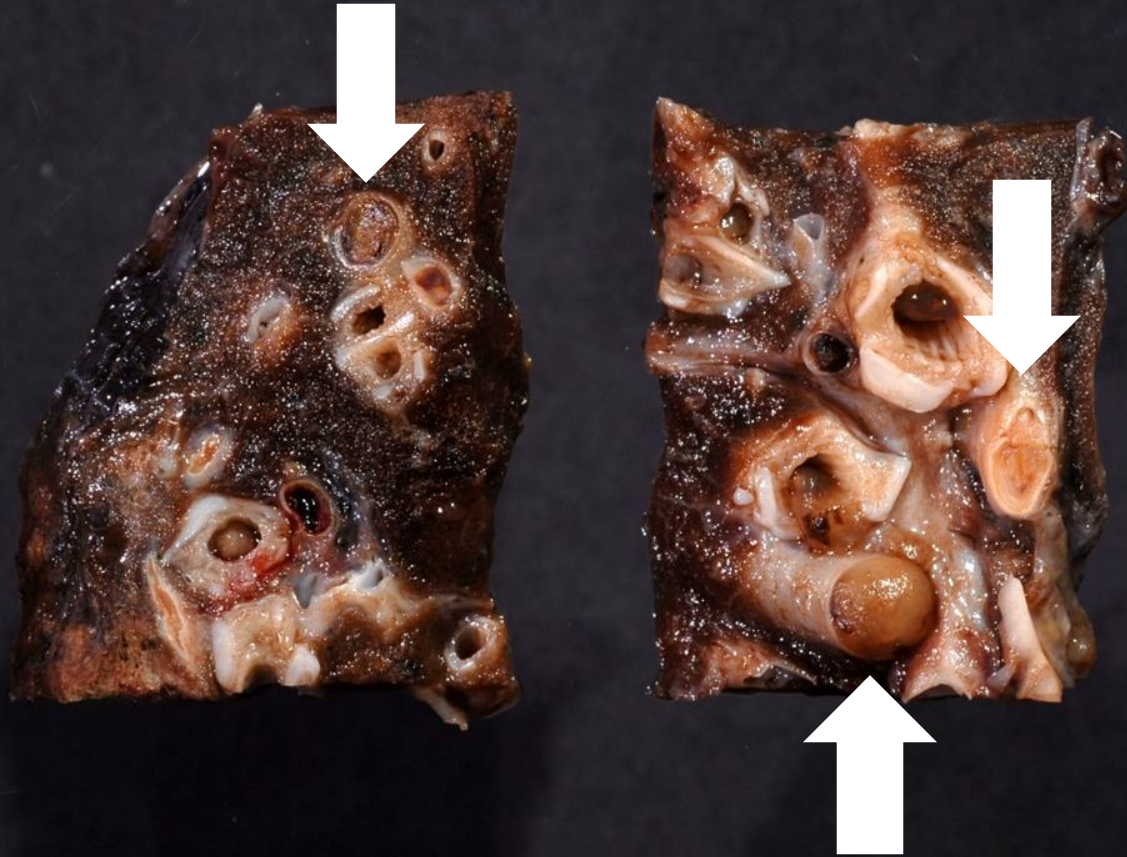
200um



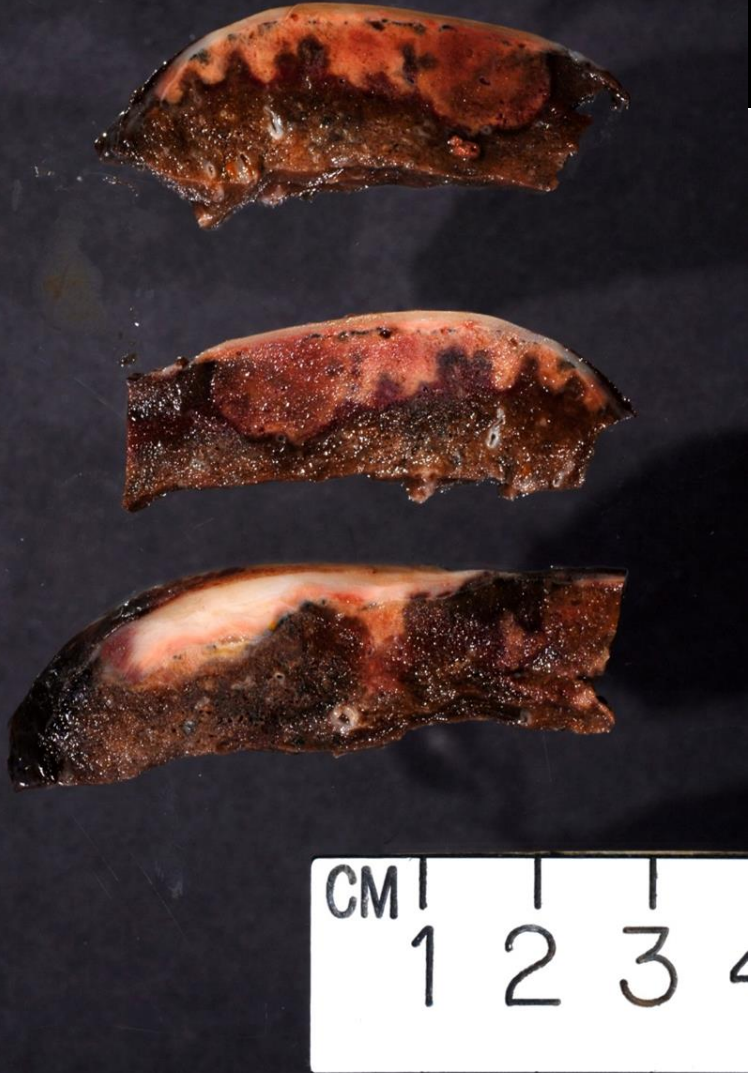
Pulmonary artery intimal sarcoma

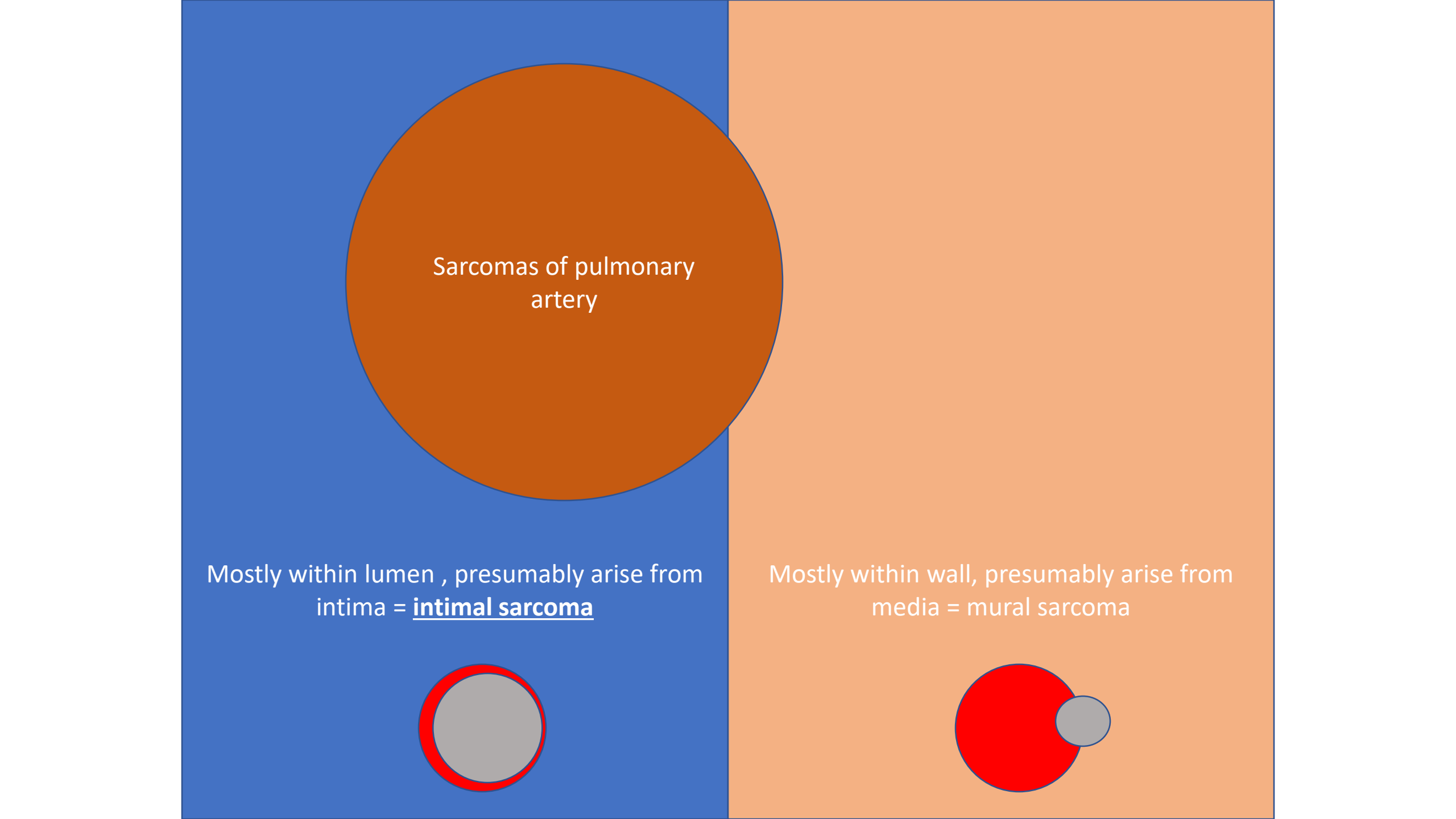


Pulmonary artery intimal sarcoma



Infarct due to pulmonary artery intimal sarcoma





The diagram is divided into two vertical panels. The left panel has a blue background and contains a large orange circle representing a sarcoma within the lumen of a pulmonary artery. Below it is a small diagram of a vessel with a red ring (intima) and a grey center (lumen). The right panel has an orange background and contains a large red circle representing a sarcoma within the vessel wall. Below it is a small diagram of a vessel with a red wall and a grey center. Text labels describe the location and presumed origin of these sarcomas.

Sarcomas of pulmonary artery

Mostly within lumen , presumably arise from intima = intimal sarcoma

Mostly within wall, presumably arise from media = mural sarcoma

The diagram is a conceptual map of sarcoma types. It features a large blue rectangular area on the left and a large orange rectangular area on the right, separated by a vertical line. In the blue area, there are two circles: an orange one at the top and a green one at the bottom. The orange circle is labeled 'Pulmonary artery intimal sarcoma' and the green circle is labeled 'Aorta or cardiac intimal sarcoma'. The text 'Undifferentiated sarcoma' is placed in the blue area between these two circles. In the orange area, a list of sarcoma types is provided: 'Leiomyosarcoma', 'Rhabdomyosarcoma', 'Angiosarcoma', 'Osteosarcoma', and 'Chondrosarcoma'.

Pulmonary
artery intimal
sarcoma

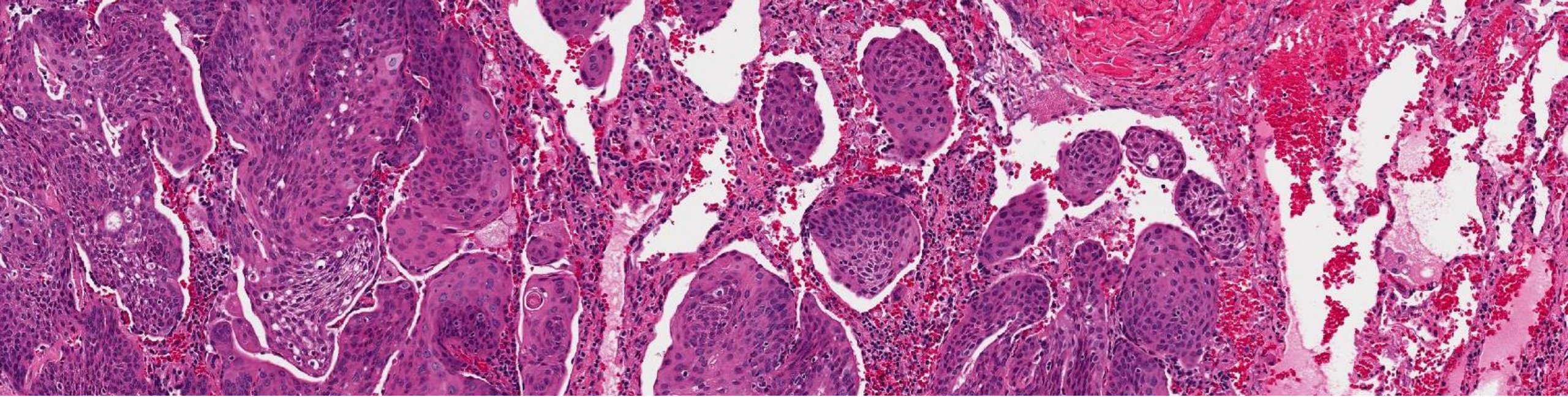
Undifferentiated sarcoma

Aorta or cardiac
intimal sarcoma

Leiomyosarcoma
Rhabdomyosarcoma
Angiosarcoma
Osteosarcoma
Chondrosarcoma

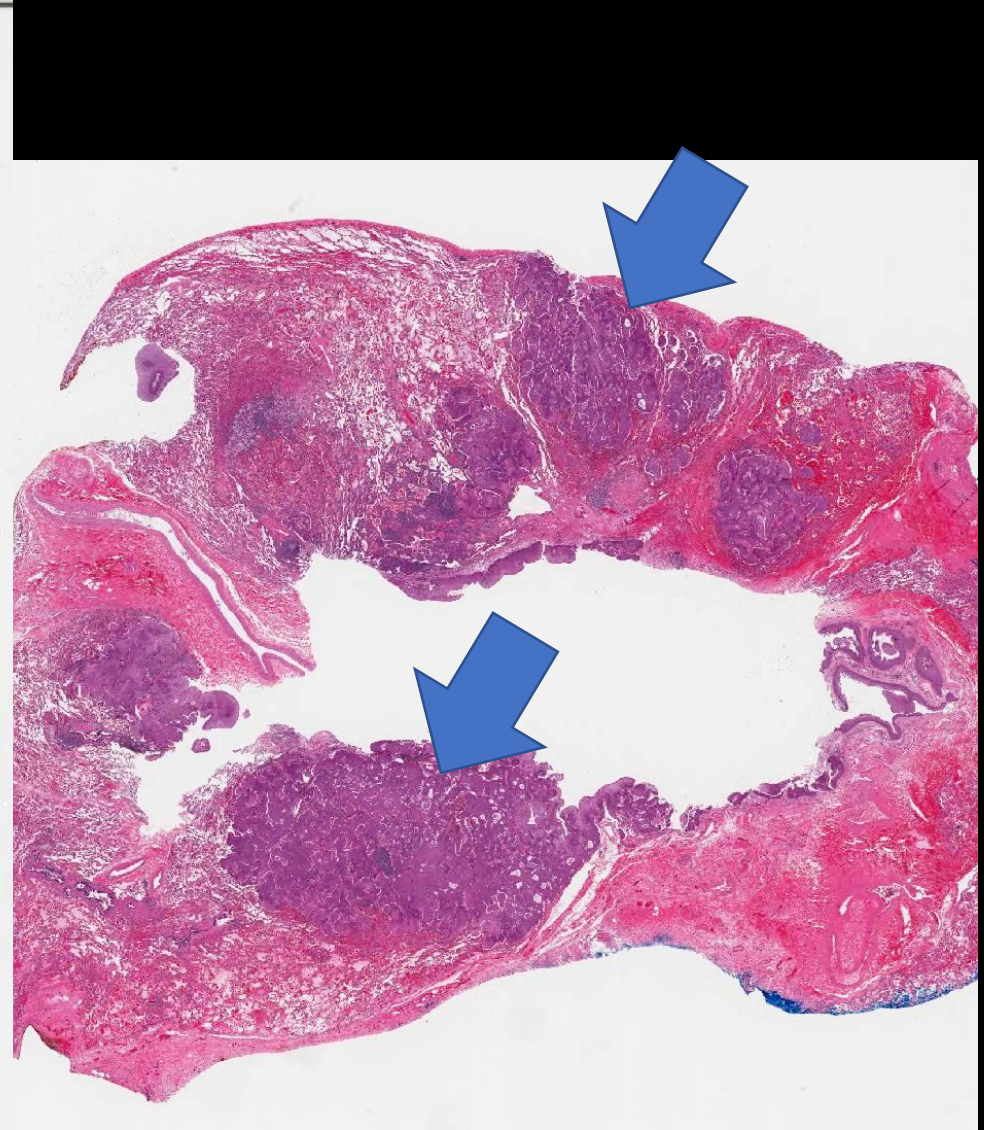
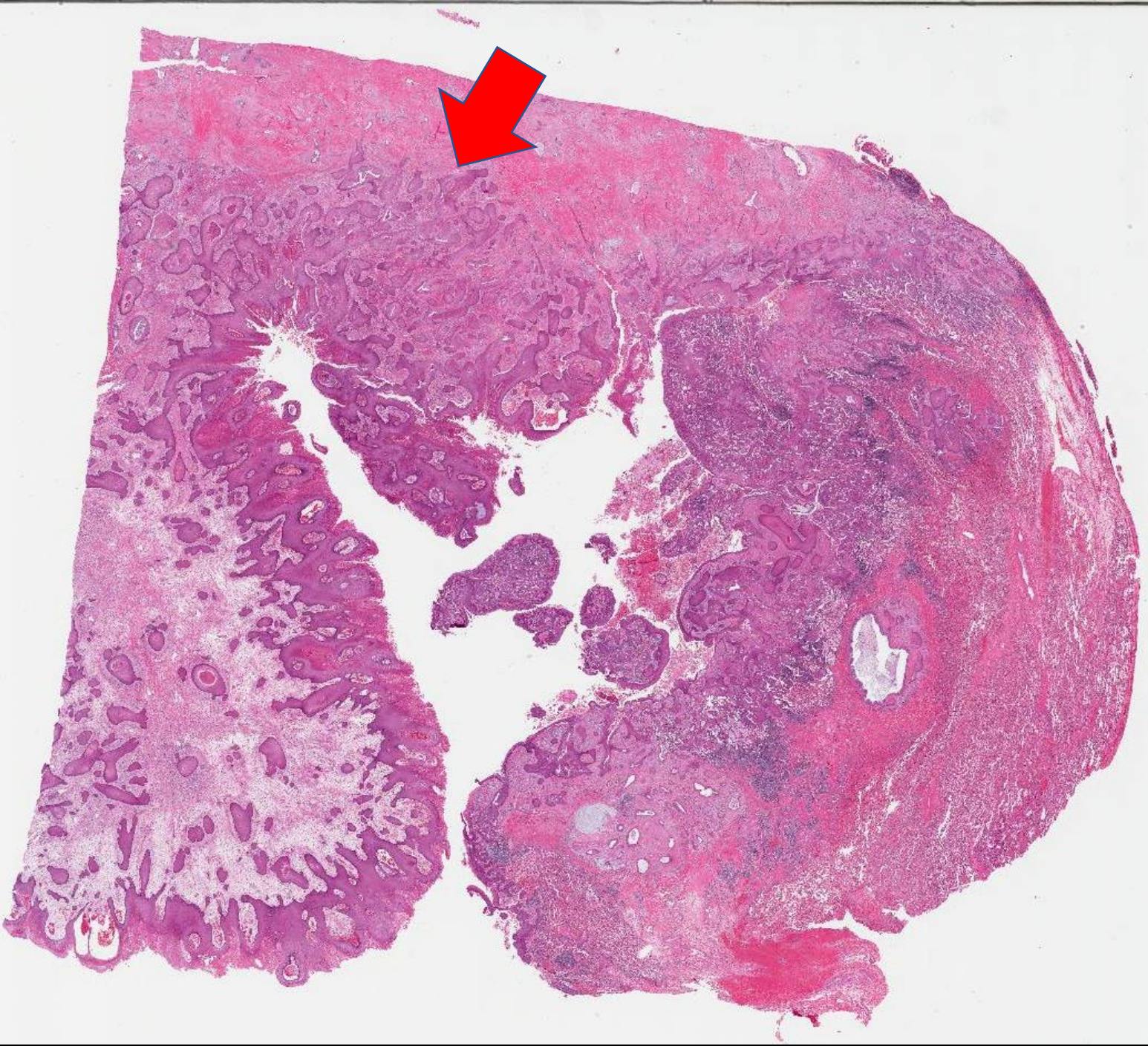
PULMONARY ARTERY INTIMAL SARCOMA

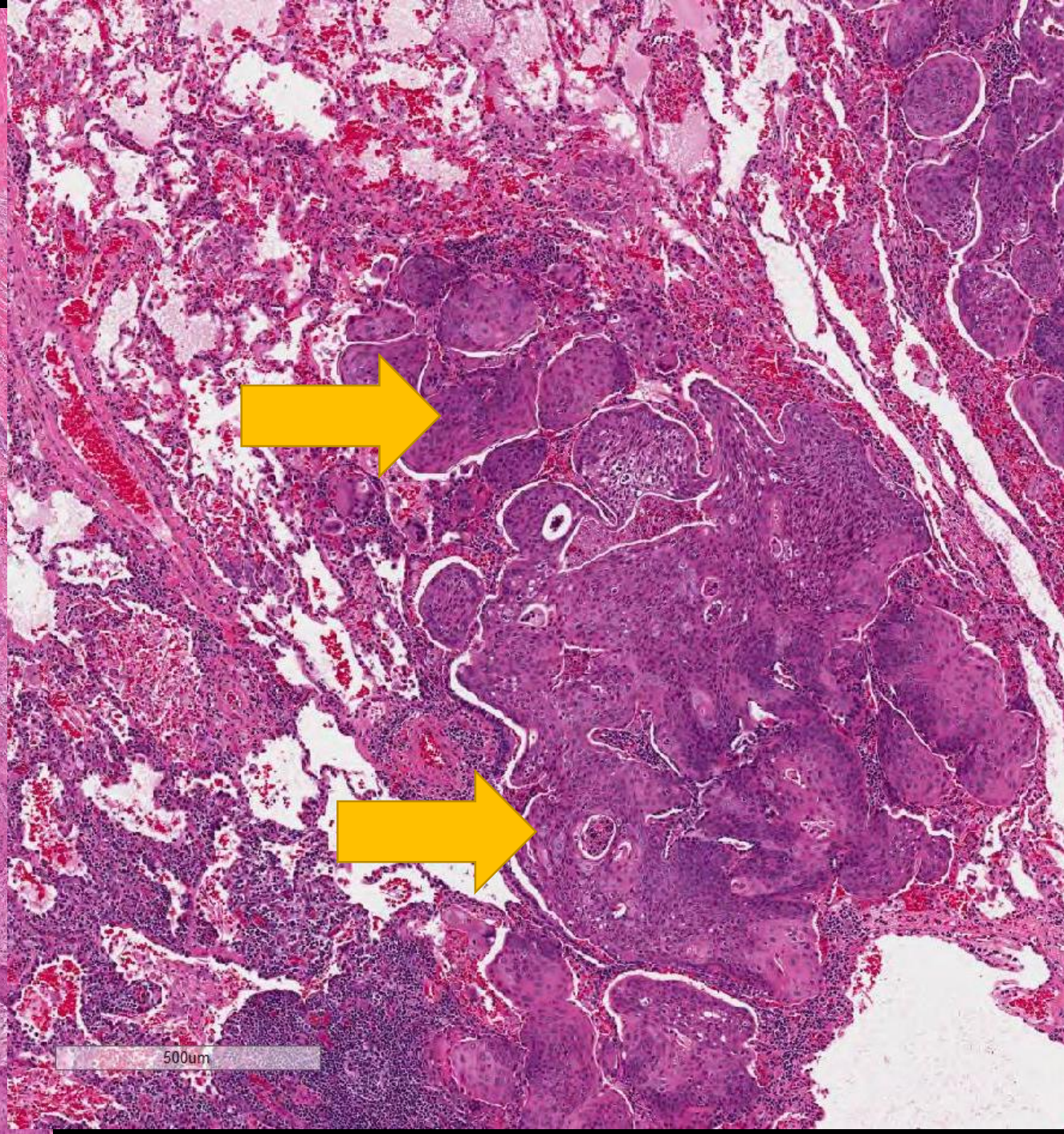
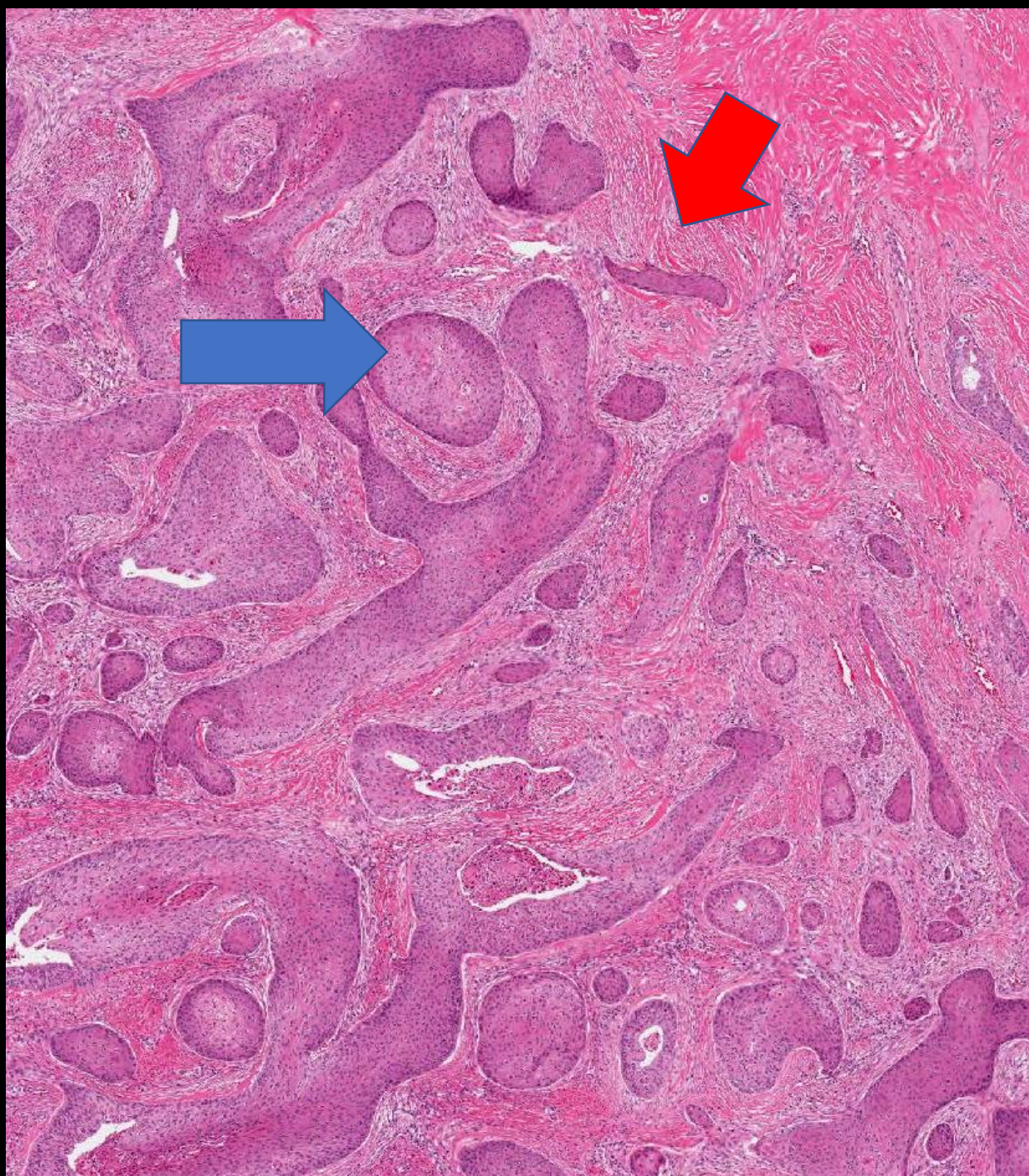
- Clinical: non-resolving pulmonary thrombus, mass within pulmonary artery
- H&E: poorly differentiated malignant neoplasm
- Immunohistochemistry: Not very helpful (Keratin neg, MDM2 may be overexpressed)
- How to confirm? Location!!



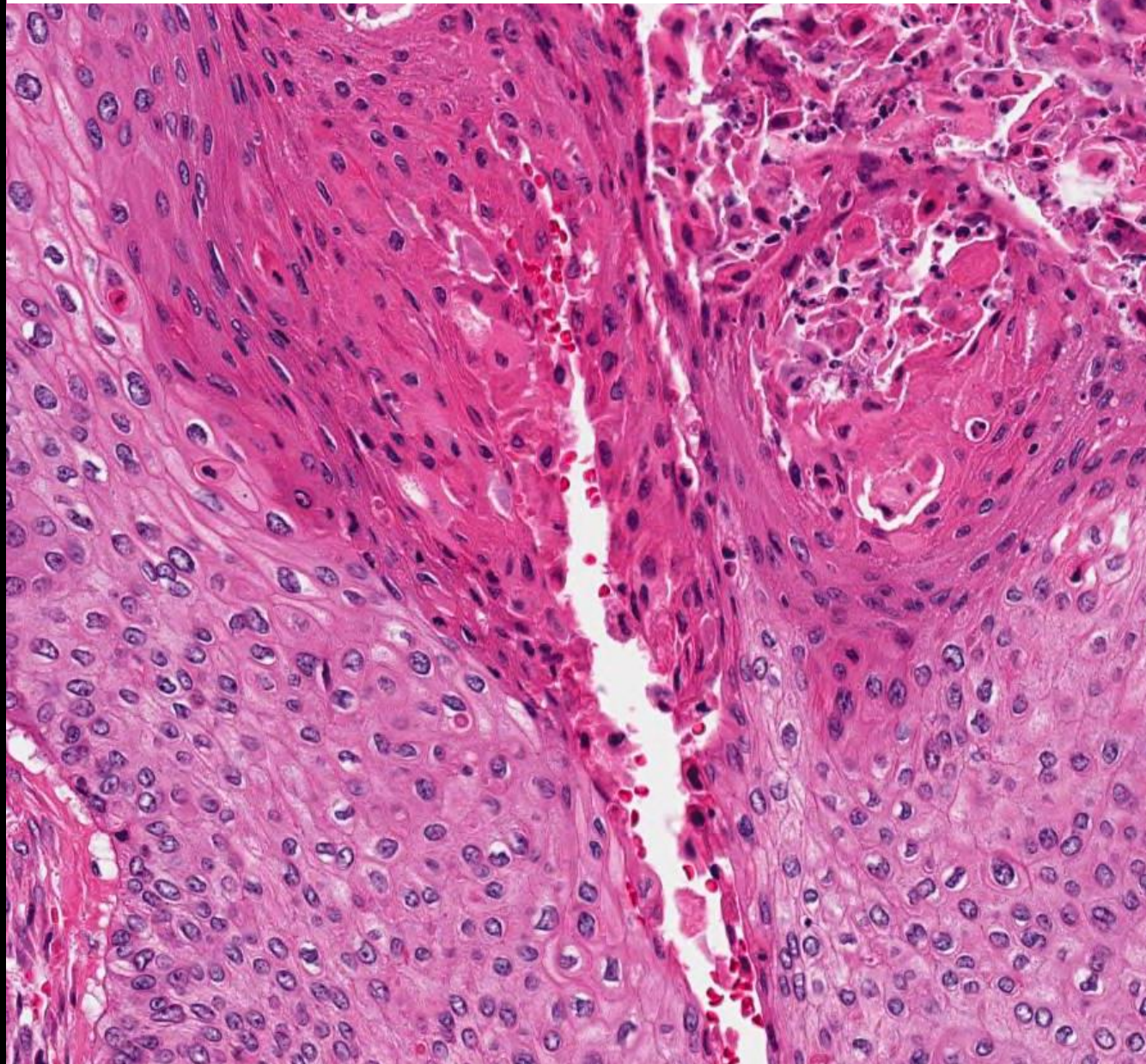
BENIGN OR MALIGNANT?

TUMOR 8

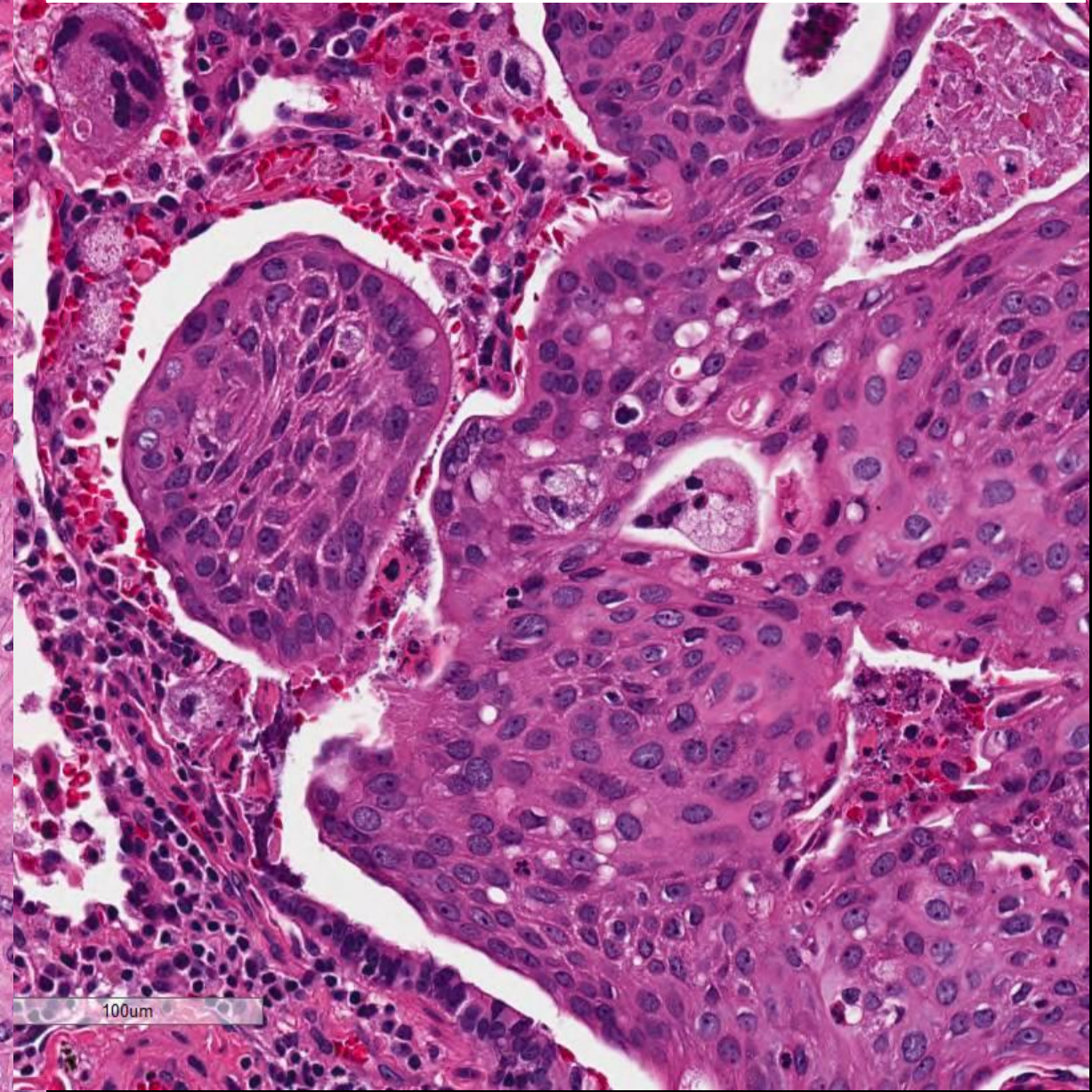




Squamous cell sarcoma

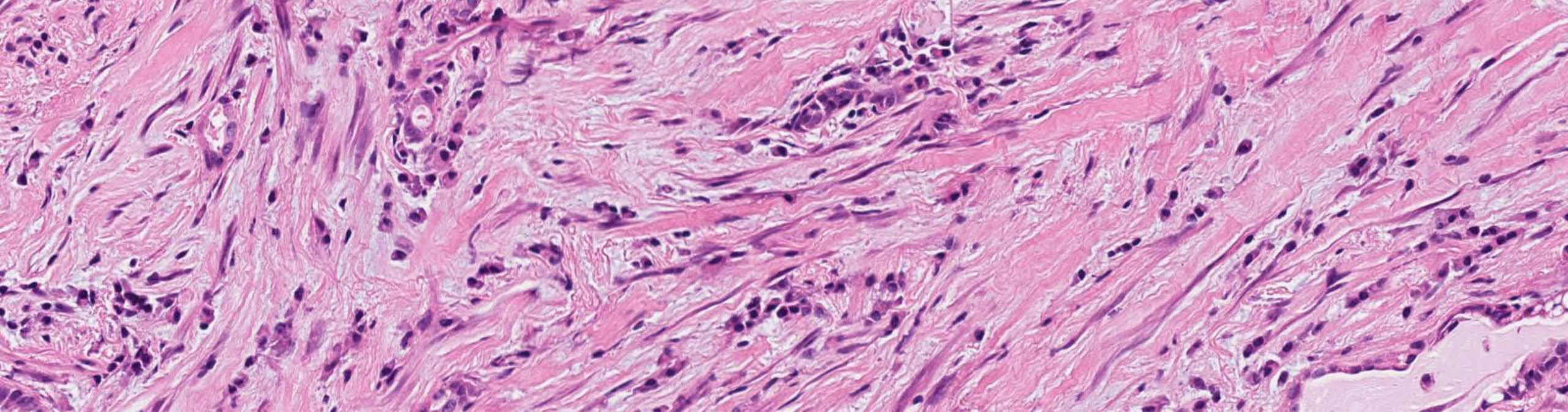


Squamous papillomatosis



SQUAMOUS CELL CARCINOMA ARISING IN PAPILLOMATOSIS

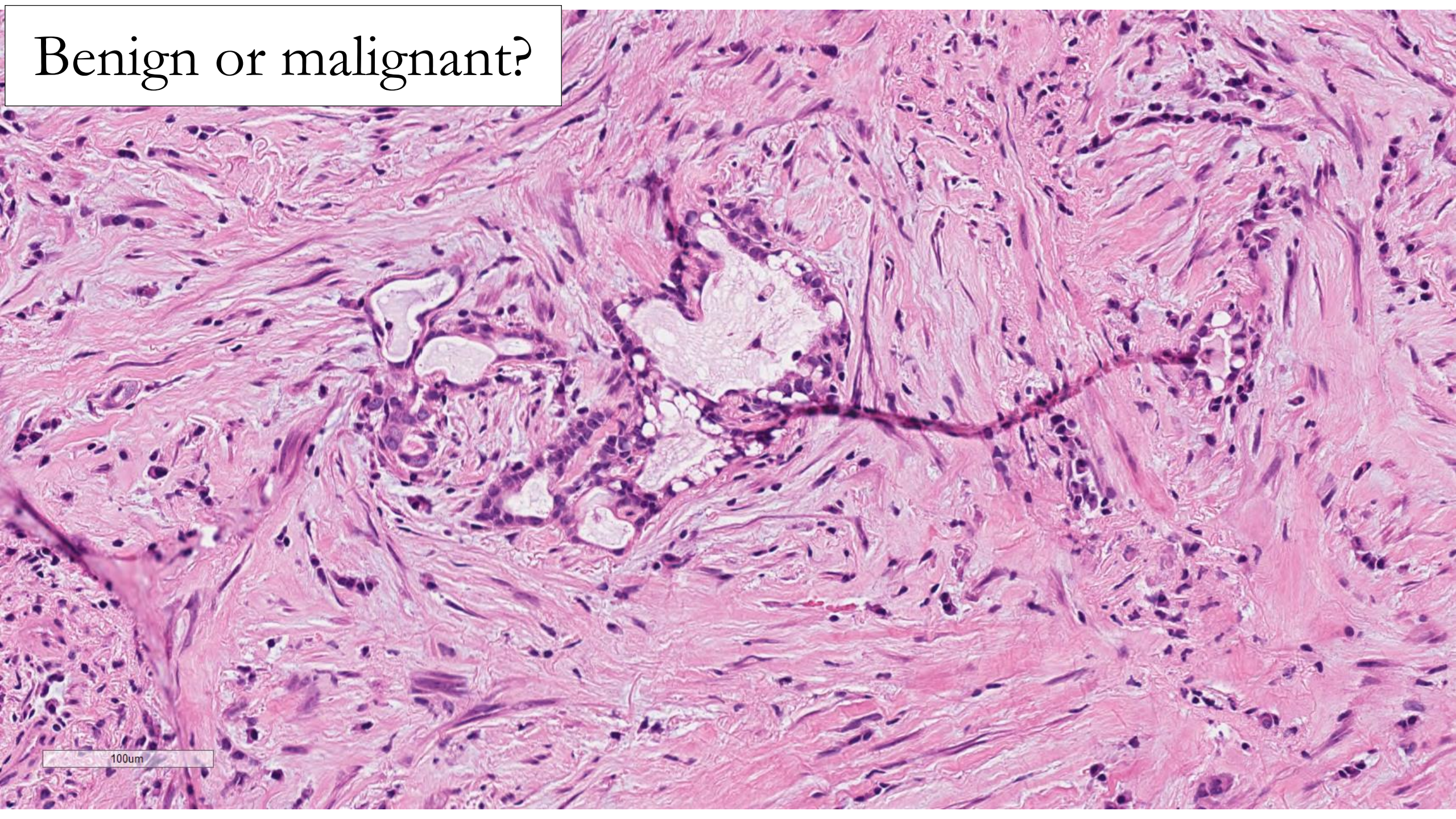
- Clinical: Recurrent tracheal papillomatosis in young patients can involve lung; multiple lung nodules
- H&E: Bland cytology, cilia (papilloma), malignant cytology, keratinization, desmoplasia (squamous cell carcinoma)
- Immunohistochemistry: both are pos for squamous markers
- How to confirm? Morphology is key!!



IGG4 DISEASE?

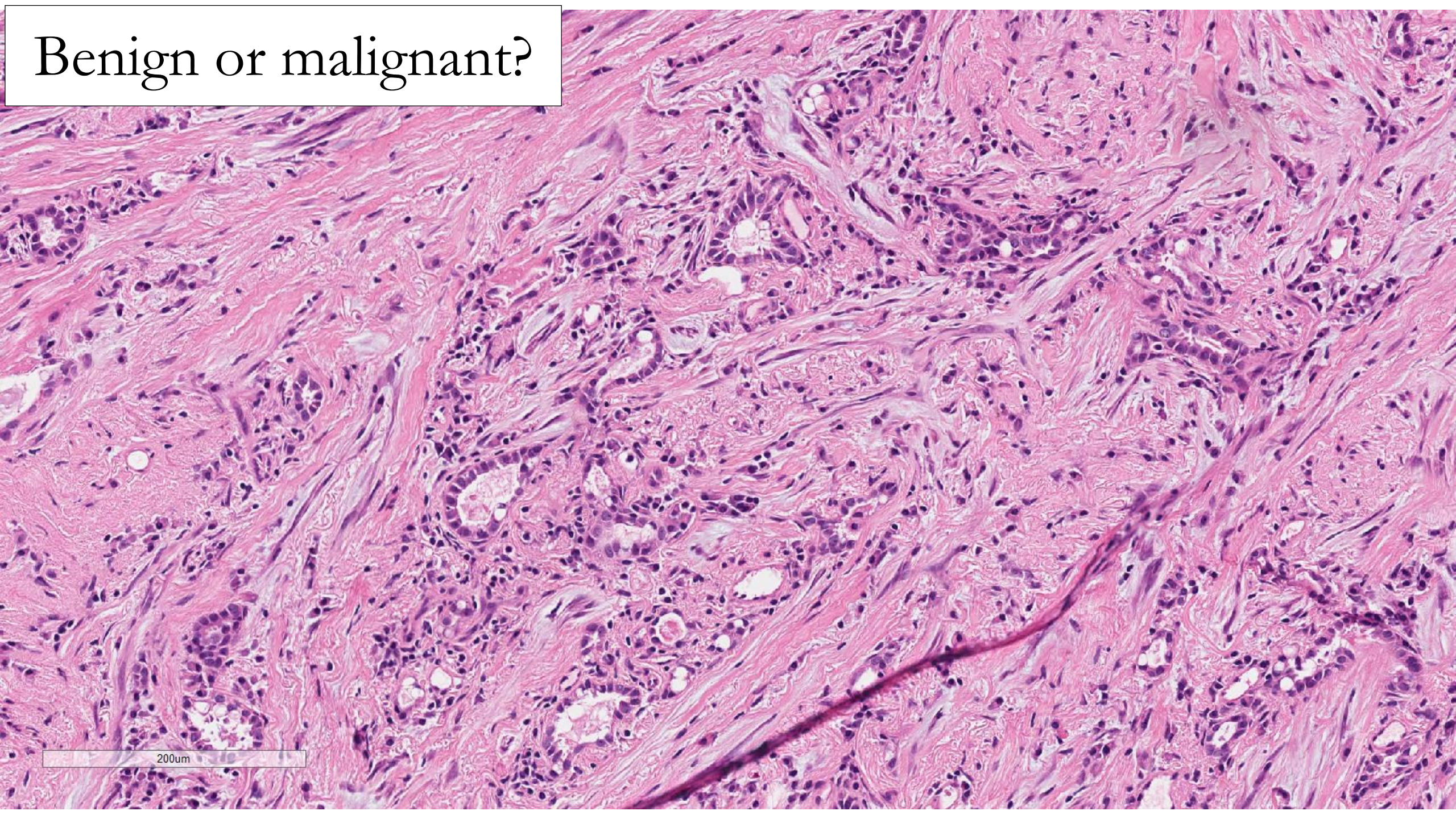
TUMOR 9

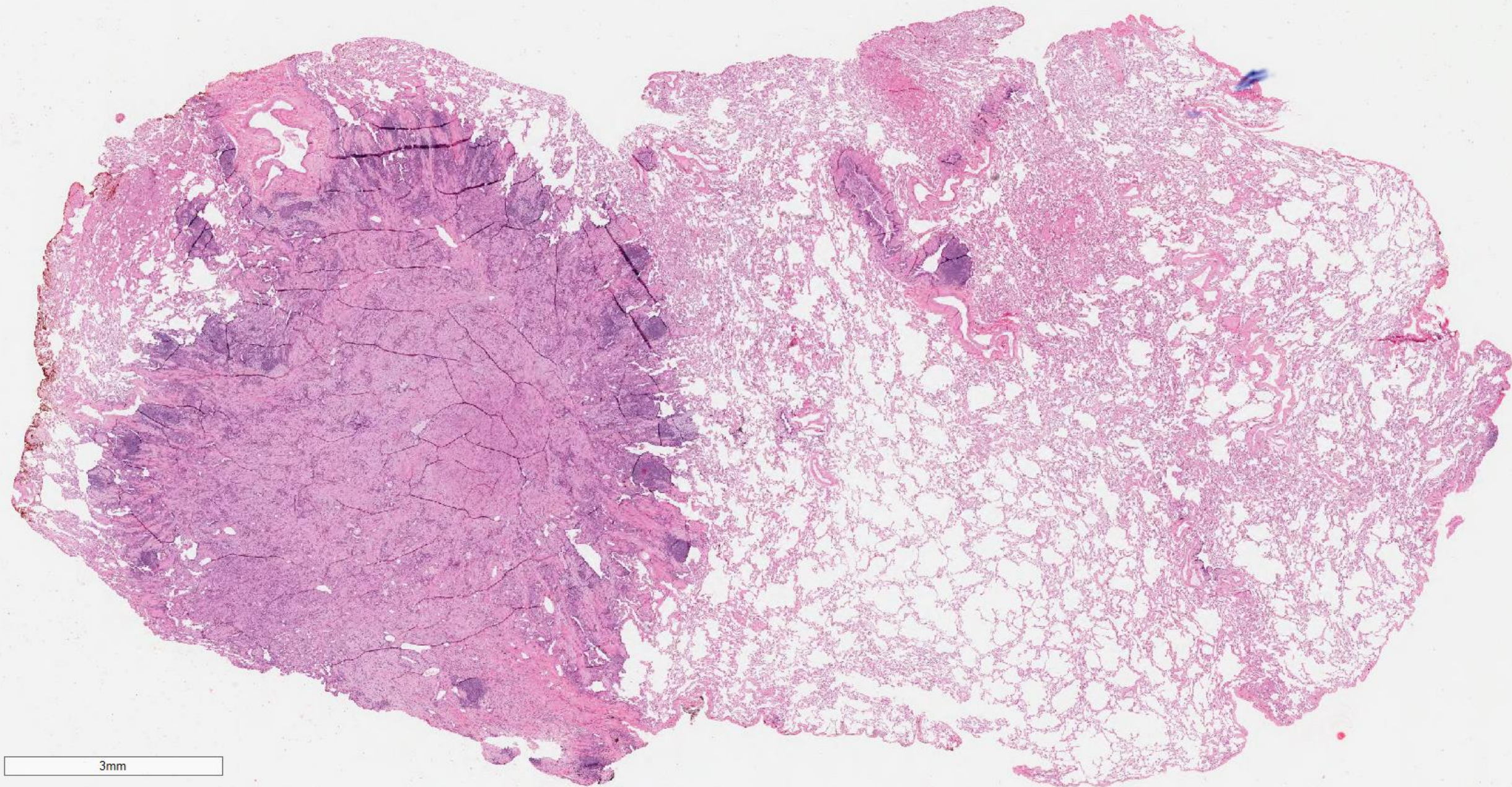
Benign or malignant?



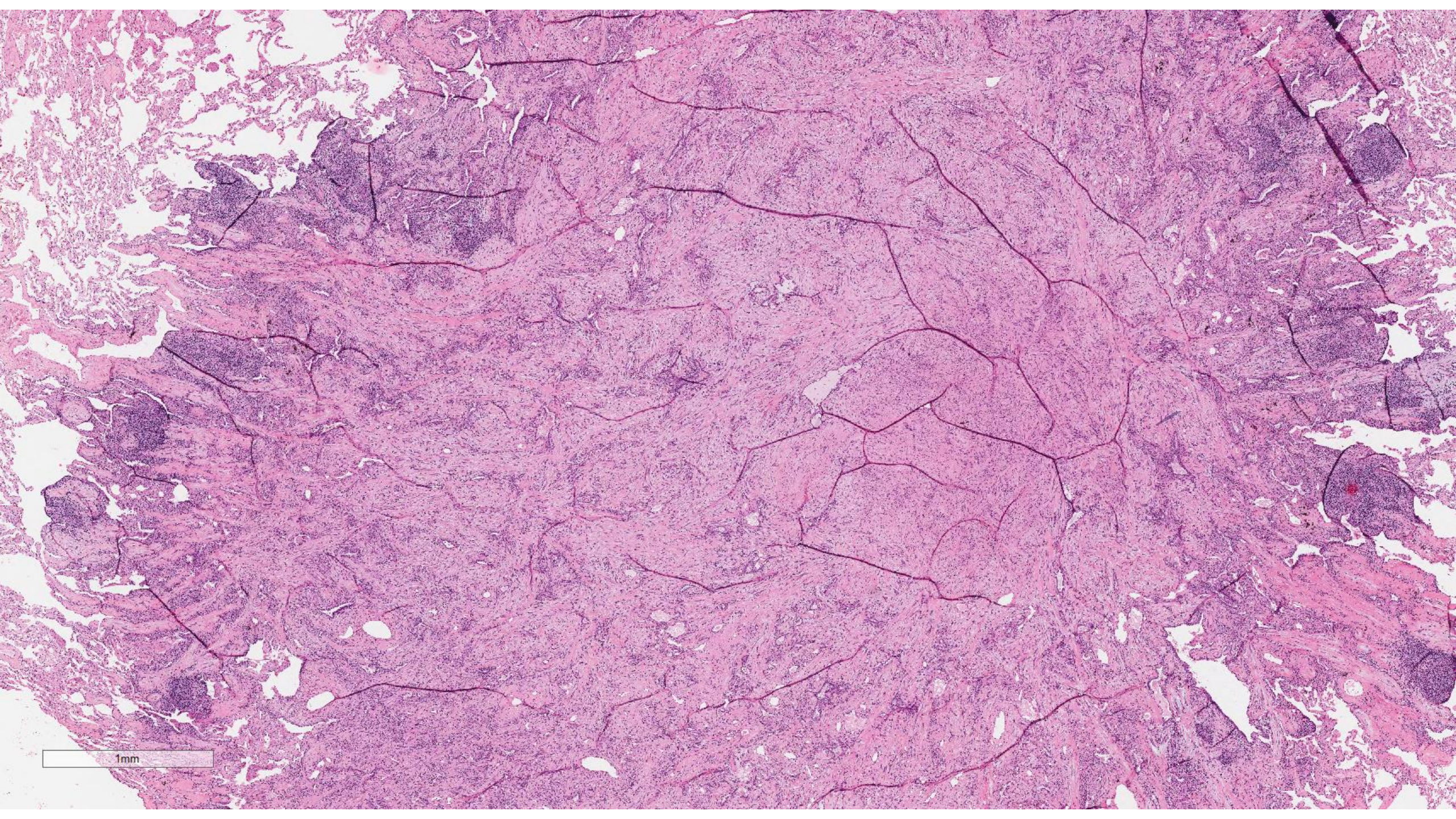
100um

Benign or malignant?

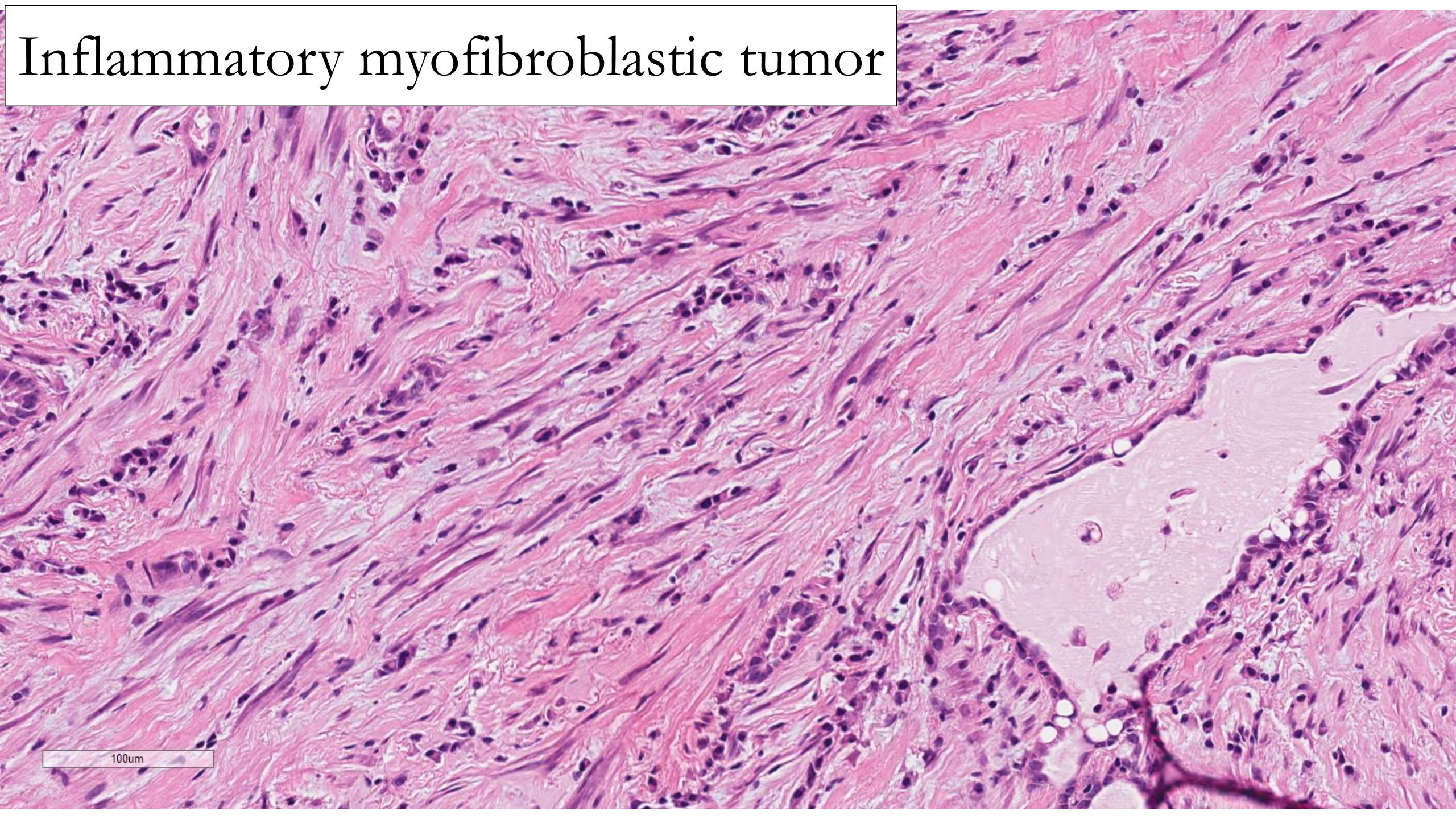




3mm

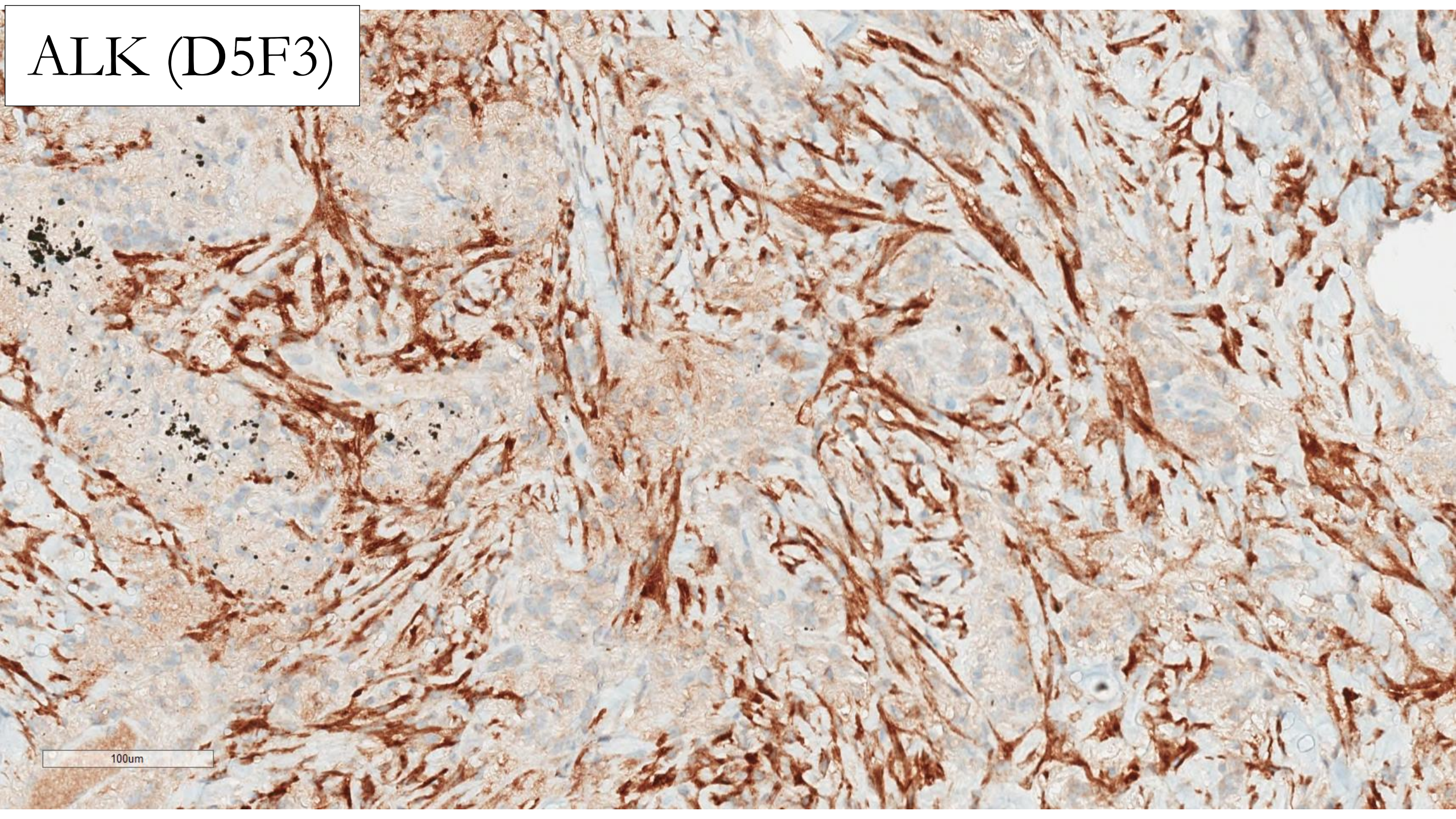


Inflammatory myofibroblastic tumor



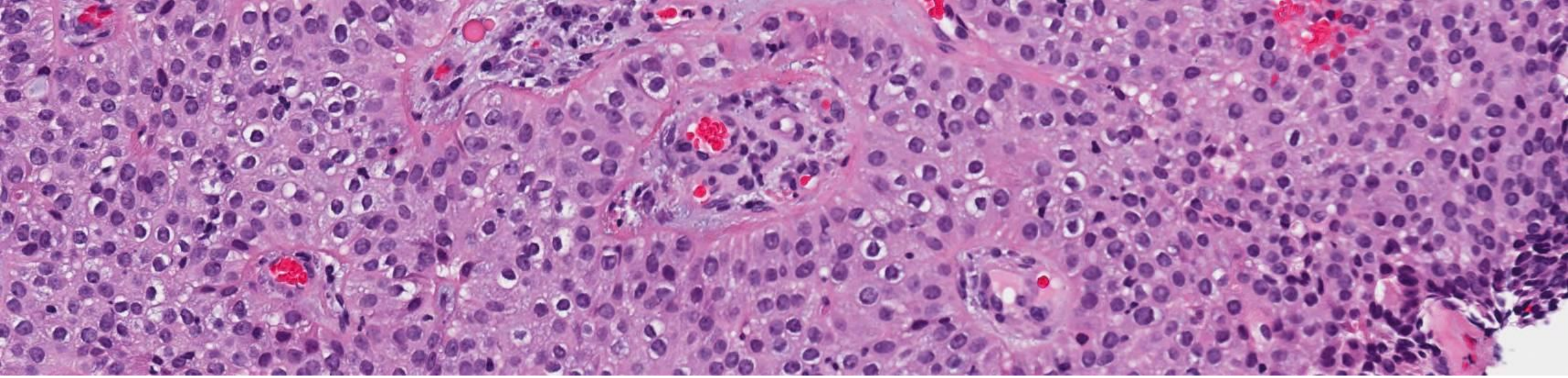
100um

ALK (D5F3)



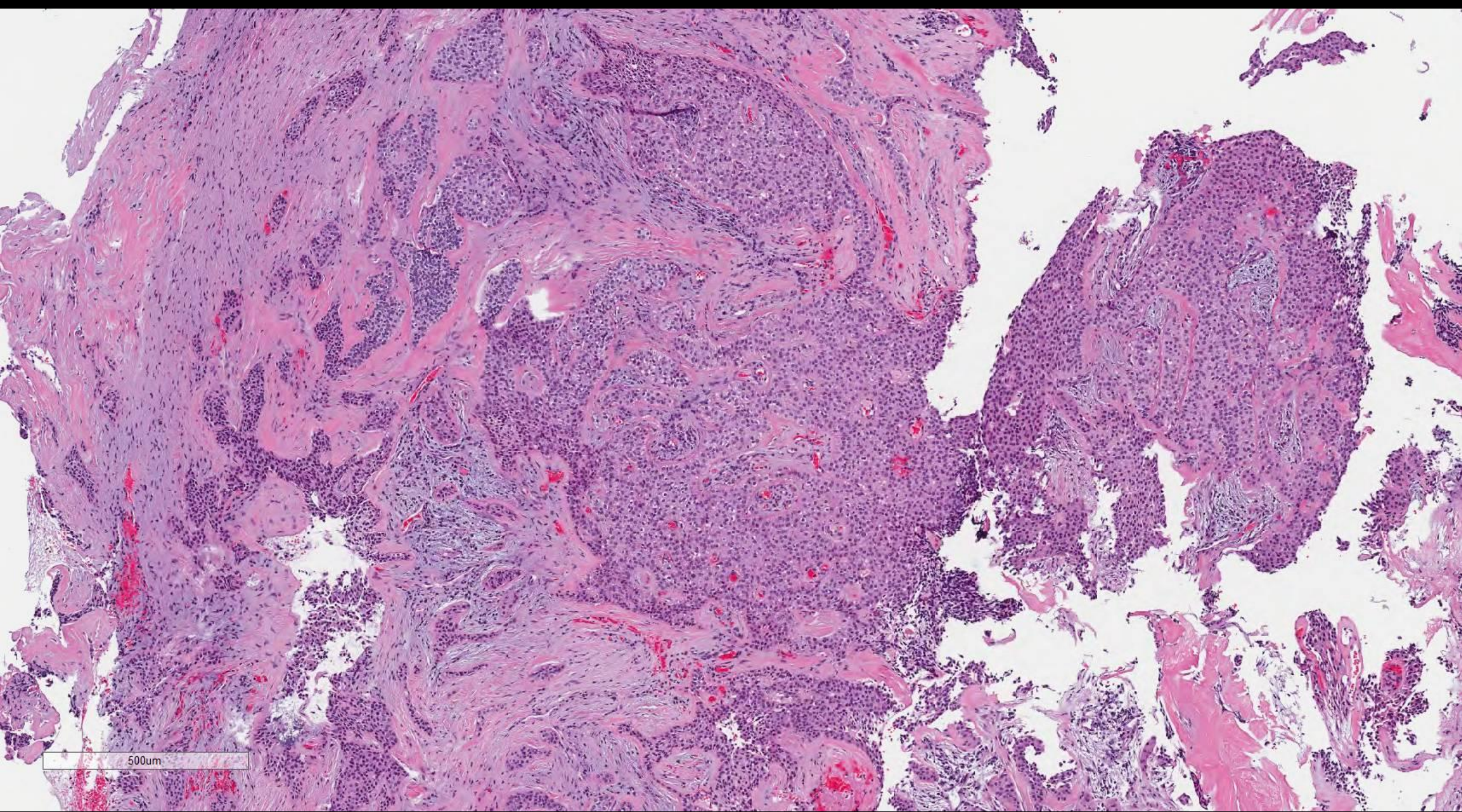
INFLAMMATORY MYOFIBROBLASTIC TUMOR

- Clinical: Lung mass in young patient
- H&E: Bland elongated spindle cells (spindle cell neoplasm) + many plasma cells
- Immunohistochemistry: ALK + (try D5F3!), SMA +, IgG4 + cells common
- How to confirm? ALK (D5F3) IHC or ALK FISH



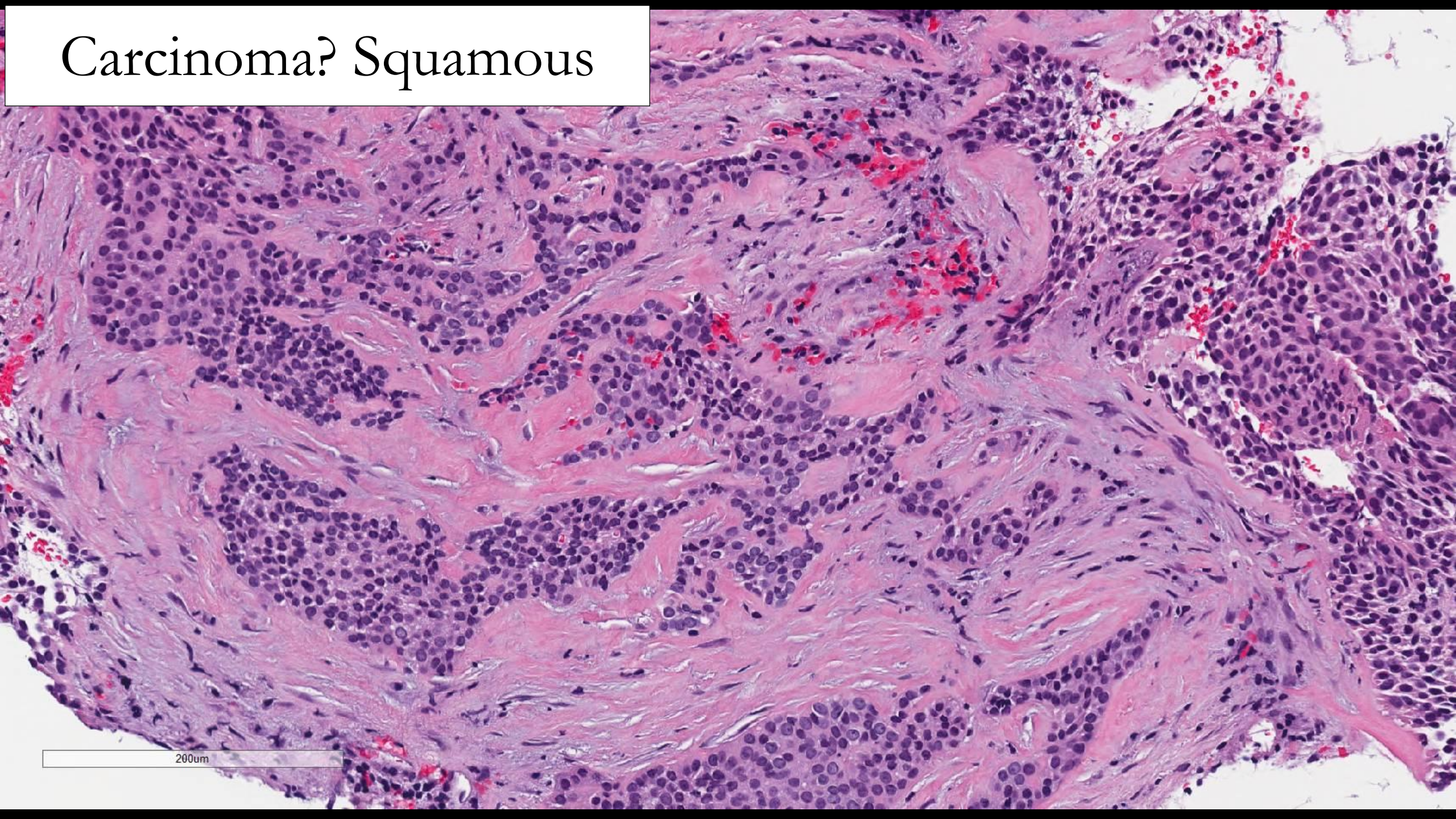
SQUAMOUS CELL CARCINOMA?

TUMOR 10



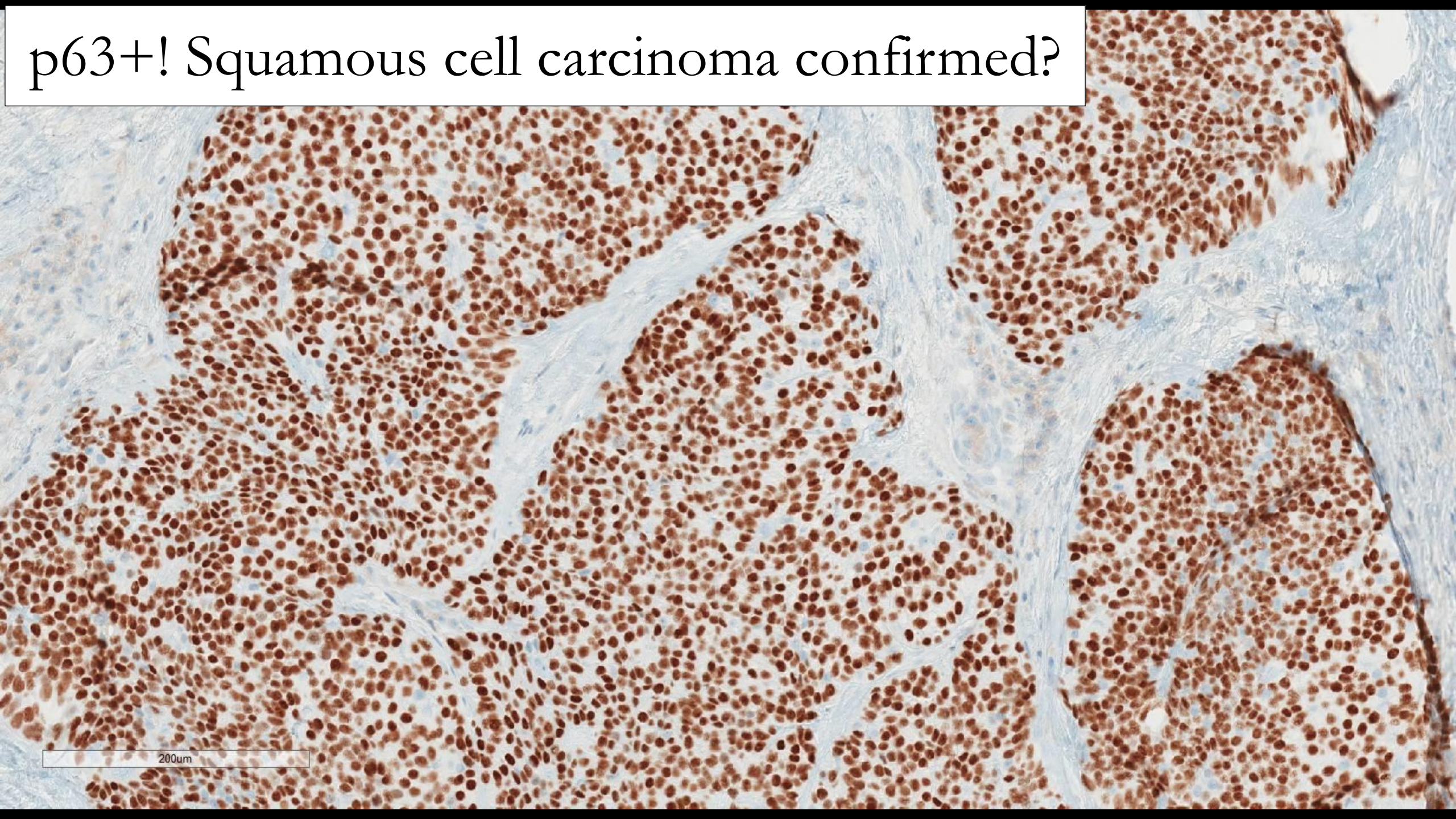
500um

Carcinoma? Squamous

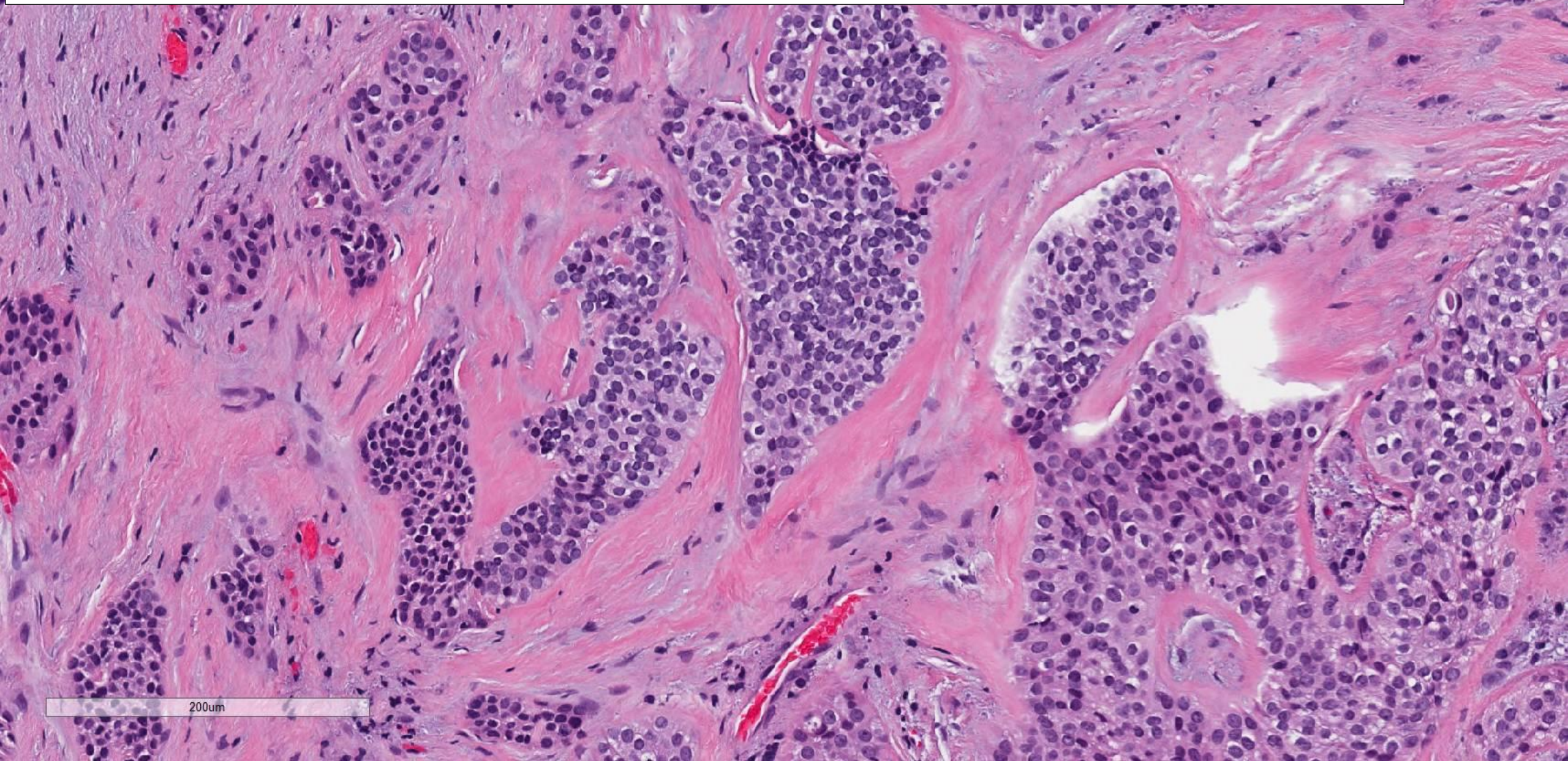


200um

p63+! Squamous cell carcinoma confirmed?



Pos for EWSR1 fusion by NGS: Clear cell carcinoma



Clear cell carcinoma: not that “clear”



100um

CLEAR CELL CARCINOMA

- Clinical: Mostly endobronchial lesions
- H&E: Bland cytology, basement membrane material, cytoplasmic clearing, occasional mucin droplet
- Immunohistochemistry: Can be misleading. TTF-1 neg, p63/p40 pos.
- How to confirm? FISH or NGS: *EW/SR1* translocation

A histological section of tissue, likely from the endometrium, stained with hematoxylin and eosin (H&E). The image shows numerous glandular structures of varying sizes, some containing secretory material. The glands are lined by a layer of cells, and the surrounding stroma is densely cellular. A central white rectangular box contains the text "Thank you!".

Thank you!

300um