

# Southbay June 2024 Webcases





# Disclosures

## June 3, 2024

The activity planners and faculty listed below have no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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**Activity Planners/Moderator:**

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Megan Troxell, MD, PhD  
Dave Bingham, MD

# Wine Selection

## *For the Tortellini*



- Medium bodied Rioja
- Blend of red and white grapes makes this an unusual wine
- Very elegant, flavorful, and delicious wine

4 bottles (1 per table)

## *2 options for the Steak*



- Medium to full bodied California style Cabernet blend
- Fruit forward and delicious

2 bottles

(ask your server for a glass)



- Medium to full bodied Rioja
- Fruit, spice, and citrus zest
- Racy and beautiful

2 bottles

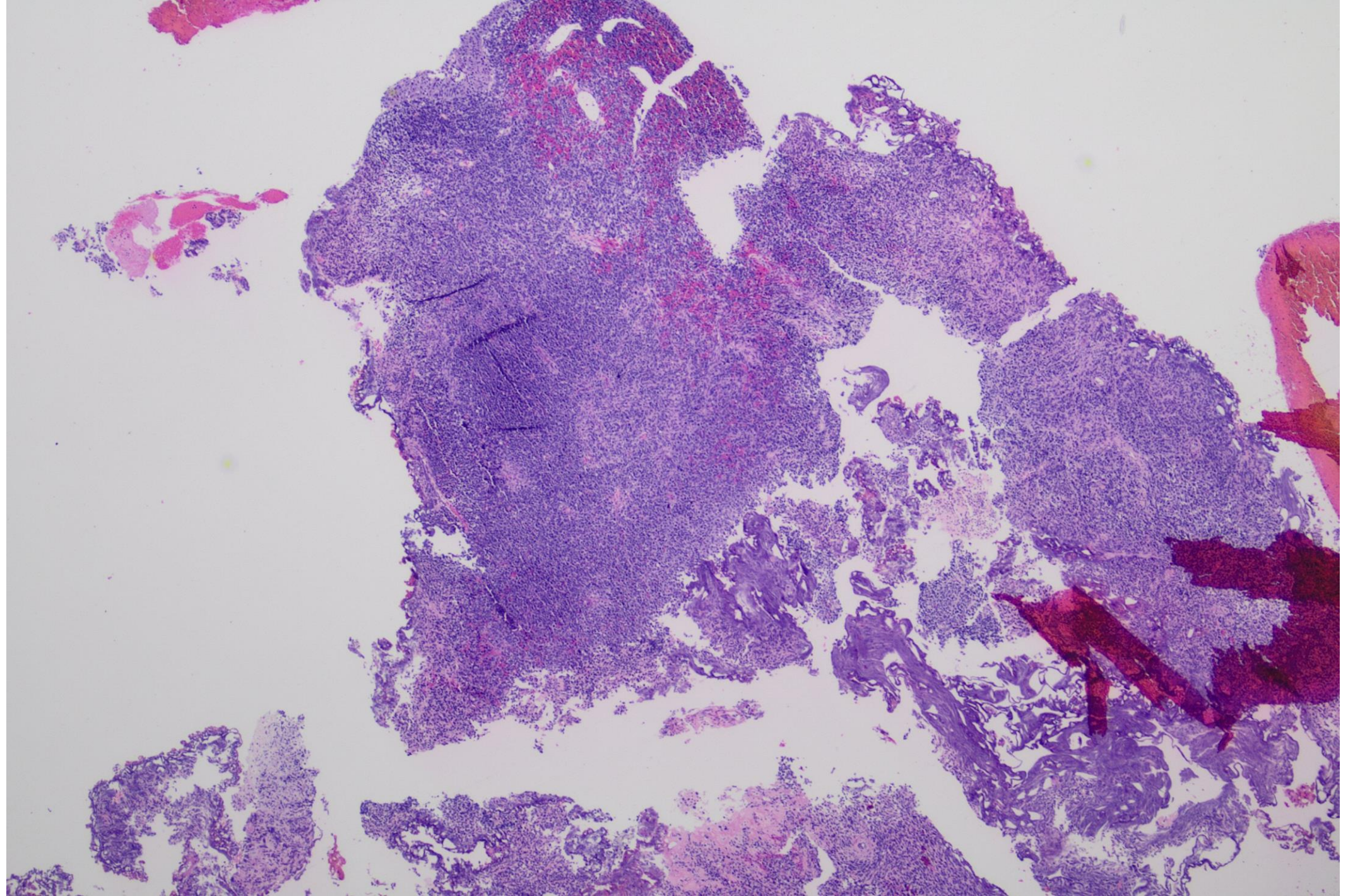
(ask your server for a glass)

24-0601

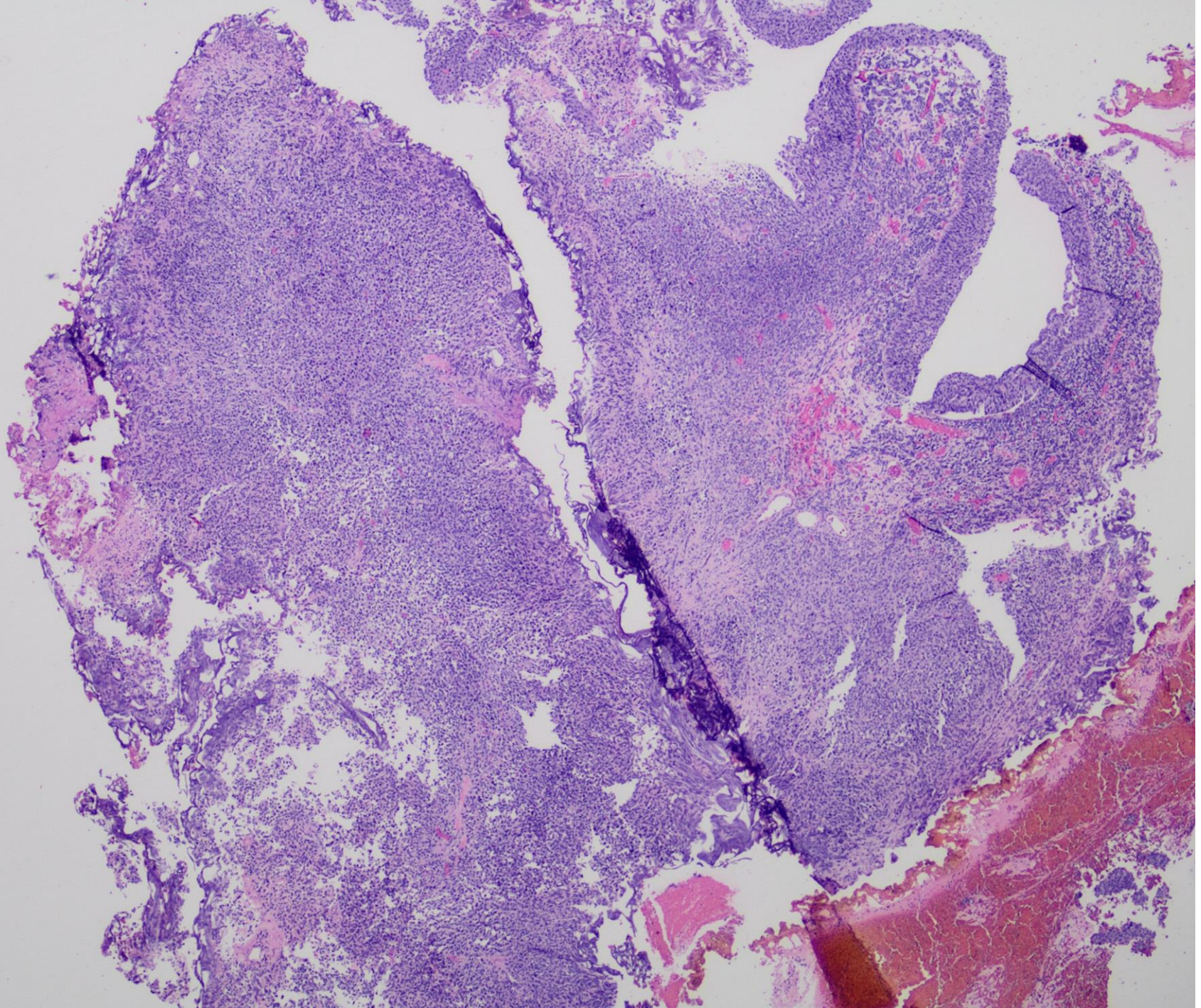
**Armen Khararjian; Kaiser Permanente**

Older aged male with bladder mass

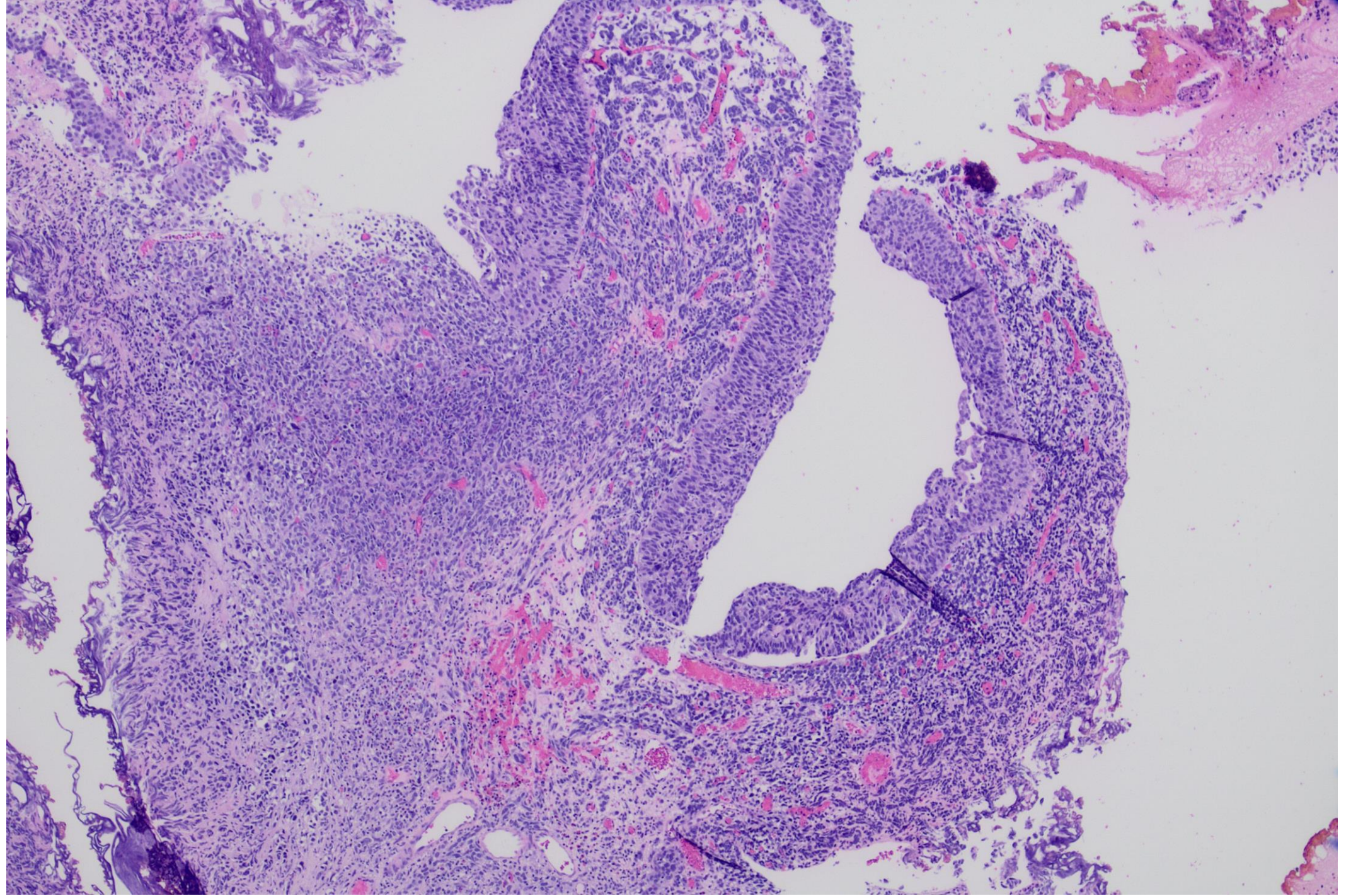




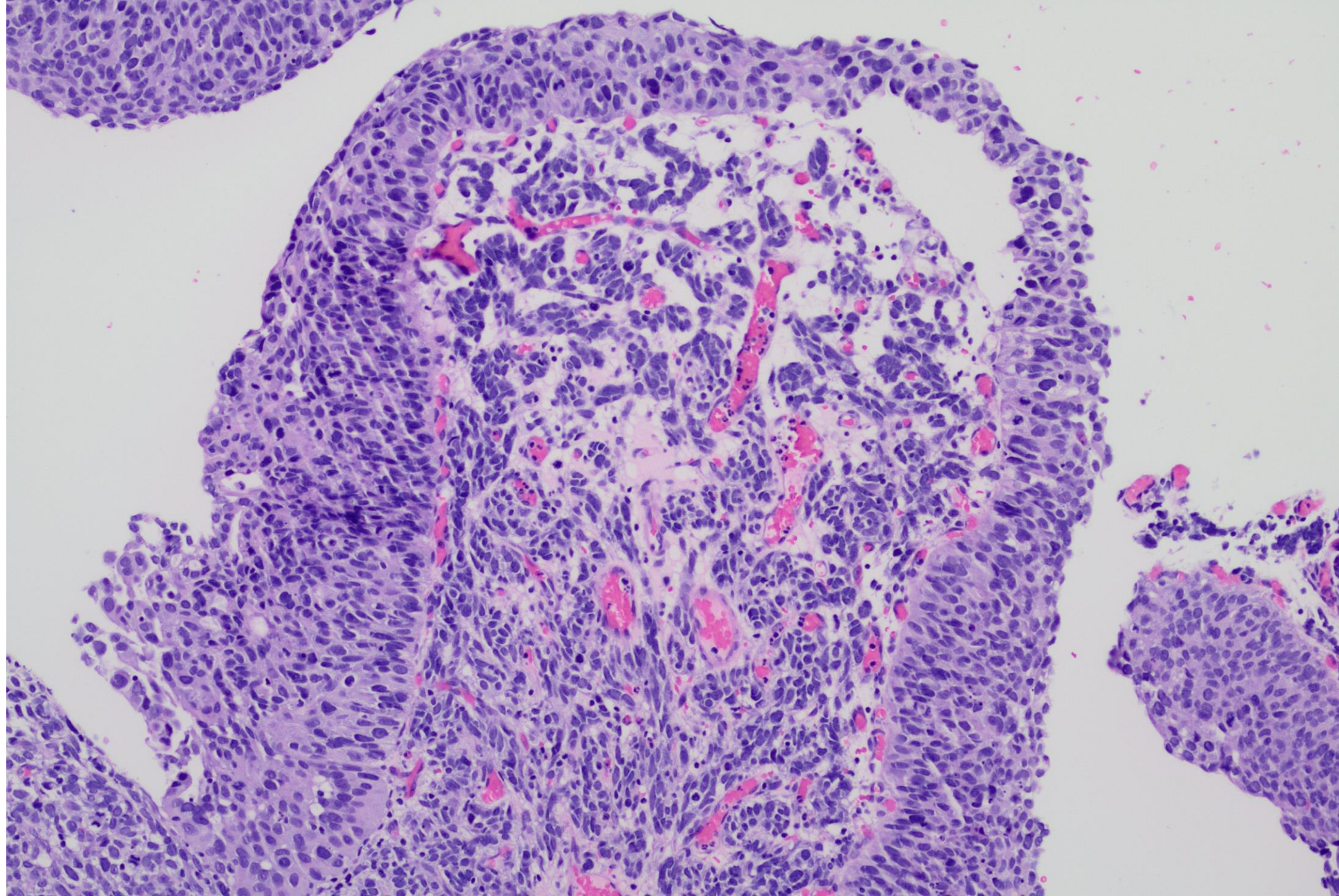




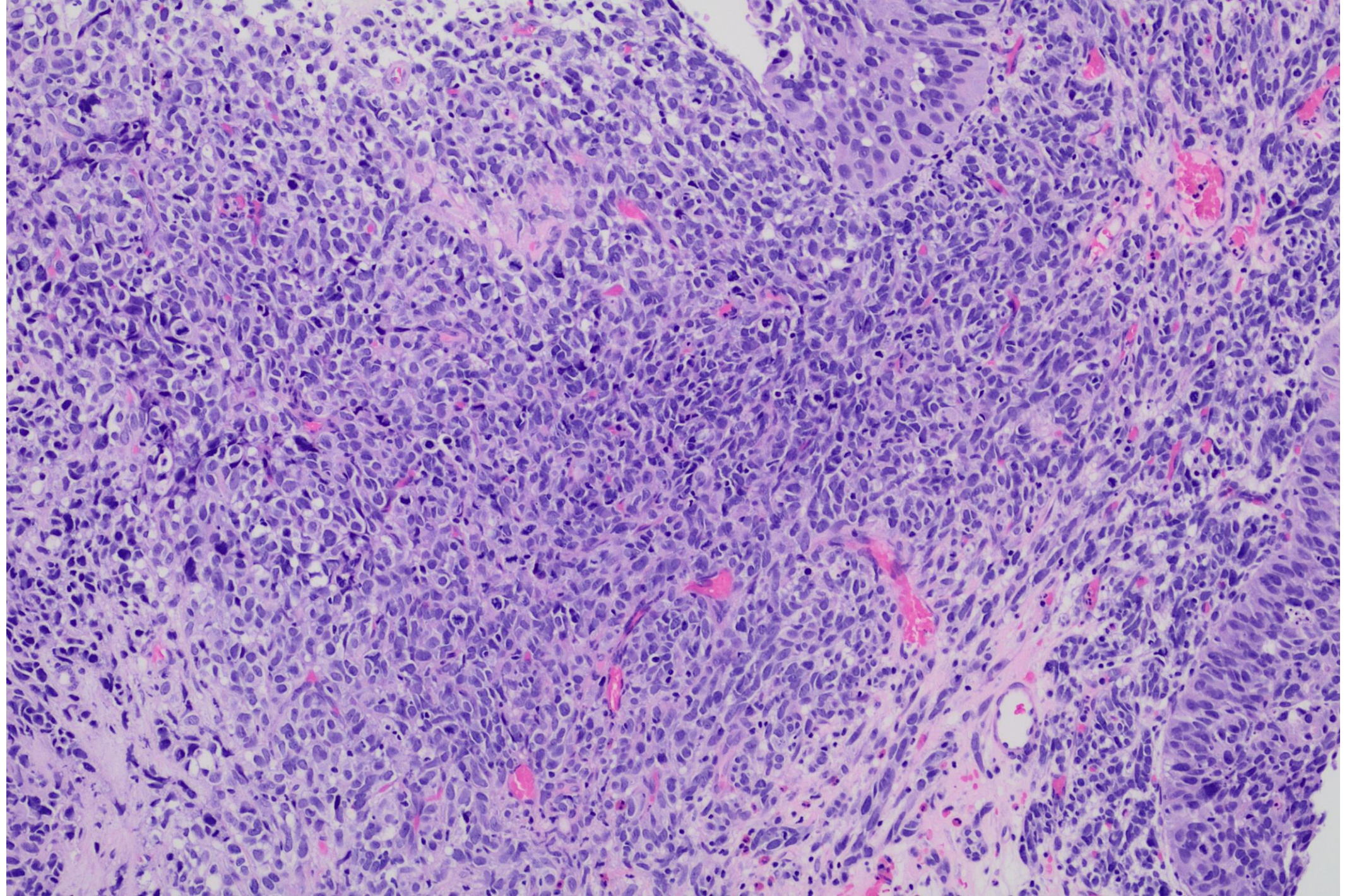




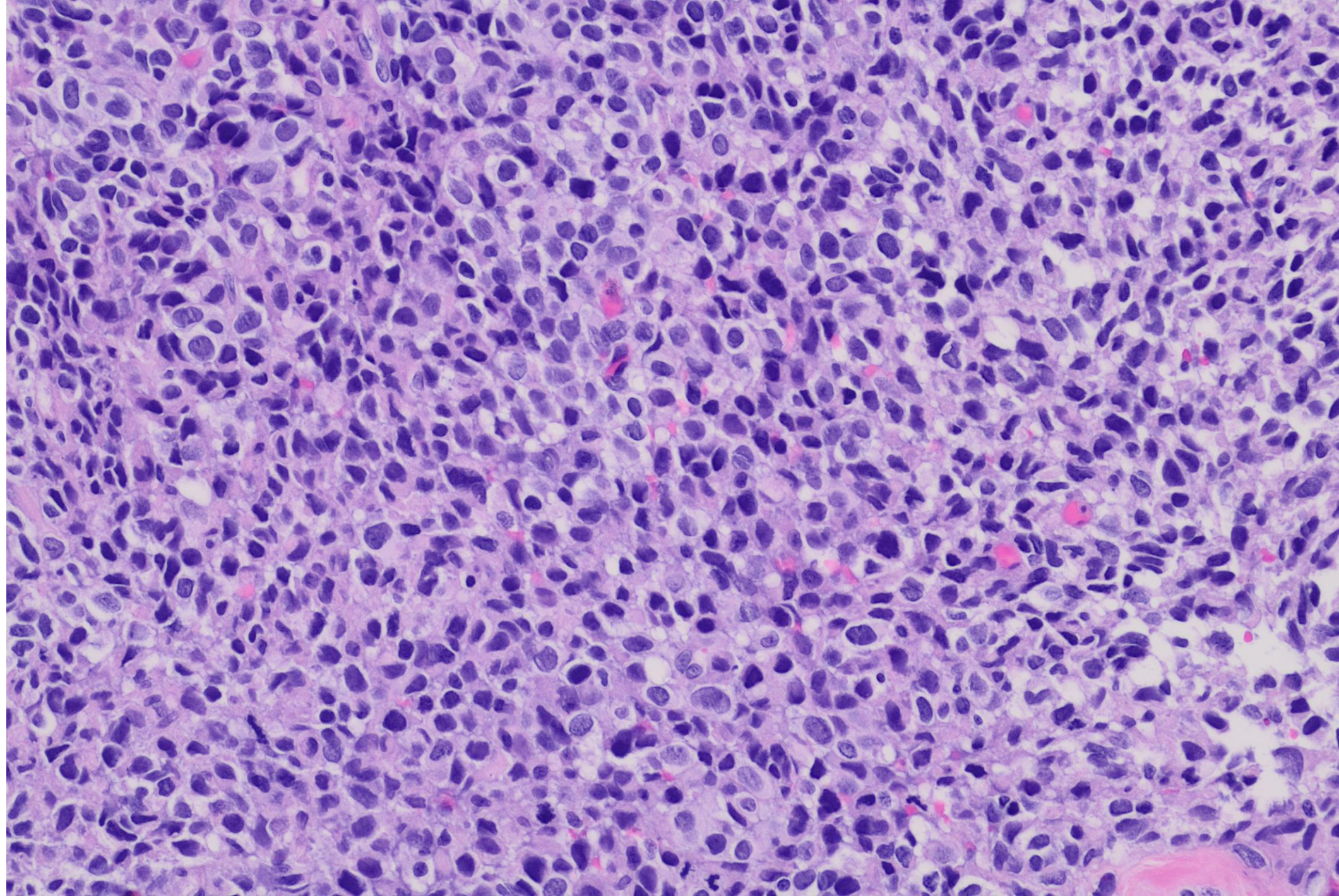




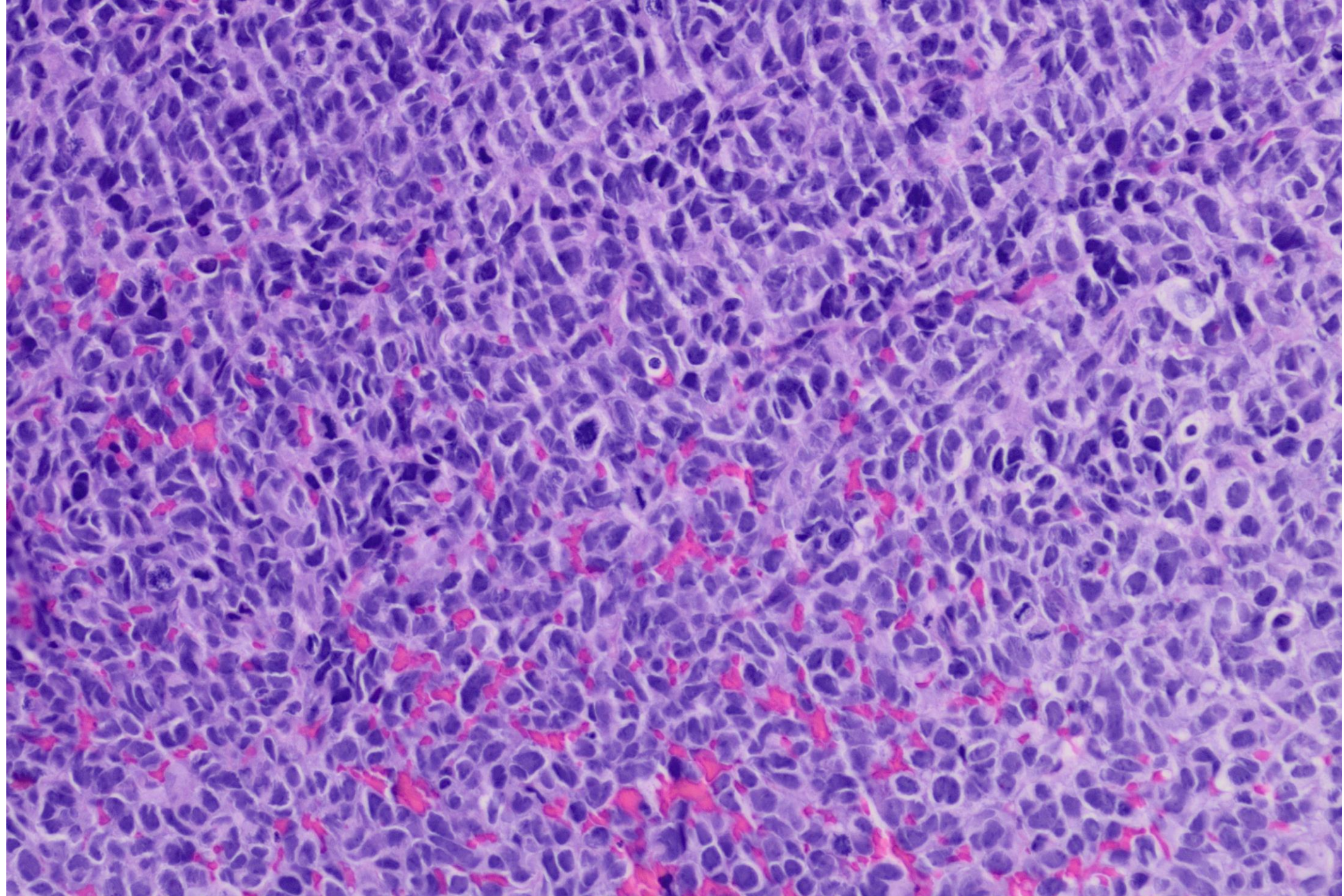




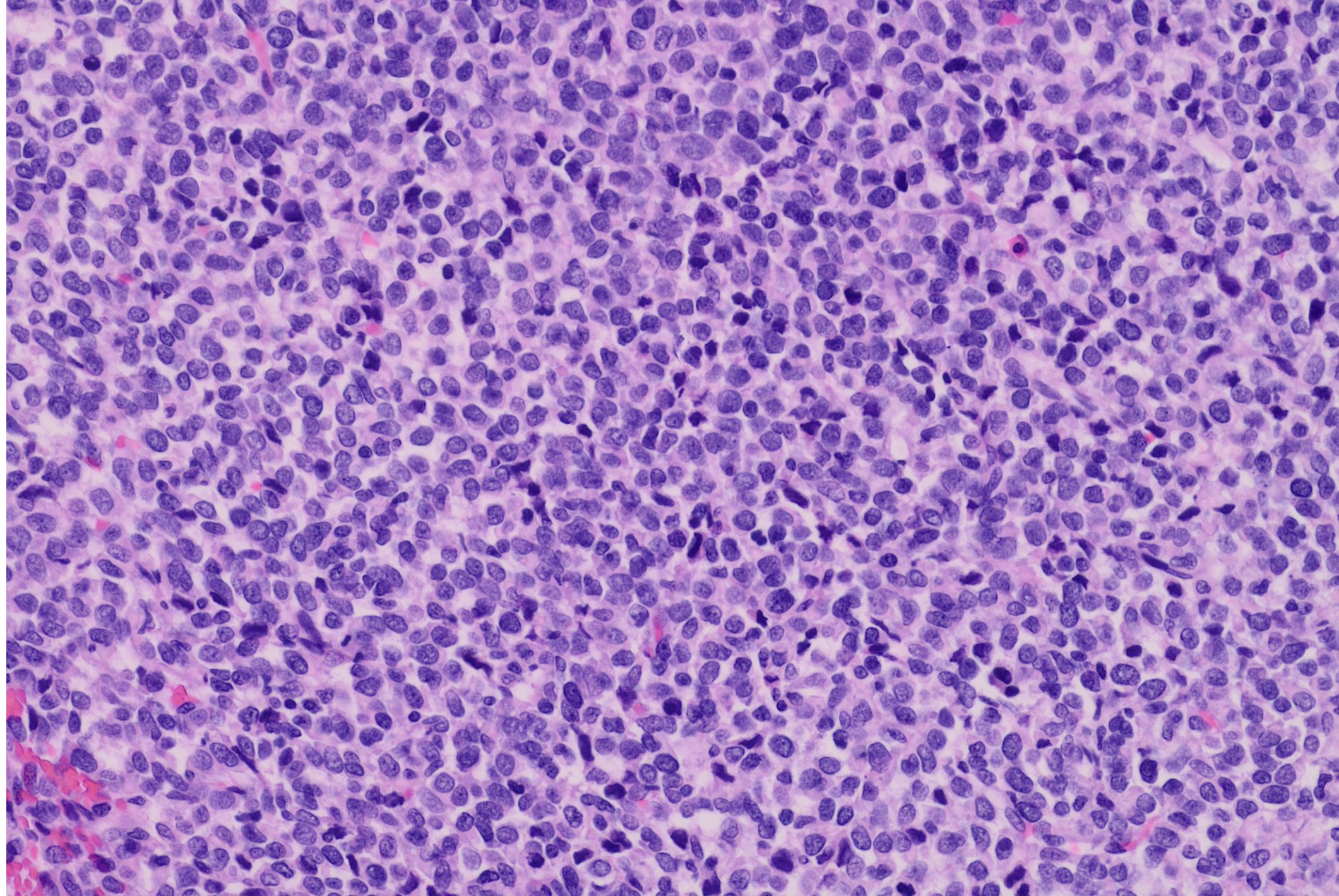




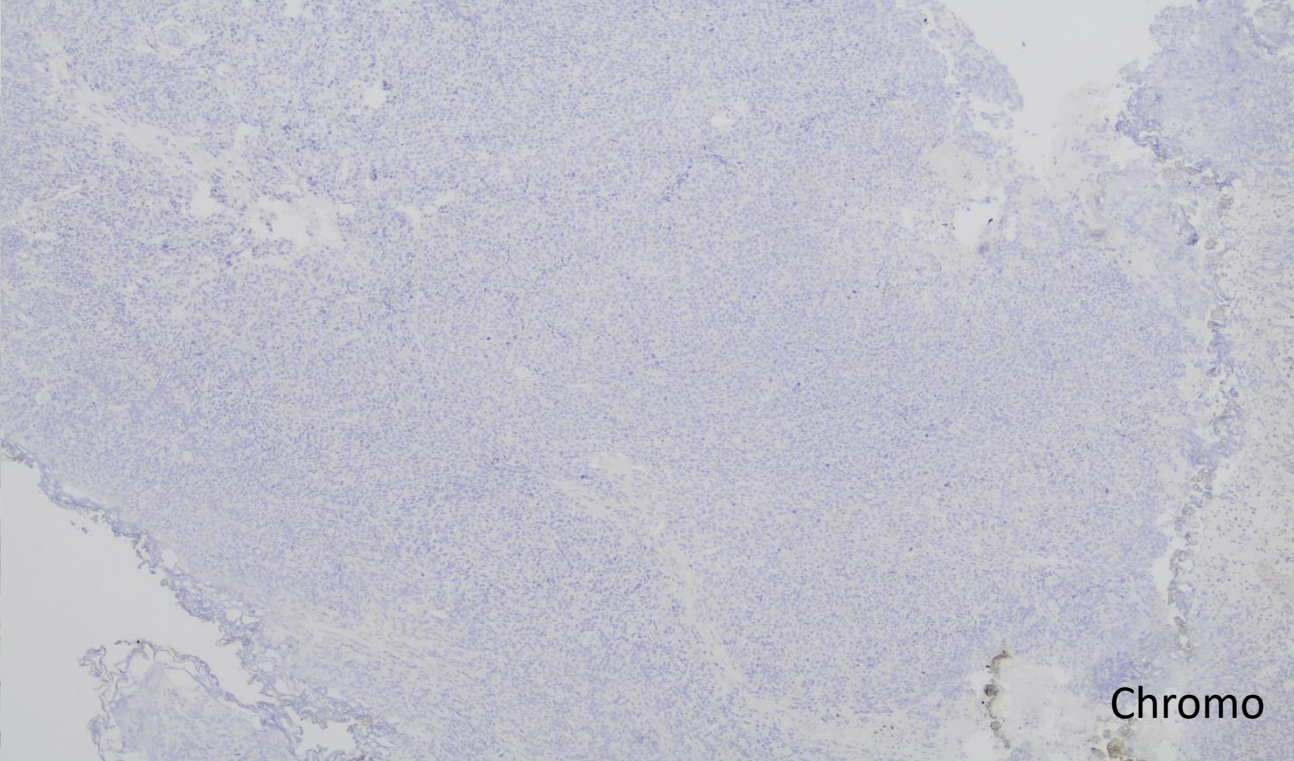
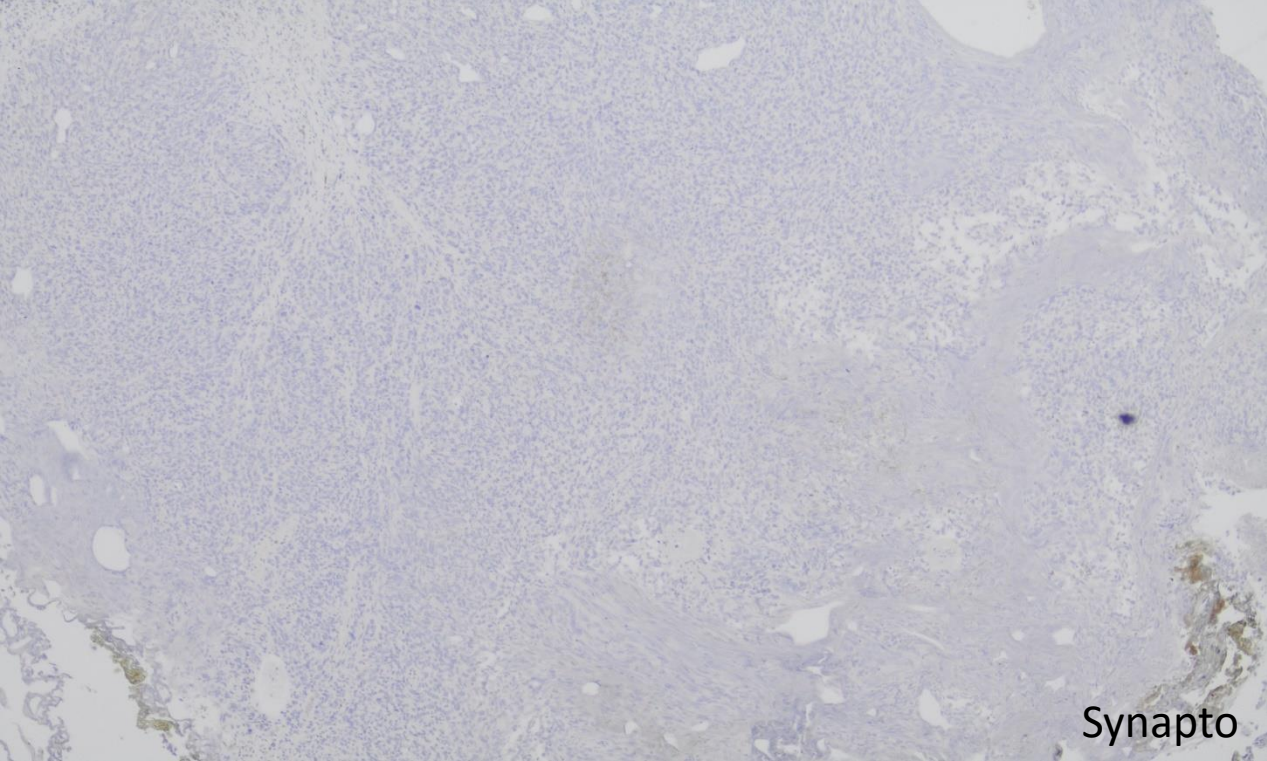
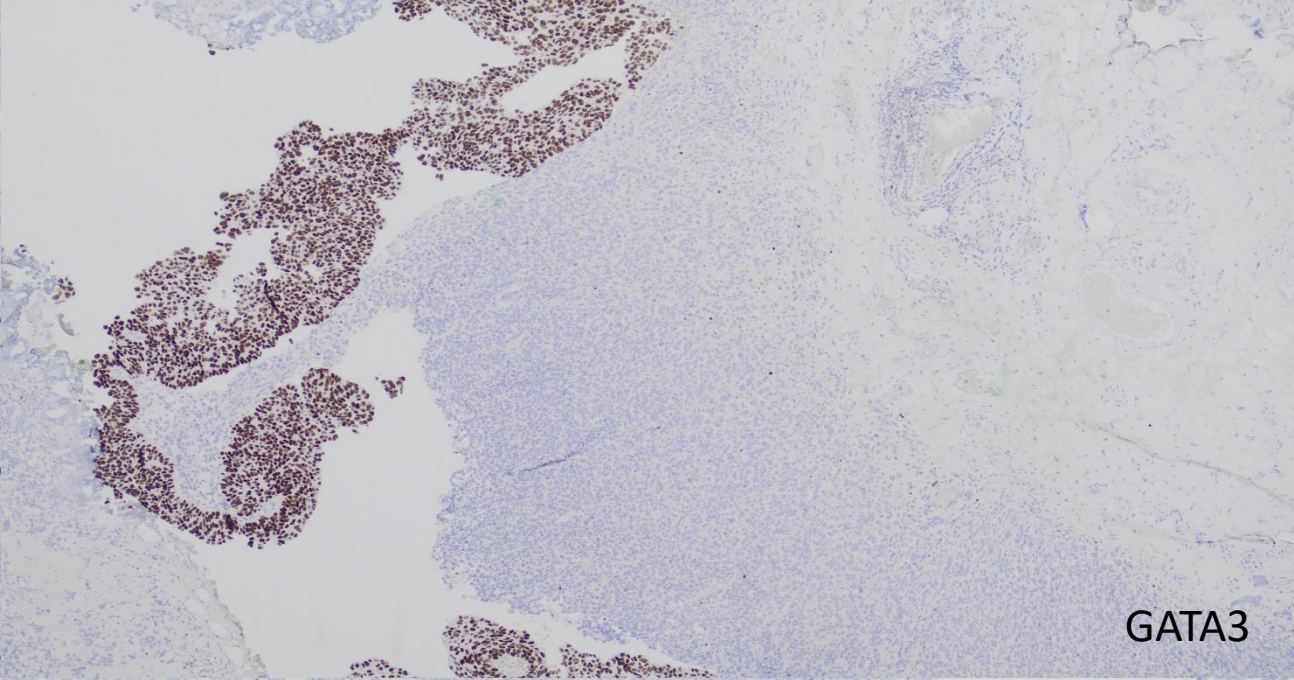
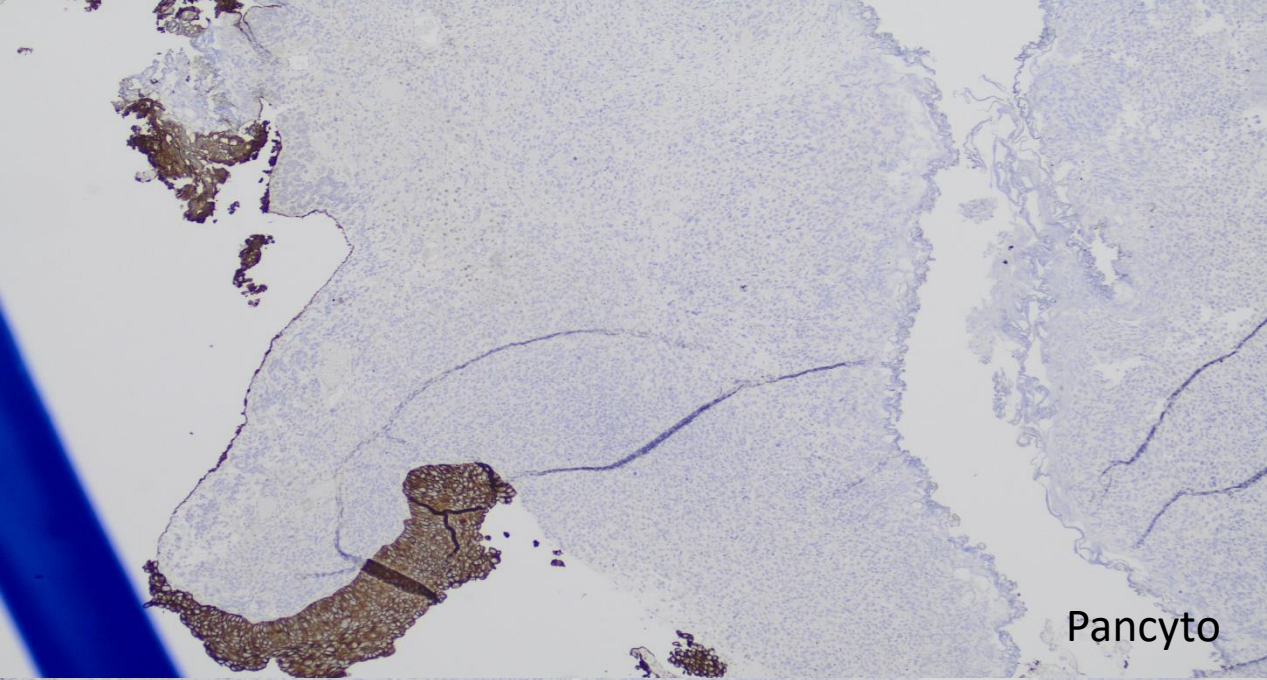










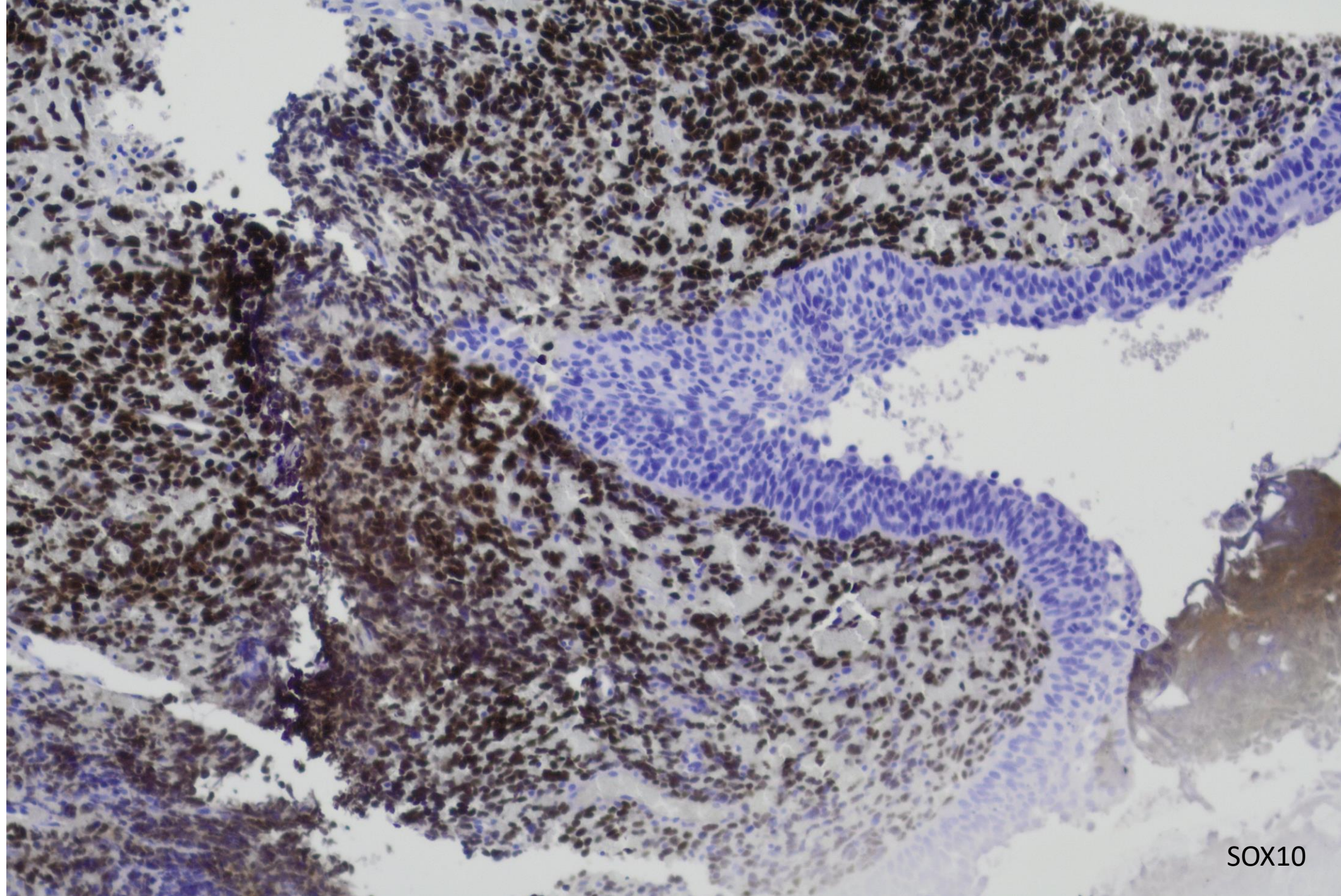




# DIAGNOSIS?

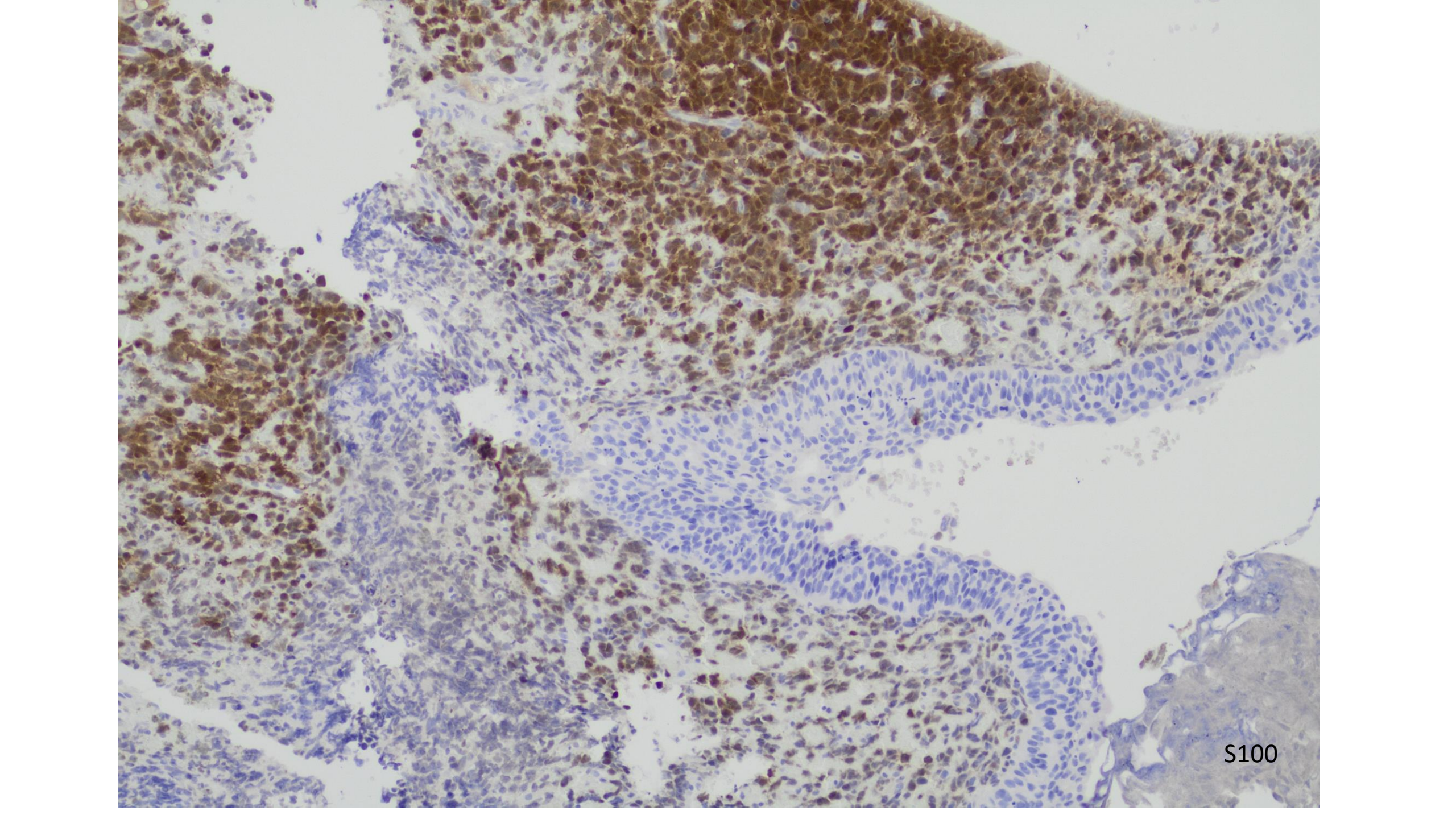






SOX10

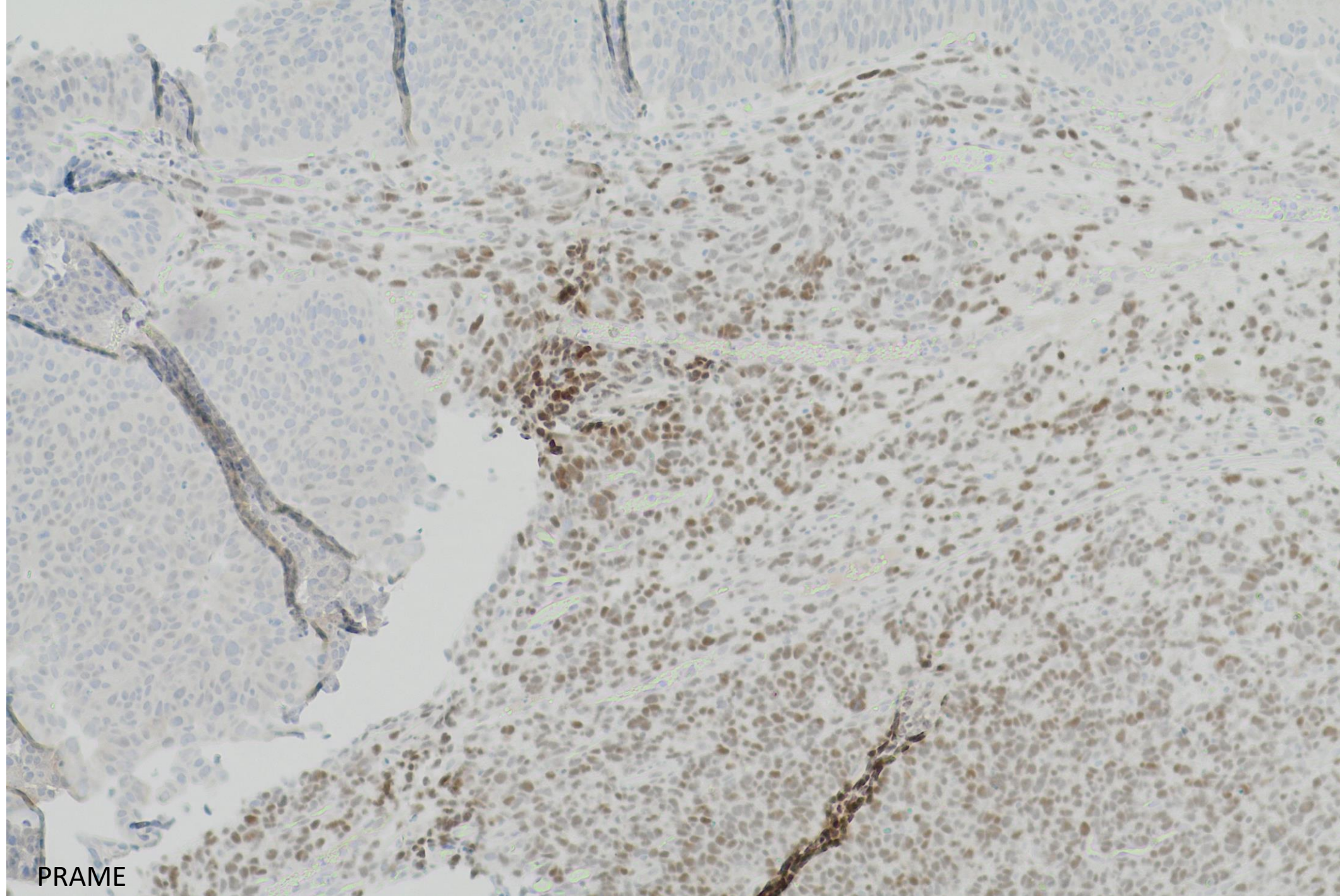




A histological slide showing a tissue section stained for S100 protein. The tissue is stained with hematoxylin and eosin (H&E), showing blue nuclei and pink cytoplasm/extracellular matrix. The S100 protein is visualized as brown staining, primarily localized to the nuclei of the cells. The tissue appears to be a stratified epithelium, possibly from the skin or a mucosal surface, with a clear transition from the stained, brown nuclei to the blue-stained nuclei of the underlying layers. The brown staining is most prominent in the upper layers of the tissue, indicating a high concentration of S100 protein in those cells.

S100





PRAME



# Other Stains

- HMB45 negative
- MelanA negative
- CD3 negative
- CD20 negative
- EMA negative
- P63 negative

# Discussion

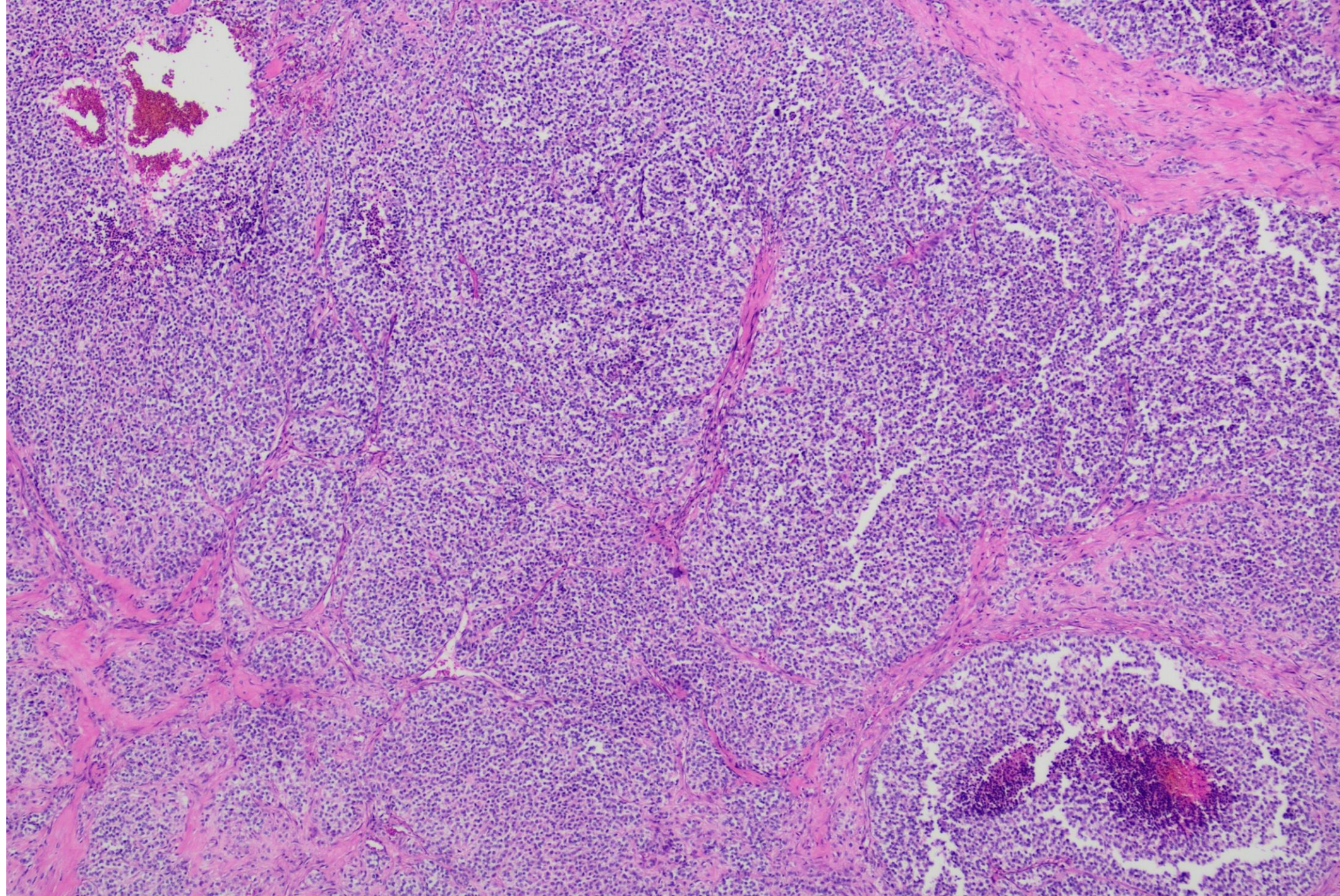
- Differential Diagnosis
  - Sarcomatoid carcinoma arising out of HG urothelial CA
    - Sarcomatoid component has melanocytic/neural differentiation
  - Primary melanoma and HG urothelial collision
    - Primary melanoma more common in females
  - Metastatic melanoma and HG urothelial collision
    - Collisions are uncommon in bladder in general
    - Derm w/u has been negative so far
  - Other?

24-0602

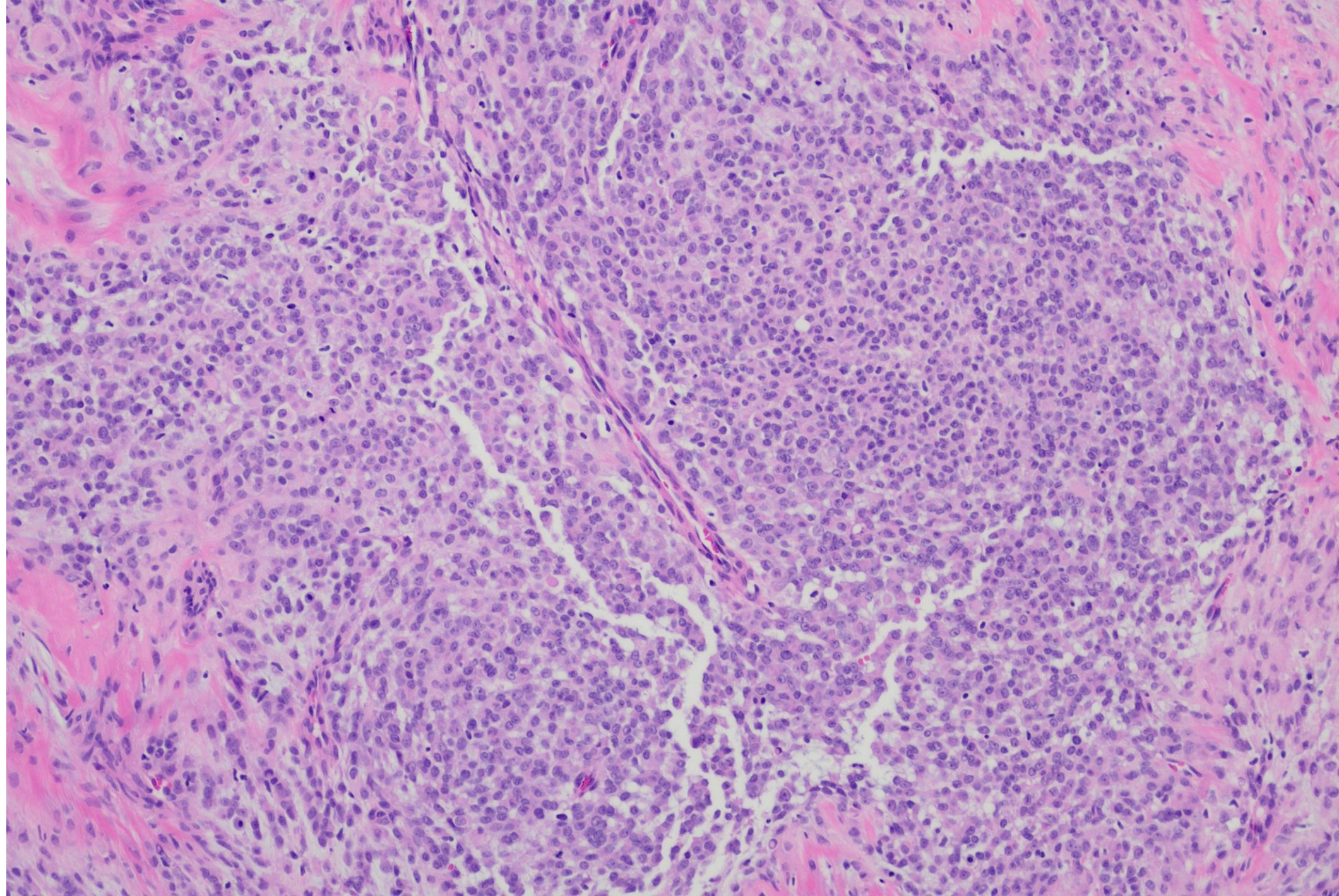
**Armen Khararjian; Kaiser Permanente**

30s male with chin lesion

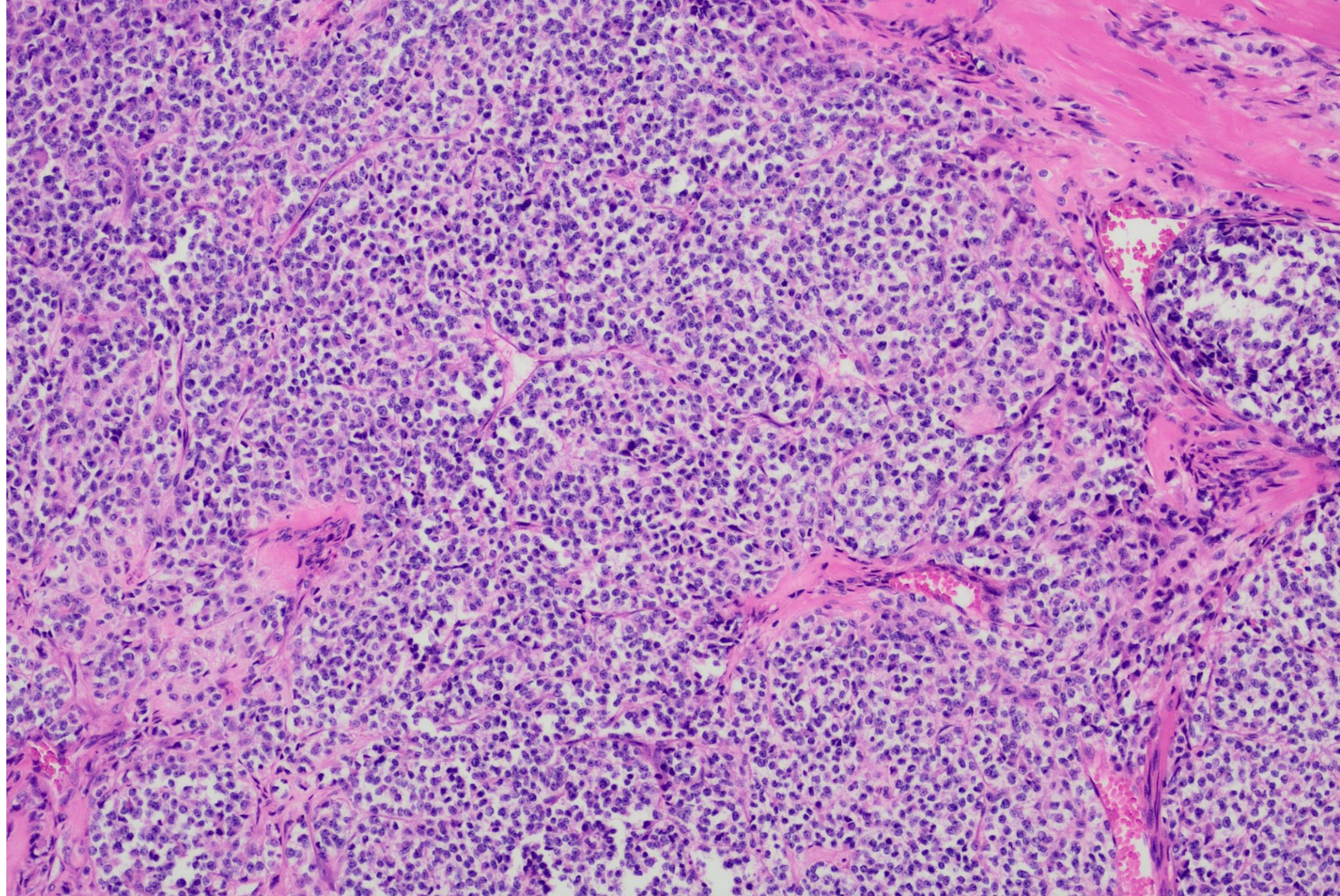




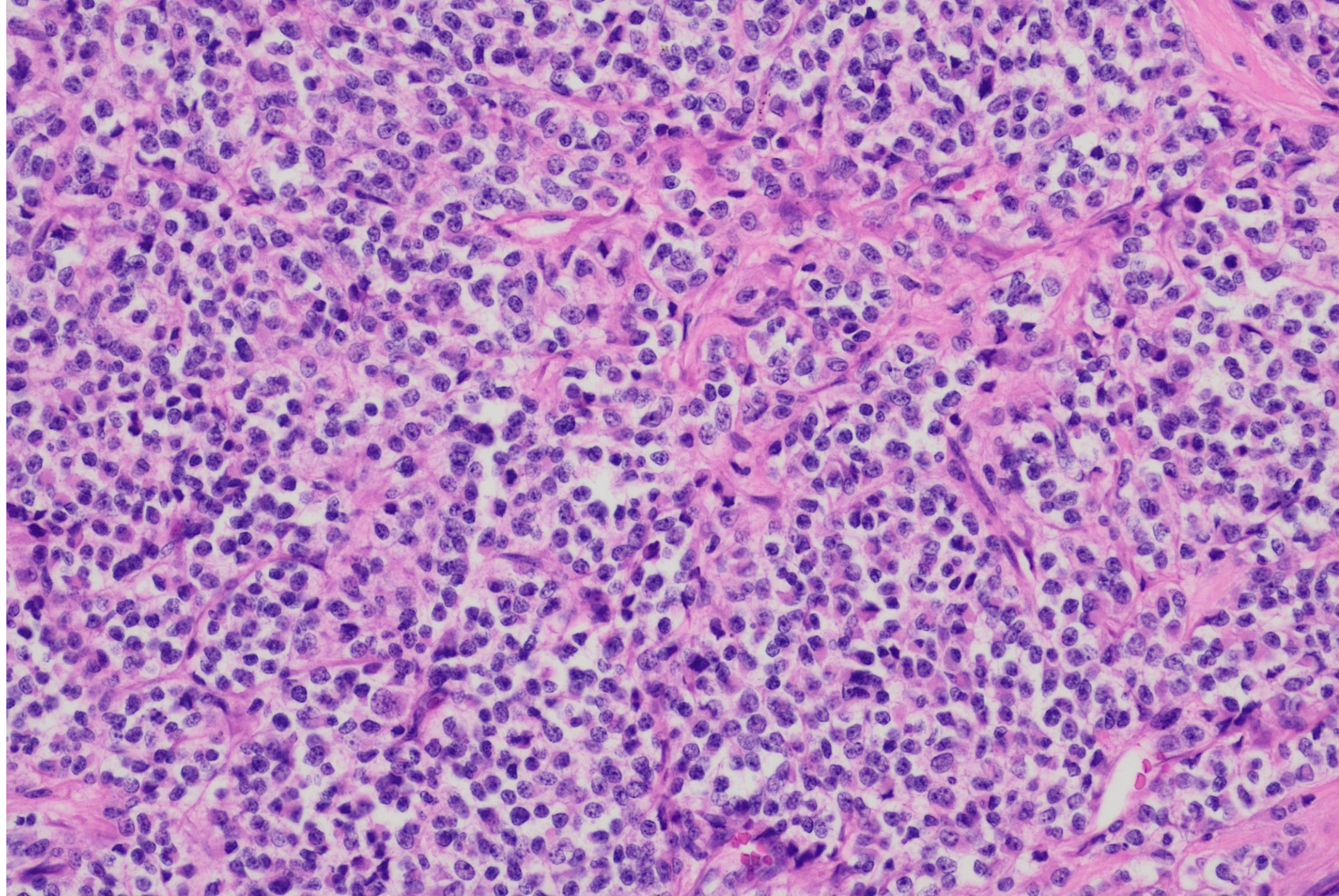




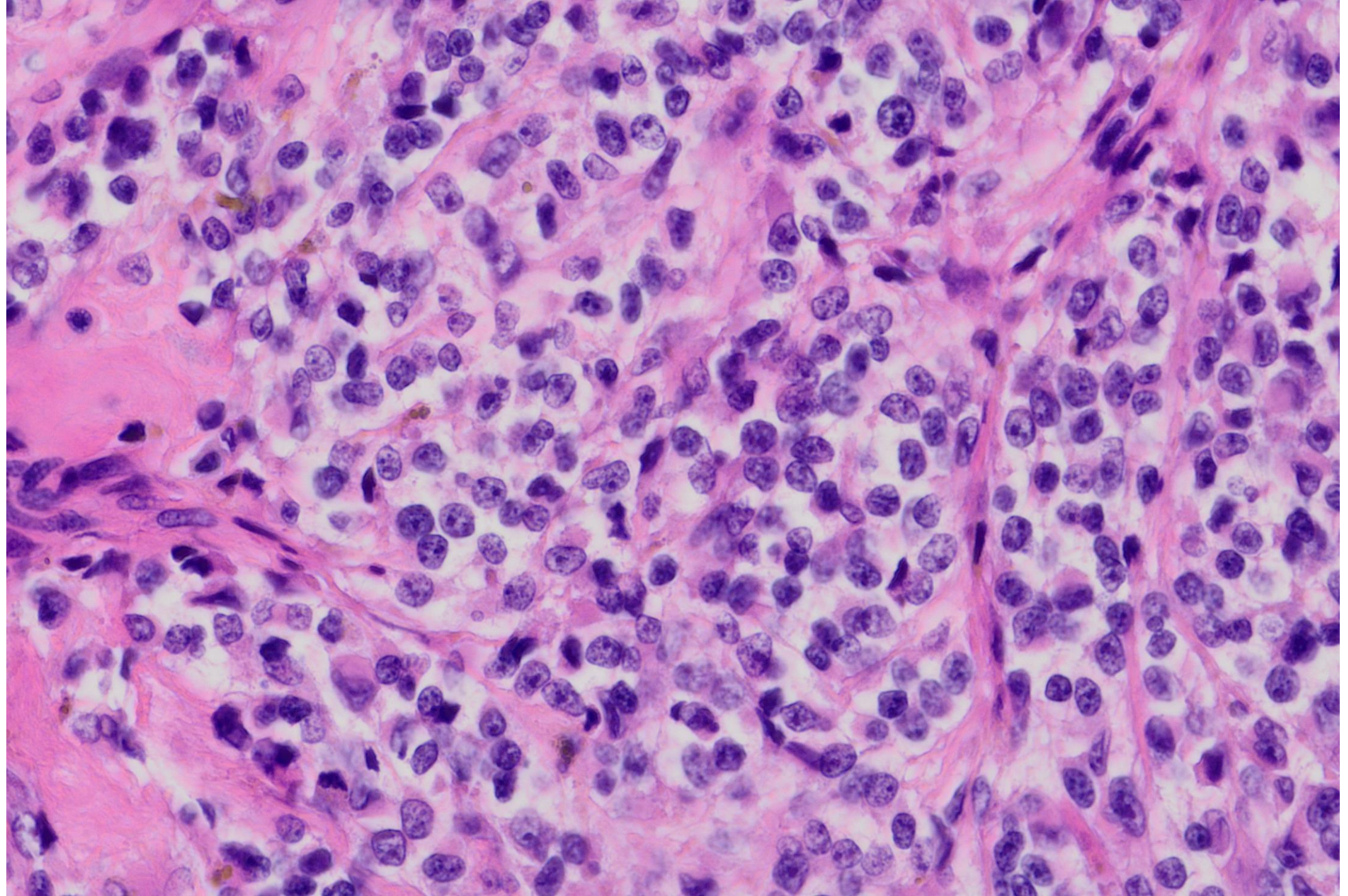




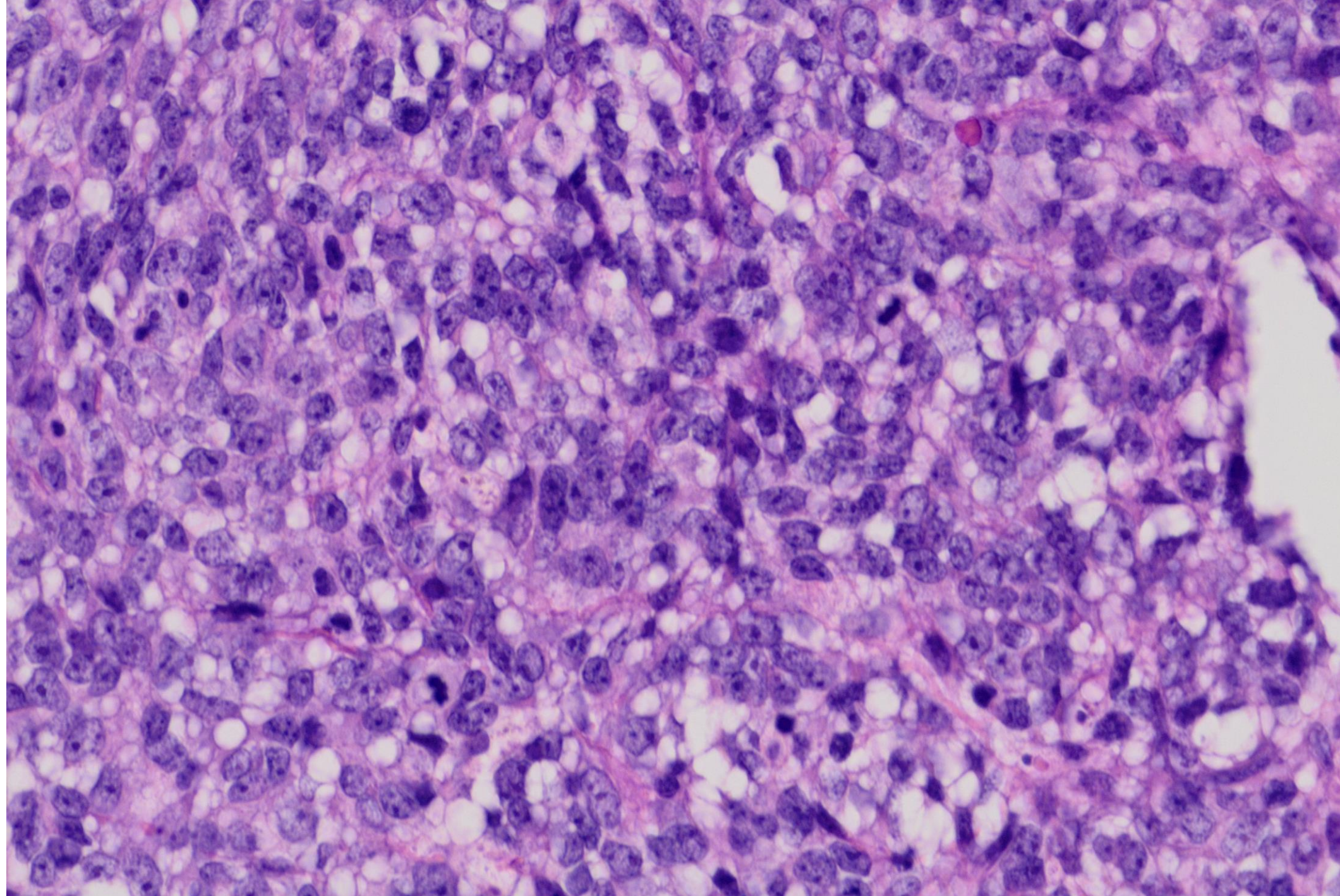




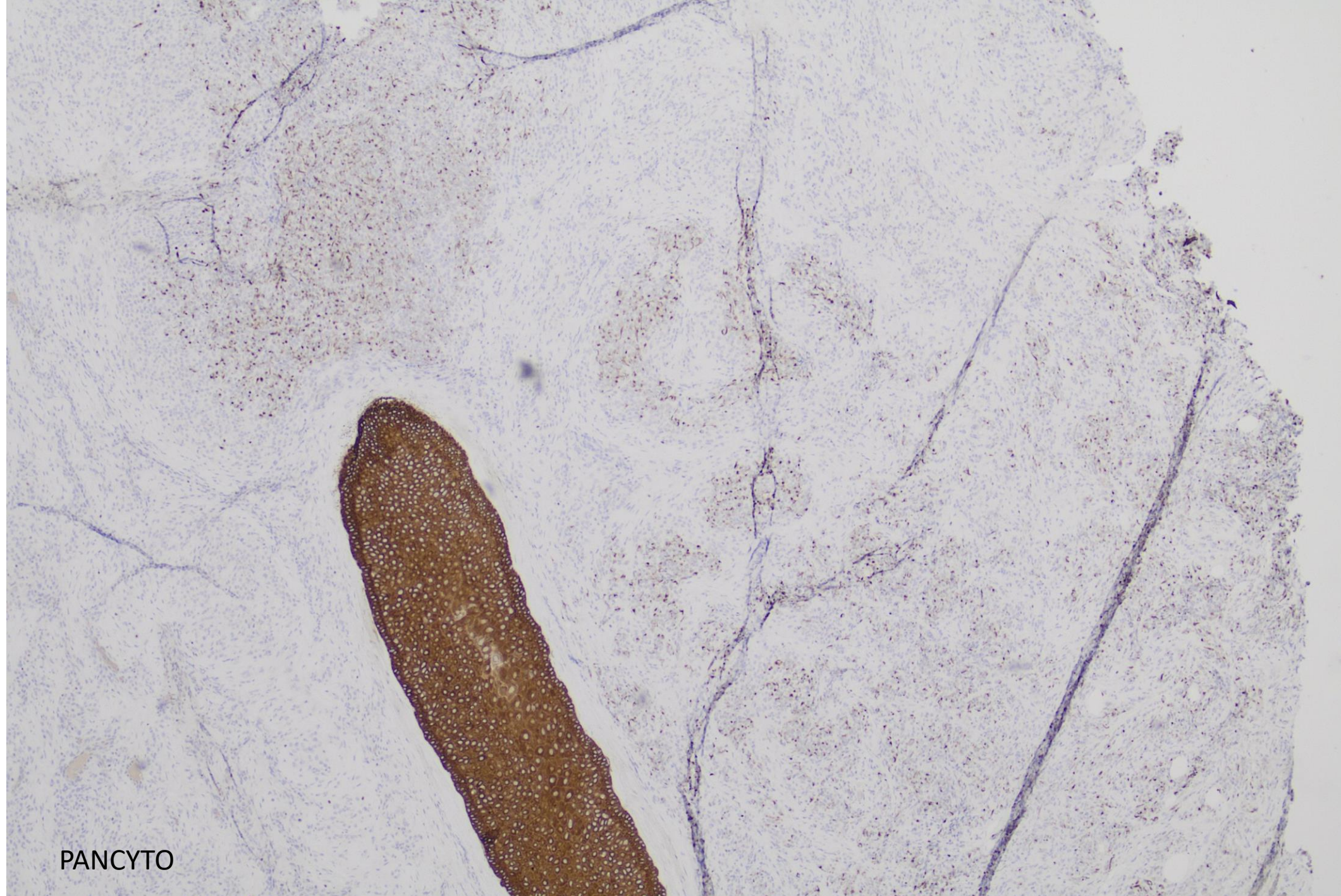






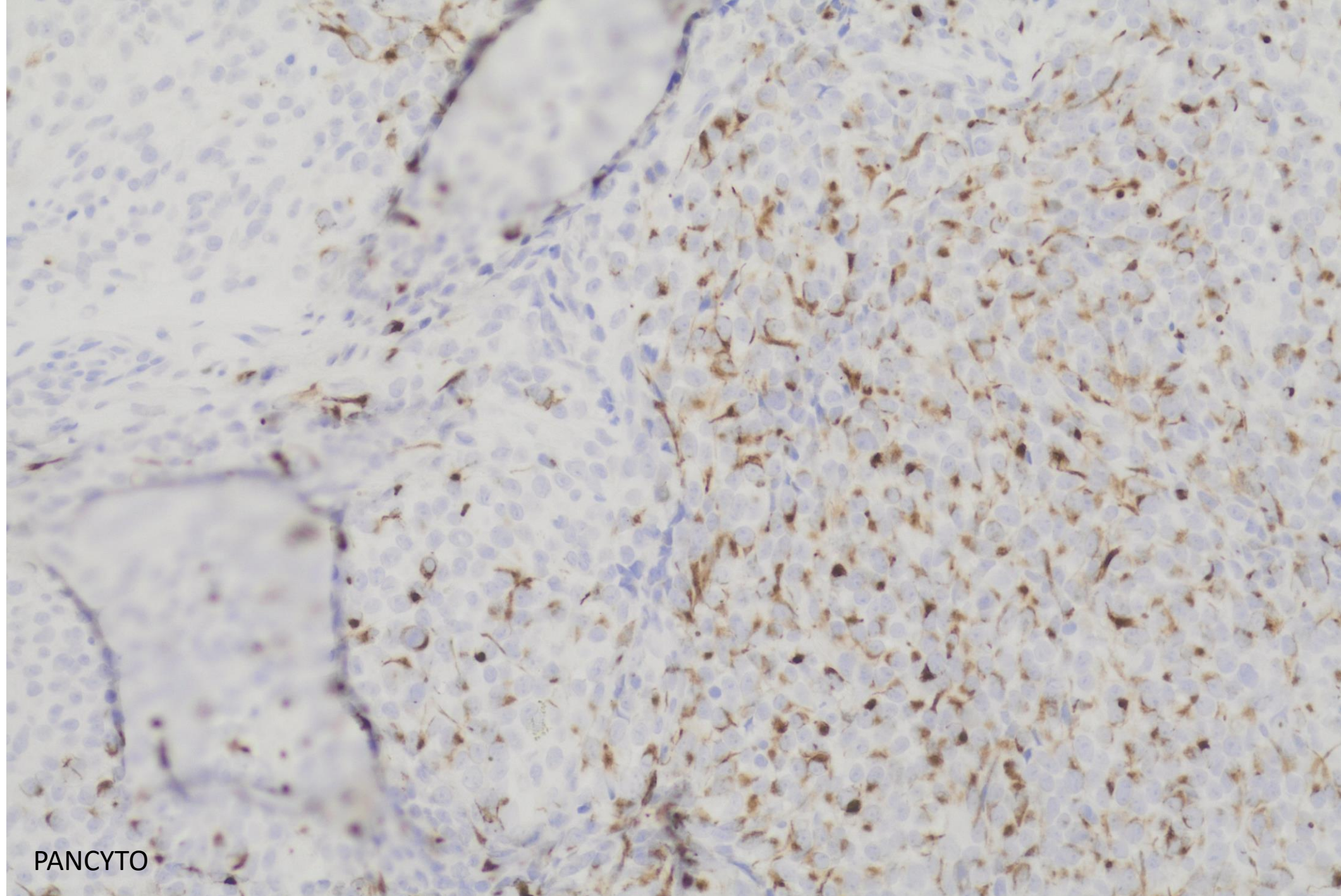






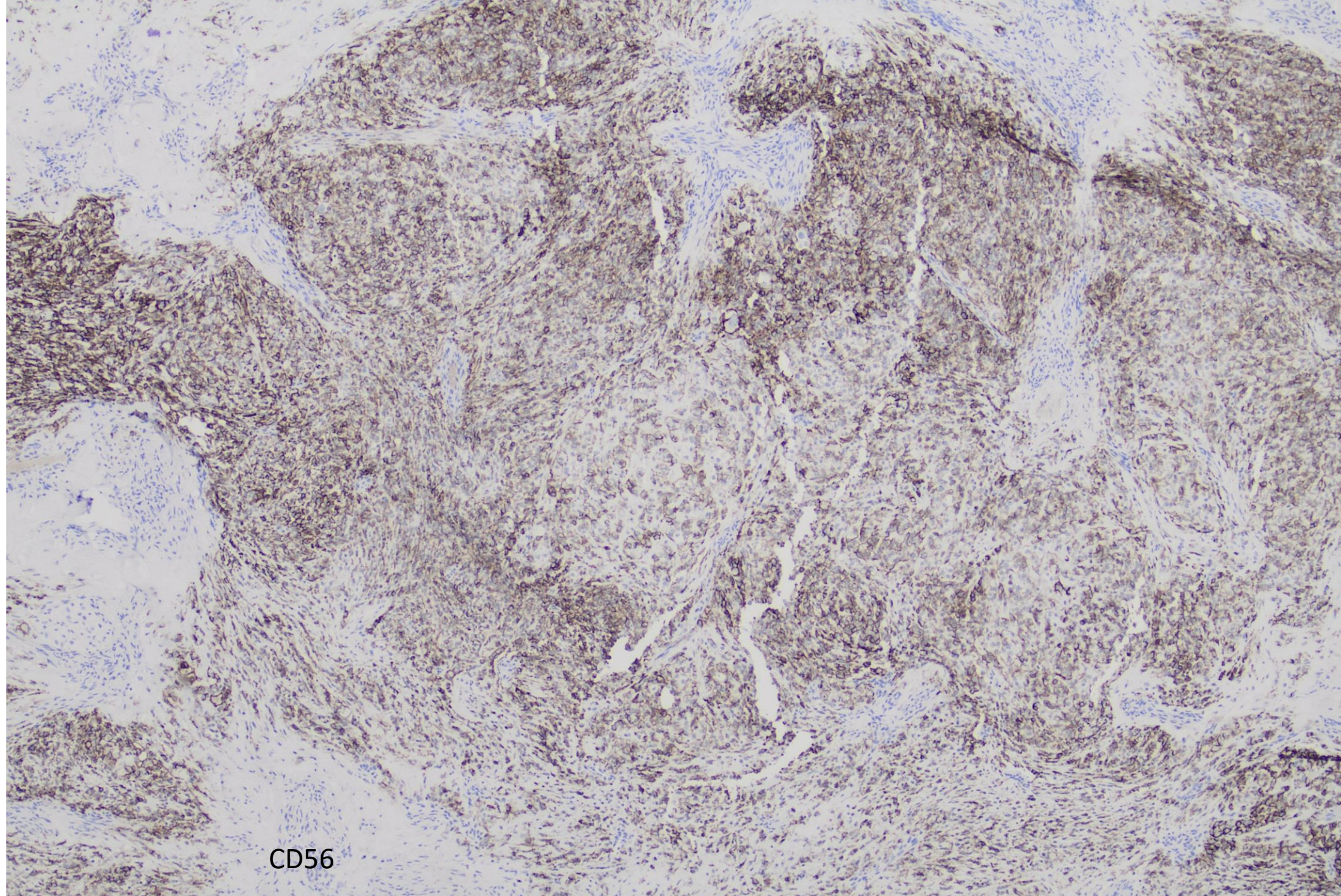
PANCYTO





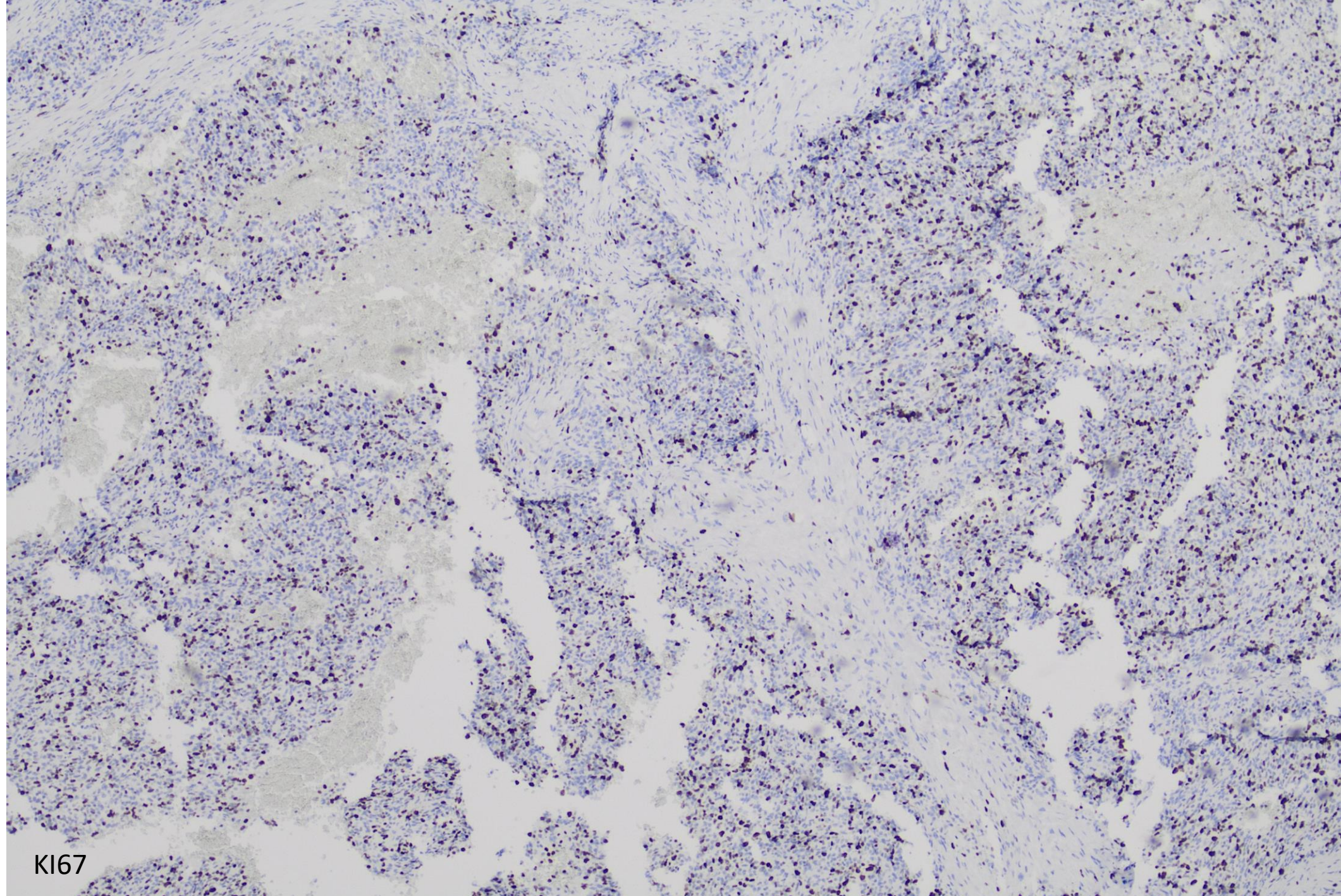
PANCYTO





CD56





KI67



# Other Negative Stains

- S100
- SOX10
- CK7
- CK20
- CD34
- ERG
- SMA
- DESMIN
- SYNAPTOPHYSIN
- CHROMOGRANIN
- CD3
- CD20
- INI Retained
- EMA

# DIAGNOSIS?



# Molecular

A CIC::DUX4 gene fusion was detected by RNA sequencing. This result is consistent with a diagnosis of Undifferentiated Round Cell Sarcoma with A CIC::DUX4 fusion (PMID: 28346326).



# Undifferentiated Round Cell Sarcoma with CIC-DUX4 Rearrangement

- <1% of sarcomas – rarest of rare malignancy
- Children and young adults with soft tissue mass
  - Trunk, distal extremities, head and neck
- Rapid growing, solitary mass
- Very aggressive with high proportion showing advanced disease at diagnosis; poor prognosis
- CIC::DUX4 translocation that induces ETV6 overexpression



# Histology

- Solid and nodular growth
- Small round/ovoid cells with amphophilic cytoplasm
- Round to oval nuclei with variable chromatin patterns
- Mitoses common
- Necrosis usually present
- Can express CD99 and WT1

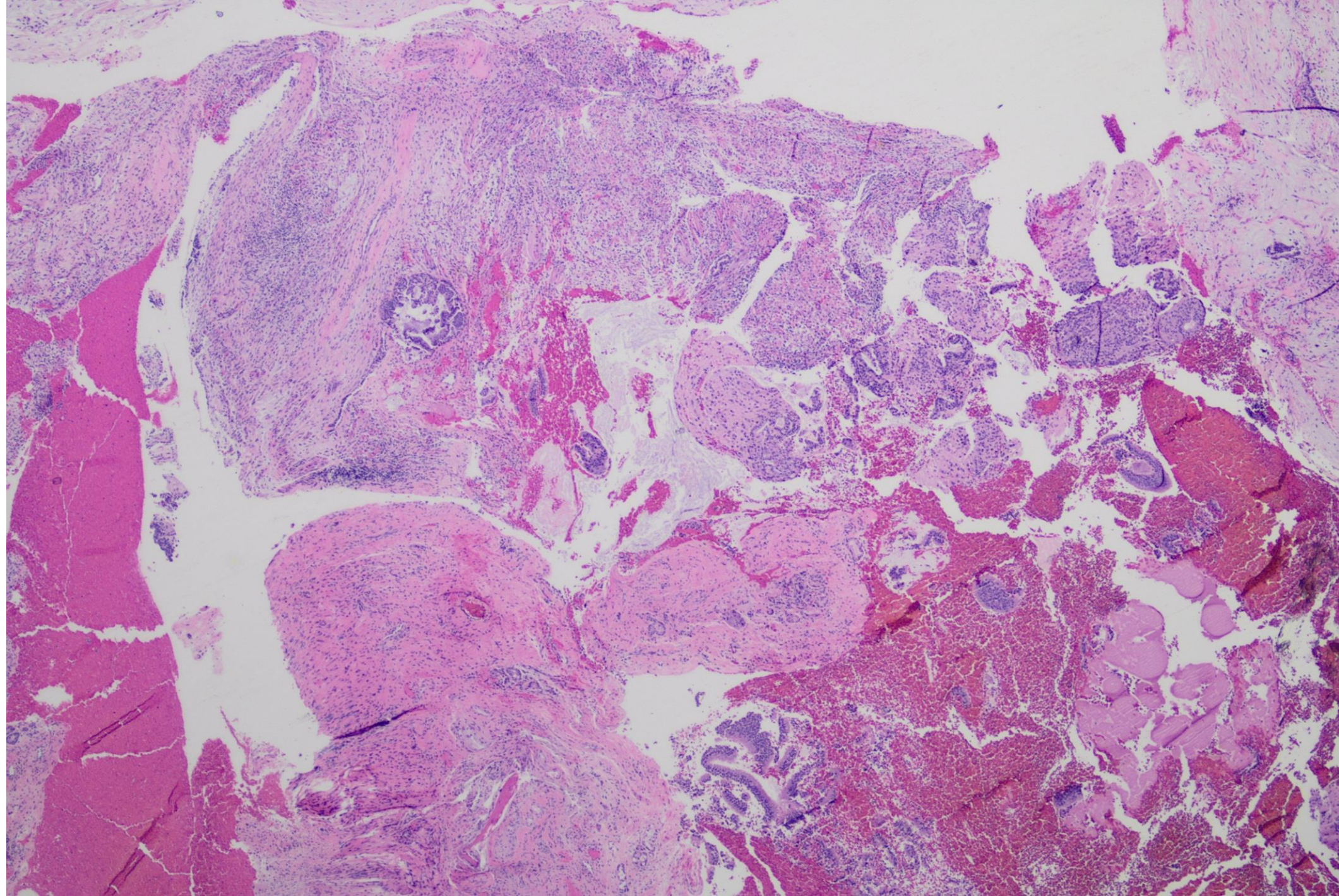


24-0603

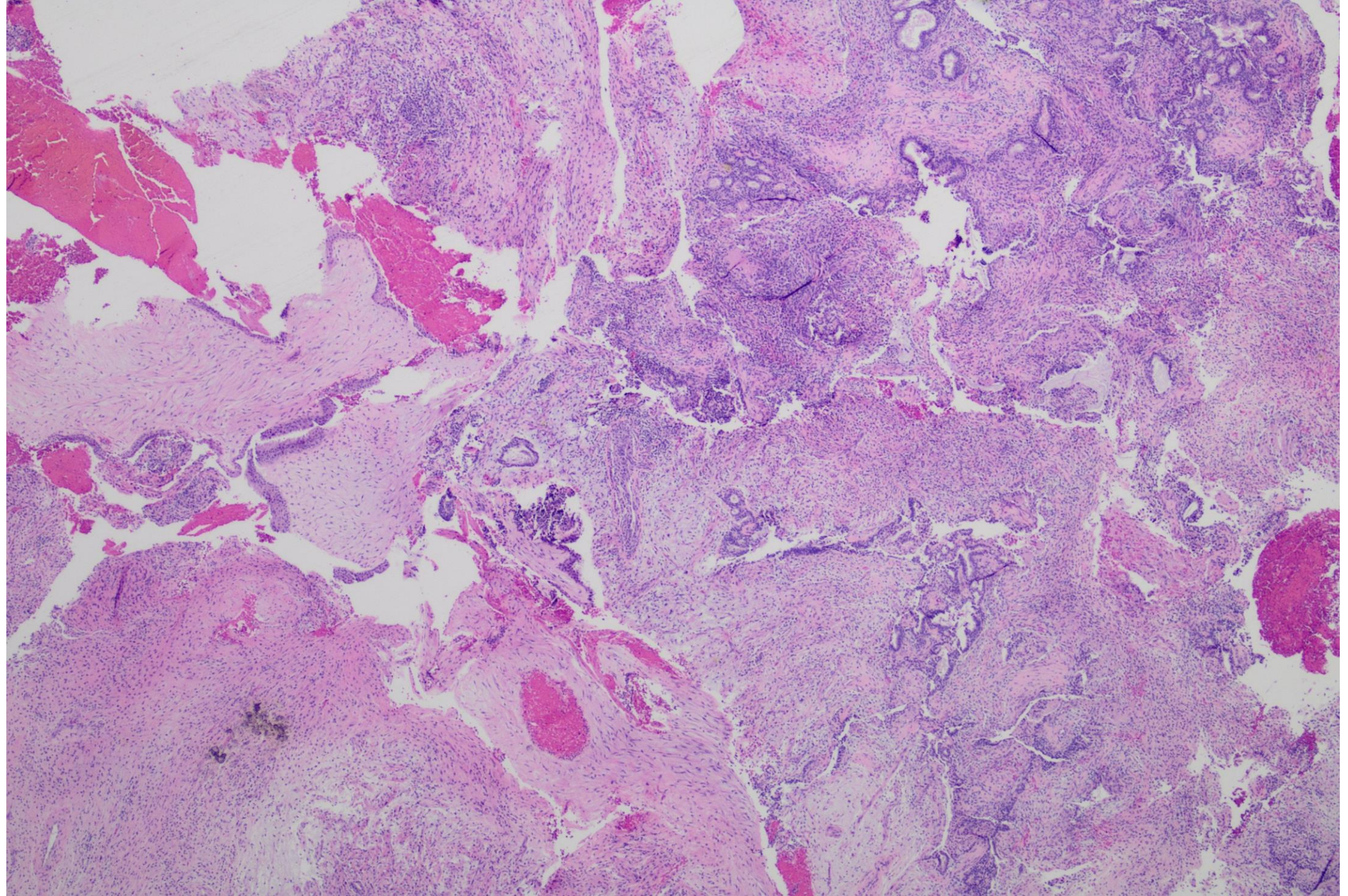
**Armen Khararjian; Kaiser Permanente**

Older aged male with a polypoid mass within the right nasal cavity and extending into the right nasopharynx

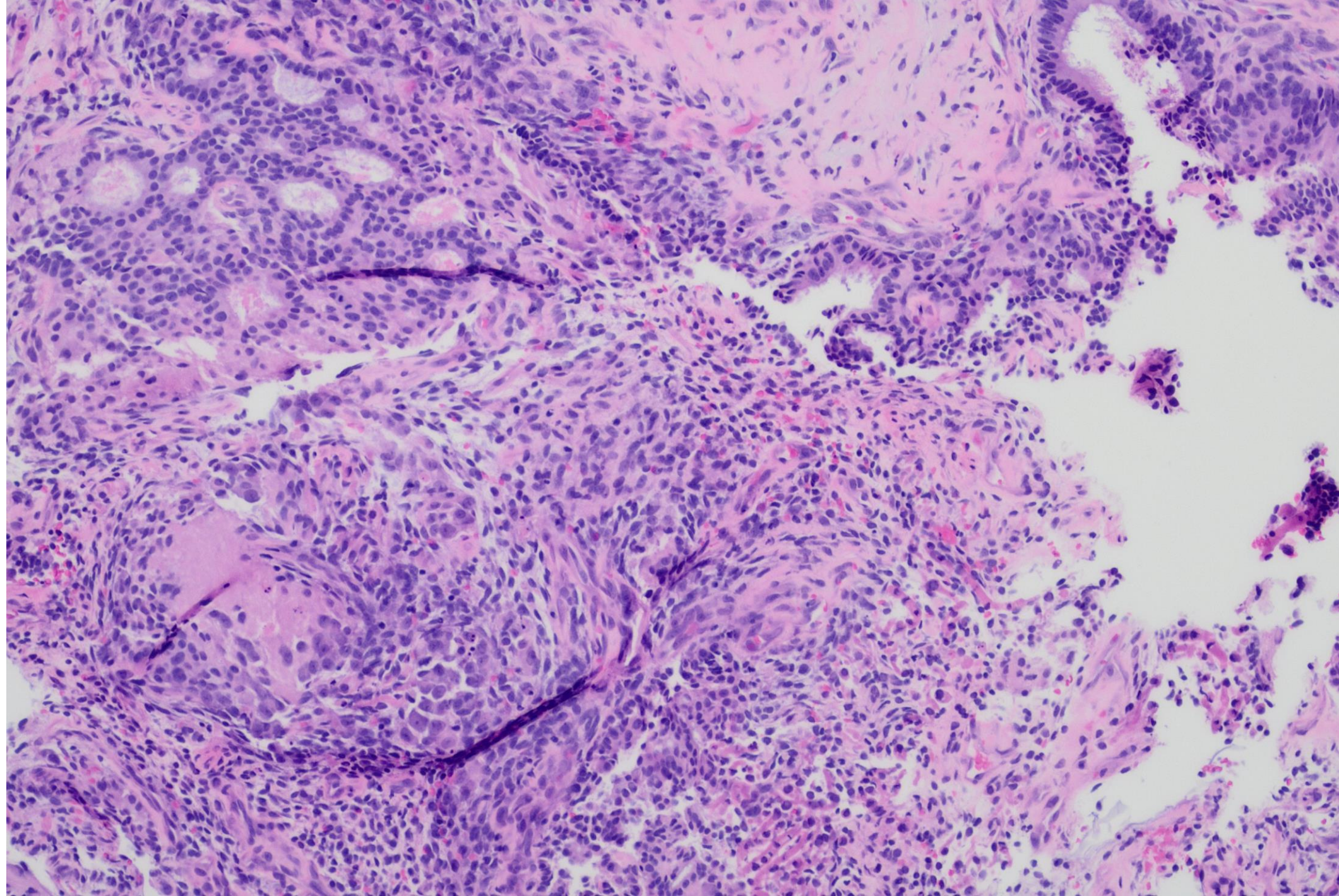




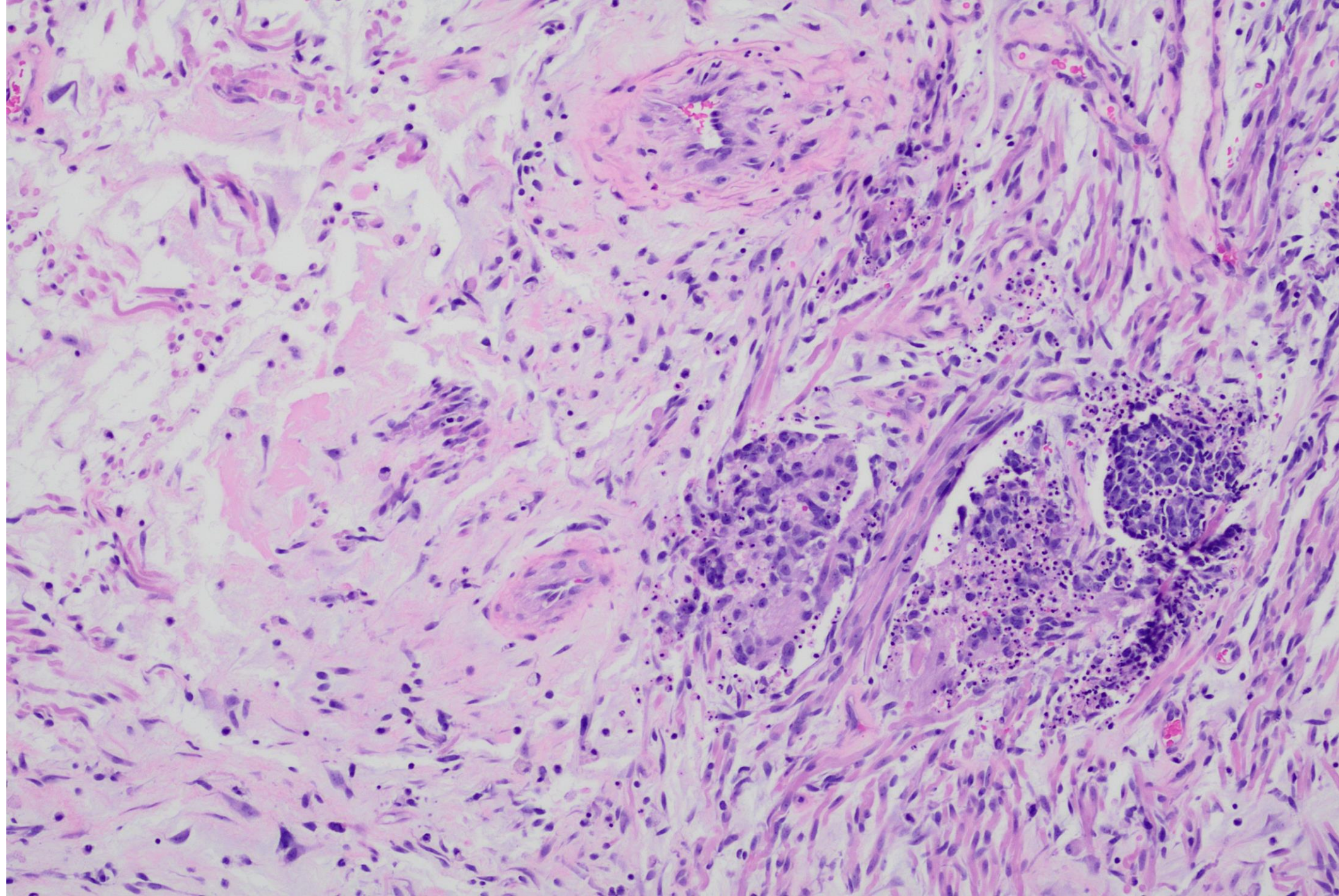




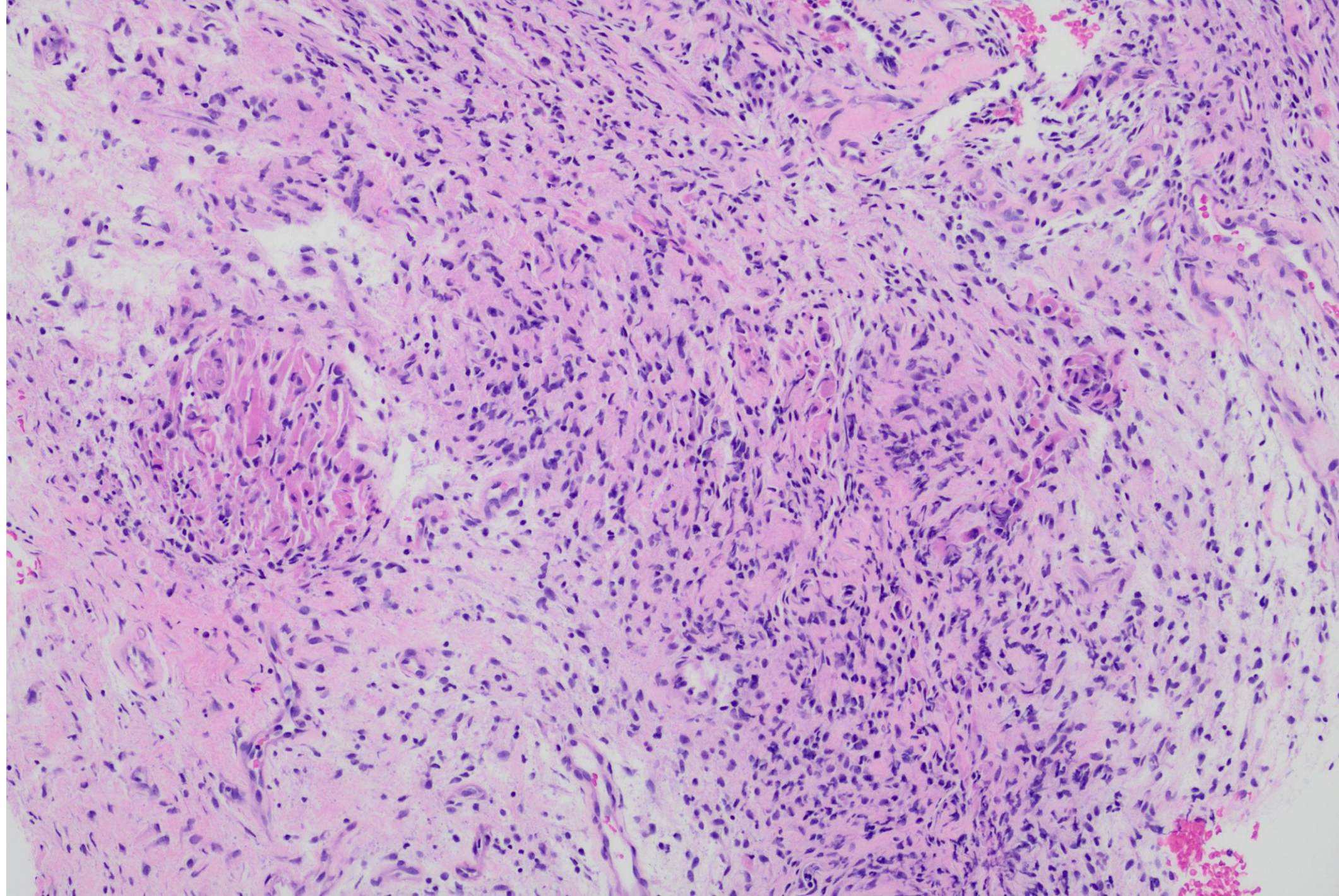




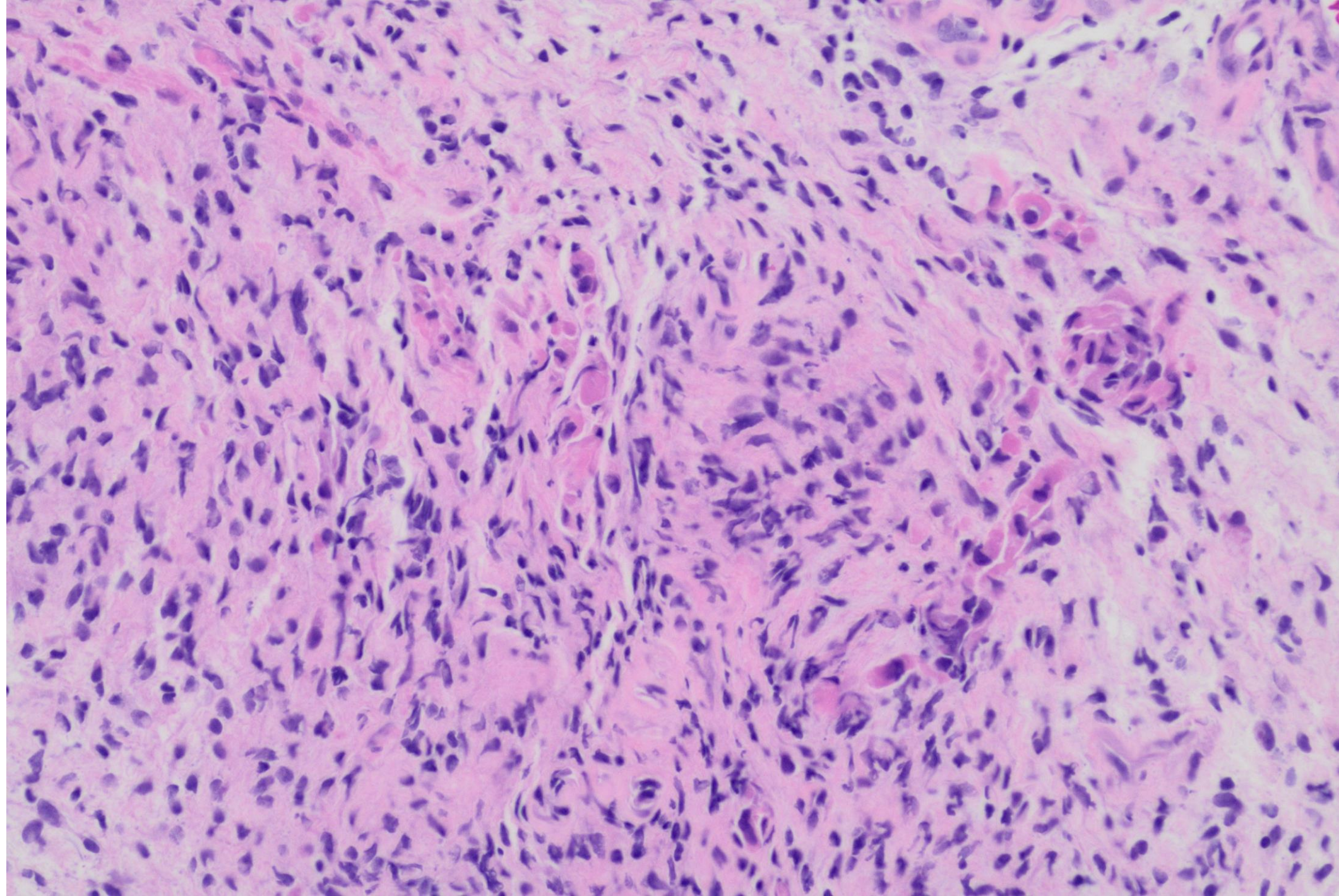




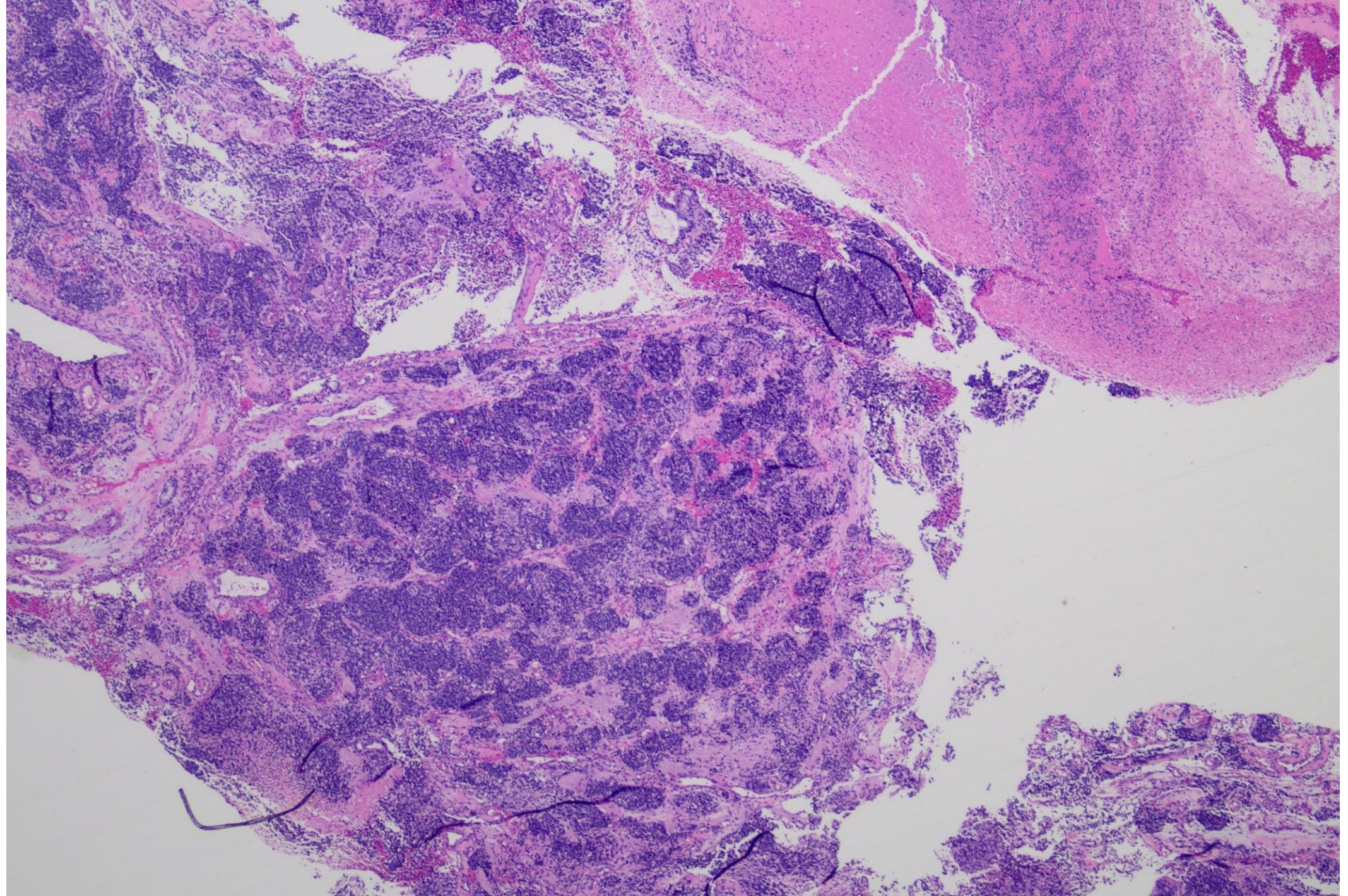




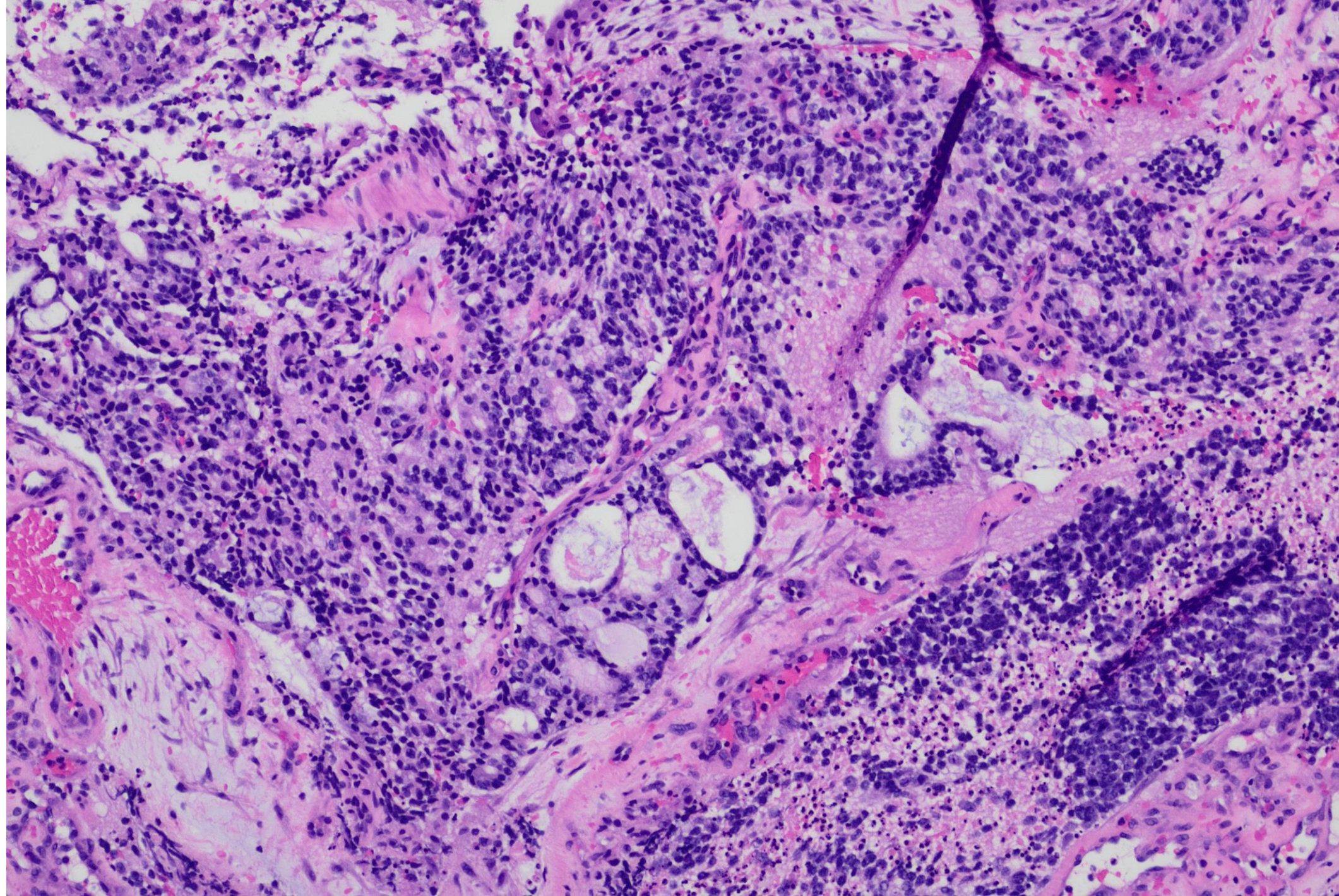




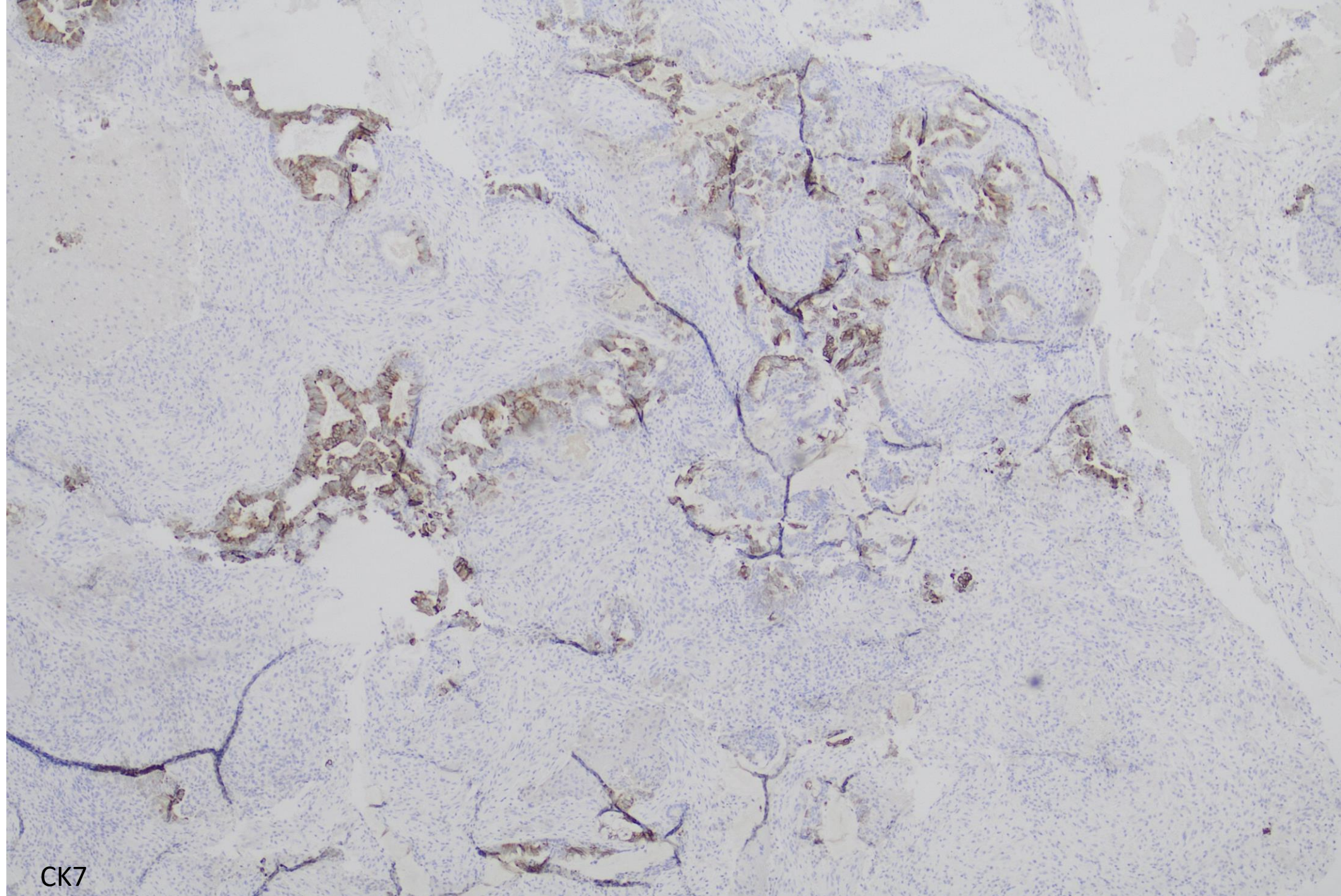






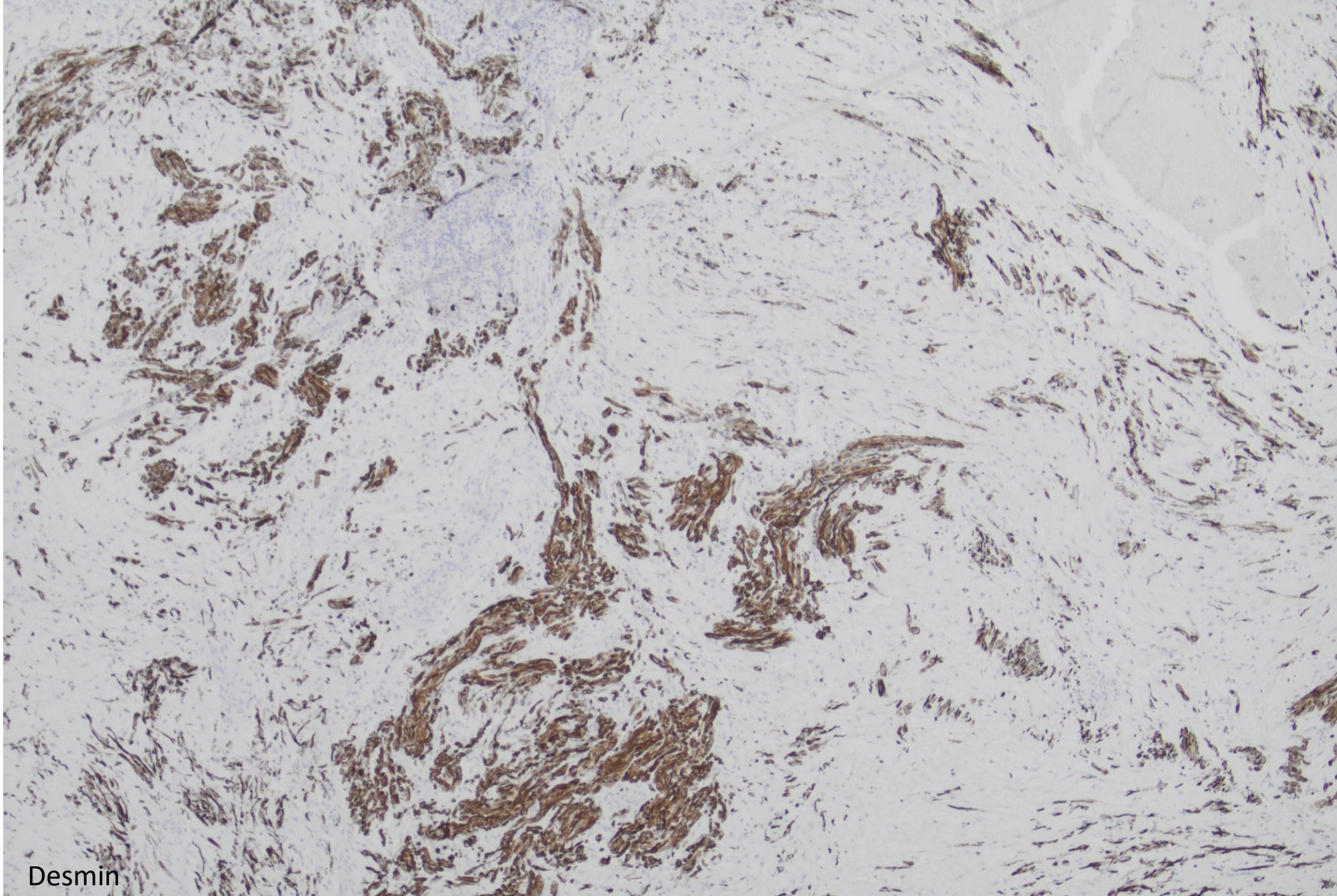






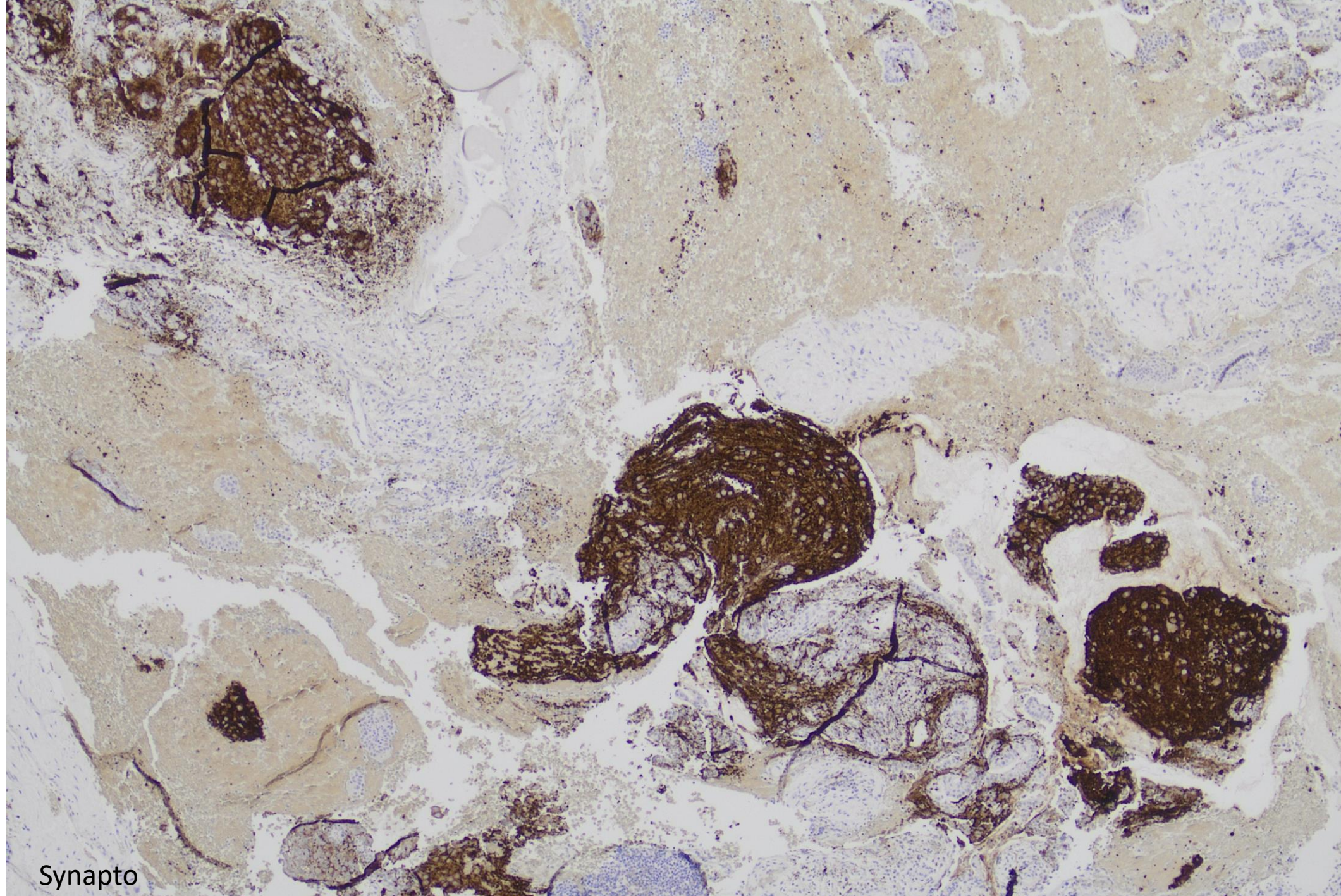
CK7





Desmin





Synapto



# DIAGNOSIS?





# Teratocarcinosarcoma

- Complex, malignant sinonasal neoplasm with immature and malignant endodermal, mesodermal, and neuroepithelial elements
- Most commonly affects middle aged men
- Likely evolves from primitive cell in olfactory membrane (considerable overlap with olfactory neuroblastoma)
  - Multiple lines of differentiation helps distinguish
- Aggressive tumor with rapid recurrence



# Histology

- Heterogenous elements
  - Carcinoma, sarcoma, immature teratoma
- Carcinoma can be adeno or squamous
- Sarcoma can be cartilage, bone, muscle, or fibroblastic
- Neural elements show primitive neuroepithelial tissue and neurofibrillary matrix
- IHC can highlight different elements
- Trisomy 12 and 1p deletion have been identified

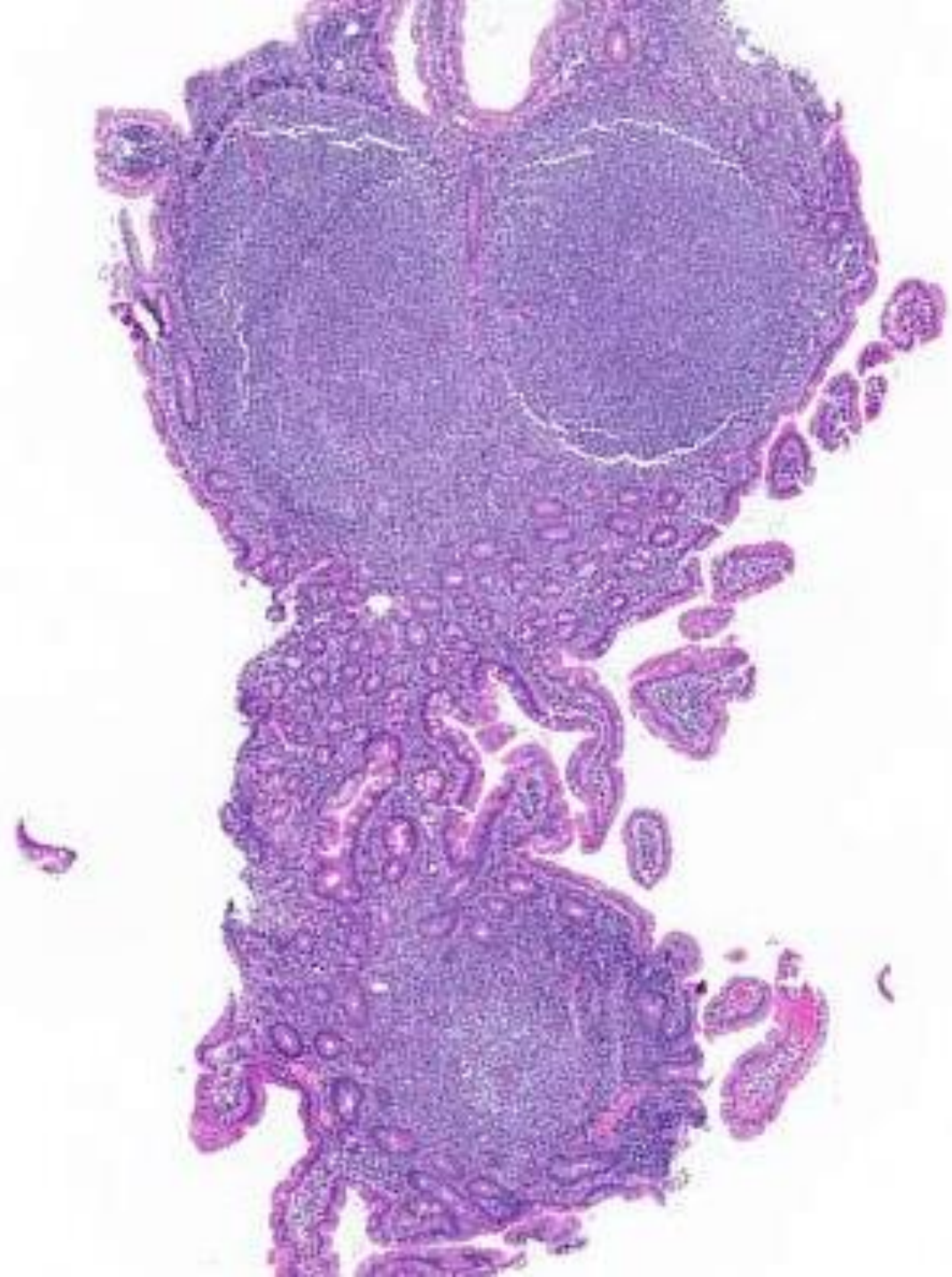
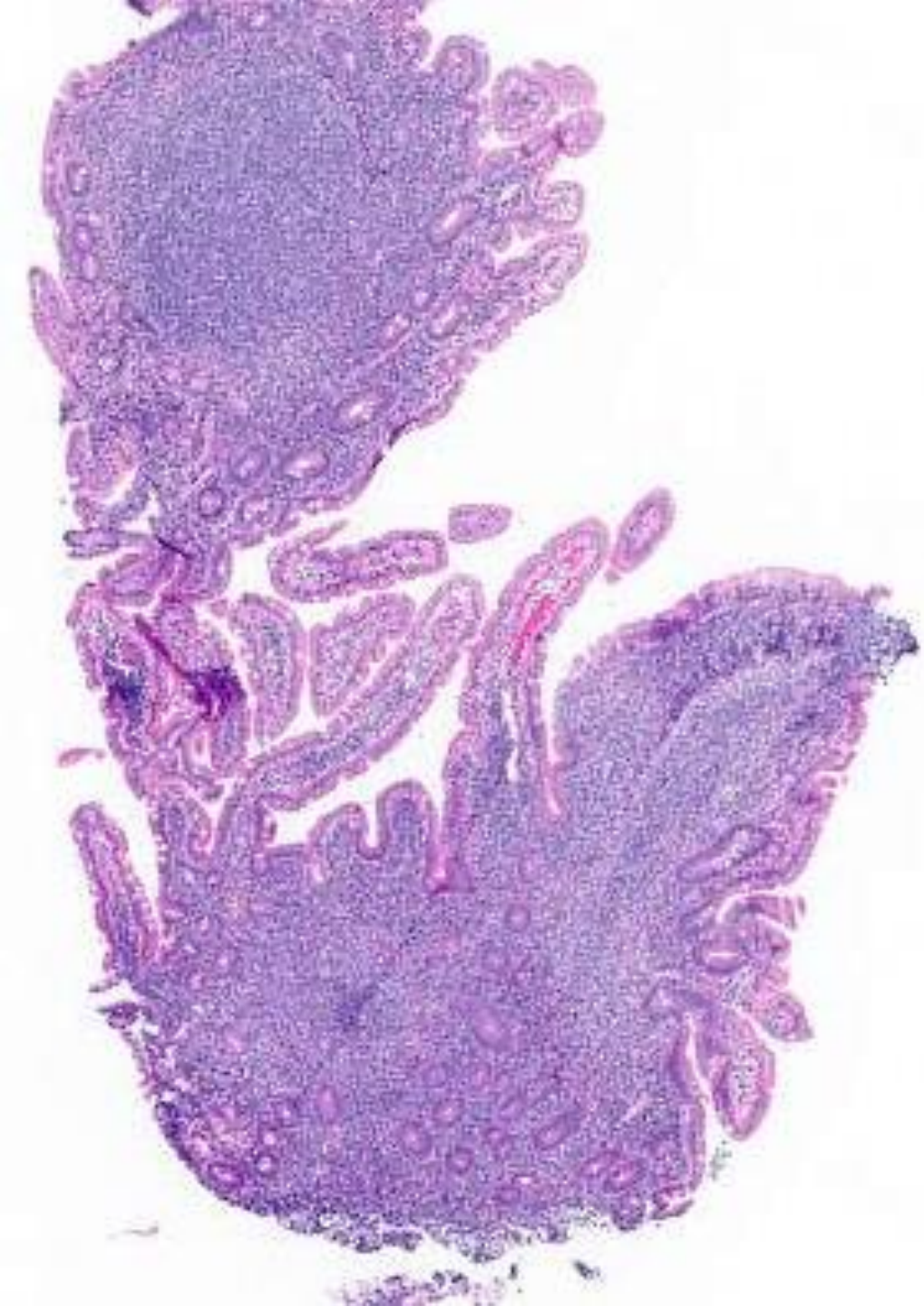


24-0604

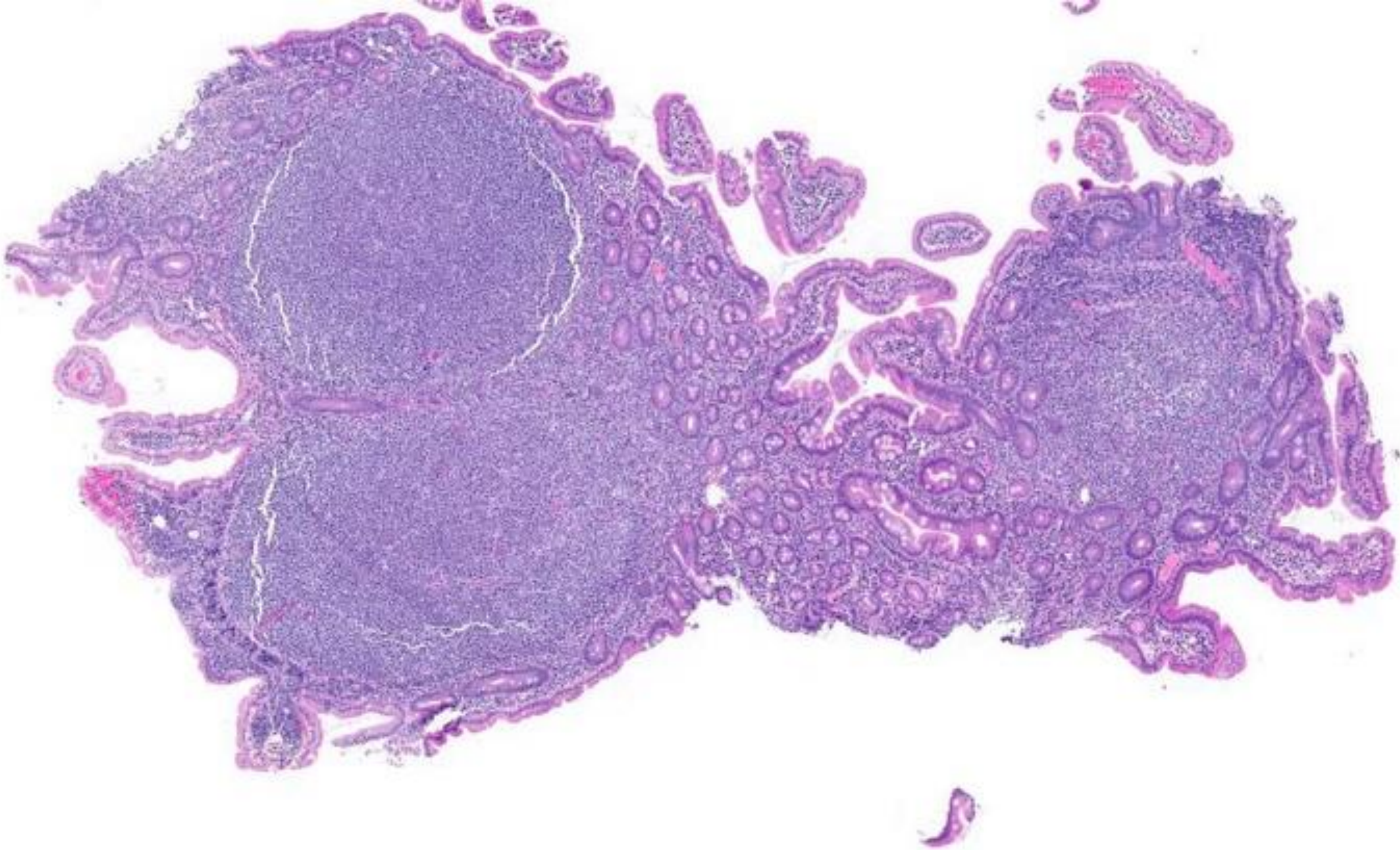
**John Higgins; Stanford**

39 year old female with GERD and “abnormal duodenal mucosa”

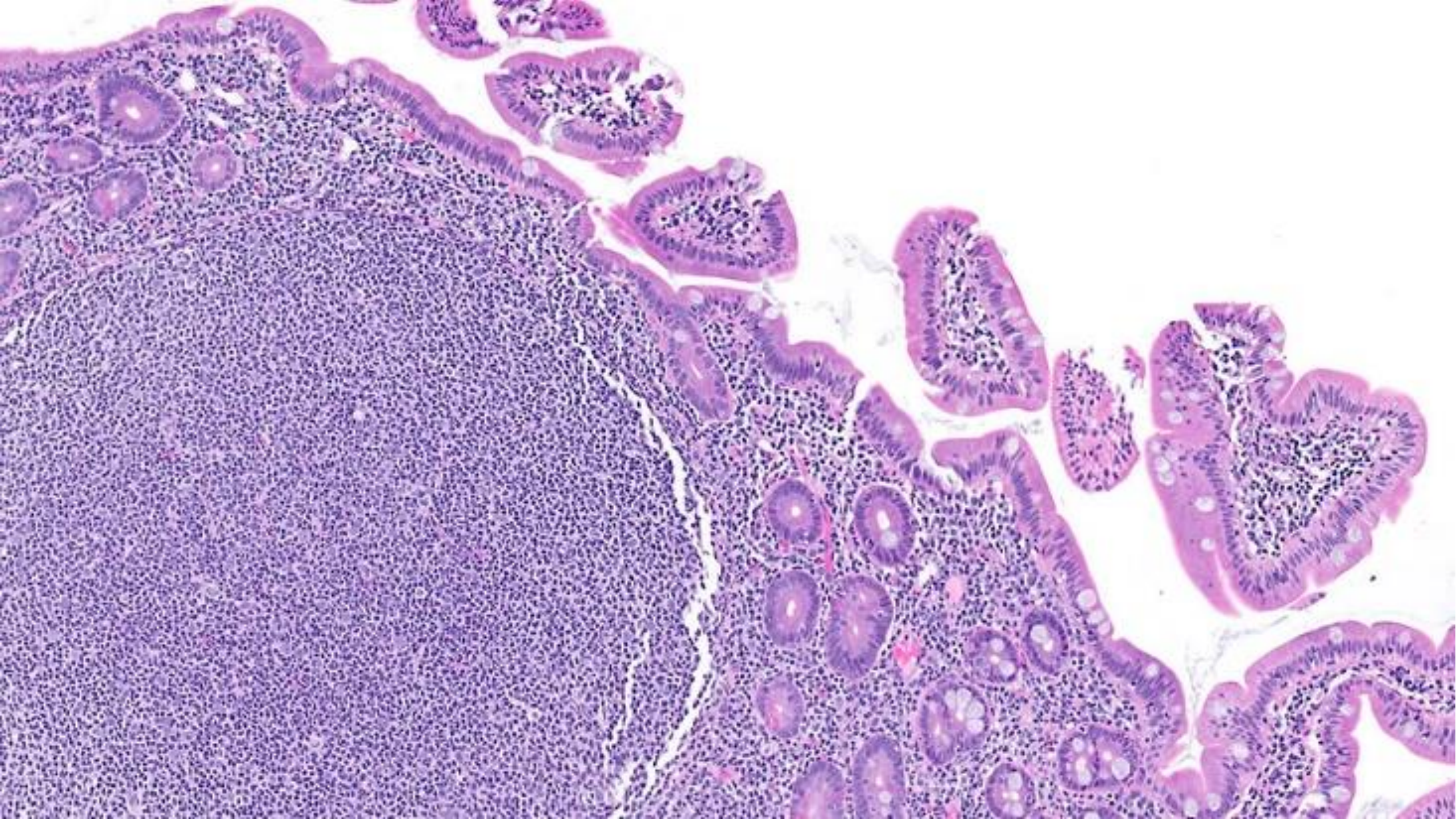




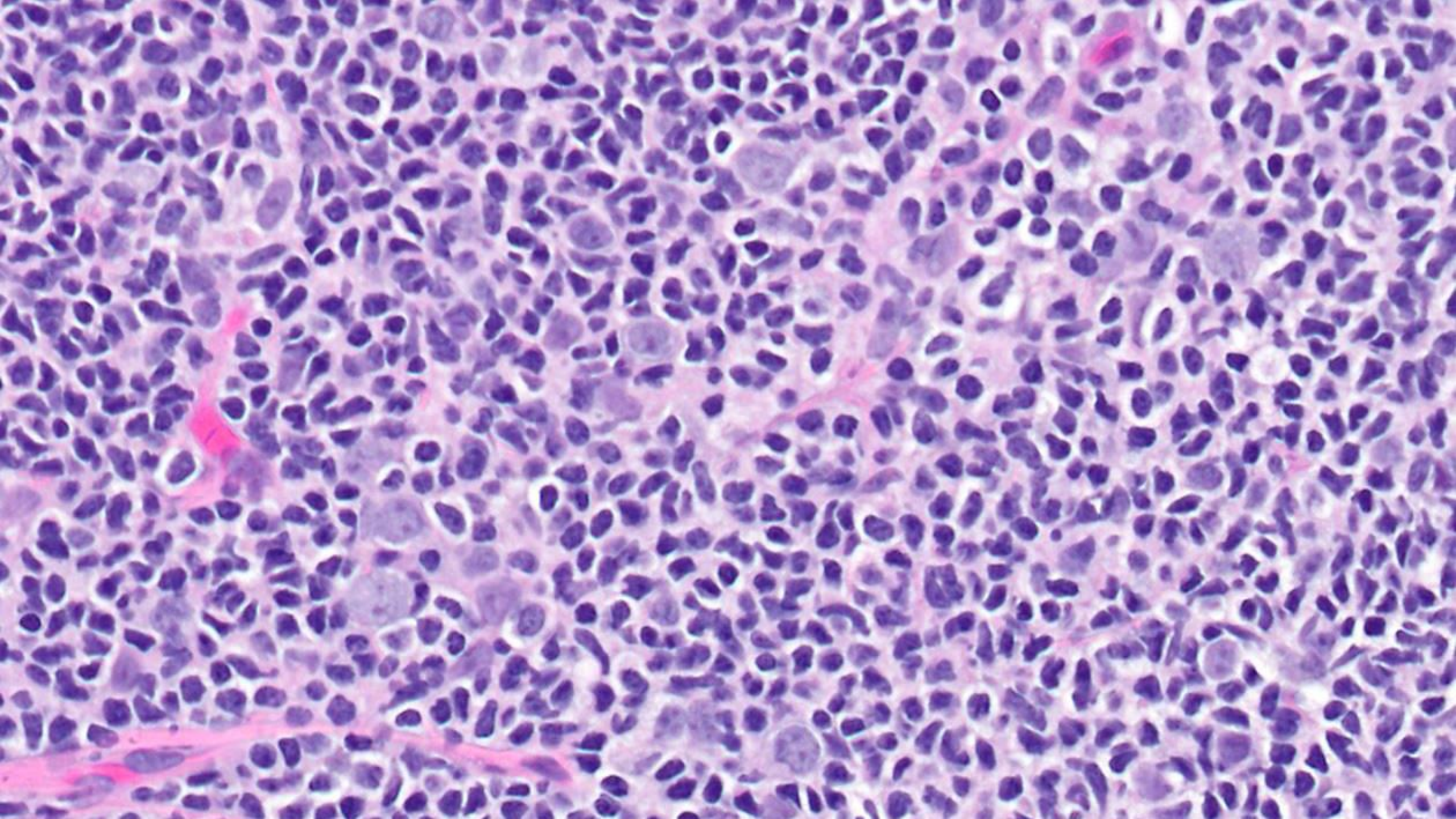




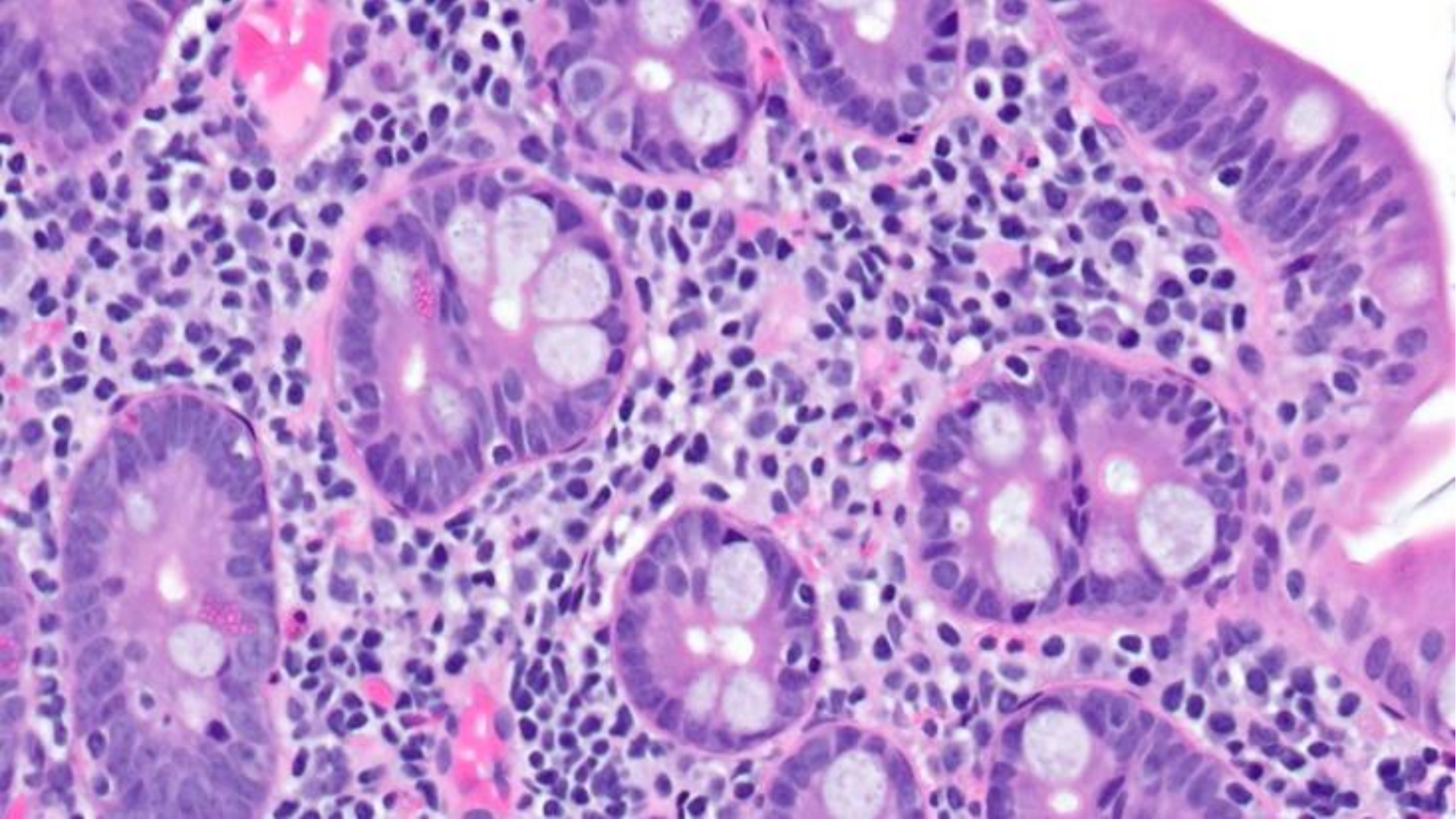














# DIAGNOSIS?

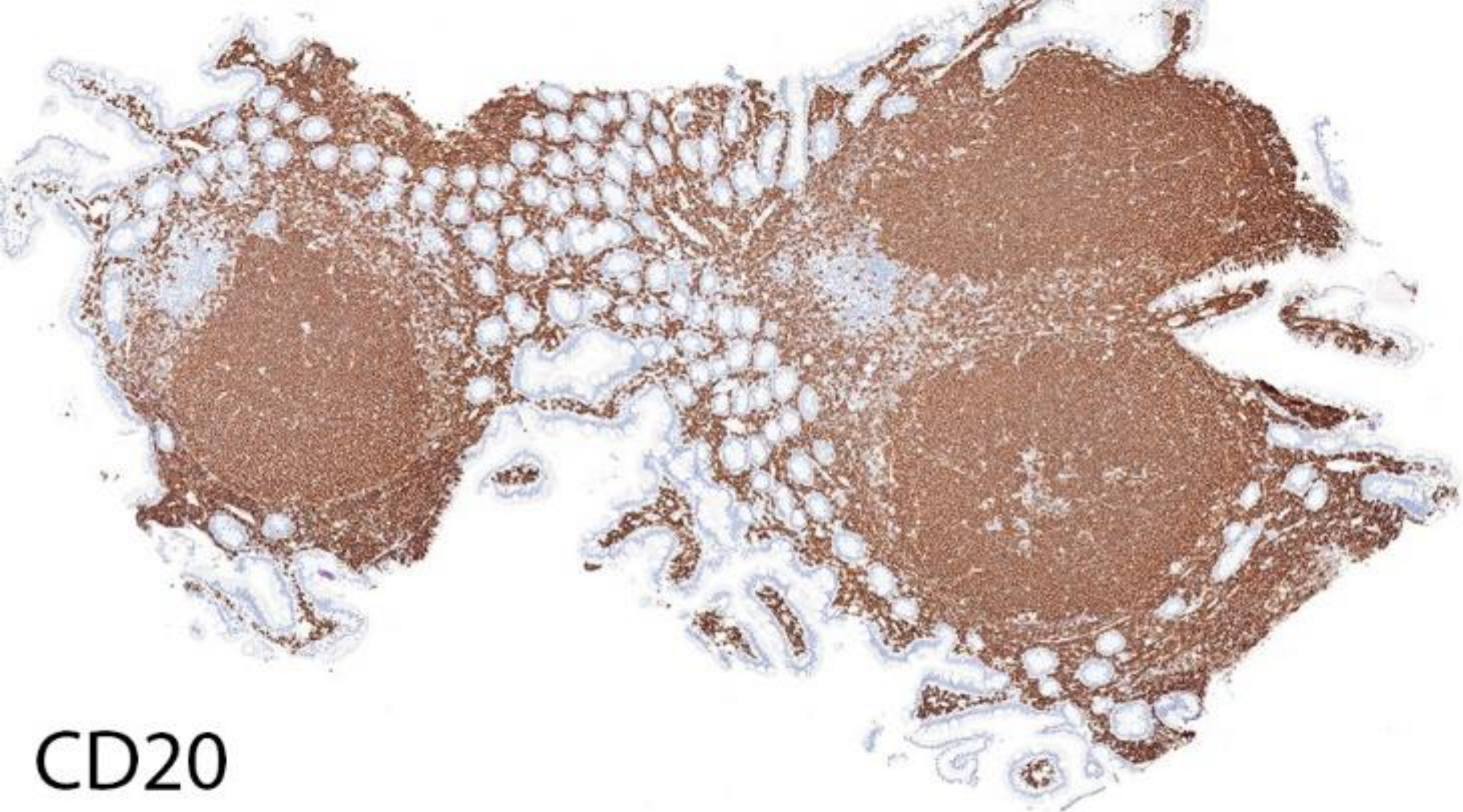




# Differential diagnosis

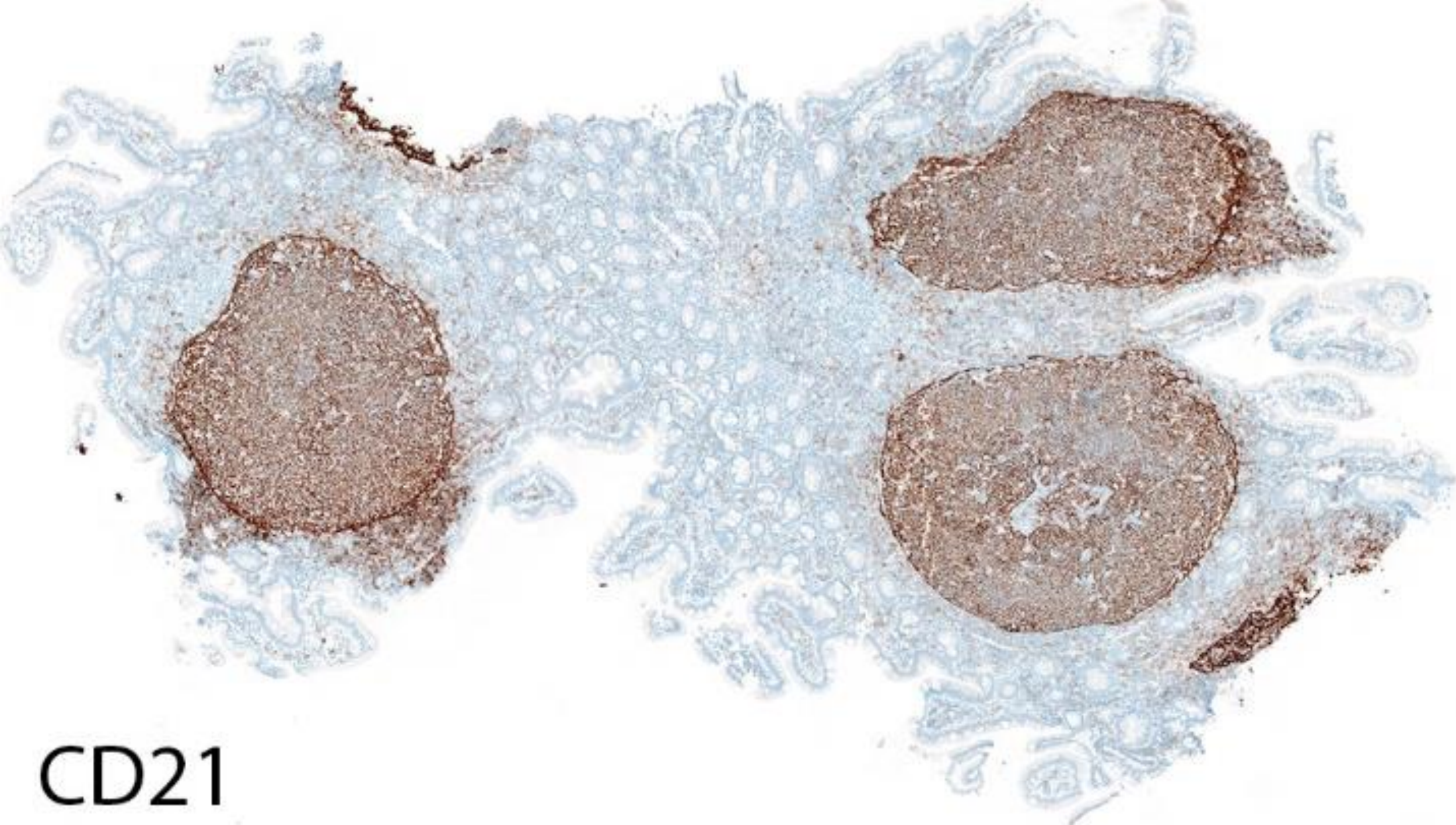
- Lymphoid hyperplasia
- Lymphoma
  - Follicular lymphoma
  - Mantle cell lymphoma
  - Marginal zone lymphoma
  - Chronic lymphocytic lymphoma/small lymphocytic lymphoma



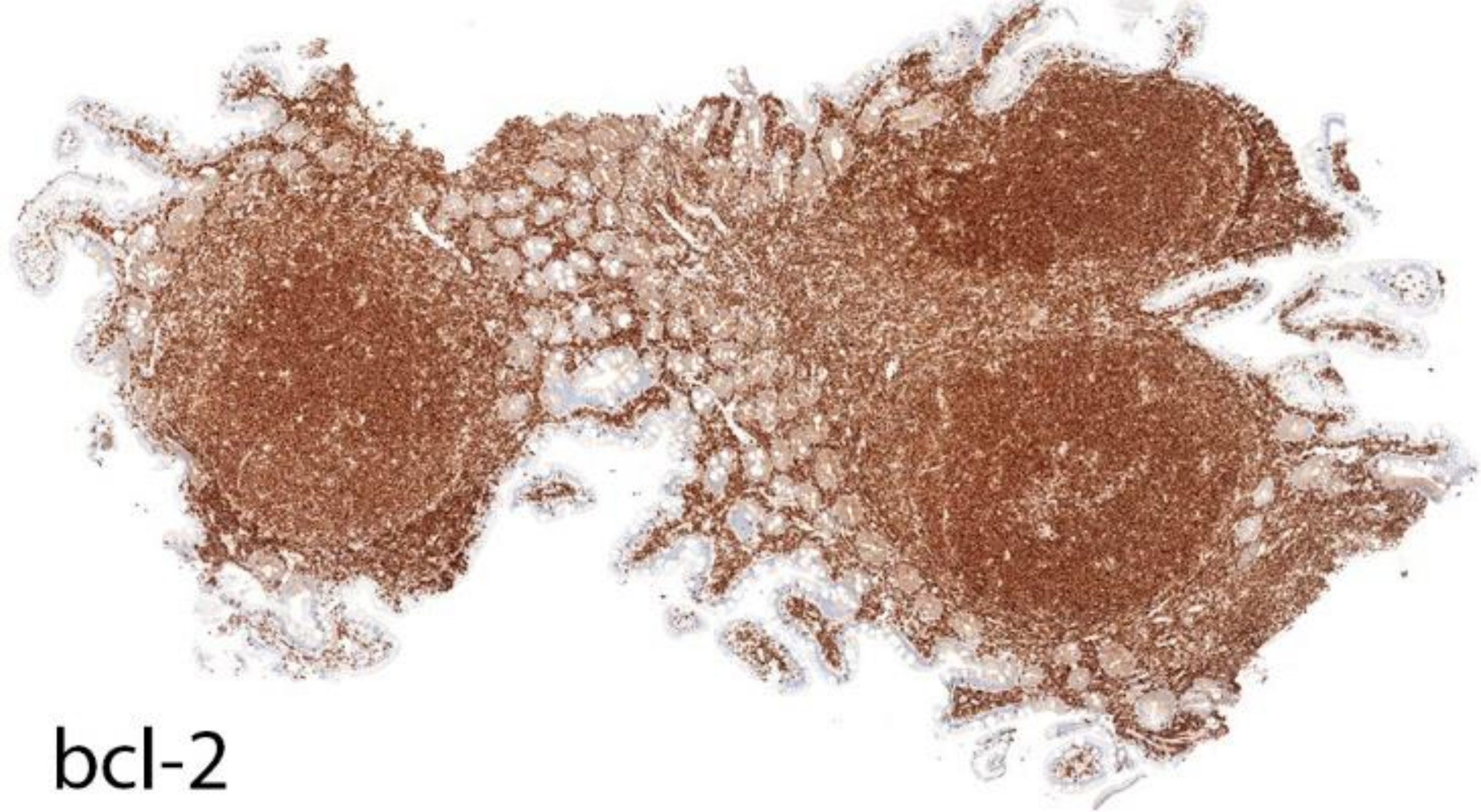


CD20









bcl-2



## Duodenal-type Follicular lymphoma

- Newly recognized entity in the 2016 World Health Organization classification update
- Usually discovered incidentally
- Immunophenotype similar to that of other FLs
- Harbors the typical t(14;18)(q32;q21) translocation
- Almost always diagnosed at a low stage and stays localized to the small intestine, most commonly the second portion of the duodenum
- 5 year progression free survival of 93%
- Other FLs are diagnosed at an advanced stage
- Duodenal involvement by systemic follicular lymphoma must be excluded clinically

Arch Pathol Lab Med. 2018 Apr;142(4):542-547

Cancer Sci (2011) 102(8):1532–1536

Virchows Arch (2020) 476:667–681



# Duodenal-type Follicular lymphoma

Arch Pathol Lab Med. 2018 Apr;142(4):542-547.

<b>Differences Between Duodenal-Type Follicular Lymphoma (D-FL), Nodal Follicular Lymphoma (NFL), and Gastrointestinal Follicular Lymphoma (GI-FL), Not of the Duodenum</b>			
	<b>D-FL</b>	<b>NFL</b>	<b>GI-FL</b>
Grade	1–2 <sup>a</sup>	1–2 or 3	1–2 or 3
Stage at presentation <sup>b</sup>	I or II	III or IV <sup>c</sup>	I–IV
BCL-6	+	+	+
CD10	+	+	+
BCL-2	+	+	+
AID	–	+	+
CD21	Peripheral of GC (duodenal pattern), 10% of follicle	Dense in GC (nodal pattern), 67% of follicle	Dense in GC (nodal pattern), 67% of follicle
CD27	+	+	–
MUM1	–	–	–
Blimp-1	–	–	–
t(14;18)	~90%	60%–90%	60%–90%
IgVH use	VH3, VH4, VH5	VH3, most cases	VH3, most cases

Abbreviations: AID, activation-induced cytidine deaminase; Blimp-1, B-lymphocyte maturation protein 1; GC, germinal center; IgVH, immunoglobulin heavy-chain variable genes; +, positive; –, negative.

<sup>a</sup> The vast majority of D-FLs are of grades 1–2. However, very rare cases that transformed to high-grade B-cell lymphoma have been reported.

<sup>b</sup> D-FL staging was by the Lugano classification; NFL and GI-FL staging was by the Ann Arbor classification.

<sup>c</sup> Most NFLs present at stages III–IV, although a minority of cases can present at a lower stage.



## Follow-up

- Evaluated by PET/CT which showed no adenopathy
- She will be followed with active surveillance and q6 months MR enterography and labs

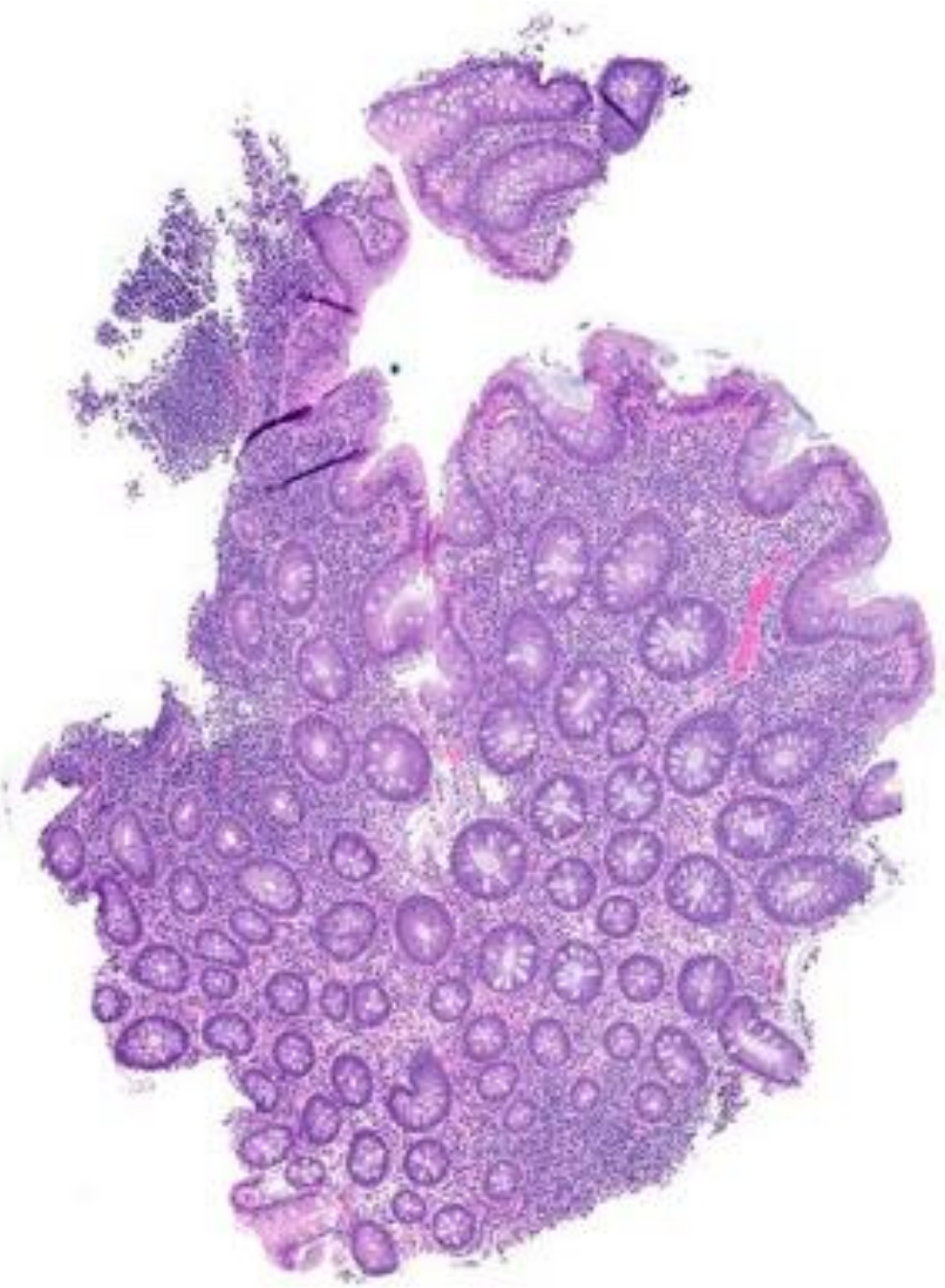
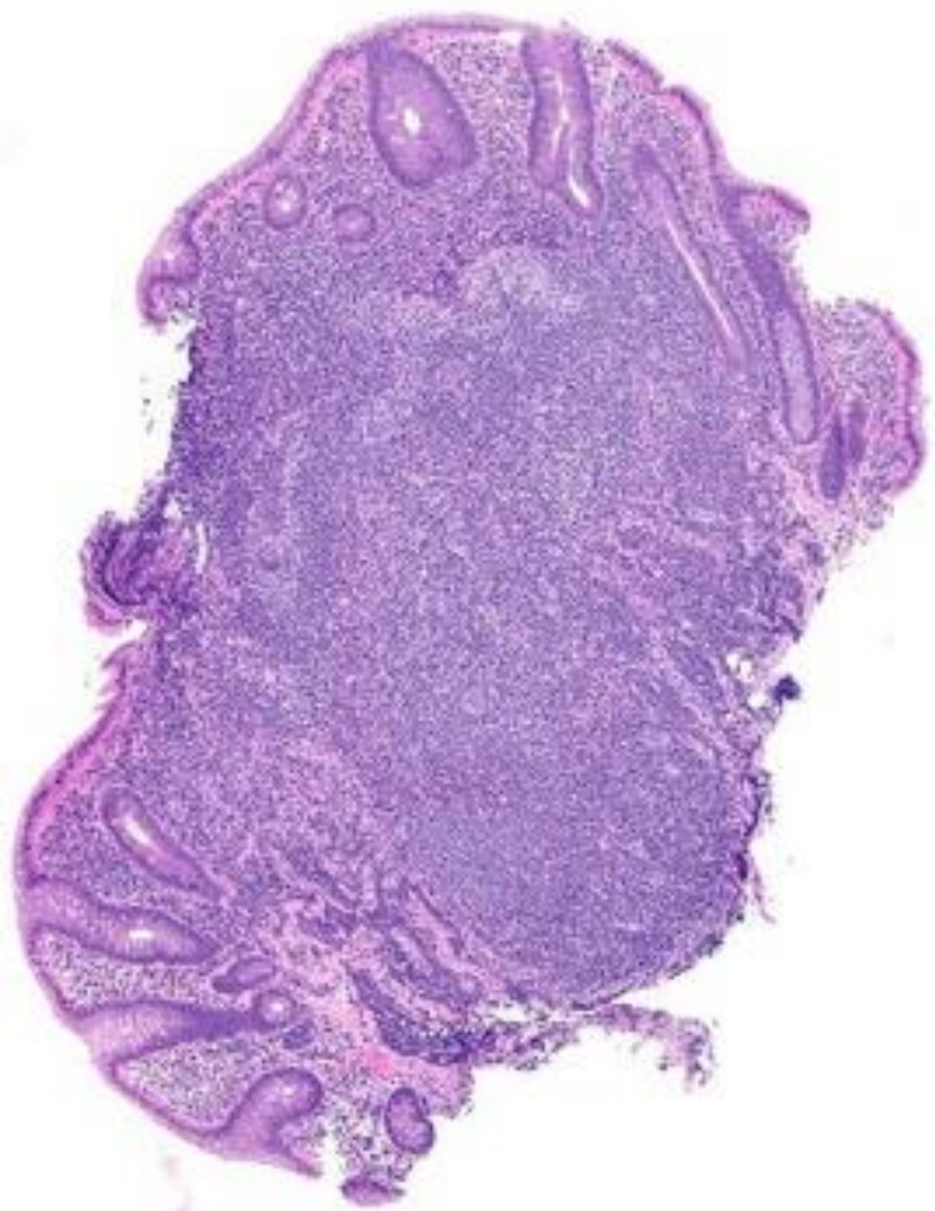


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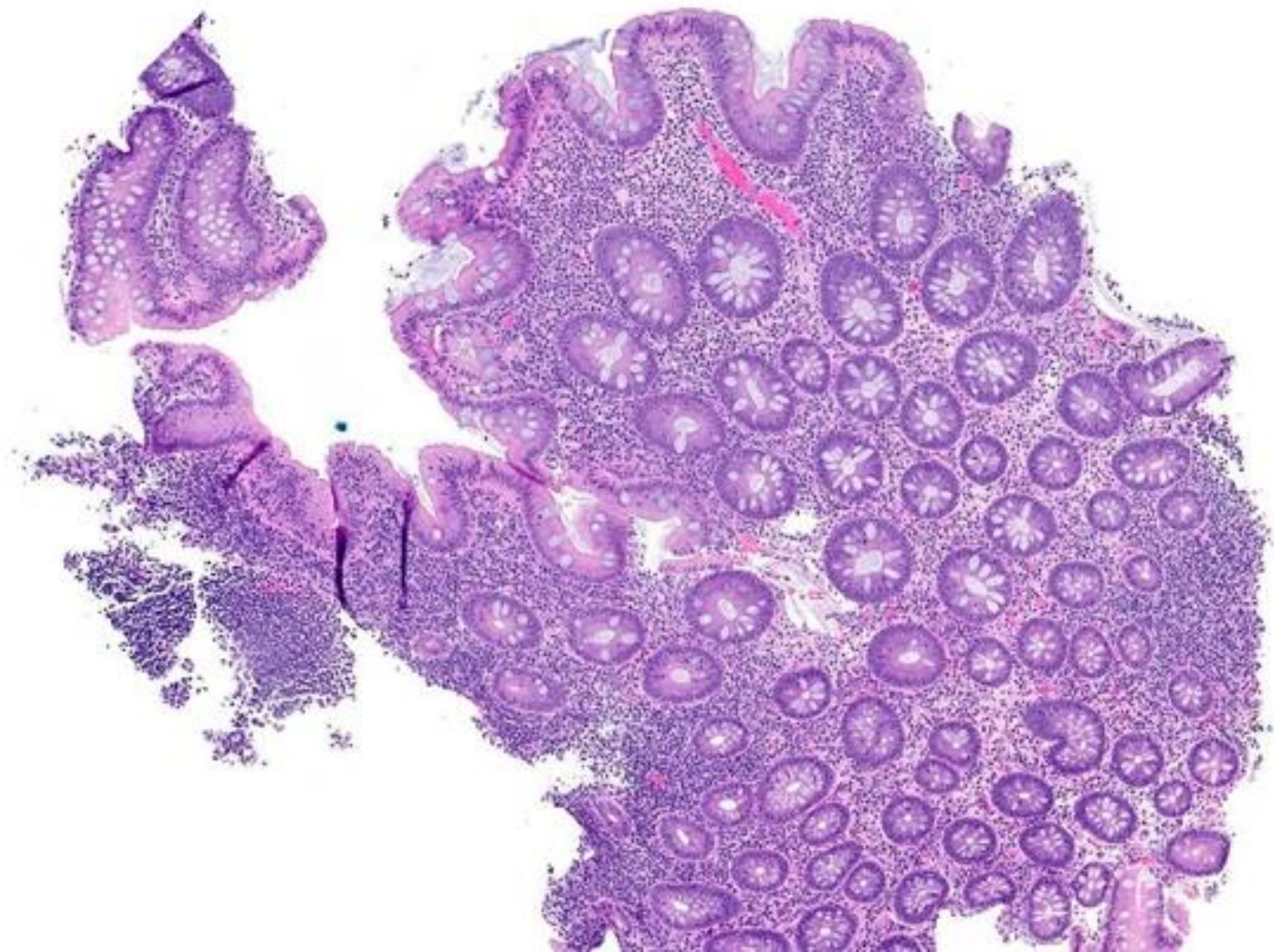
John Higgins; Stanford

72 year old male with colon polyps x2

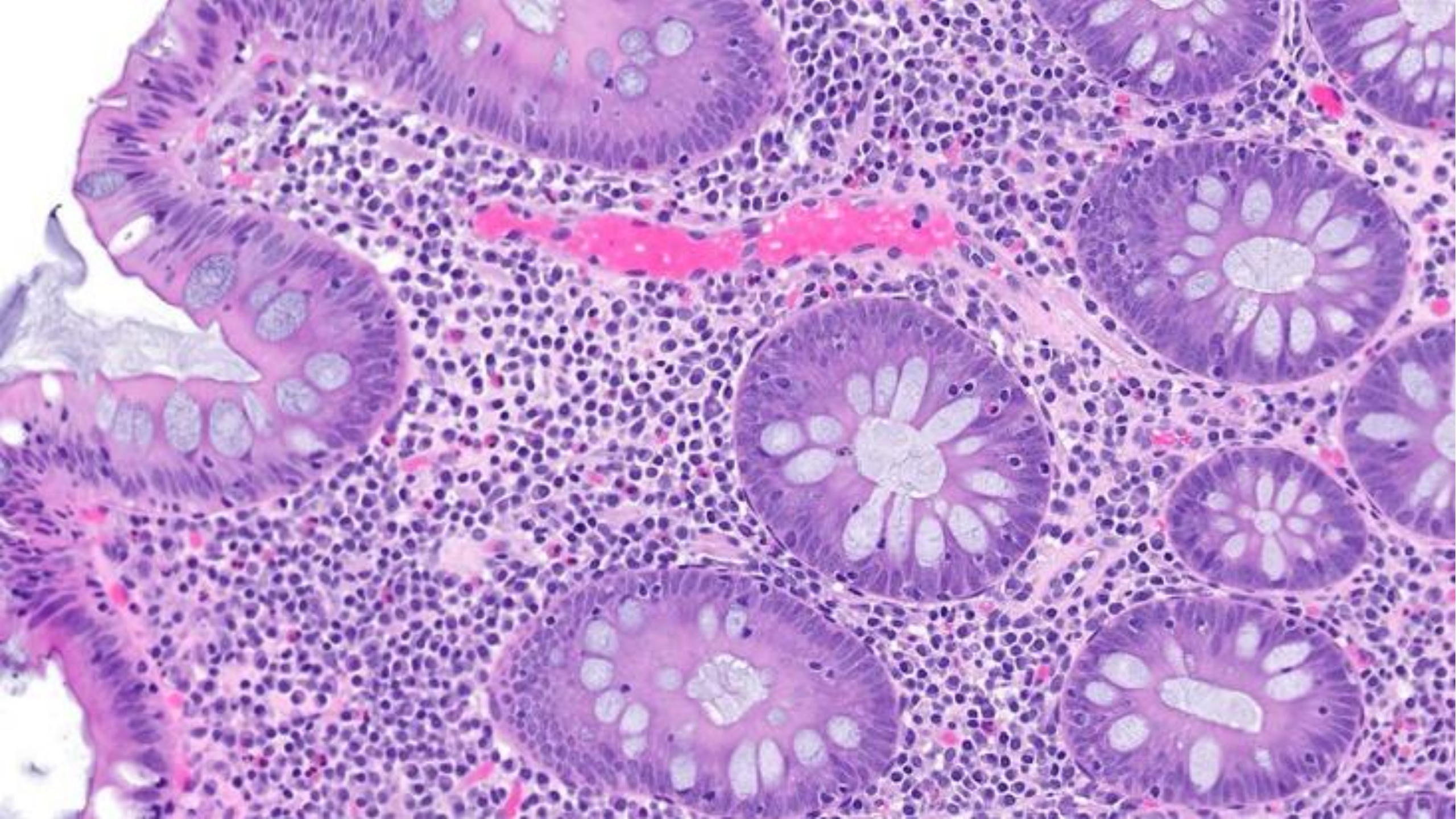




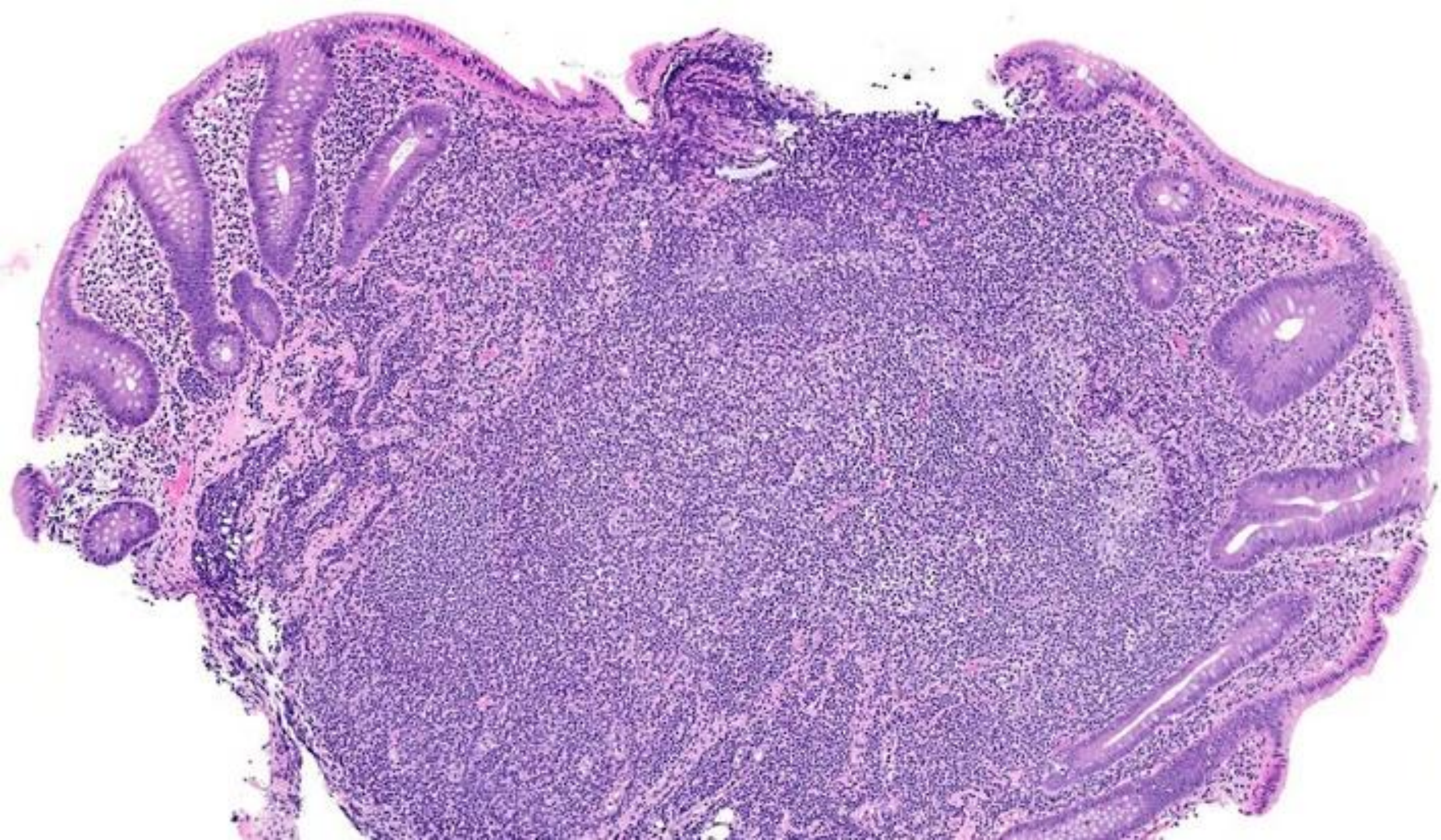




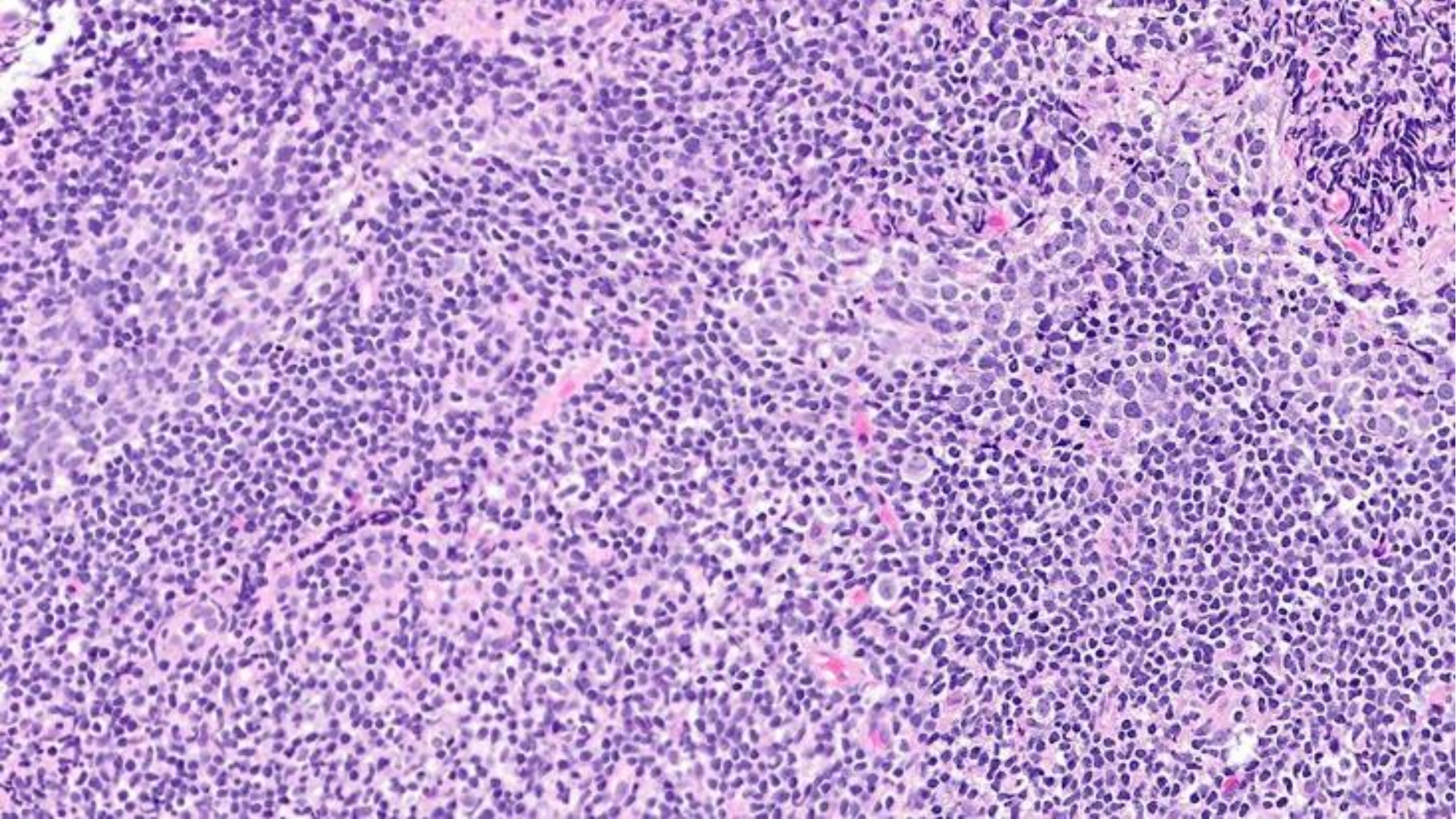




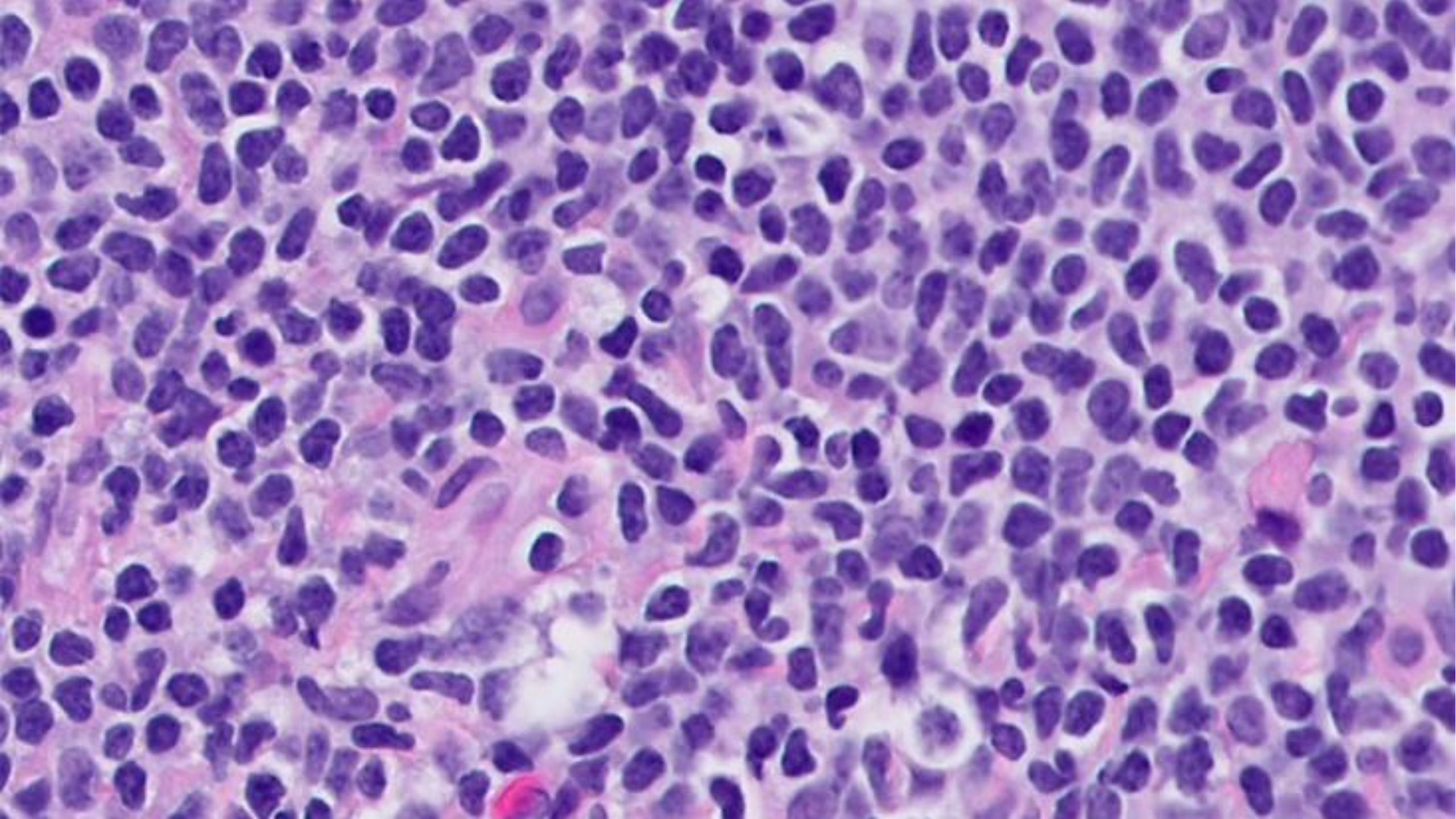














# DIAGNOSIS?





# Differential diagnosis

- Prominent lymphoid aggregate
- Lymphoid hyperplasia/infection
- Lymphoma
  - Follicular lymphoma
  - Mantle cell lymphoma
  - Marginal zone lymphoma
  - Chronic lymphocytic lymphoma/small lymphocytic lymphoma

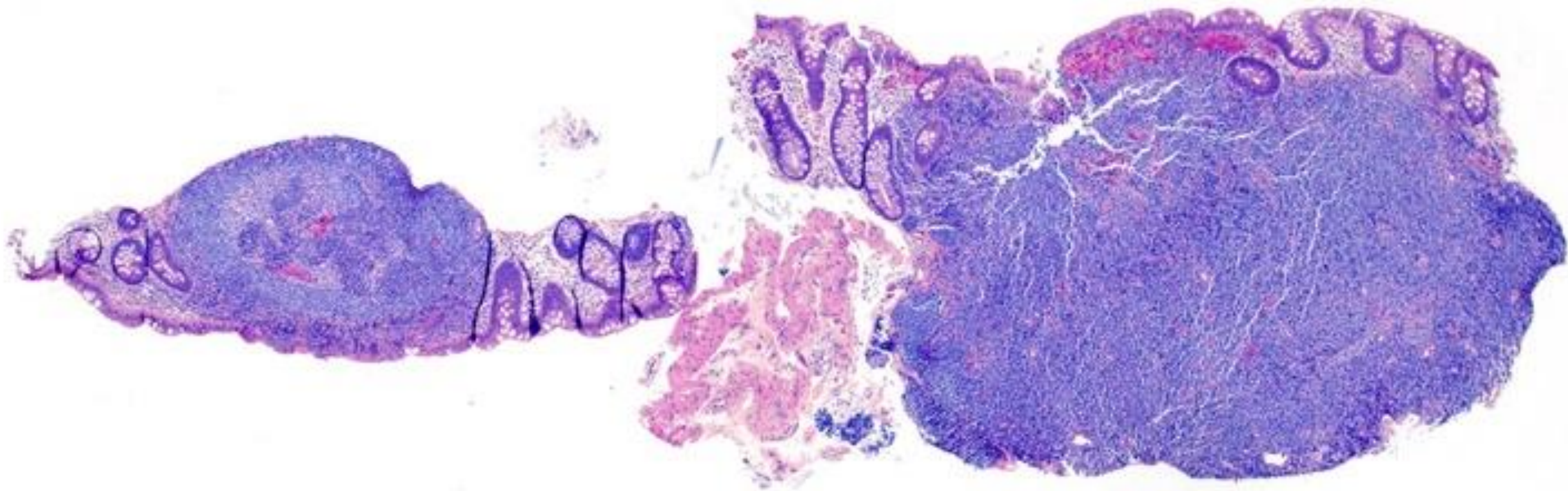


## When and how to stain

- Unusually large aggregate
- Unrecognizable architecture
- History and peripheral blood findings
- Start with B and T cell markers

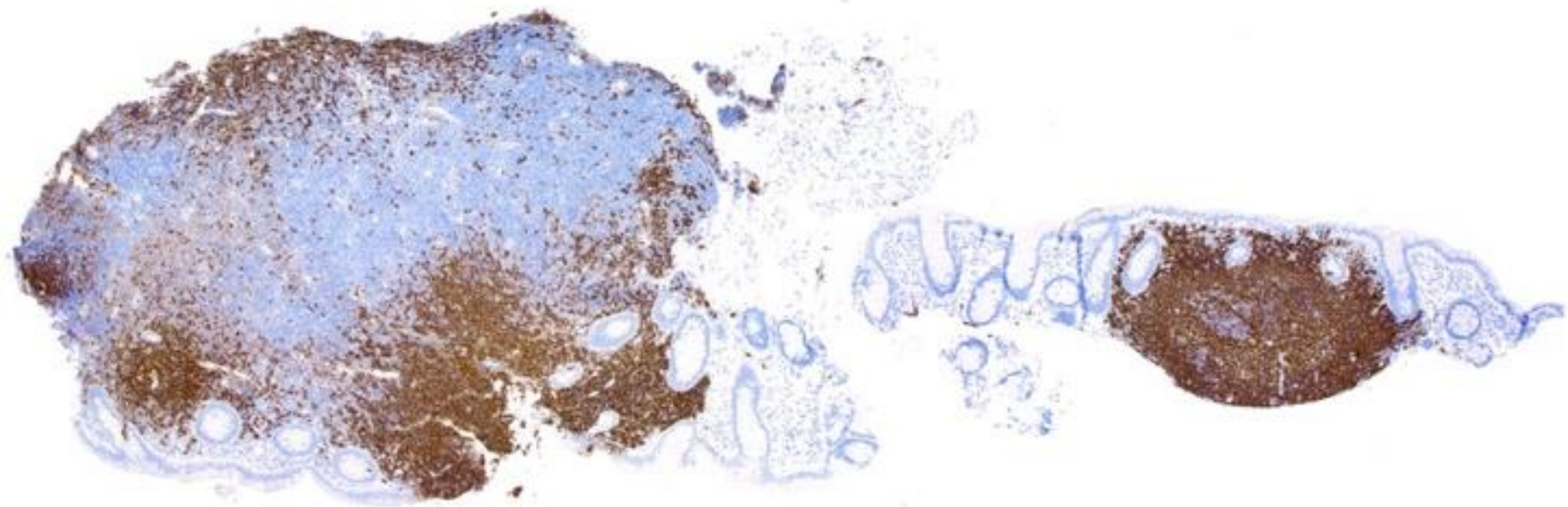


A different case



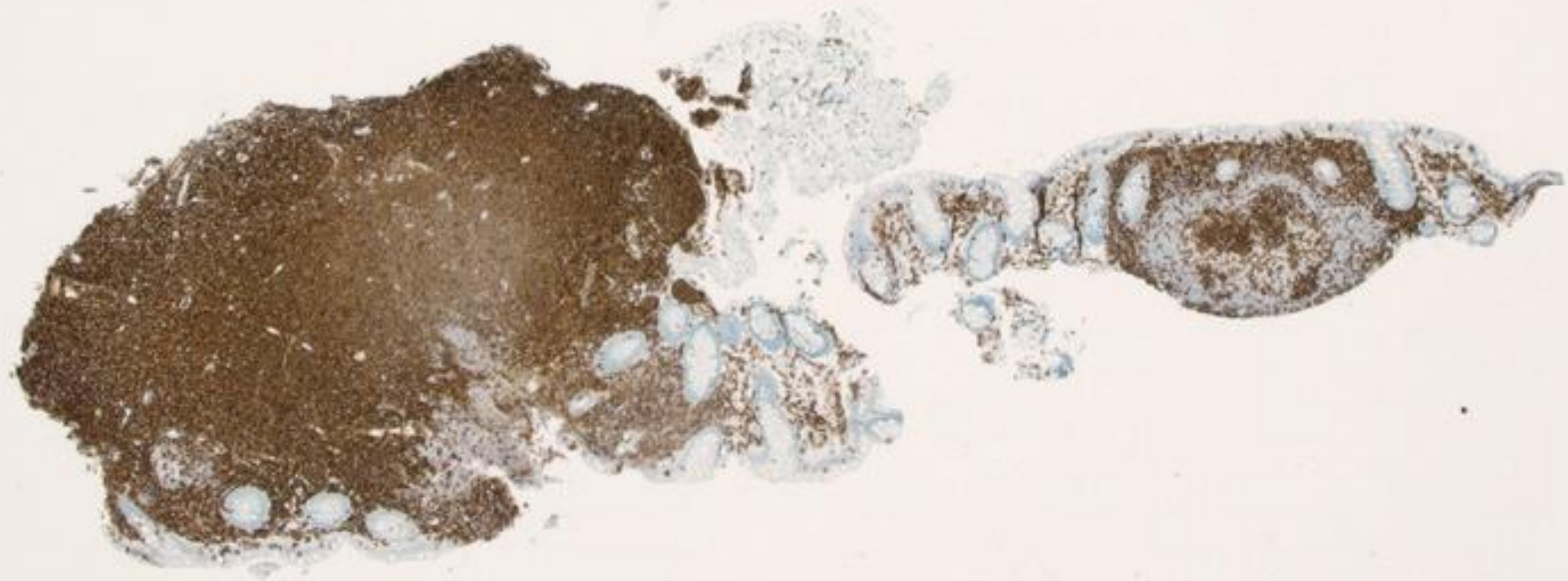


CD20





CD43

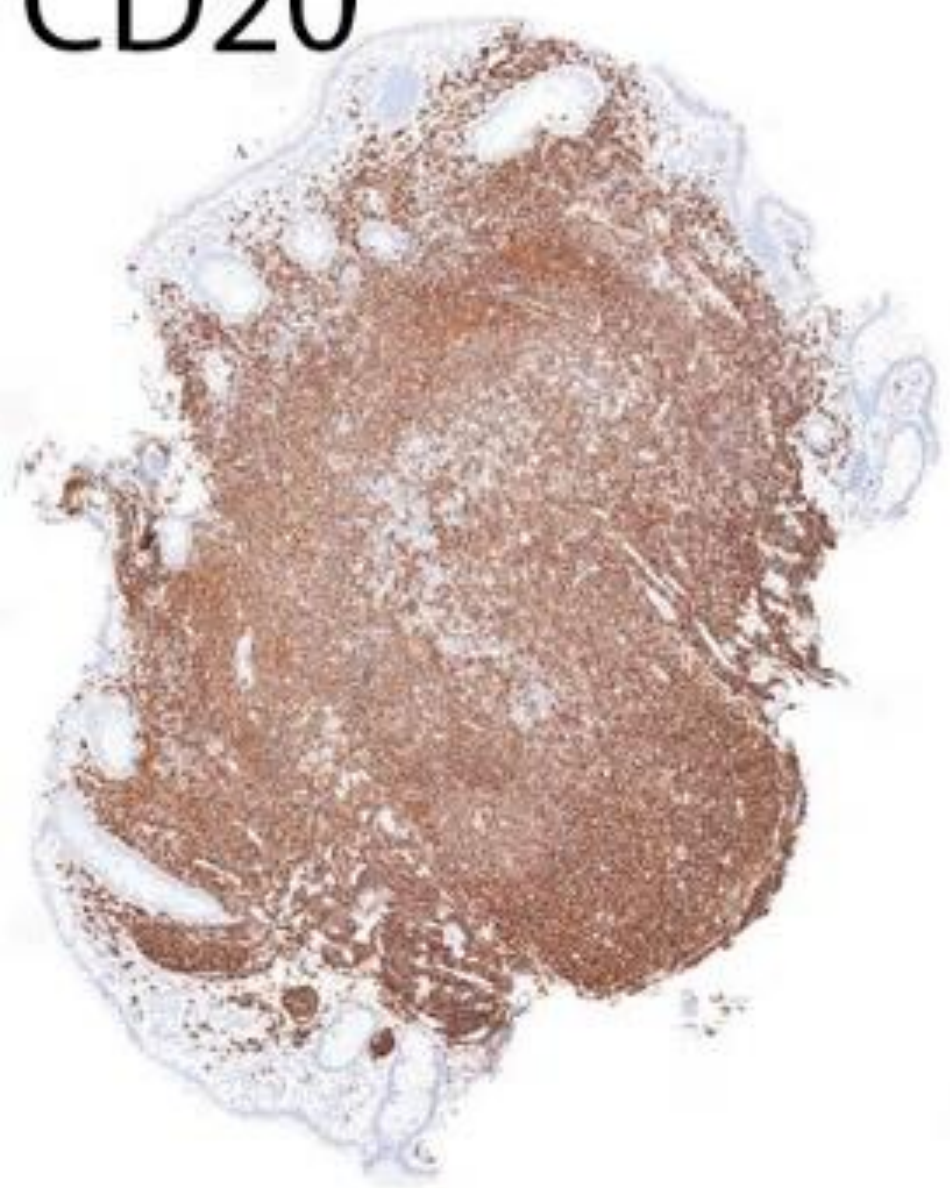




Back to our case

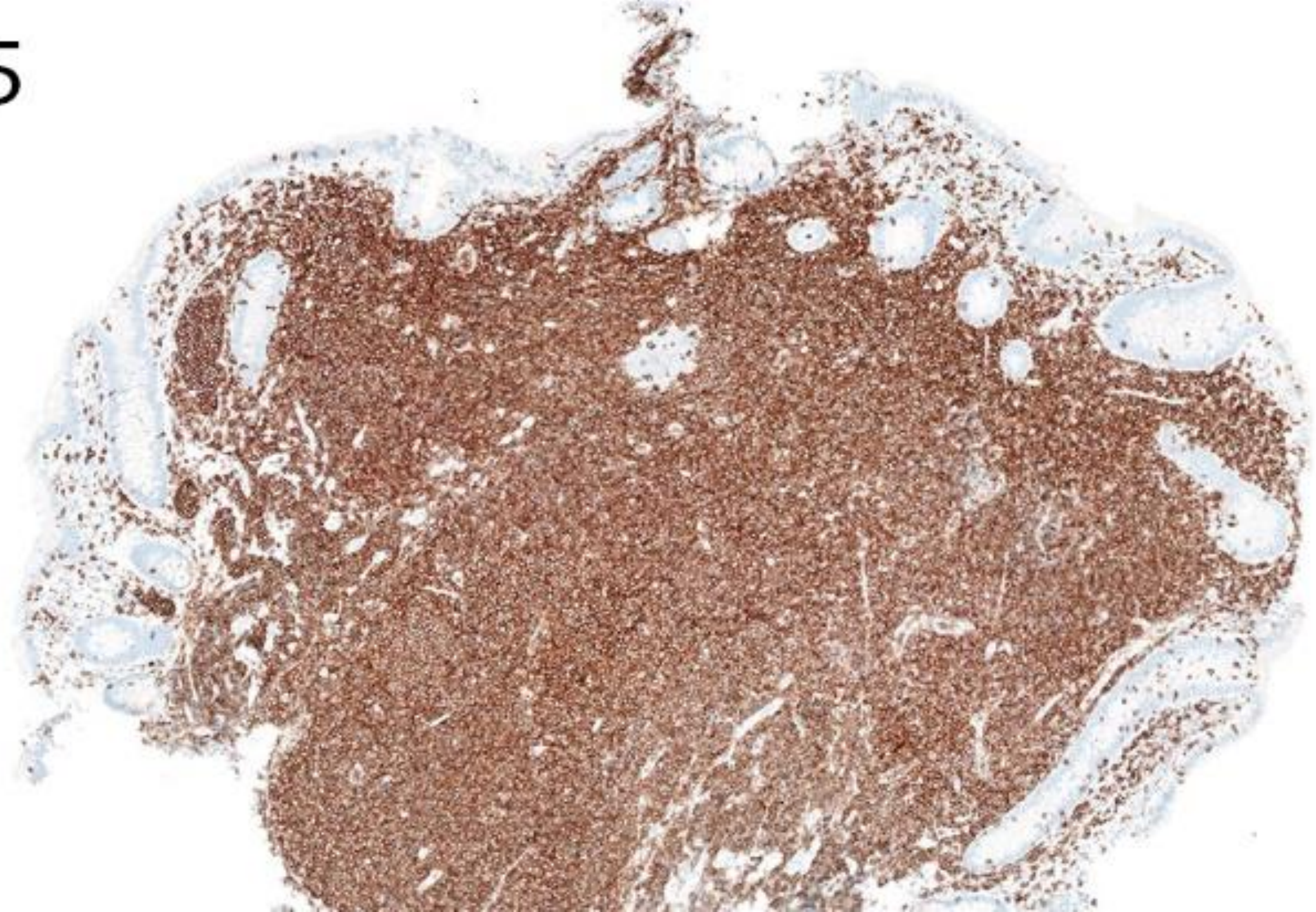


CD20



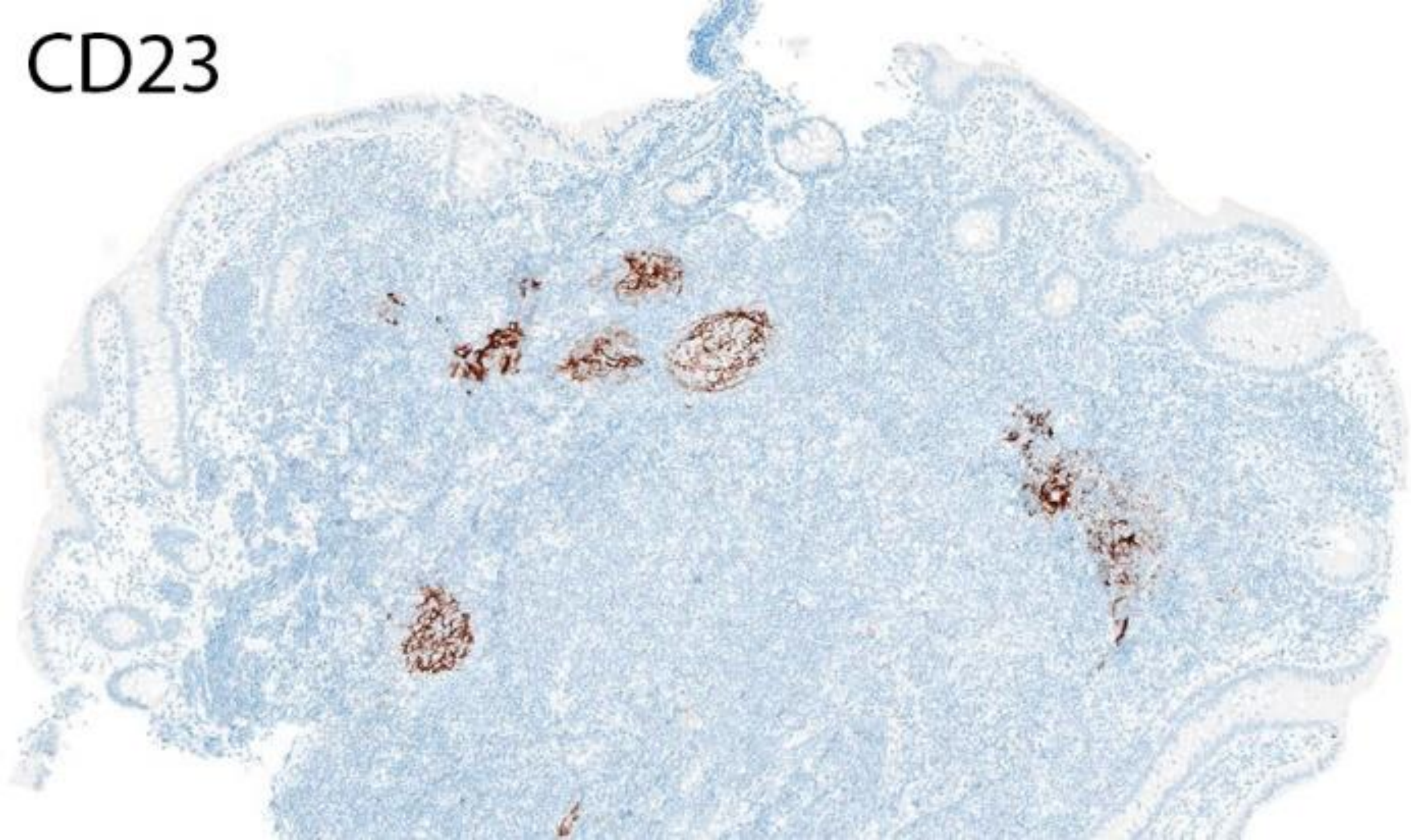


CD5



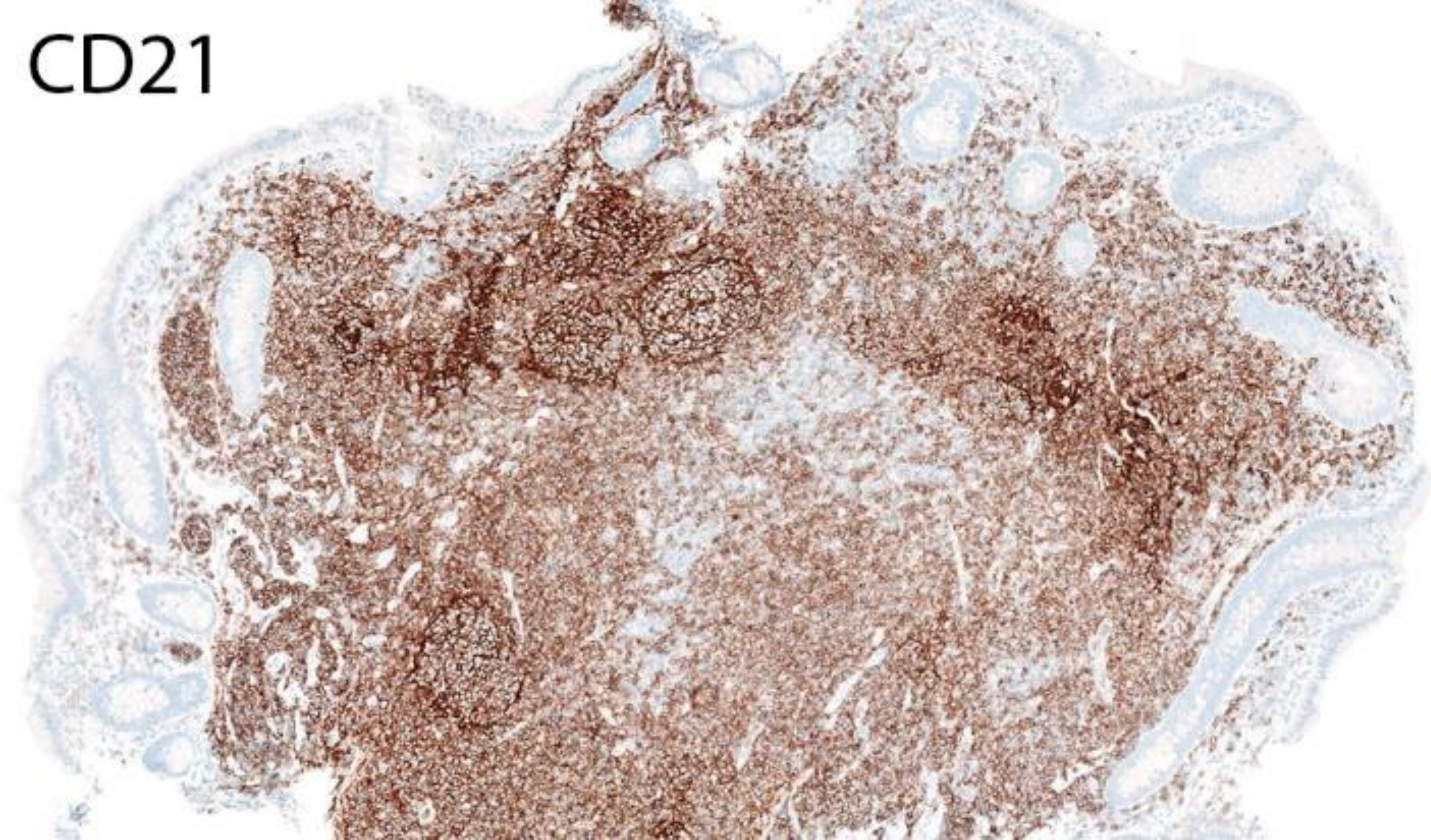


CD23



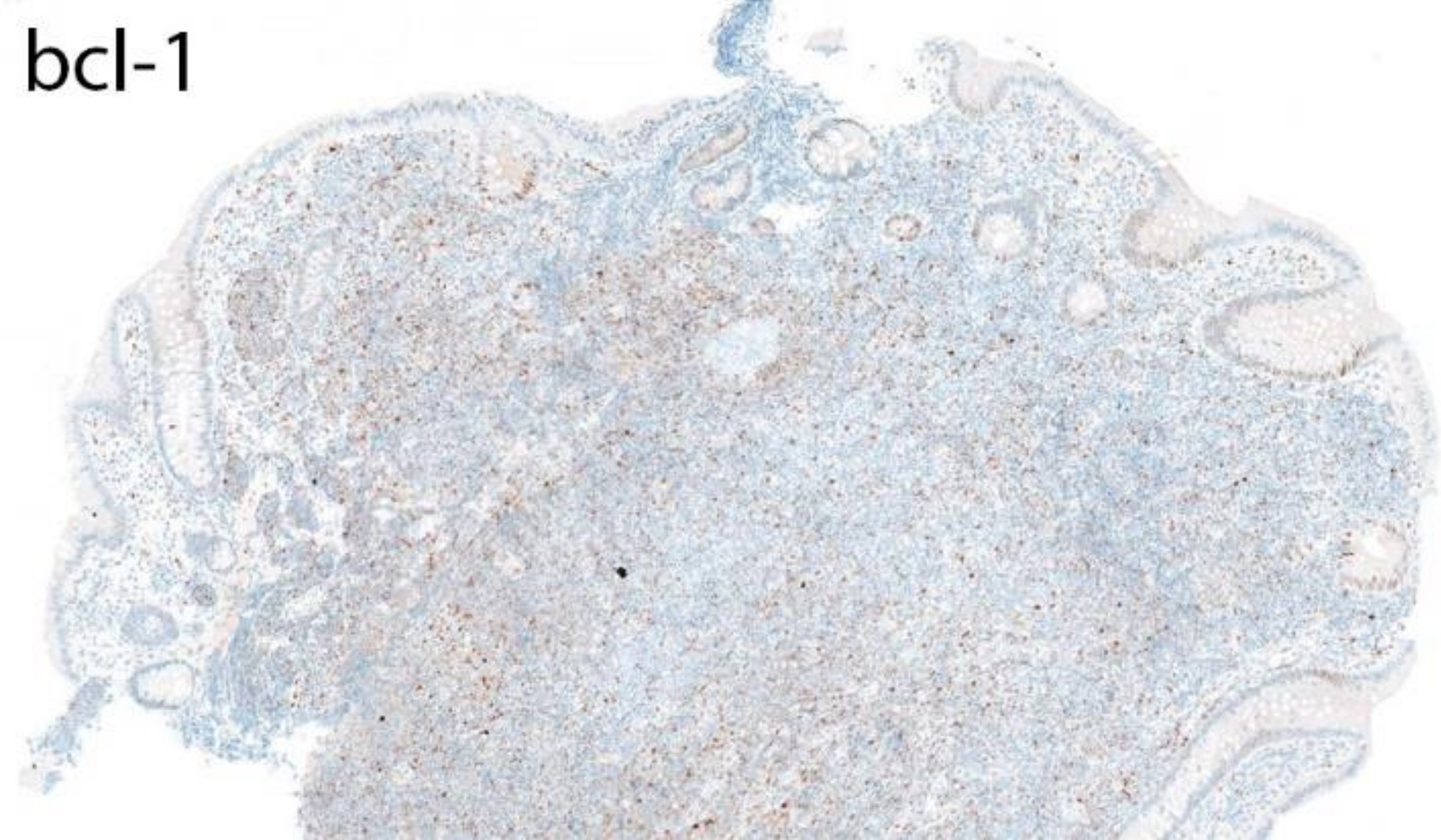


CD21



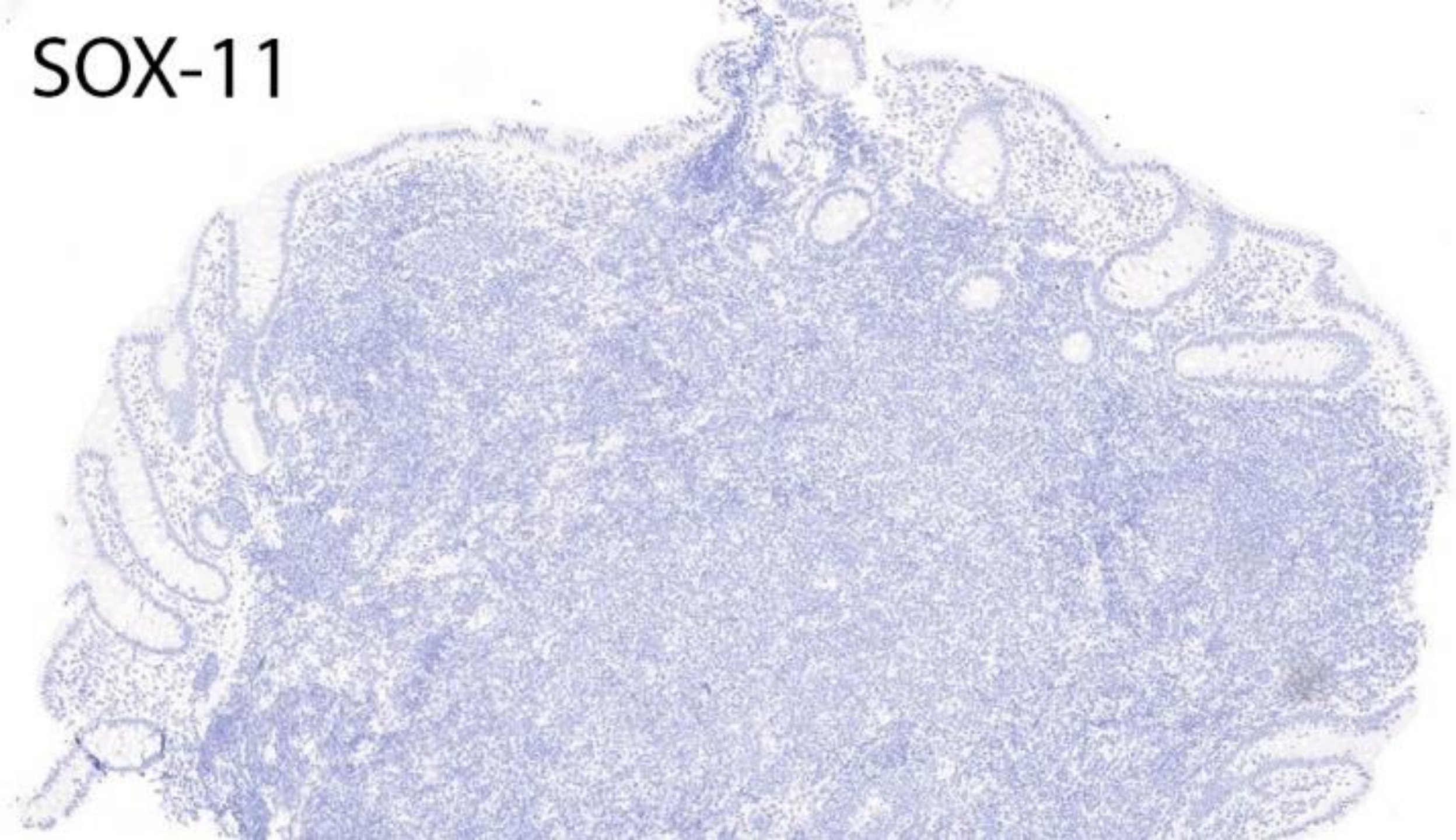


bcl-1





SOX-11





# GI mantle cell lymphoma

- Typical form is as lymphomatous polyposis in the colon
- CCND1 most common but may also be CCND2 or CCND3
- SOX11 useful for recognizing non-CCND1 cases



# Leukemic non-nodal mantle cell lymphoma

- Conventional pattern of mantle cell lymphoma involvement is nodal and bone marrow
- Indolent cases may show leukemic pattern of involvement
- Such cases are estimated to represent 3% of MCL cases
- These cases are characterized by lack of SOX11 expression
- SOX11 negative cases show 5-year overall survival of 78% versus 36%

Cancer Res. 2010 Feb 15;70(4):1408-18  
Haematologica. 2011 Aug;96(8):1121-7.



## Follow-up

- WBC 30.9 with absolute lymphocytosis
- PET/CT showed bilateral hypermetabolic cervical lymph nodes, largest 2.1 cm as well as epiglottic lesion that raised consideration for SCC
- FNA of left cervical lymph node showed involvement by MCL
- First diagnosed with MCL in 2/2020 with peripheral blood flow cytometry showing a kappa monotypic CD5/CD19/CD20 B-cell population not expressing CD23, FISH positive for CCND1/IgH gene rearrangement
- Felt to have indolent disease and plan is to continue to follow without treatment

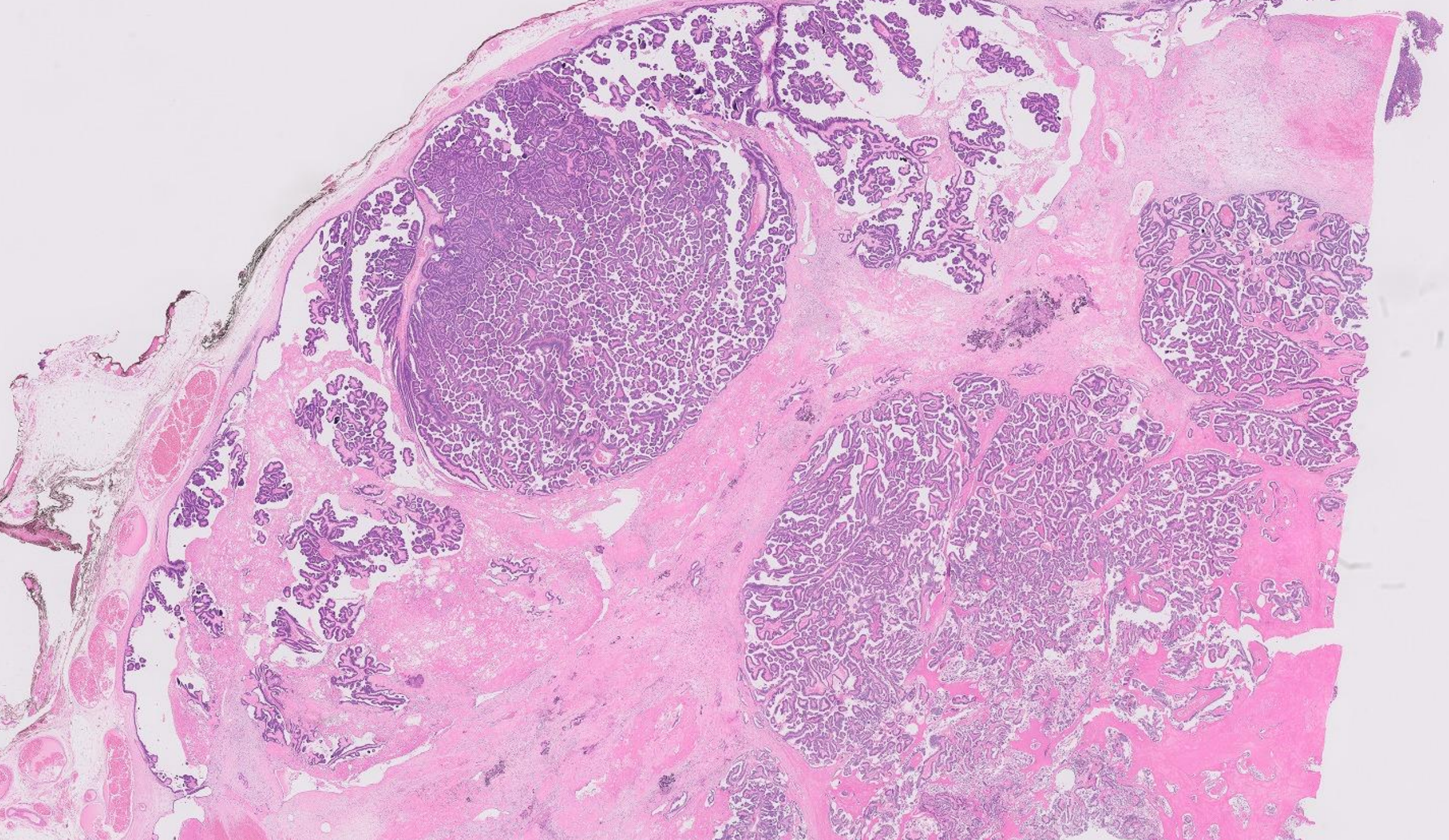


24-0606

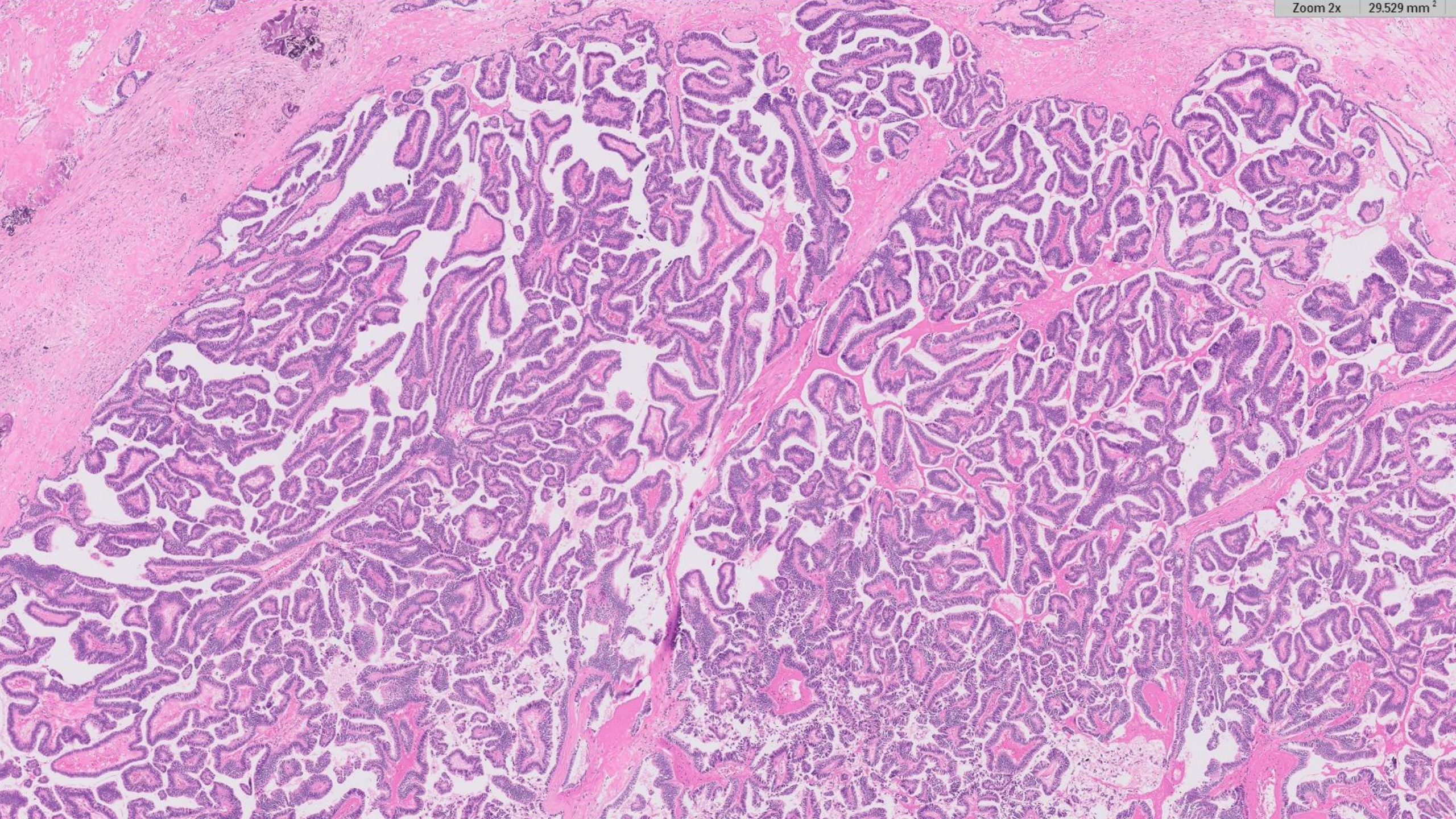
**Rabia Bhalli, Megan Troxell; Stanford**

80 year old female.....

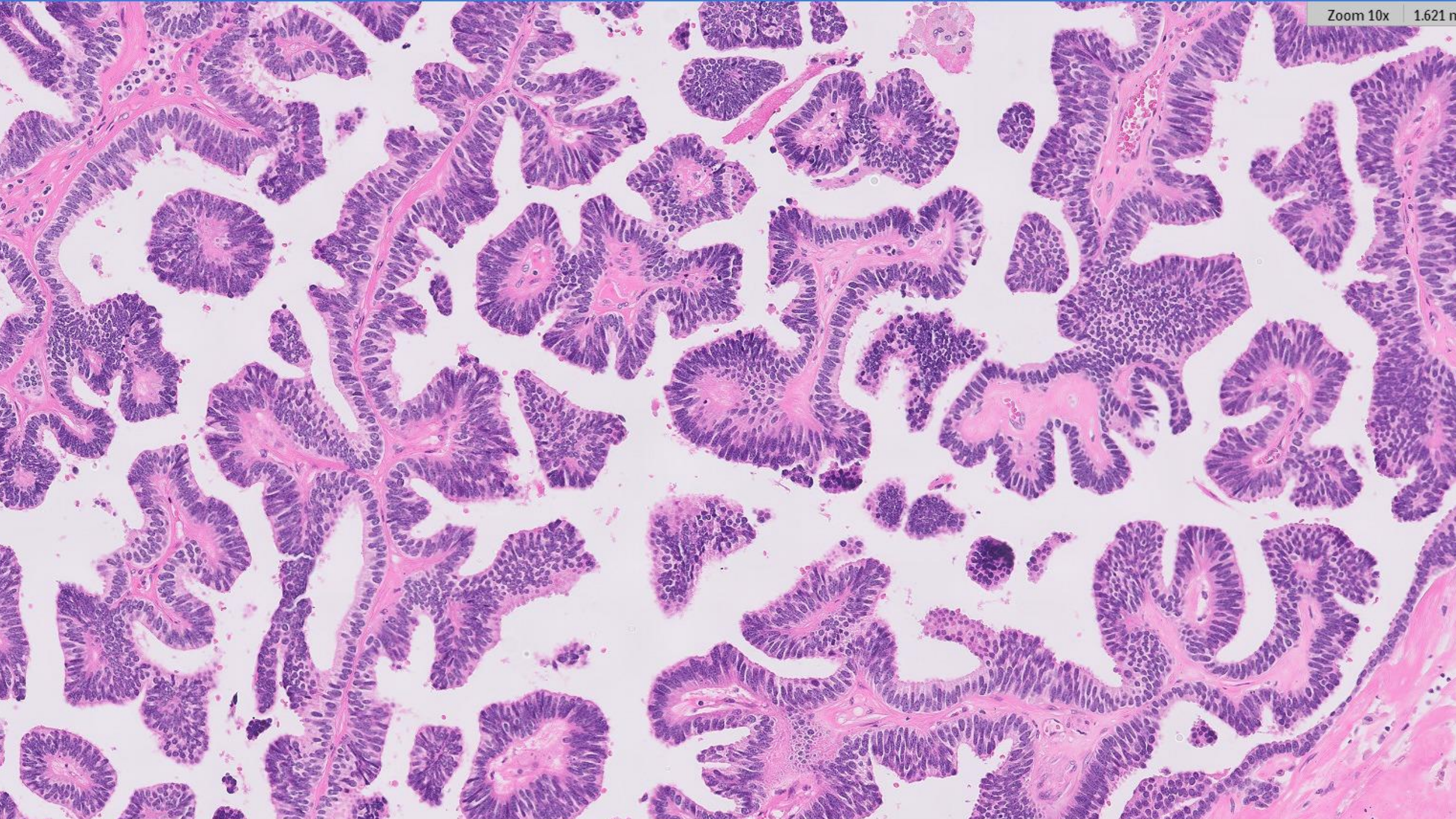




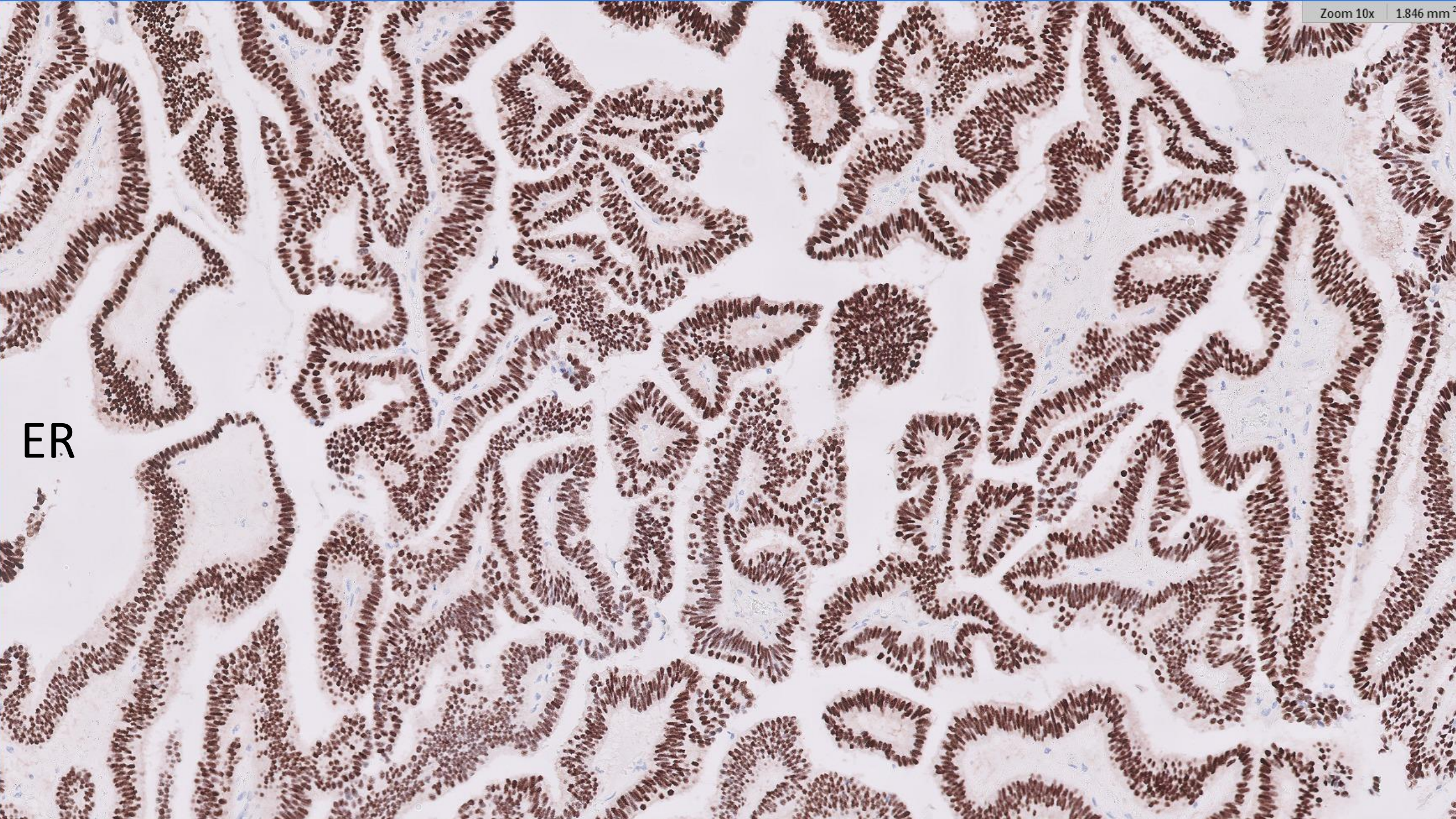












ER



# DIAGNOSIS?

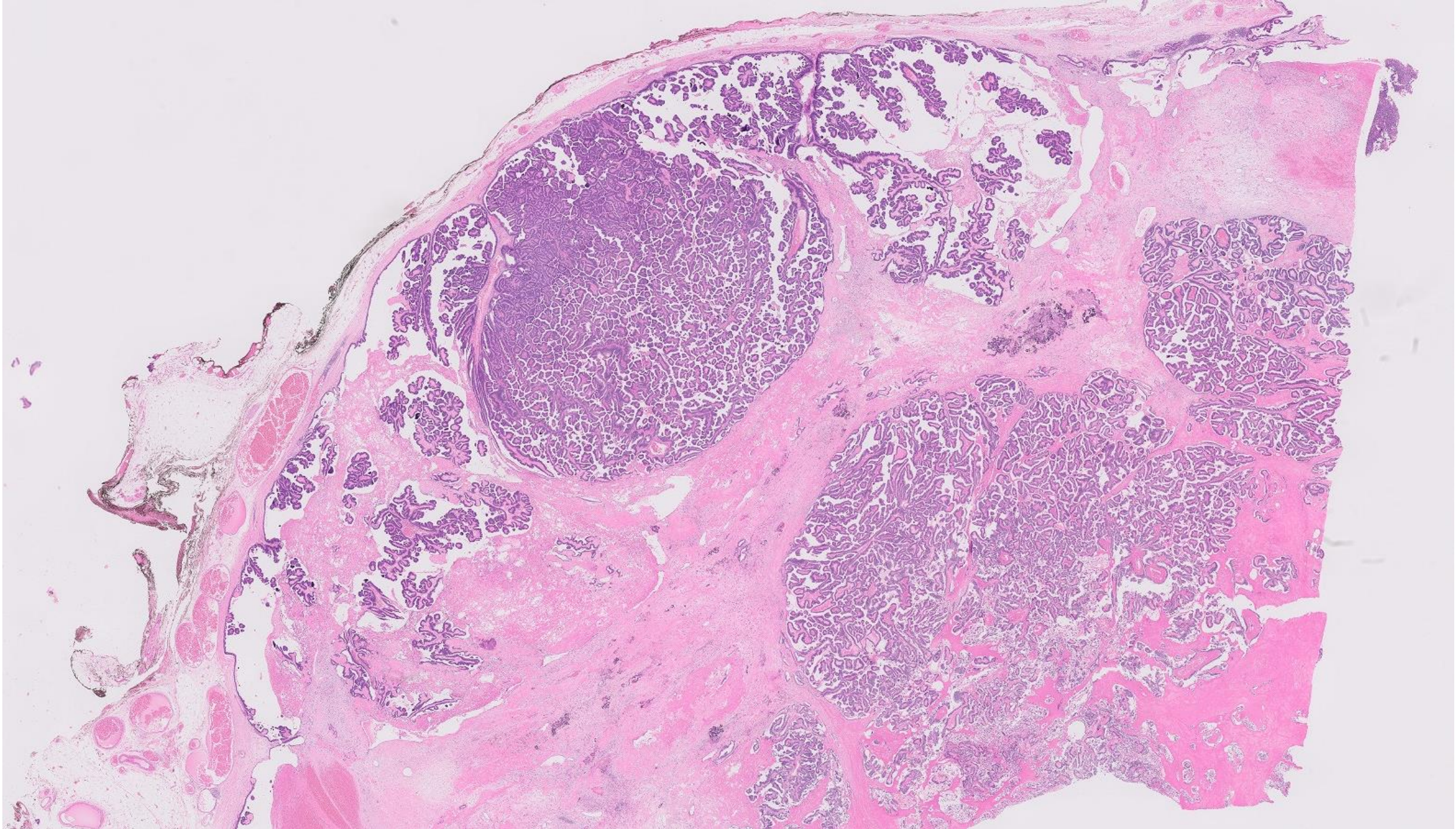




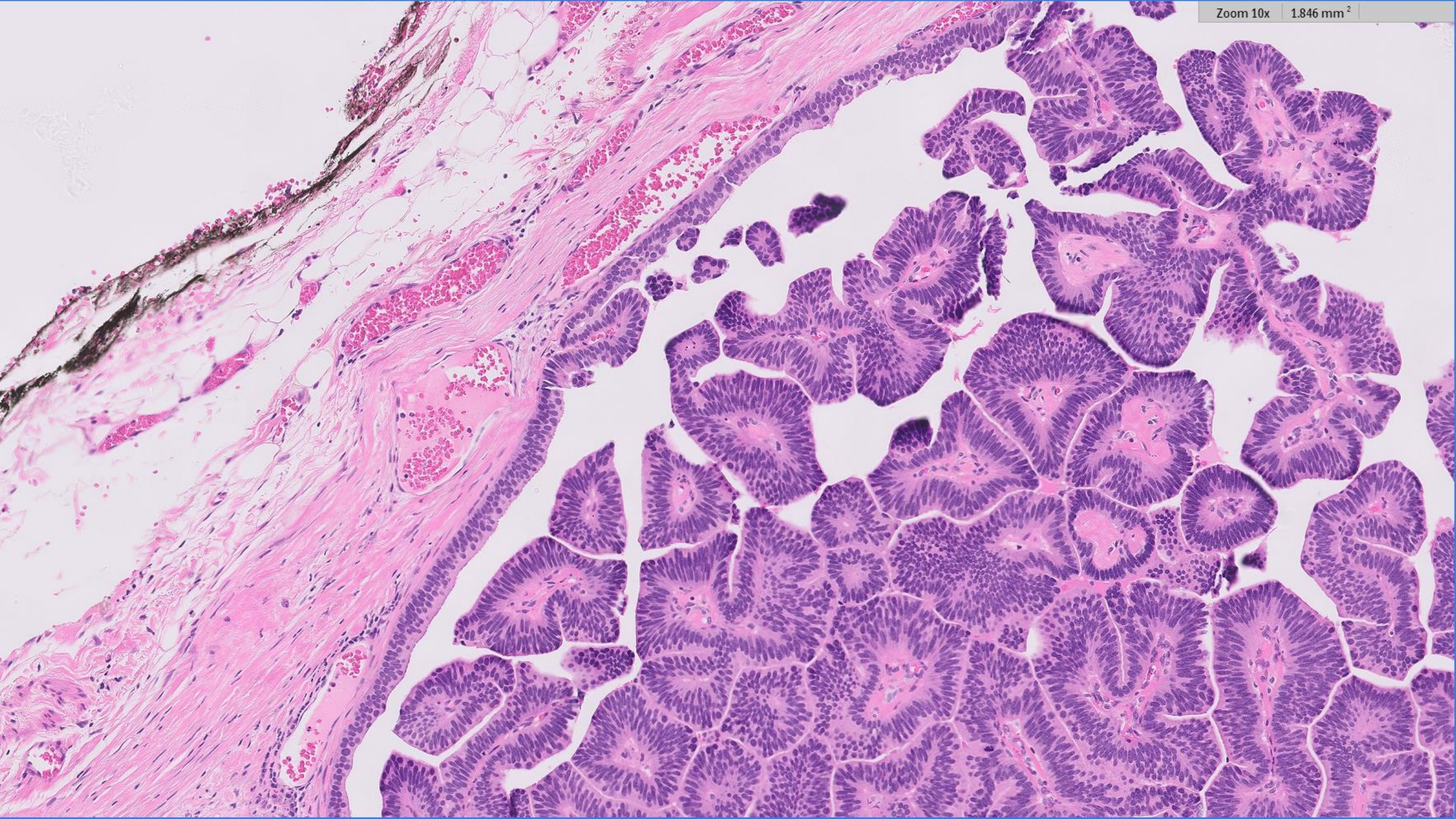


**80+yo female with a h/o right breast lumpectomy (2021) now presents with a right axilla mass (5.2x5.1x3.7 cm)**

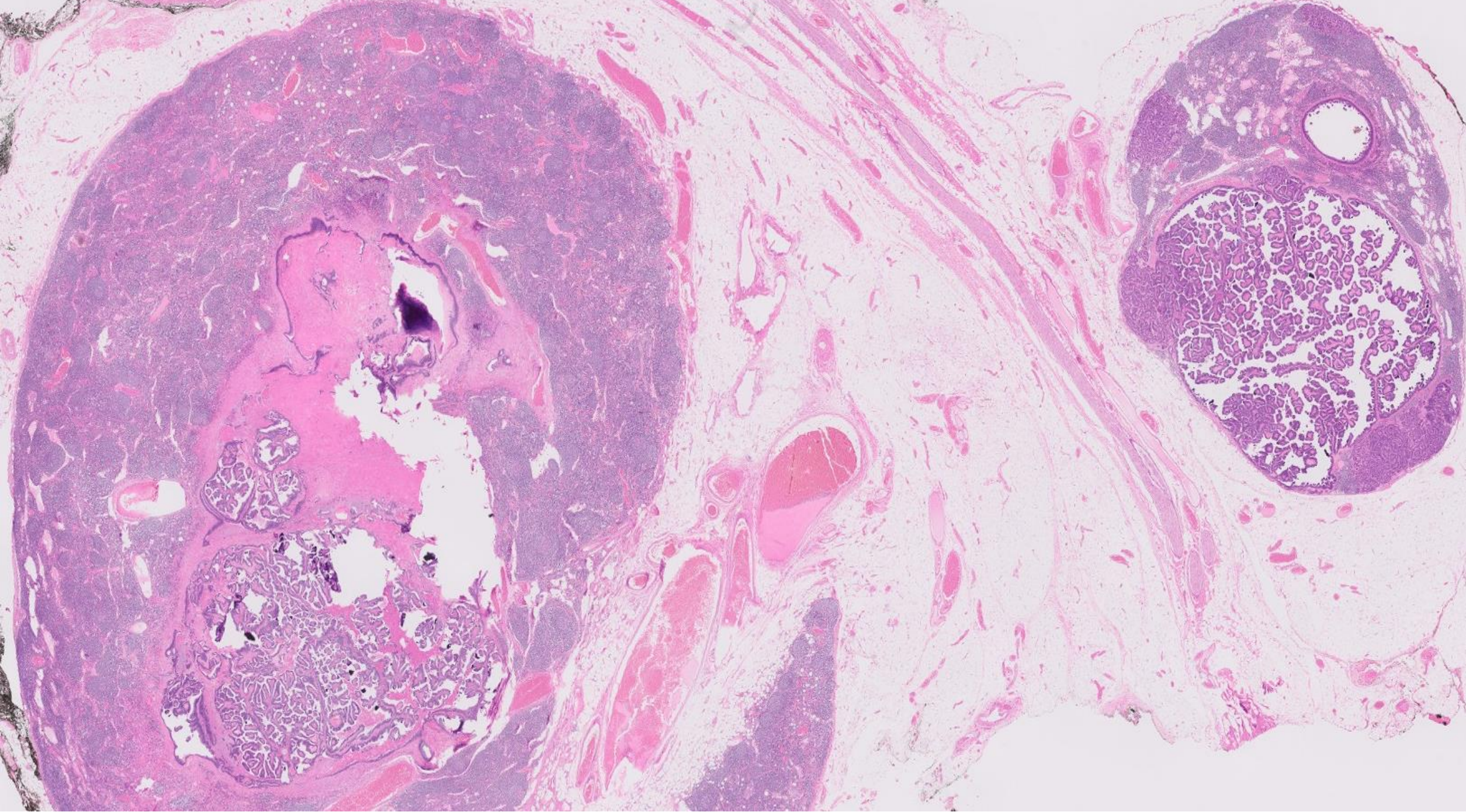














# Differential diagnosis



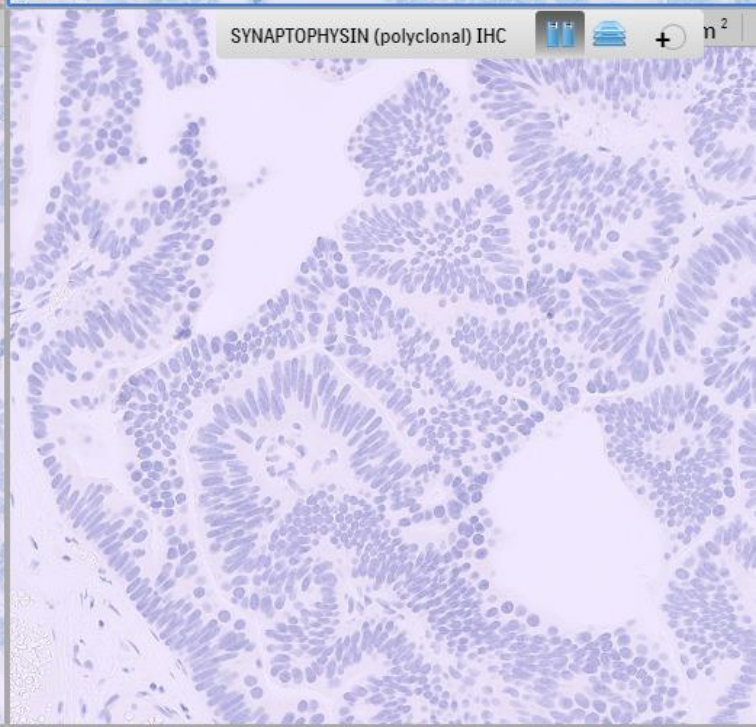
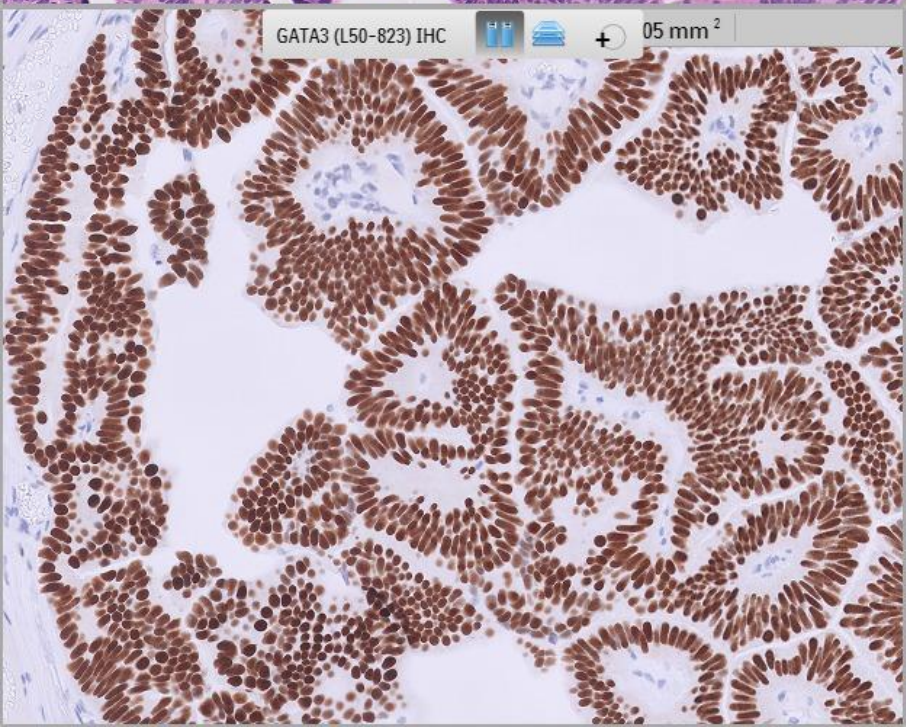
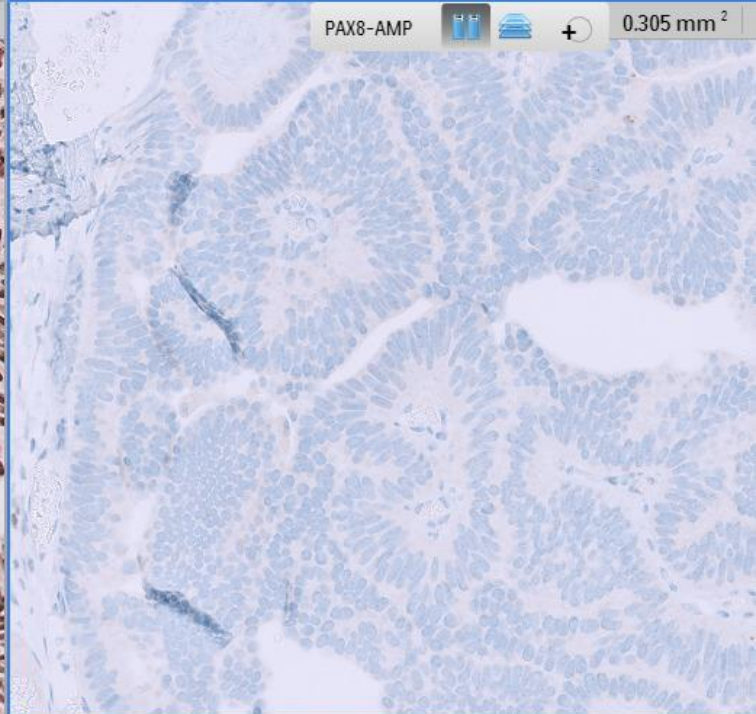
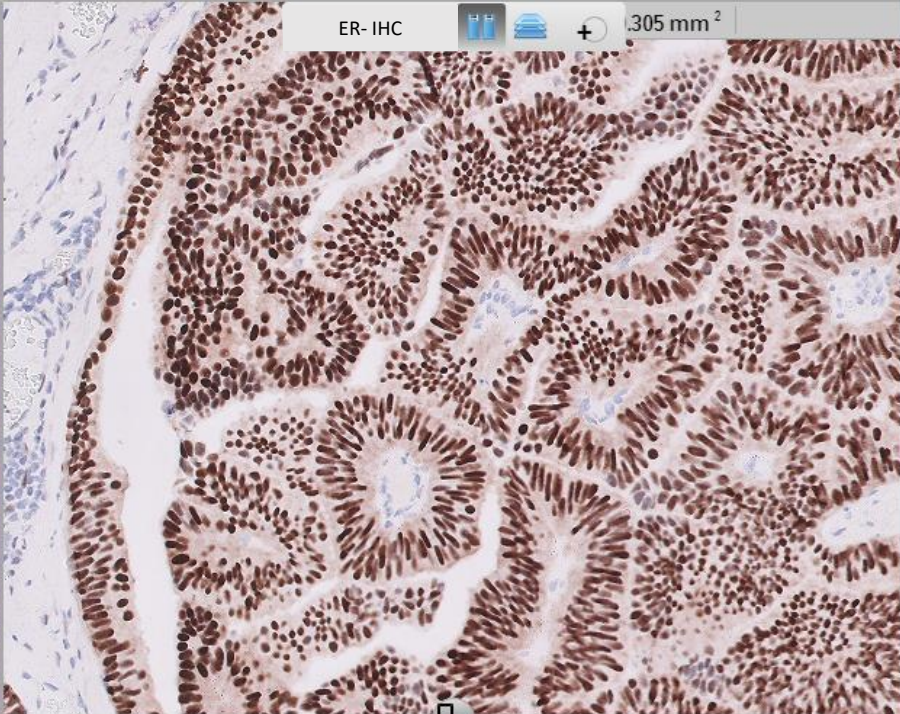
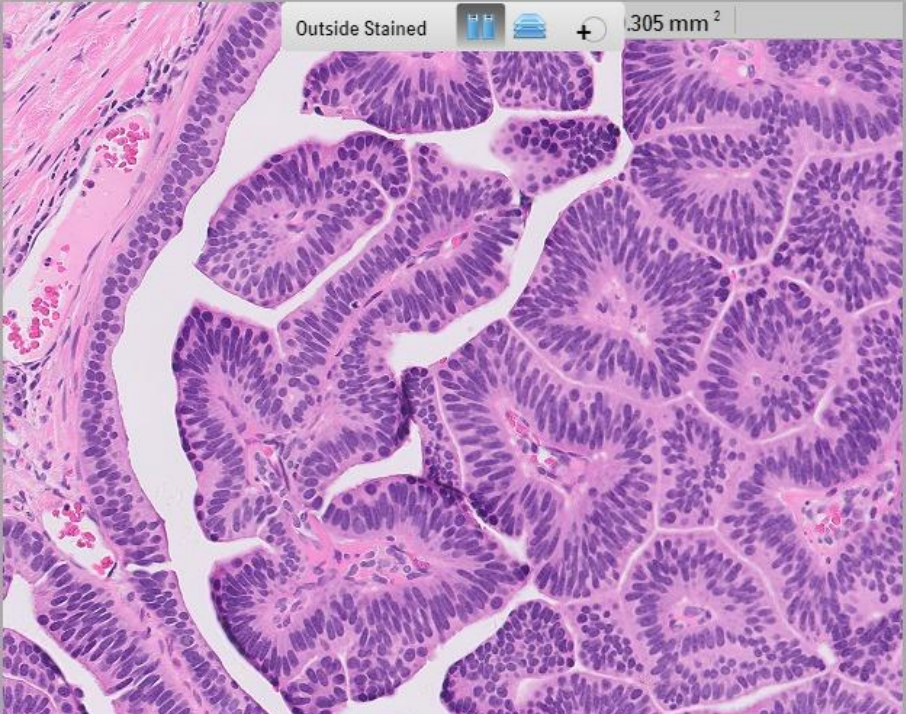
# Differential diagnosis

- Benign papillary inclusions
- Metastatic cancer with papillary architecture
  - Breast
  - Gyn
  - Thyroid
  - Renal
  - Mesothelial.... others



# Immunohistochemistry



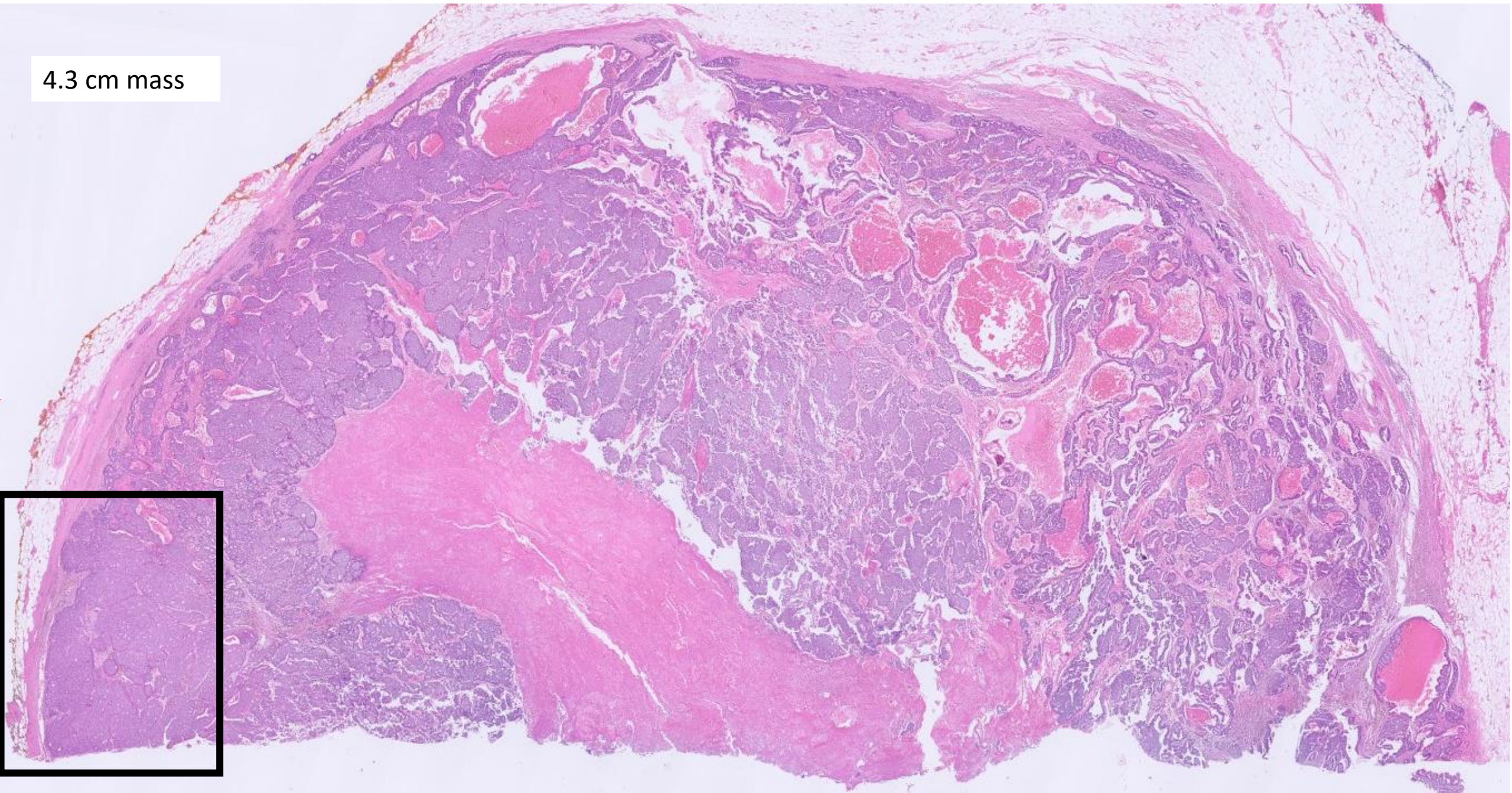




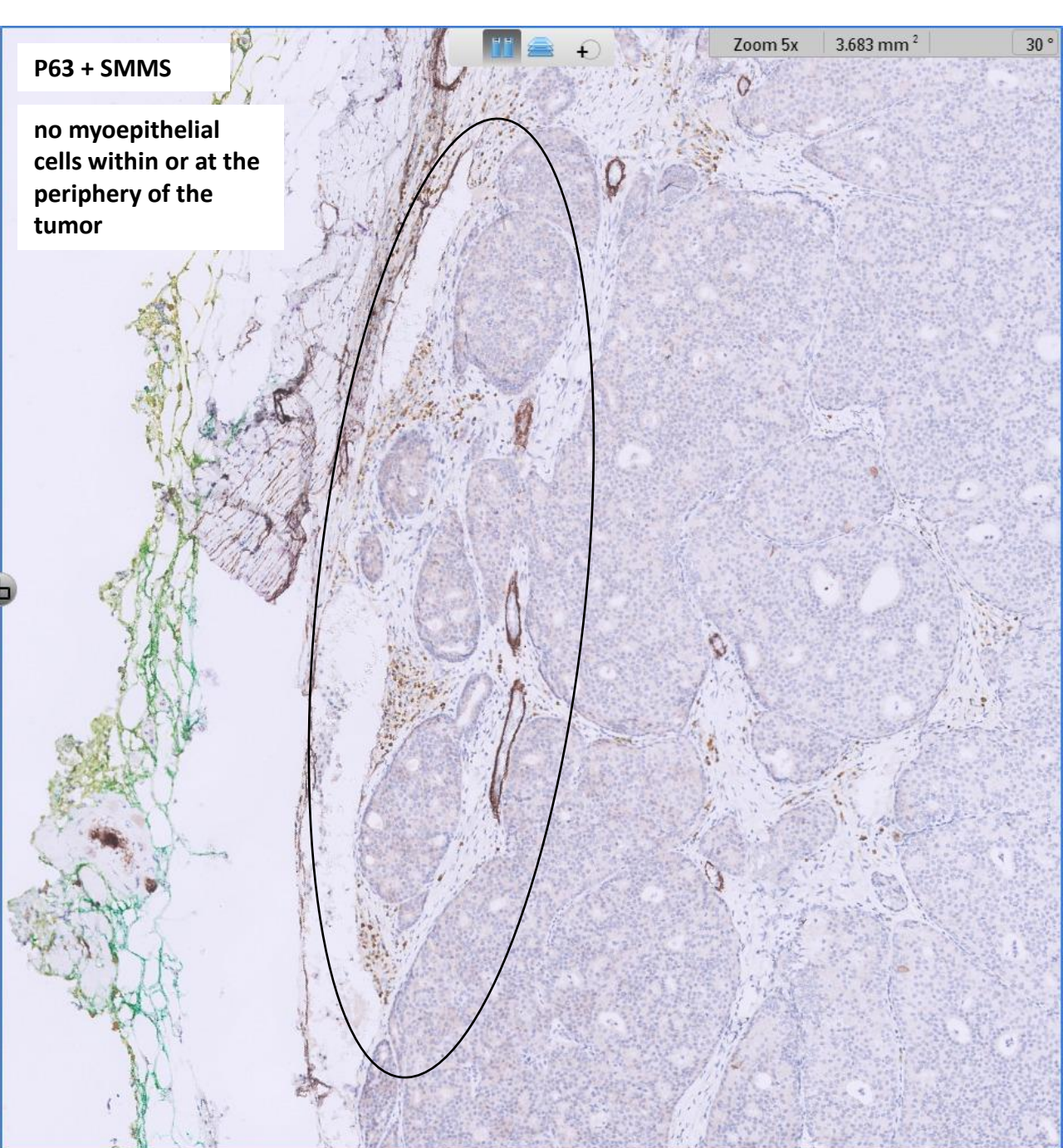
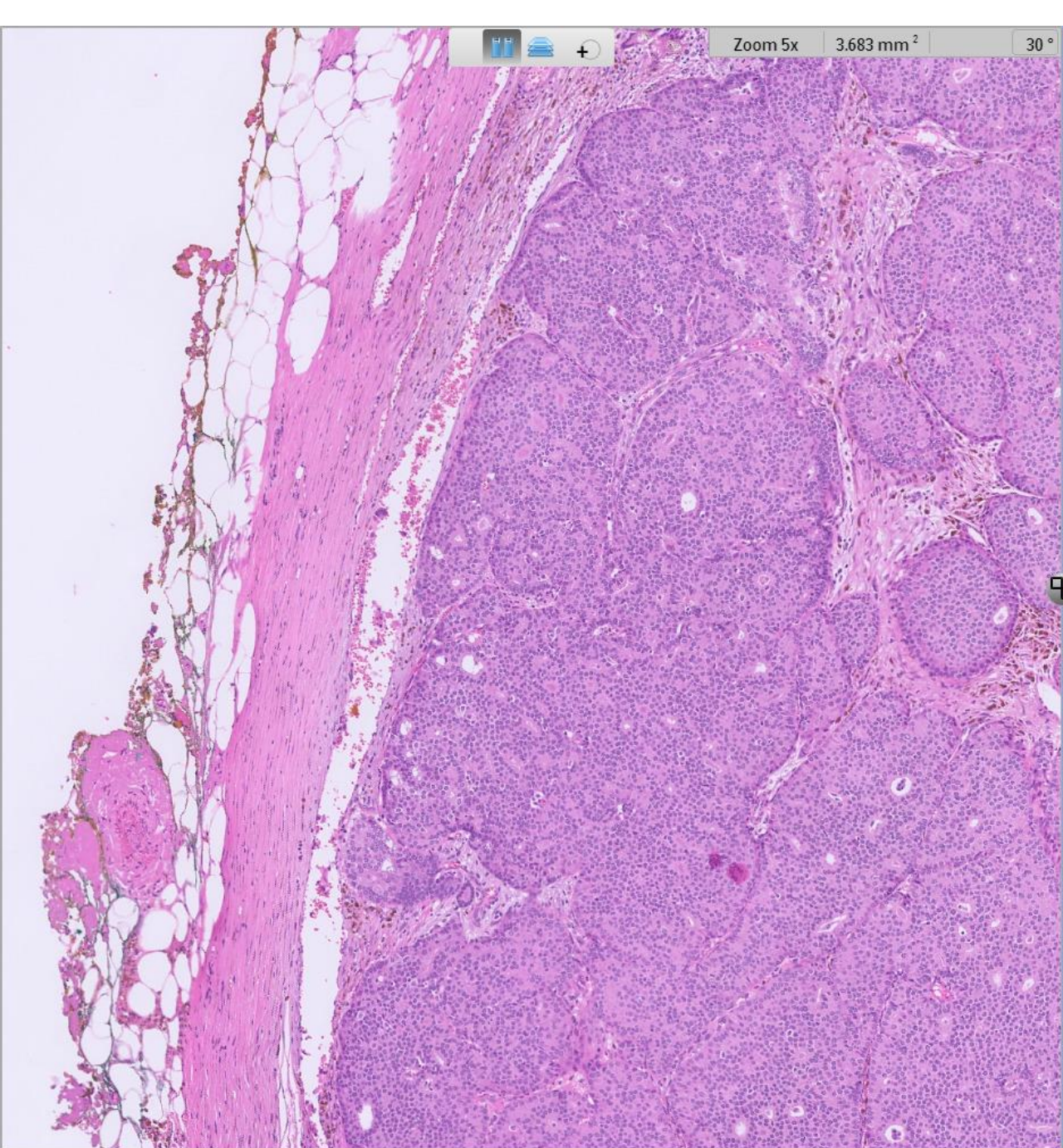
Compare to the prior resection (2021)



4.3 cm mass



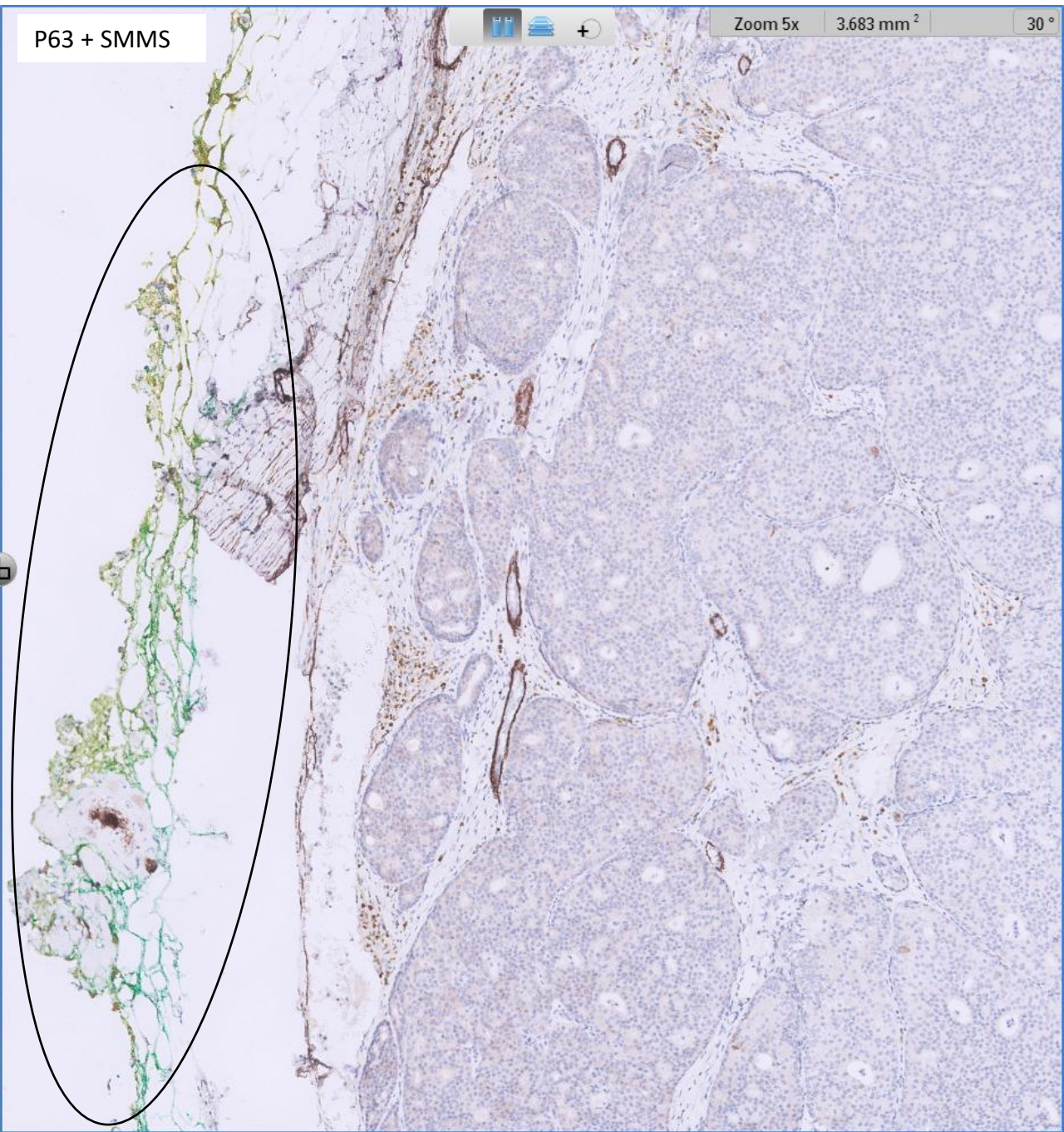
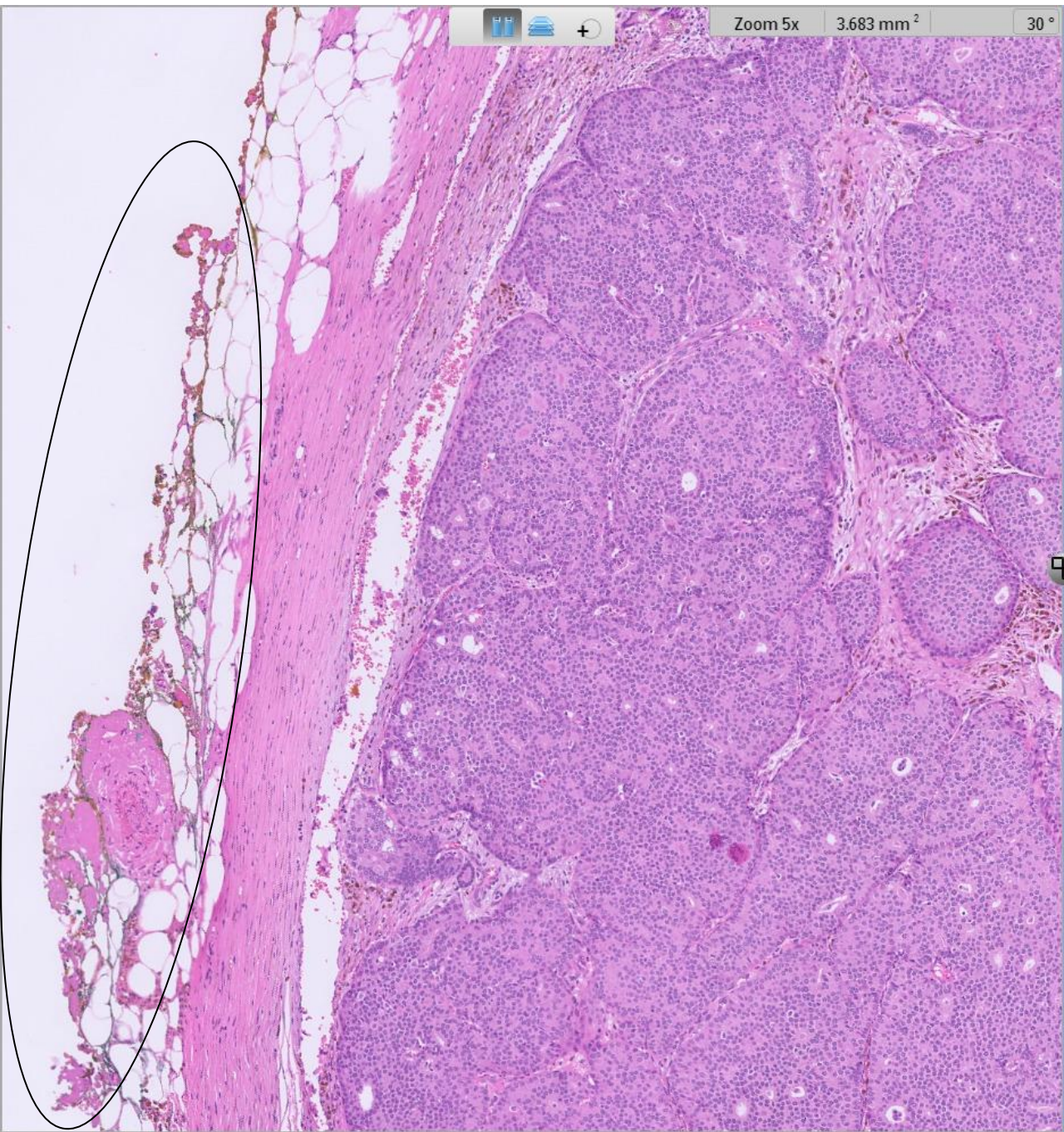




**P63 + SMMS**

**no myoepithelial  
cells within or at the  
periphery of the  
tumor**

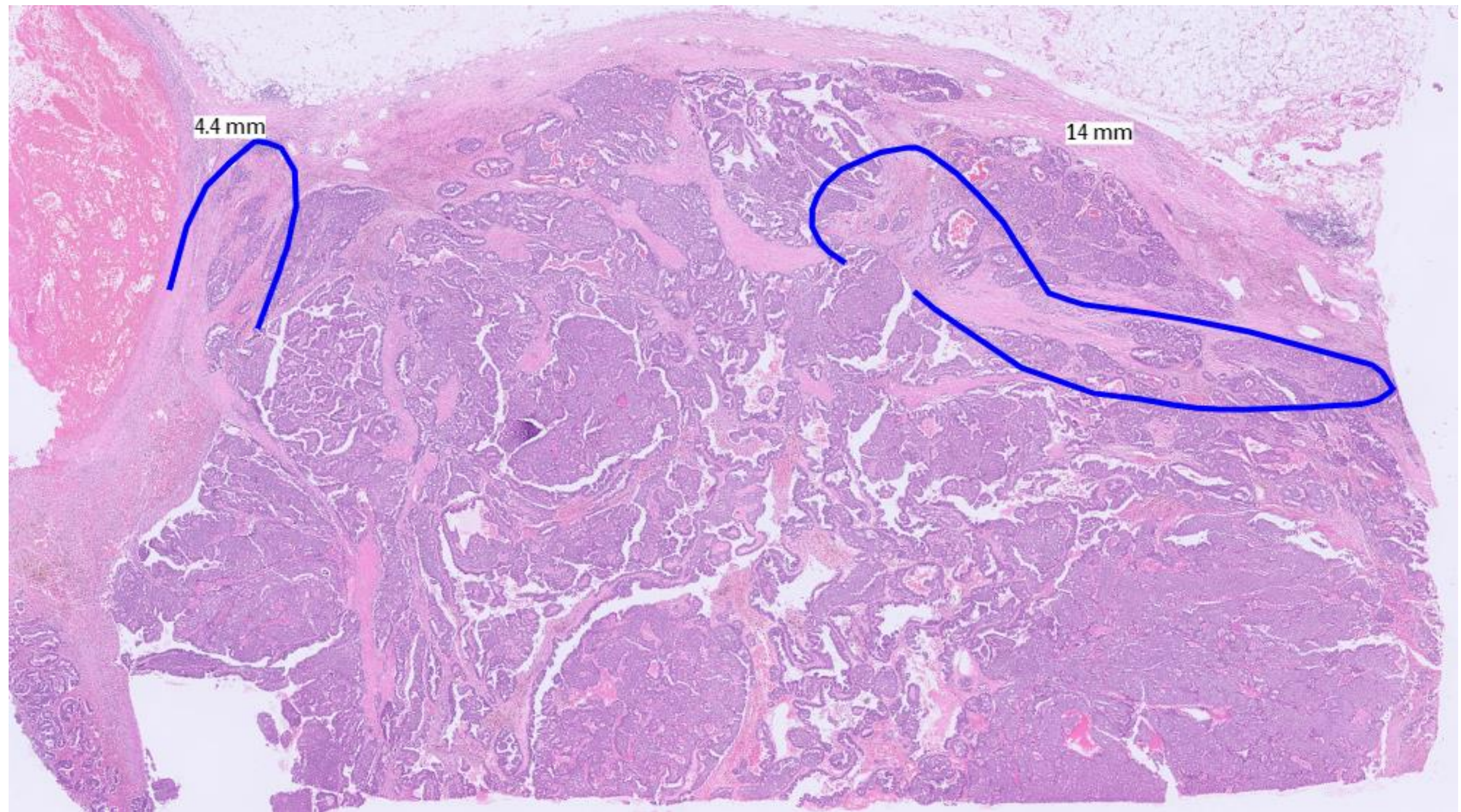




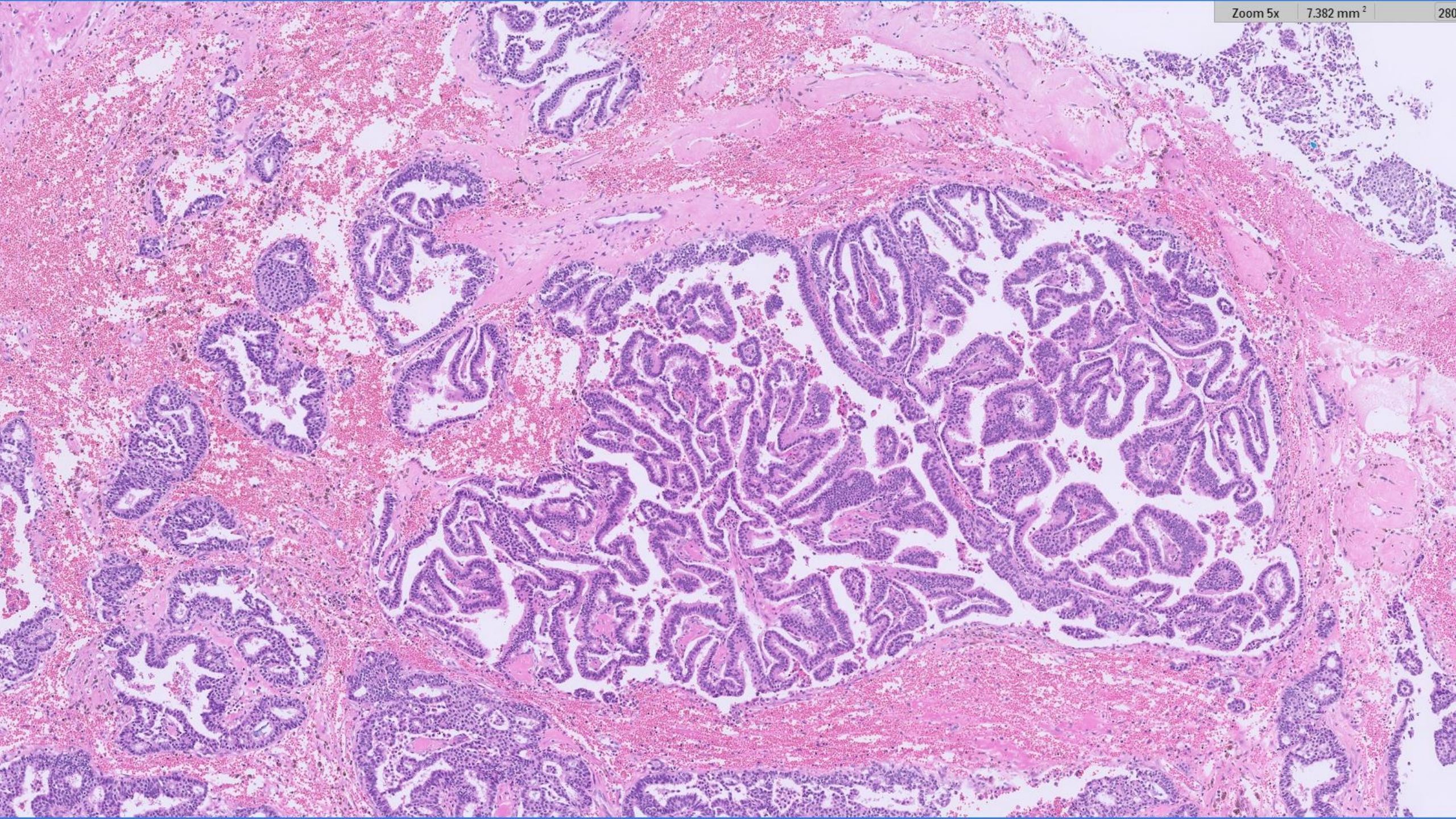


4.4 mm

14 mm









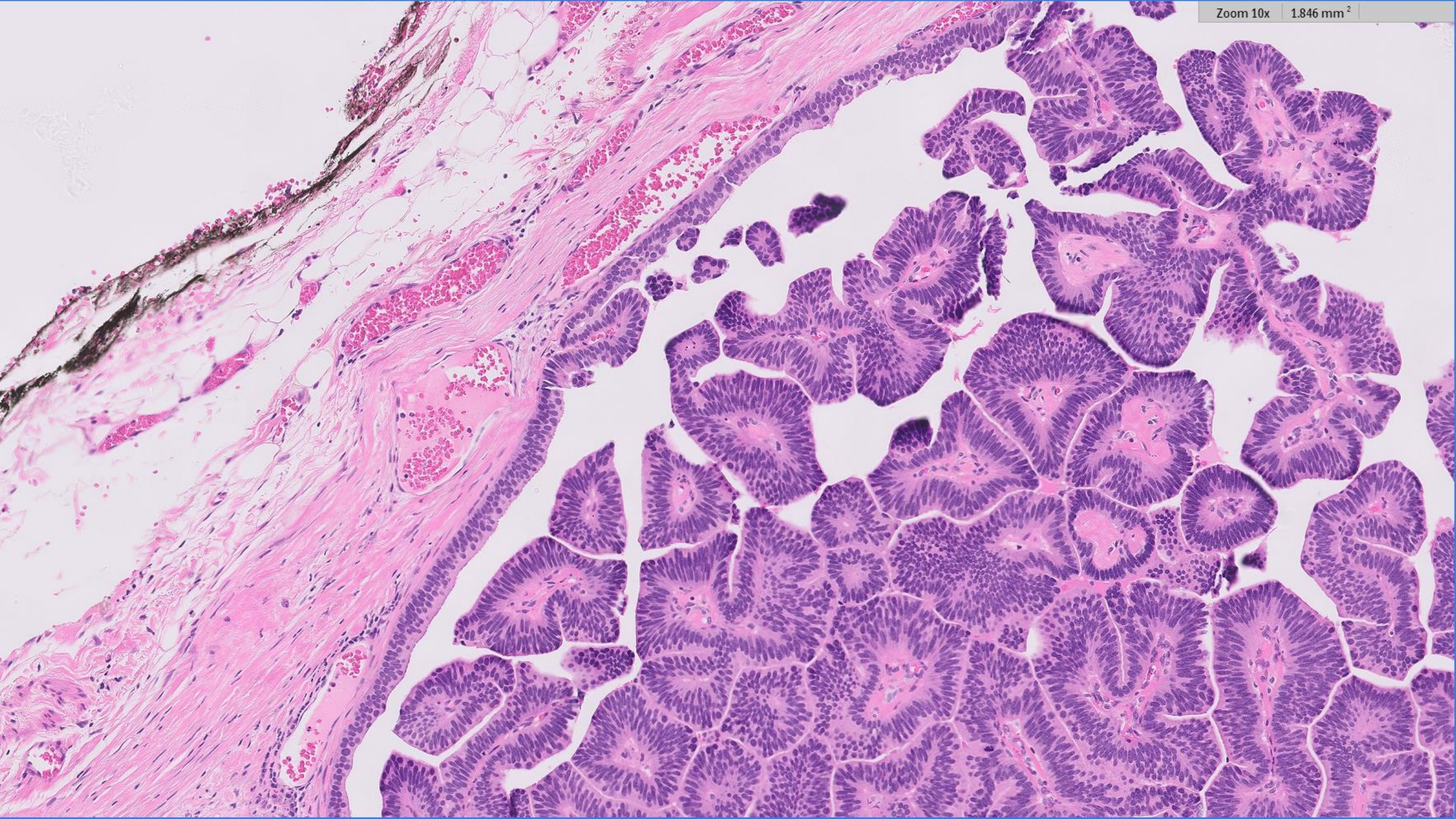
# Right Breast, Lumpectomy (Prior)

- **Invasive carcinoma with papillary pattern and fibrous capsule**

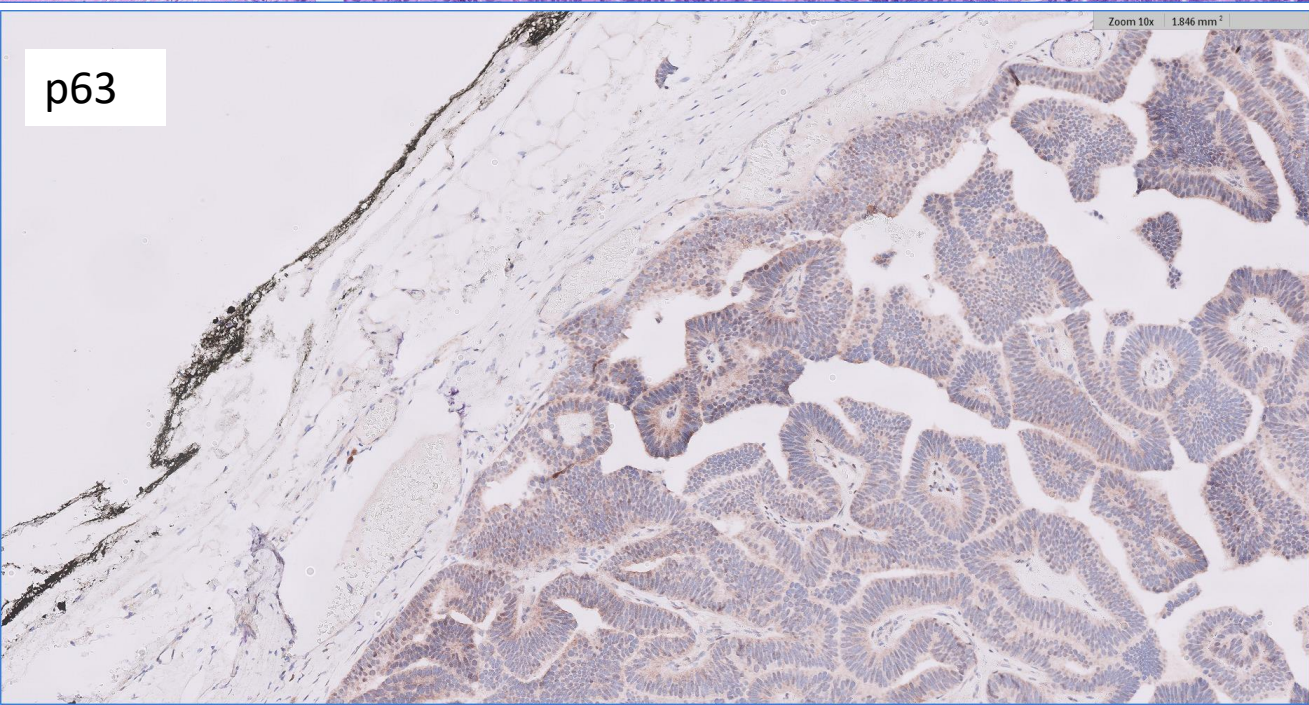
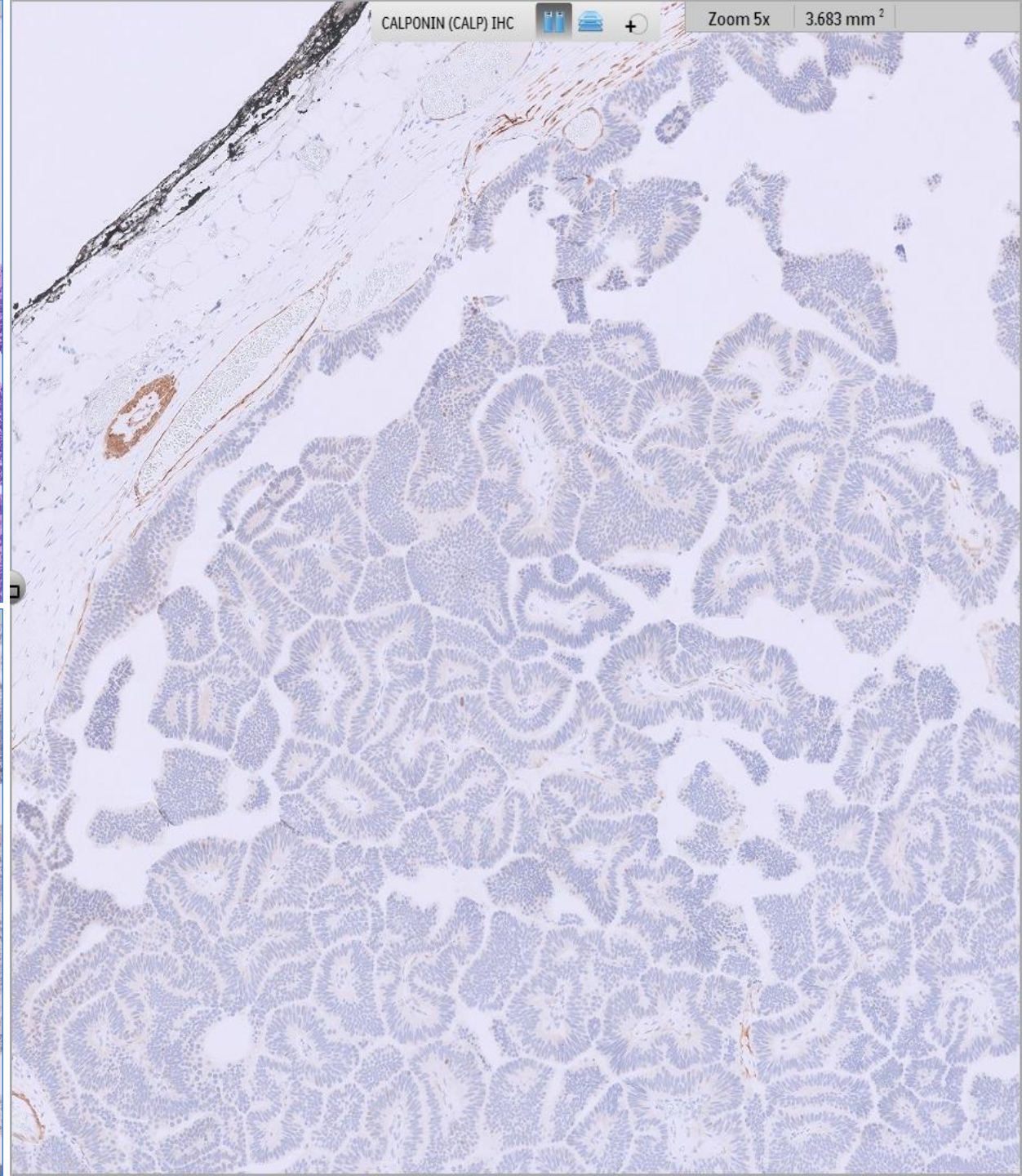
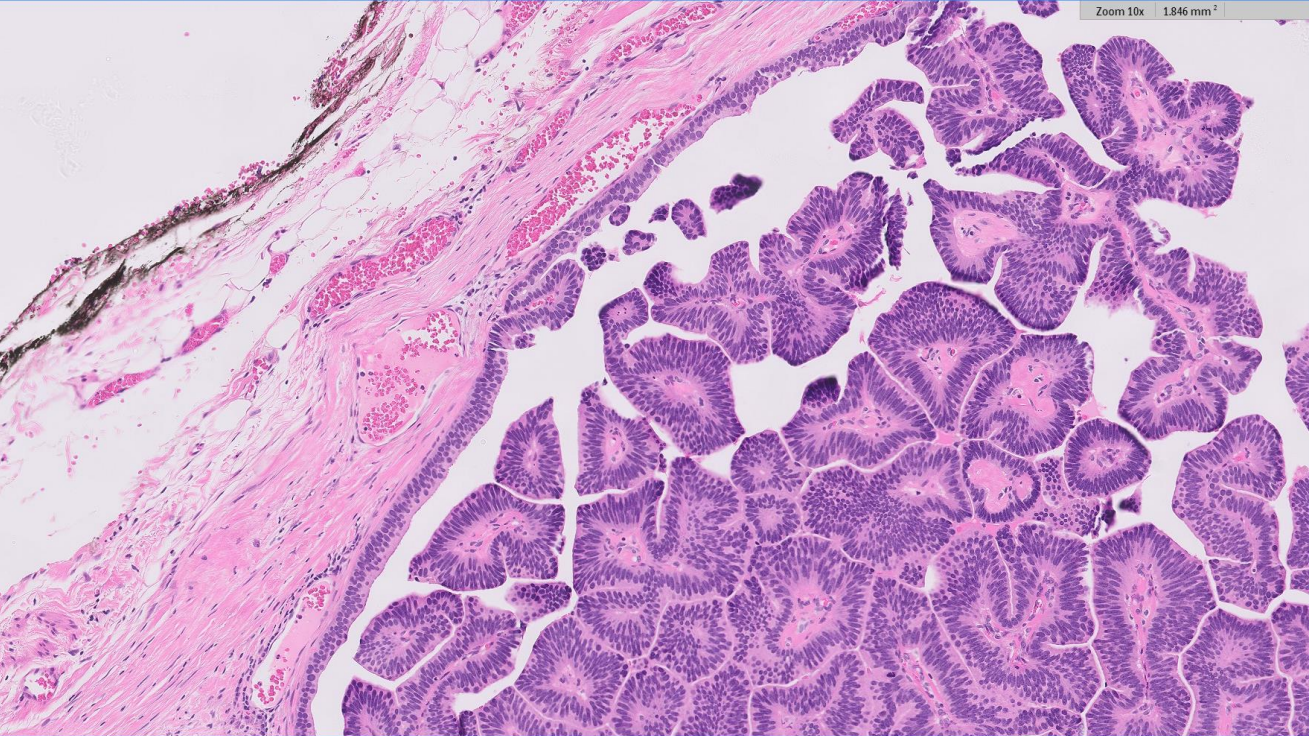
## Comment:

- This lesion does not neatly fit into any of solid papillary carcinoma, encapsulated papillary carcinoma or invasive ductal carcinoma categories.

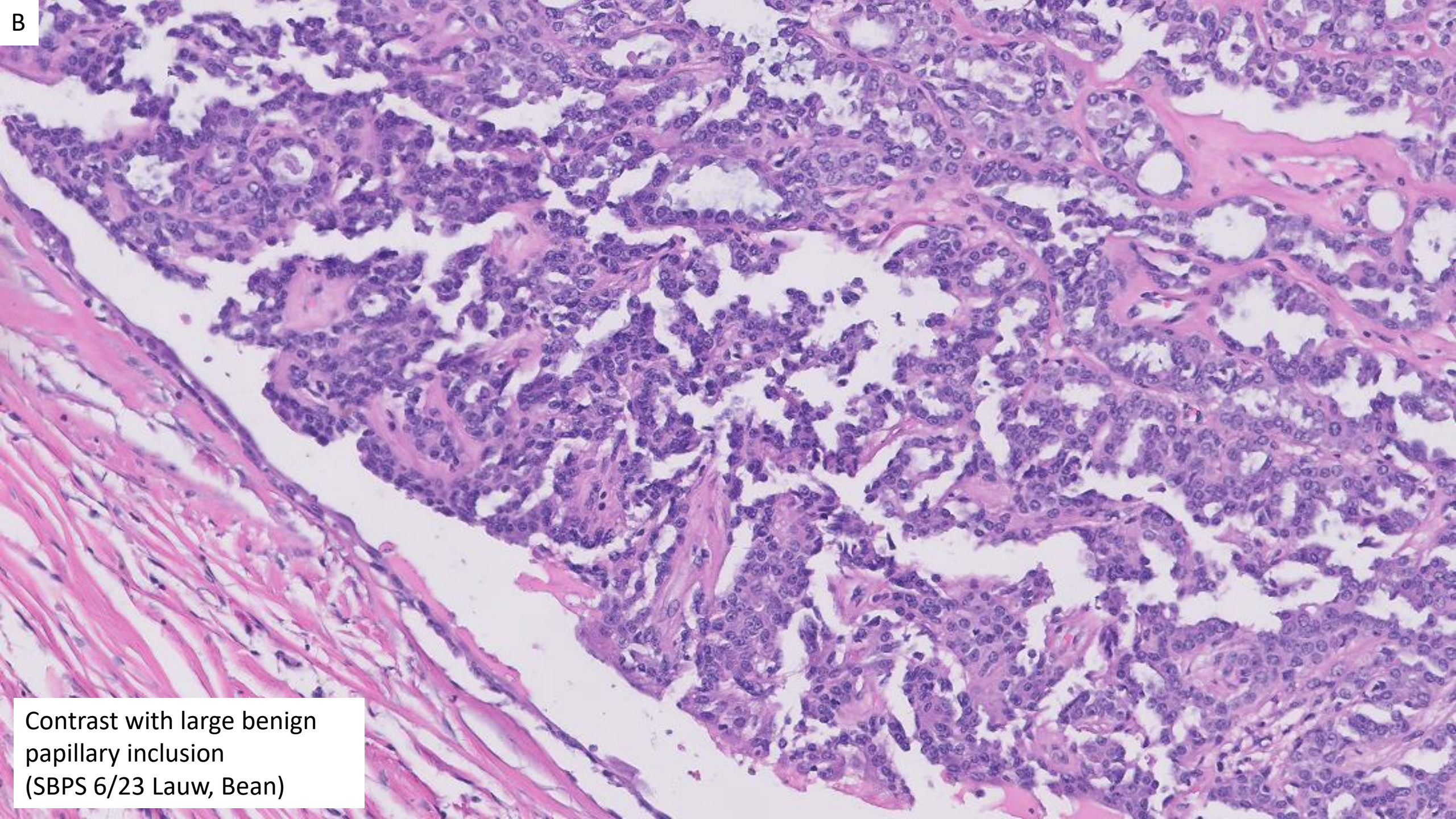








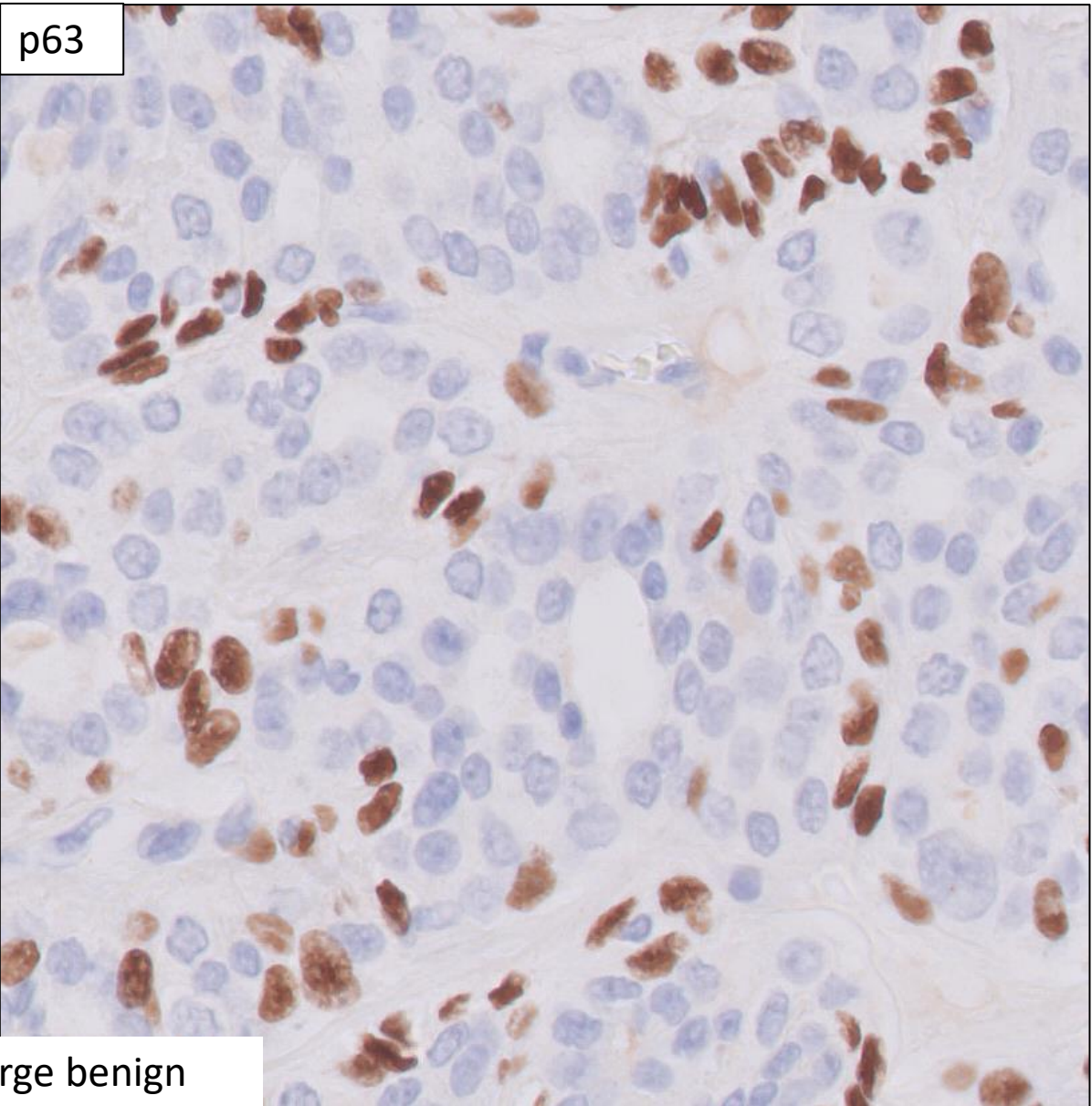
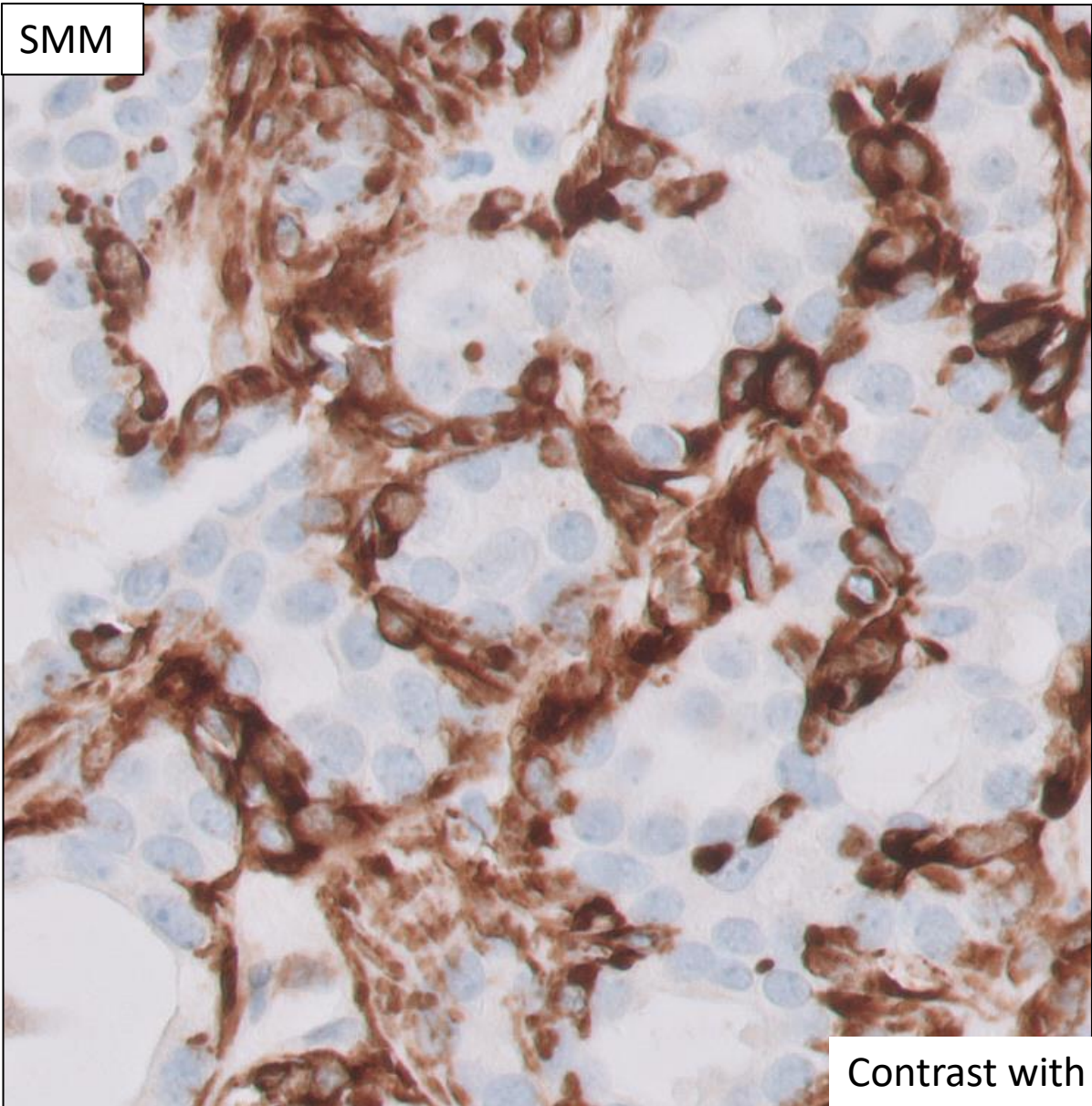




B

Contrast with large benign papillary inclusion (SBPS 6/23 Lauw, Bean)





Contrast with large benign papillary inclusion (SBPS 6/23 Lauw, Bean)



# Differential diagnosis

- Benign papillary inclusions
- Metastatic cancer with papillary architecture
  - **Breast (Metastatic papillary breast carcinoma)**
  - Ovary
  - Thyroid
  - Renal
  - Mesothelial.... others



## **“Right breast/axilla mass ”, Excision**

- **Metastatic papillary breast carcinoma in 3 of 3 lymph nodes (3/3)**
  - Two lymph nodes with macro-metastasis carcinoma (tumor foci 54 mm, 0.8 mm)
  - One lymph node with at least micro-metastatic carcinoma (tumor deposit 1.25 mm)

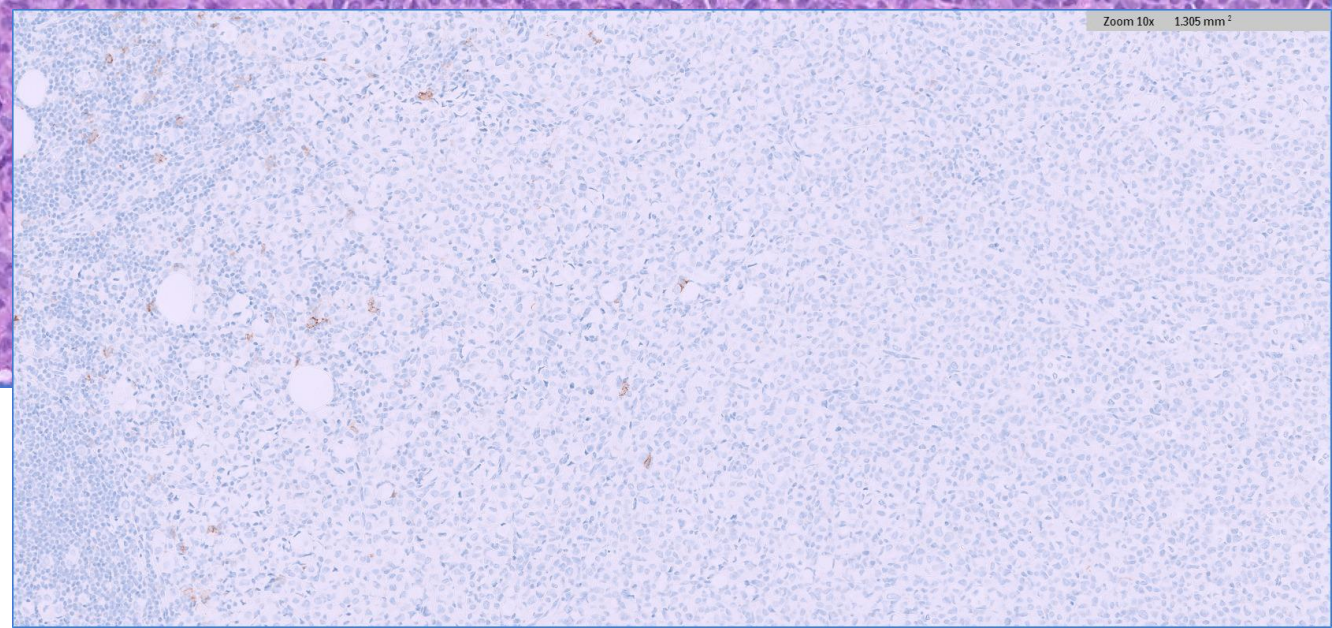
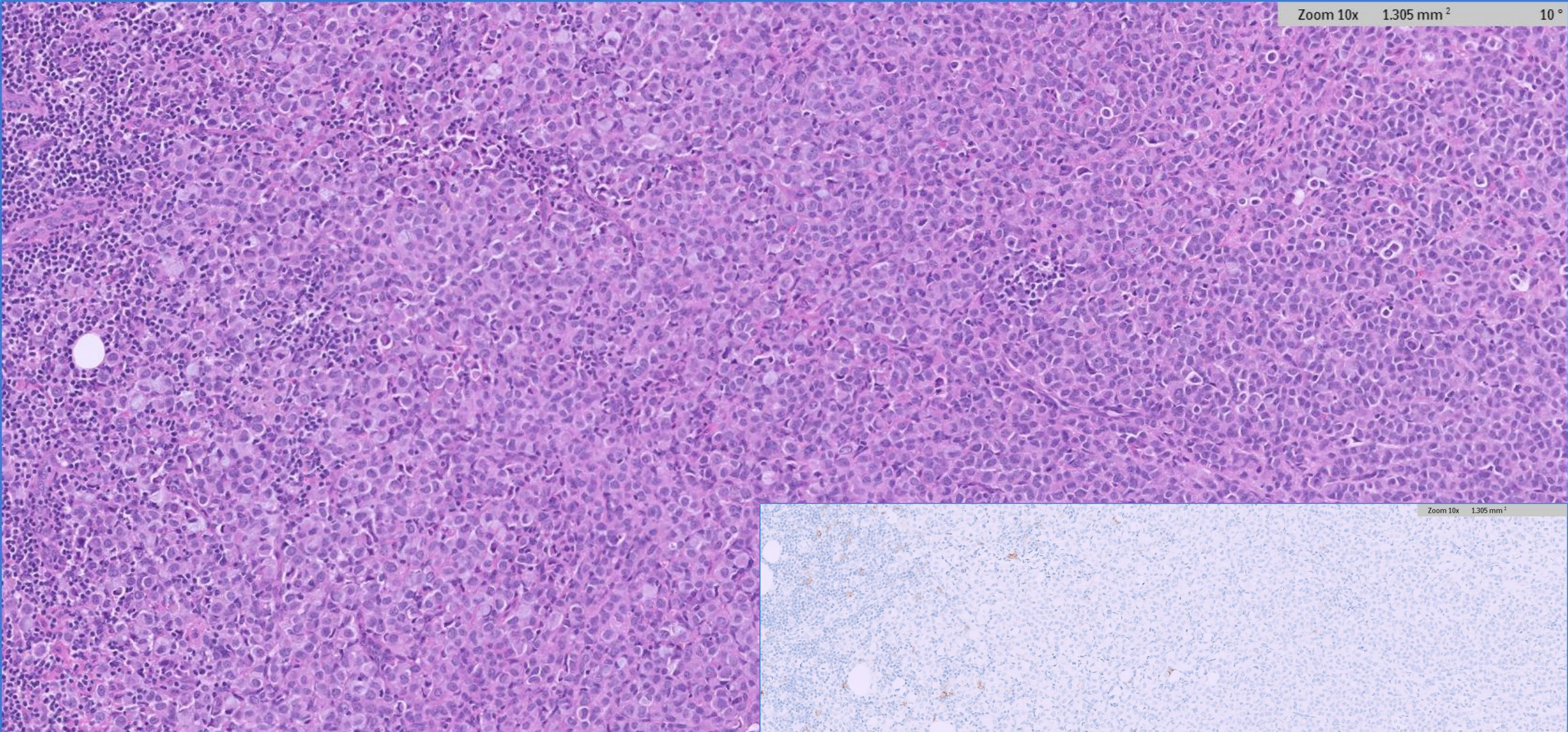


24-0607

**Rabia Bhalli, Megan Troxell; Stanford**

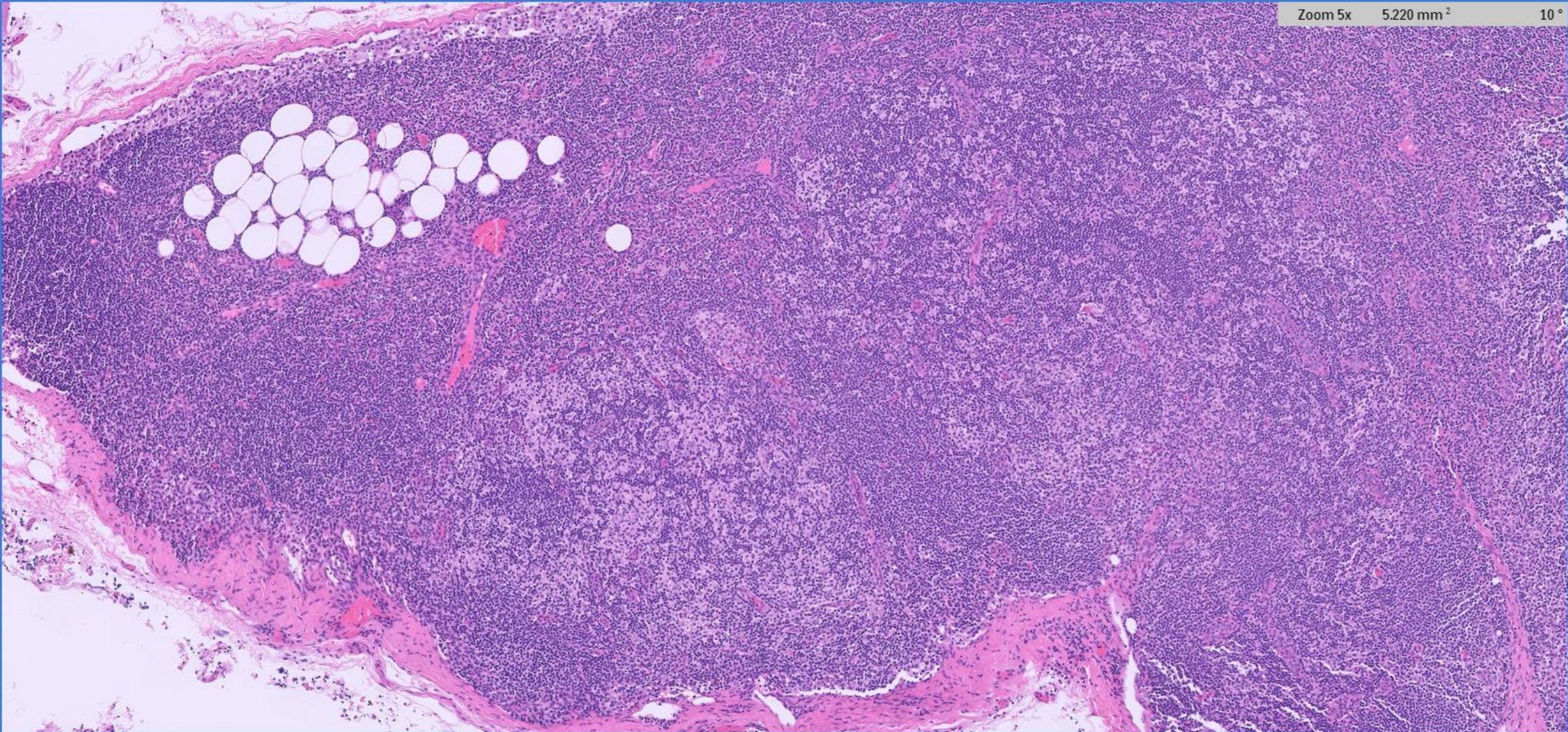
- 70+ year old woman with multiple foci of breast cancer





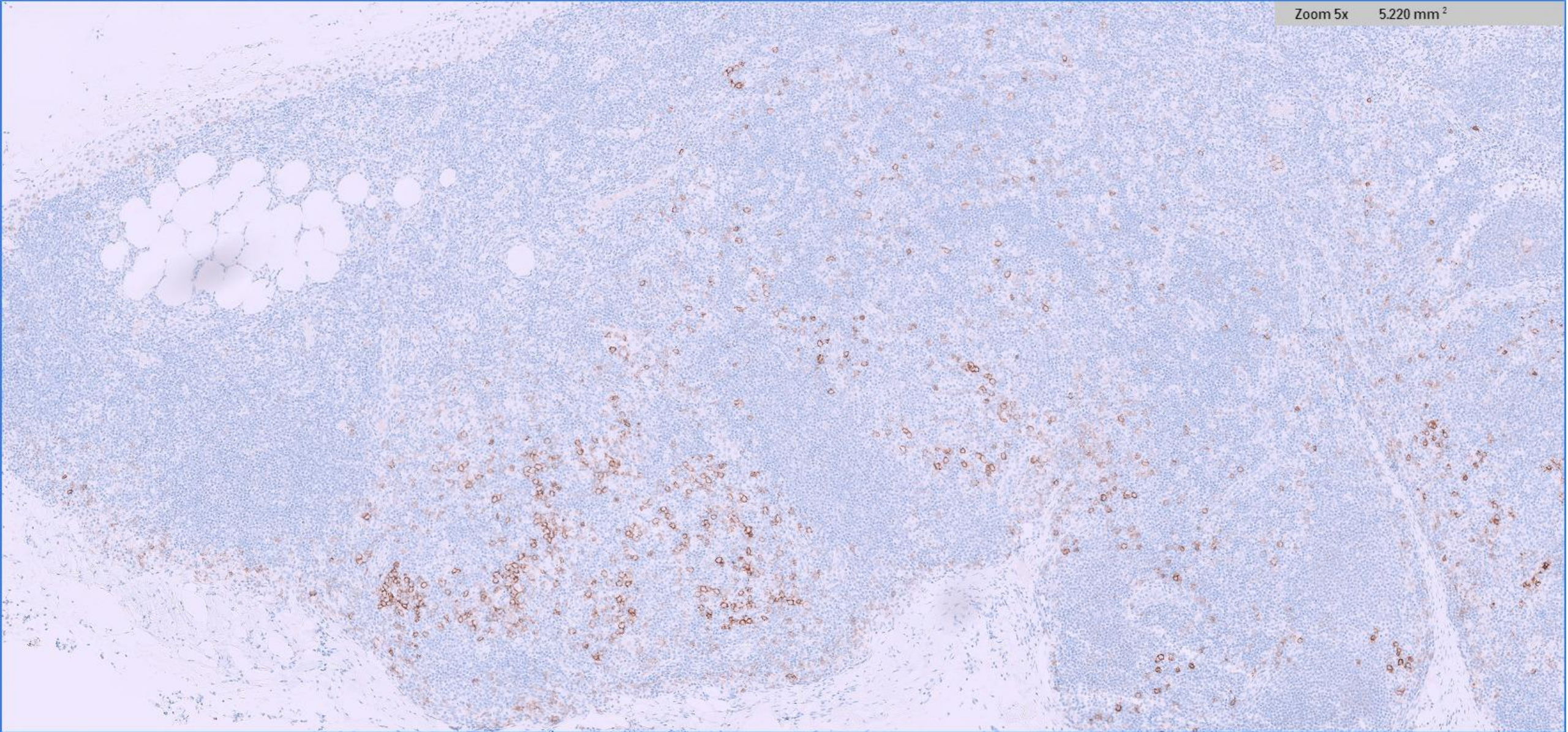
Lymph node: metastatic ILC, E-cadherin negative





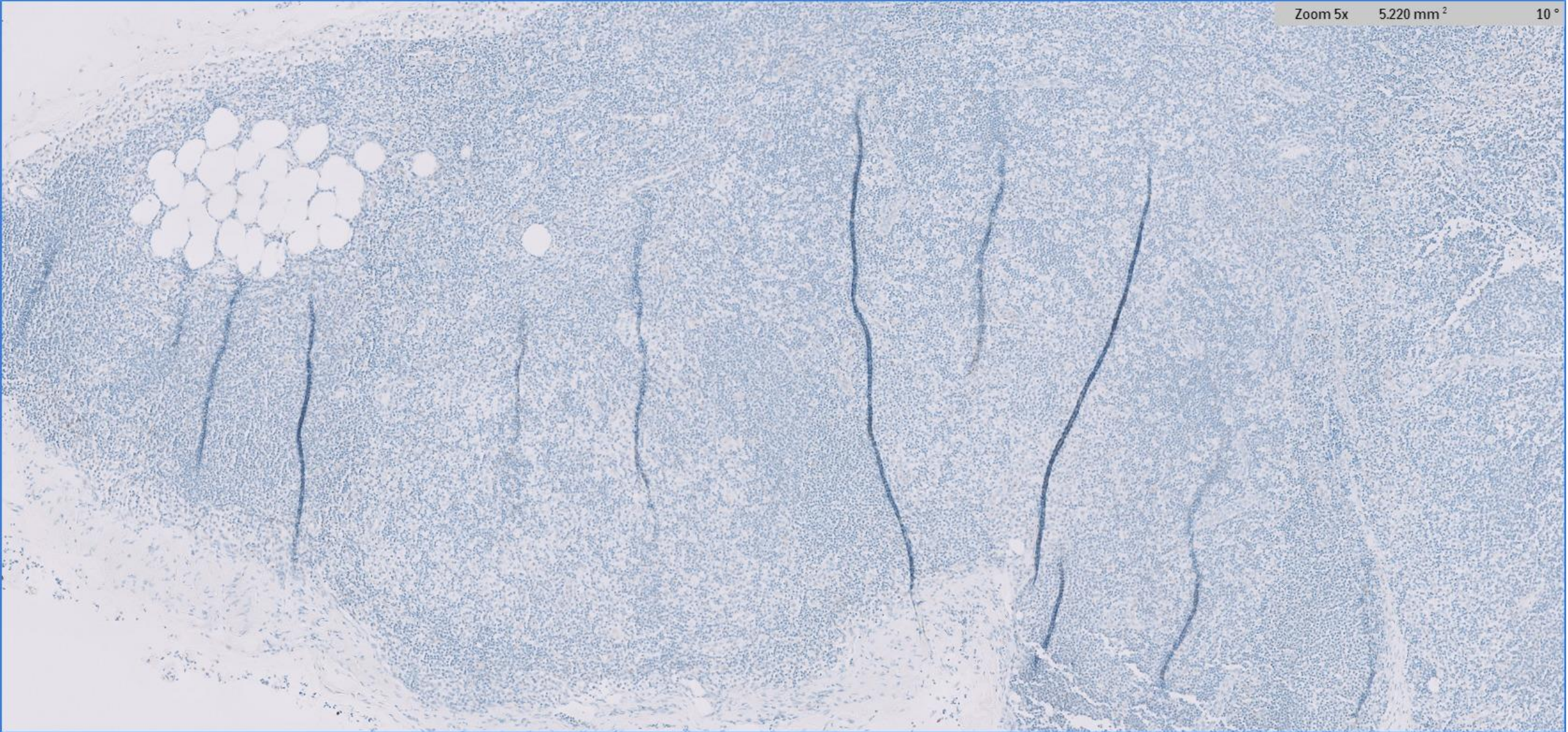
Elsewhere in node





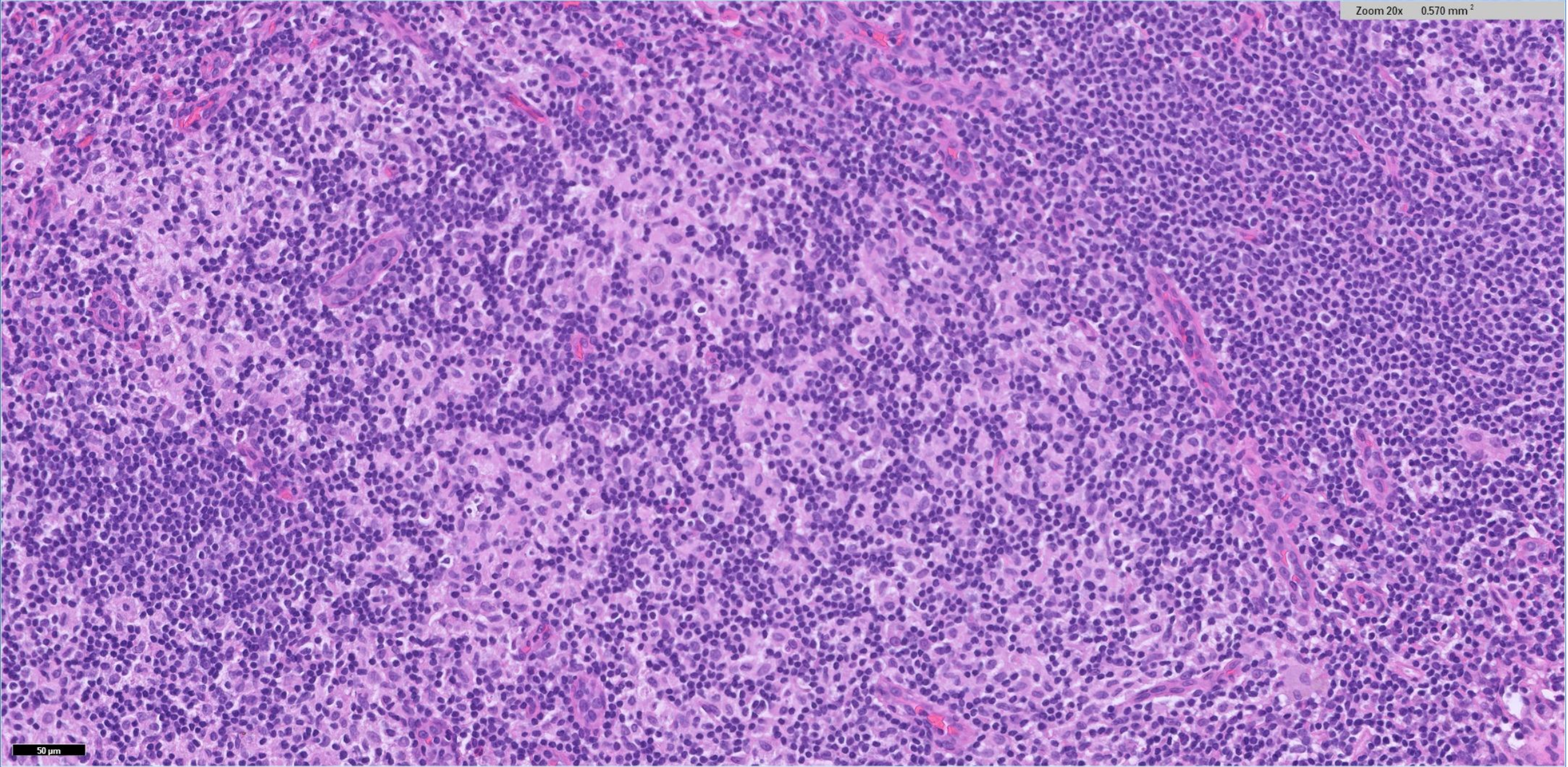
Elsewhere in node: E-cadherin





Elsewhere in node: Keratin negative





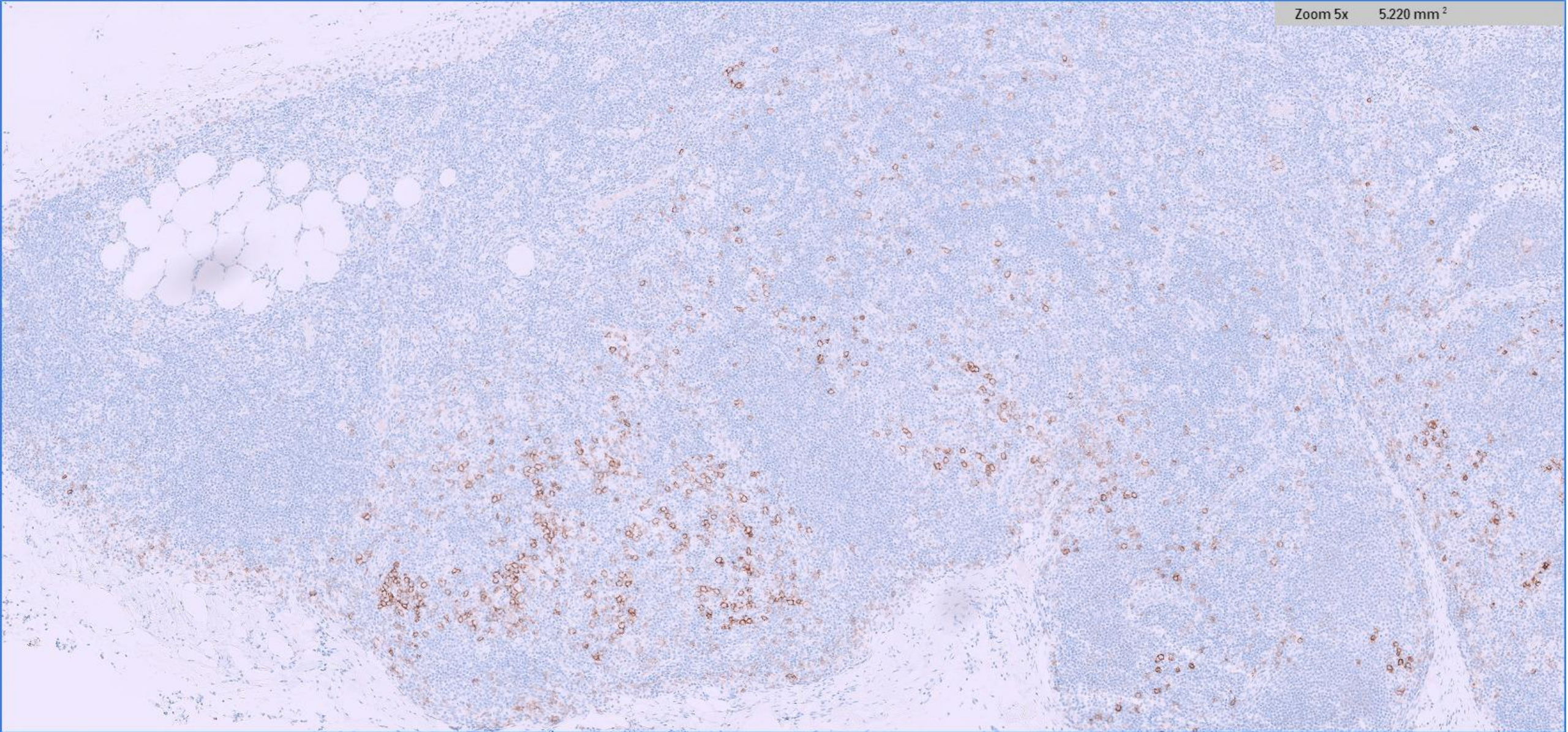
Elsewhere in node: higher power



# DIAGNOSIS?





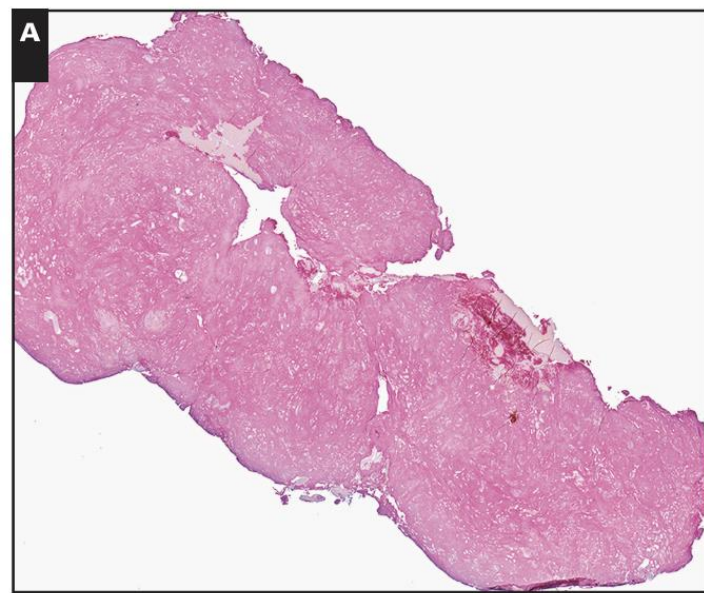


E-cadherin “Epithelial” Cadherin stains more than epithelium (*CDH1*)  
Mutated or turned off in ILC, diffuse gastric cancer and plasmacytoid UC  
NOT a reliable marker of Epithelial Differentiation

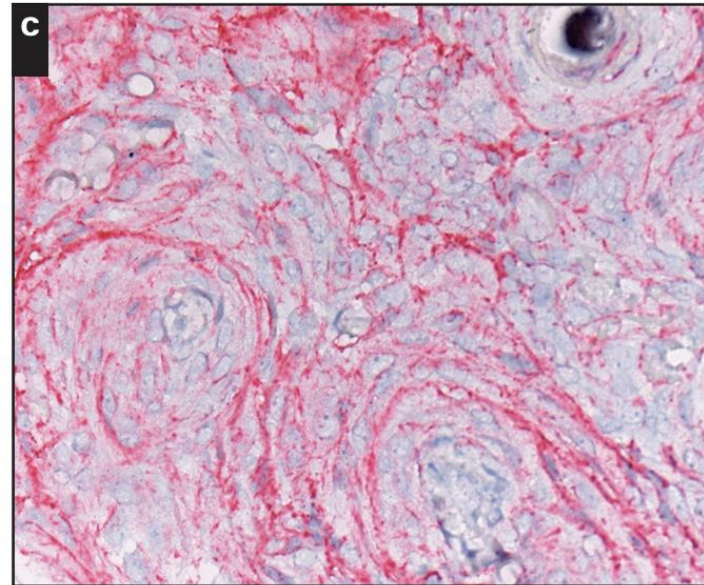


# BRAF and epithelial-mesenchymal transition in primary cutaneous melanoma: a role for Snail and E-cadherin? ☆

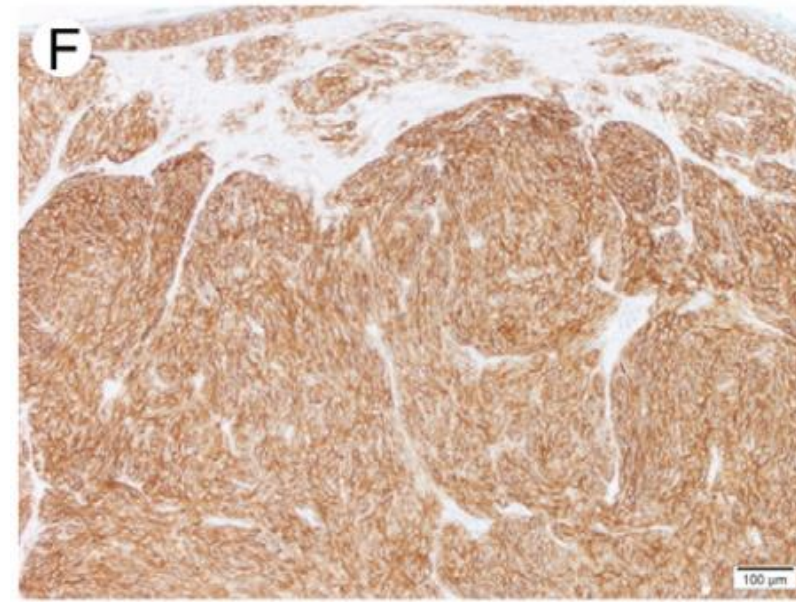
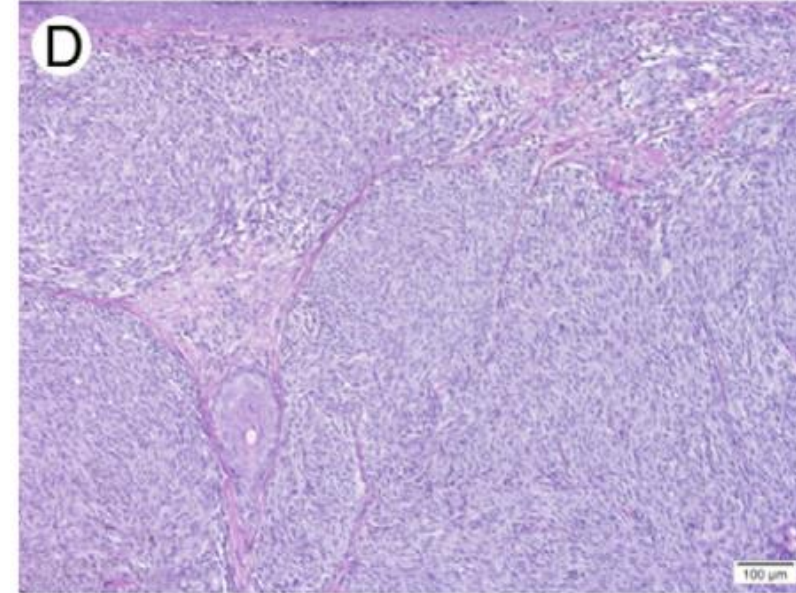
Mitchell. Hum Pathol (2016) 52. 19–27



E-cadherin + 76/77 (98%) meningiomas (red chromogen)



E-cadherin+  
60% seminomas  
90% YST testis (not shown)  
Burandt Biomarker Res '21



E-cadherin + 33/68 (48%) melanomas

## Dual Use of E-Cadherin and D2-40 Immunostaining in Unusual Meningioma Subtypes

AJCP 2015;  
144:923-934

E. Kelly S. Mrachek, MD, David Davis, HT(ASCP)QIHC, and B. K. Kleinschmidt-DeMasters, MD

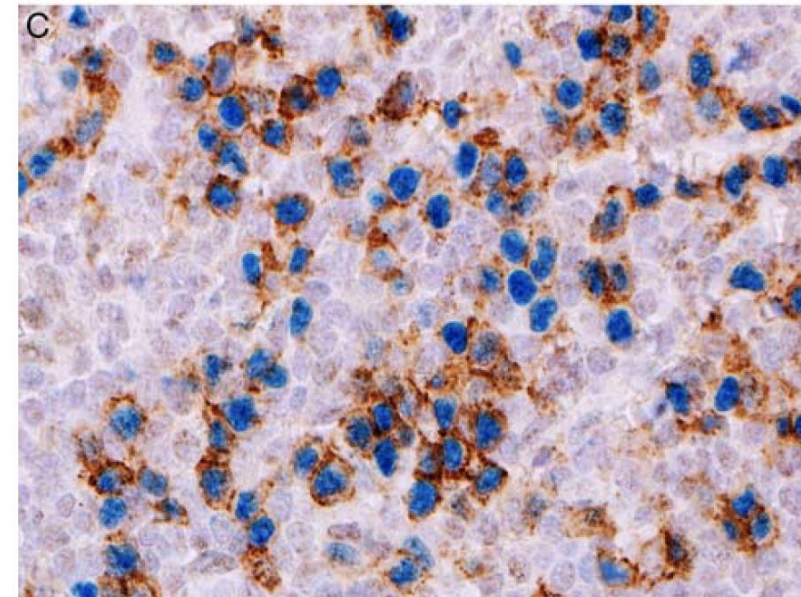


# E-cadherin in hematolymphoid populations

- Erythroid precursors
  - Acs. Arch Pathol Lab Med. 2001;125:198-201
  - Ohgami. AJCP 2014; 141:656-64
- Macrophages
- Langerhans cells
- Dendritic cells
  - May vary by activation state
- Plasmacytoid dendritic cells pDC (not in BM)
- Osteoclasts

Van den Bossche, et al. Blood. 2012;119:1623-33  
Lorenzi et al. Am J Surg Pathol 2021;45:1428–1438

Reactive lymph node  
pDC marker blue  
E-cadherin brown

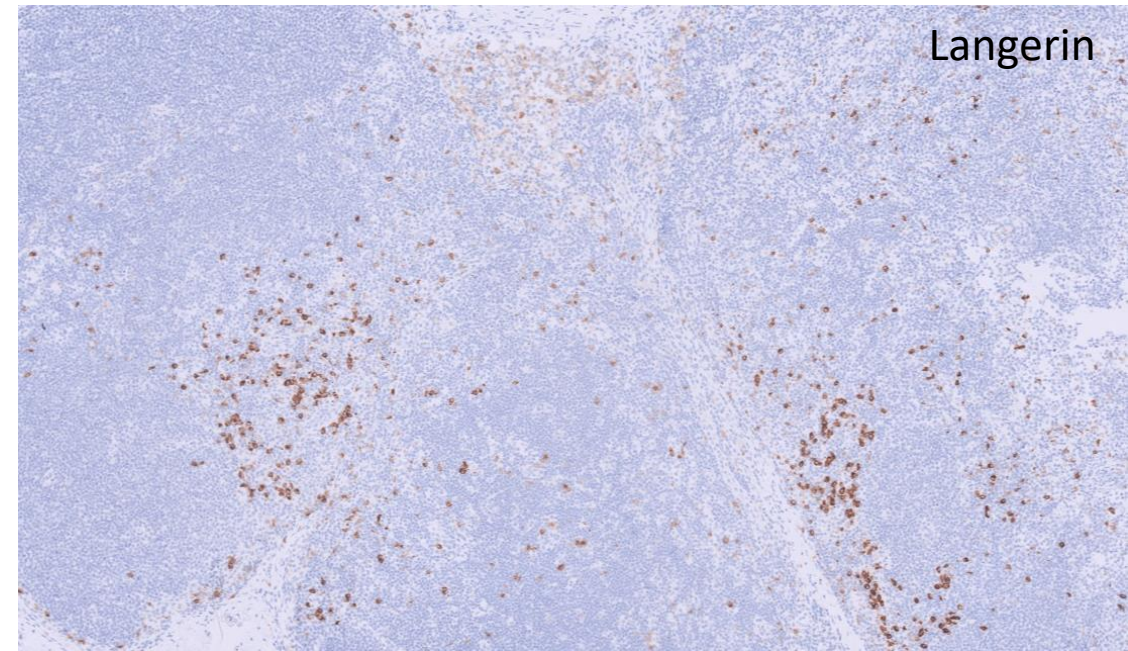
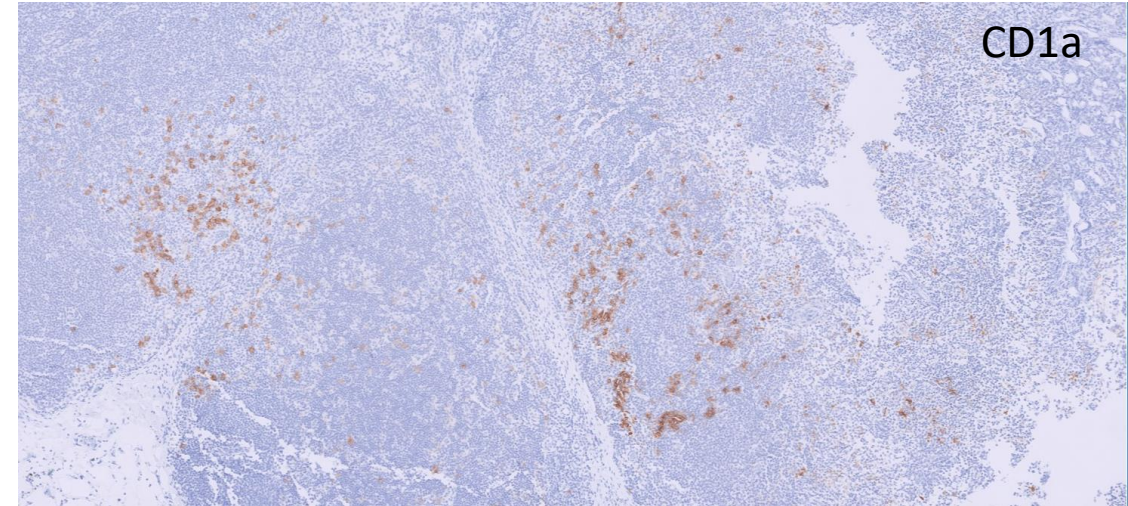




# Back to our case

- CD123: negative
- IRF8: negative
- CD1a: positive
- CD68: probably positive
- Langerin: positive
- S100: positive

→ Langerhans cells (dermatopathic LAN)





# Take home points

- E-cadherin stains much more than carcinoma
- Not an reliable epithelial marker
- Do not call E-cadherin+ in lymph node metastatic carcinoma

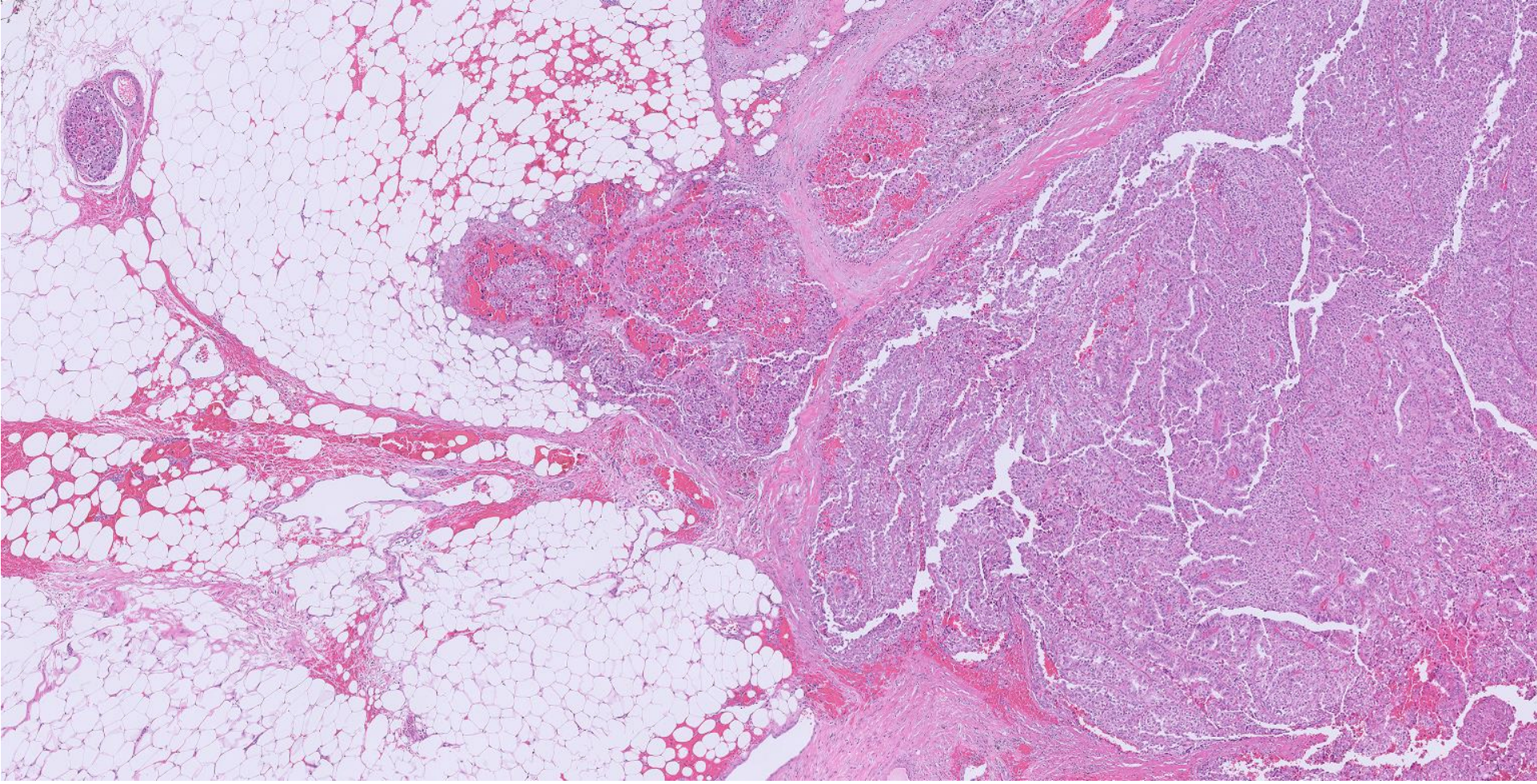


24-0608

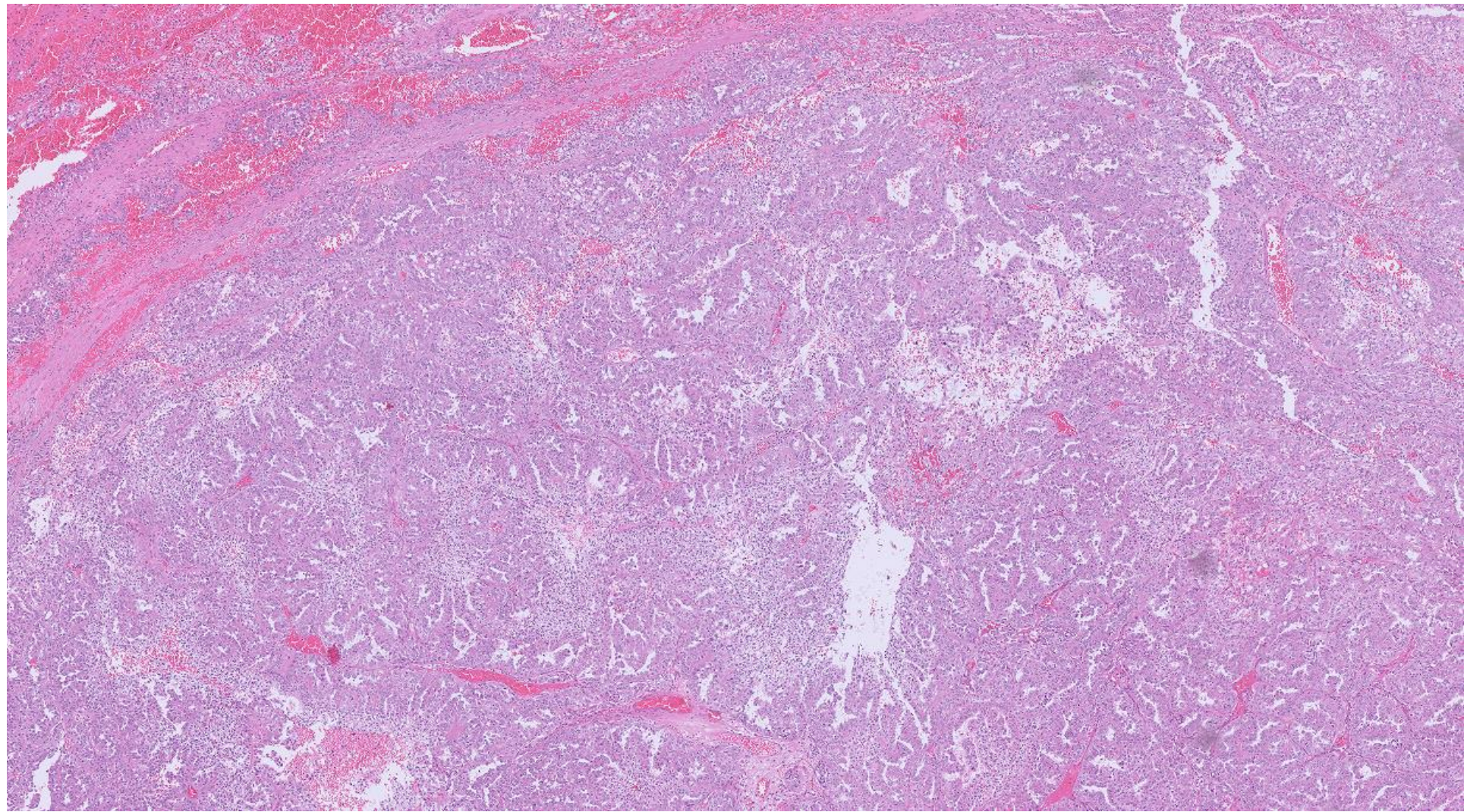
**Susan Potterveld, Ankur Sangoi; Stanford**

79-year-old male patient presents with a left renal mass and undergoes robotic radical nephrectomy. FISH negative for *TFE3* gene rearrangement

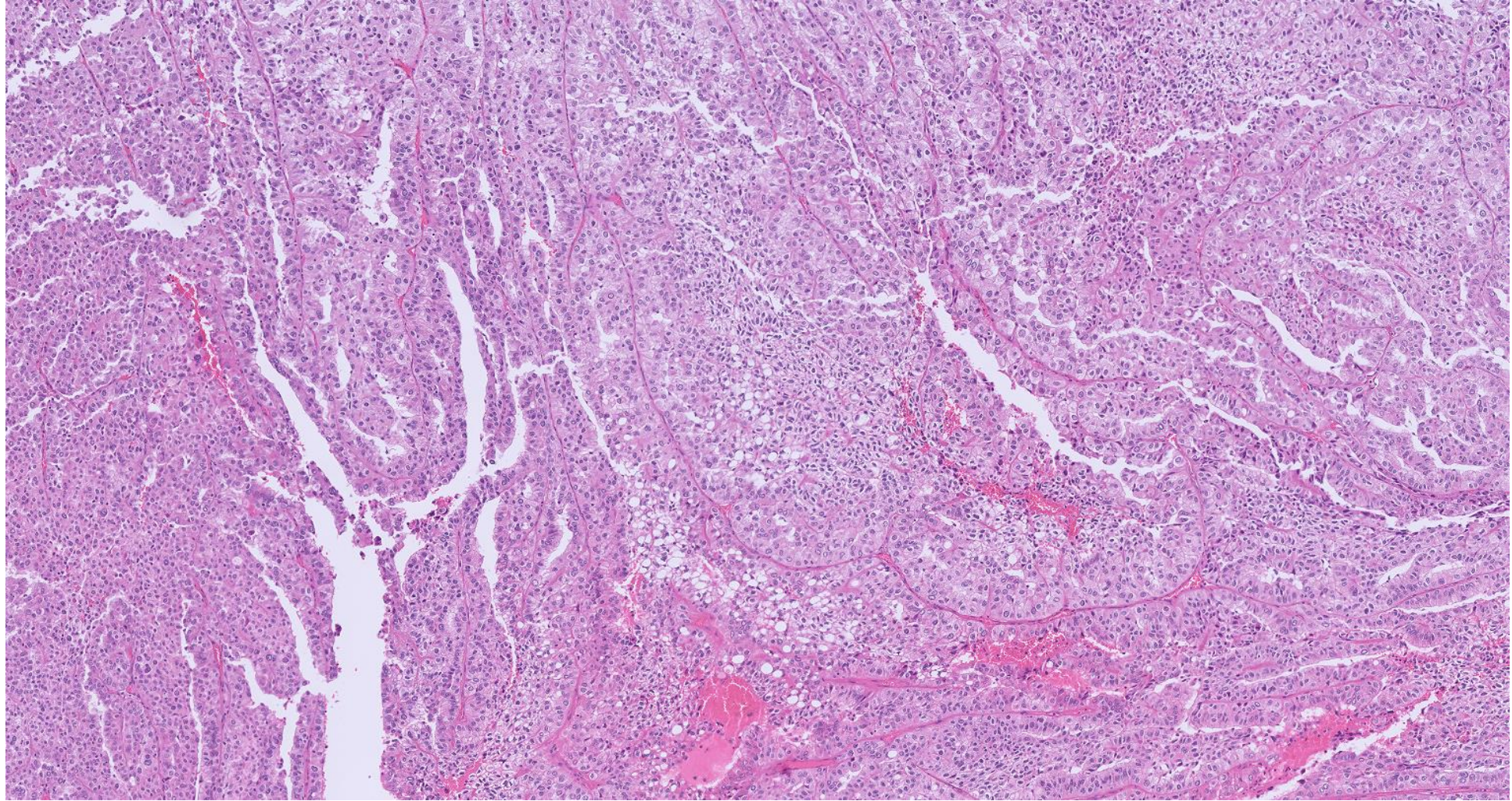




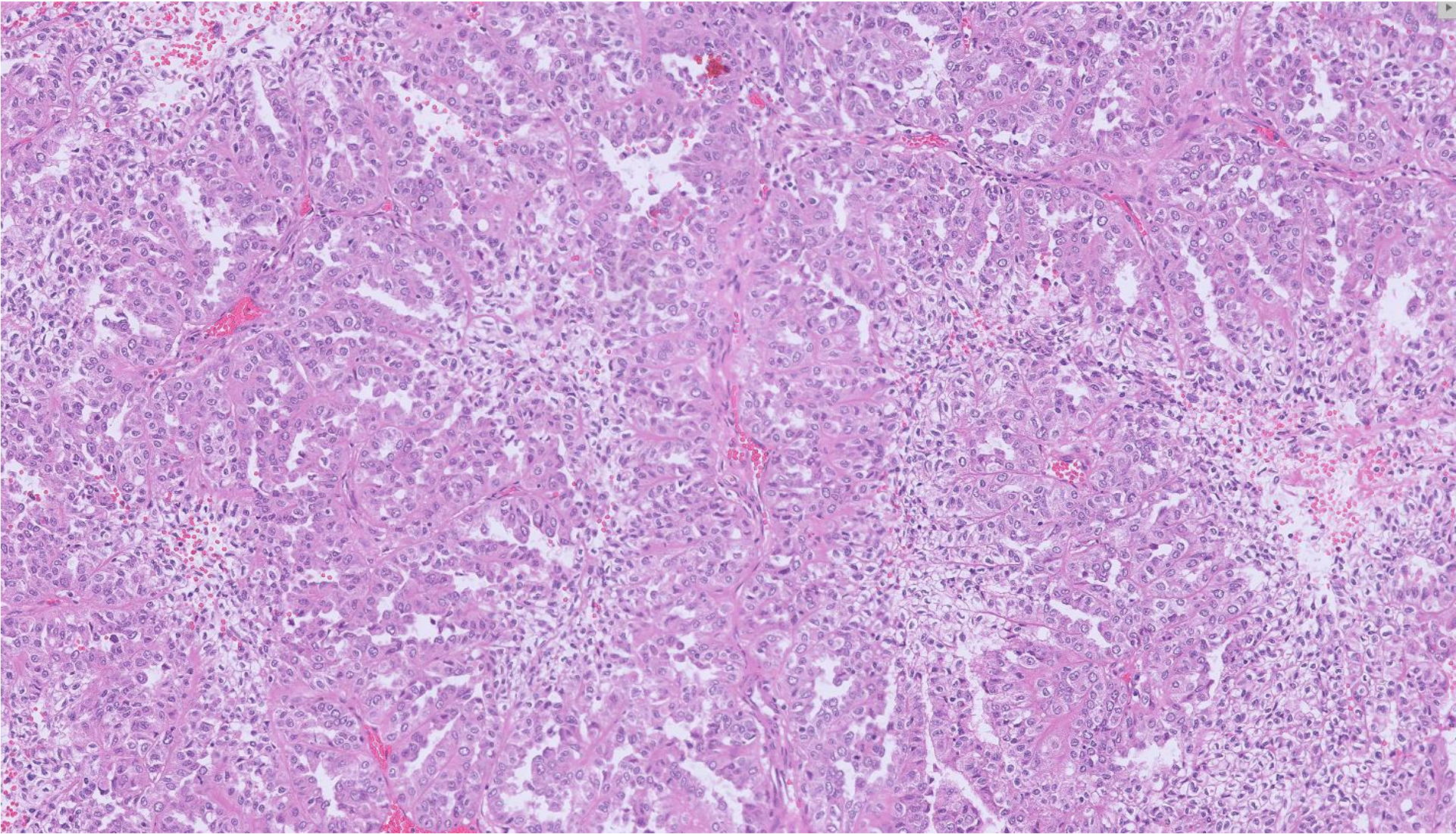




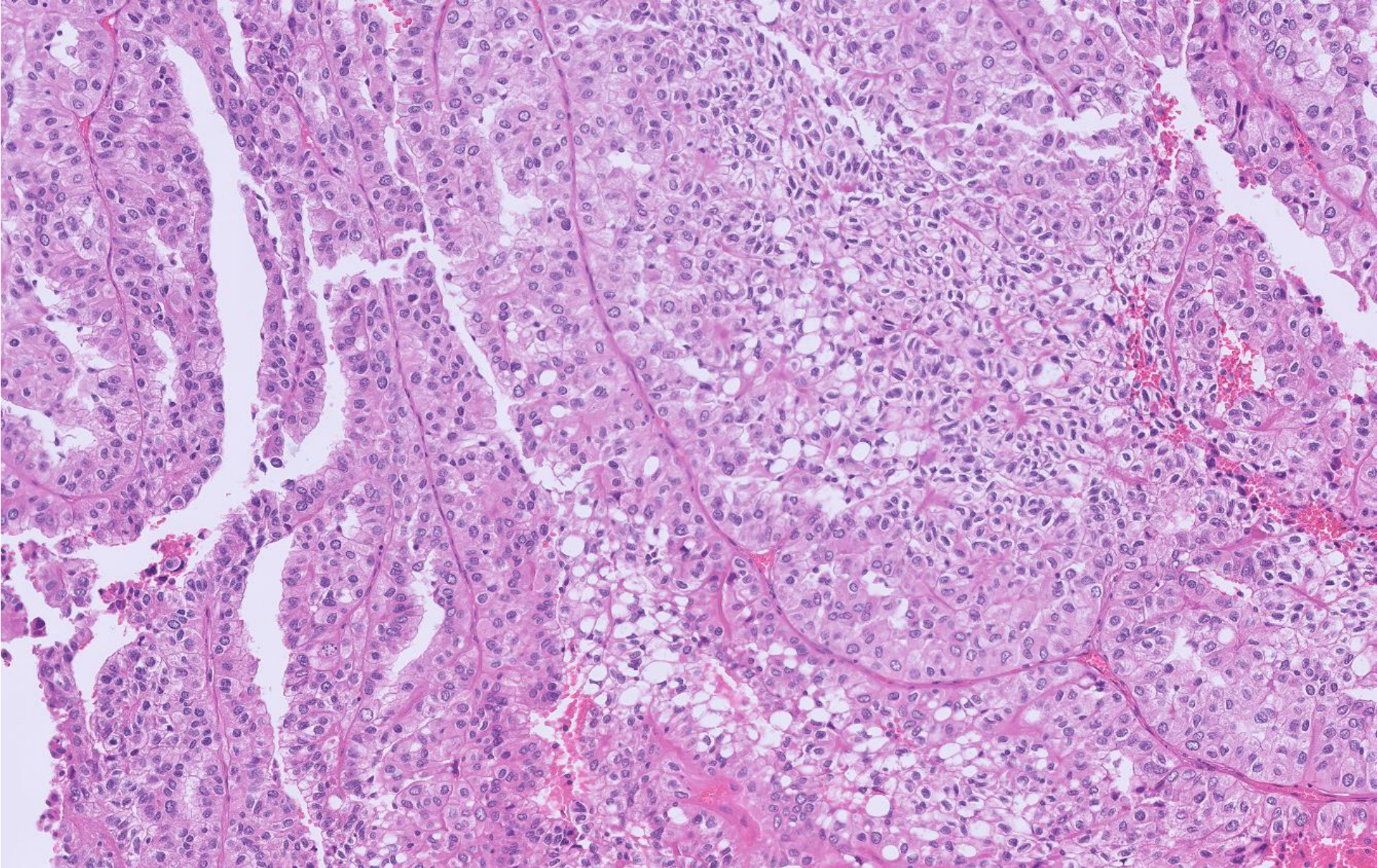




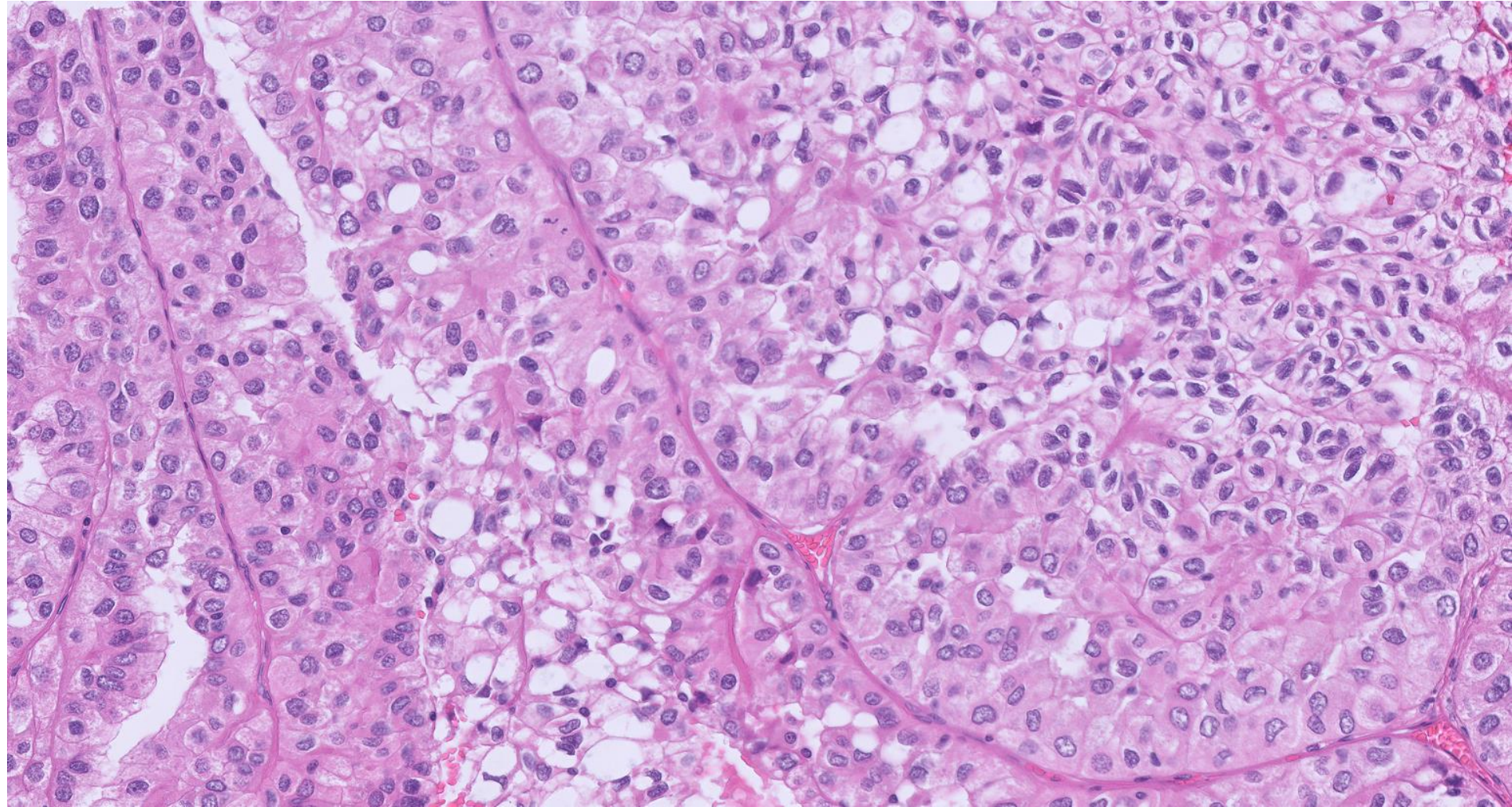














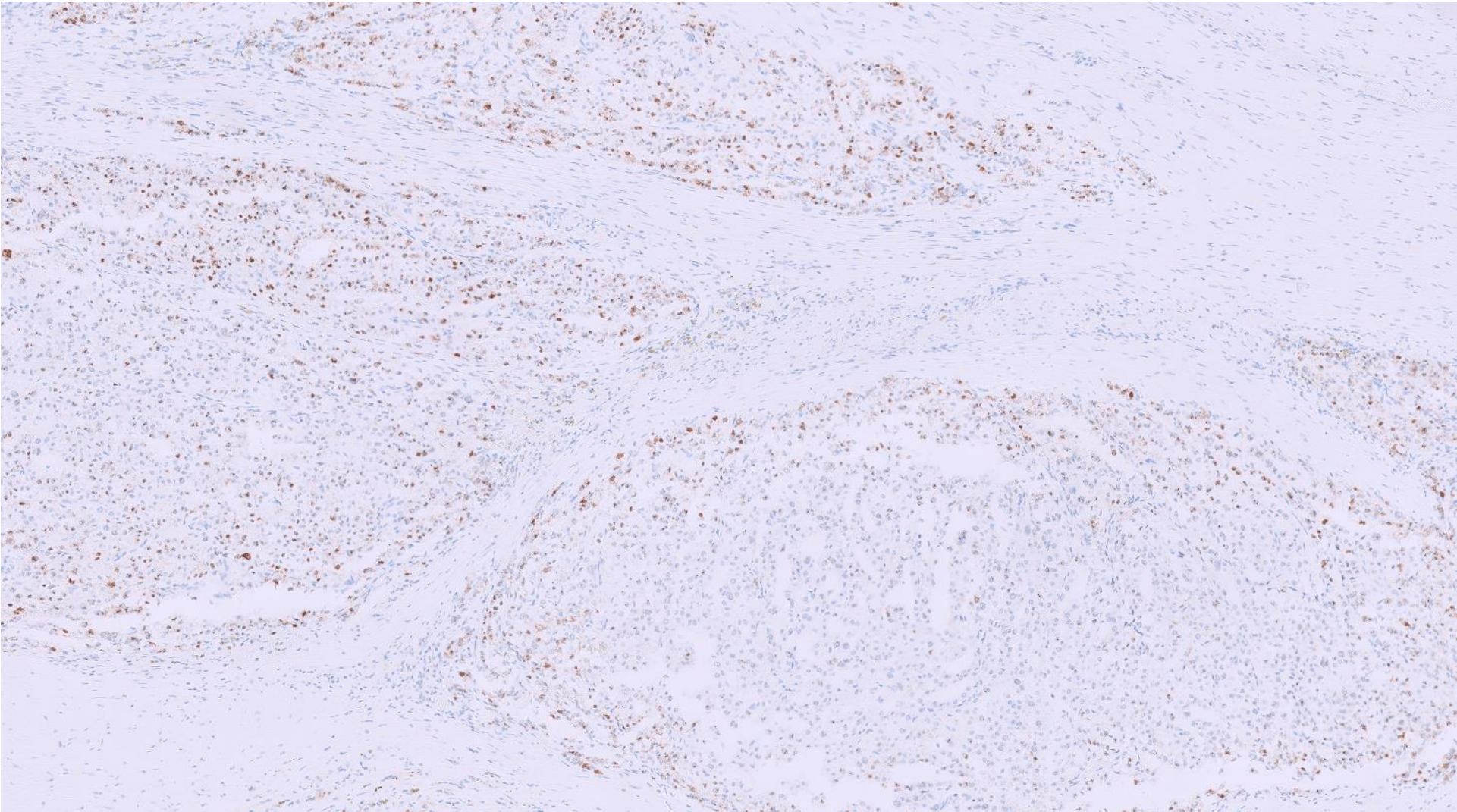
FISH negative for *TFE3* gene rearrangement



# DIAGNOSIS?

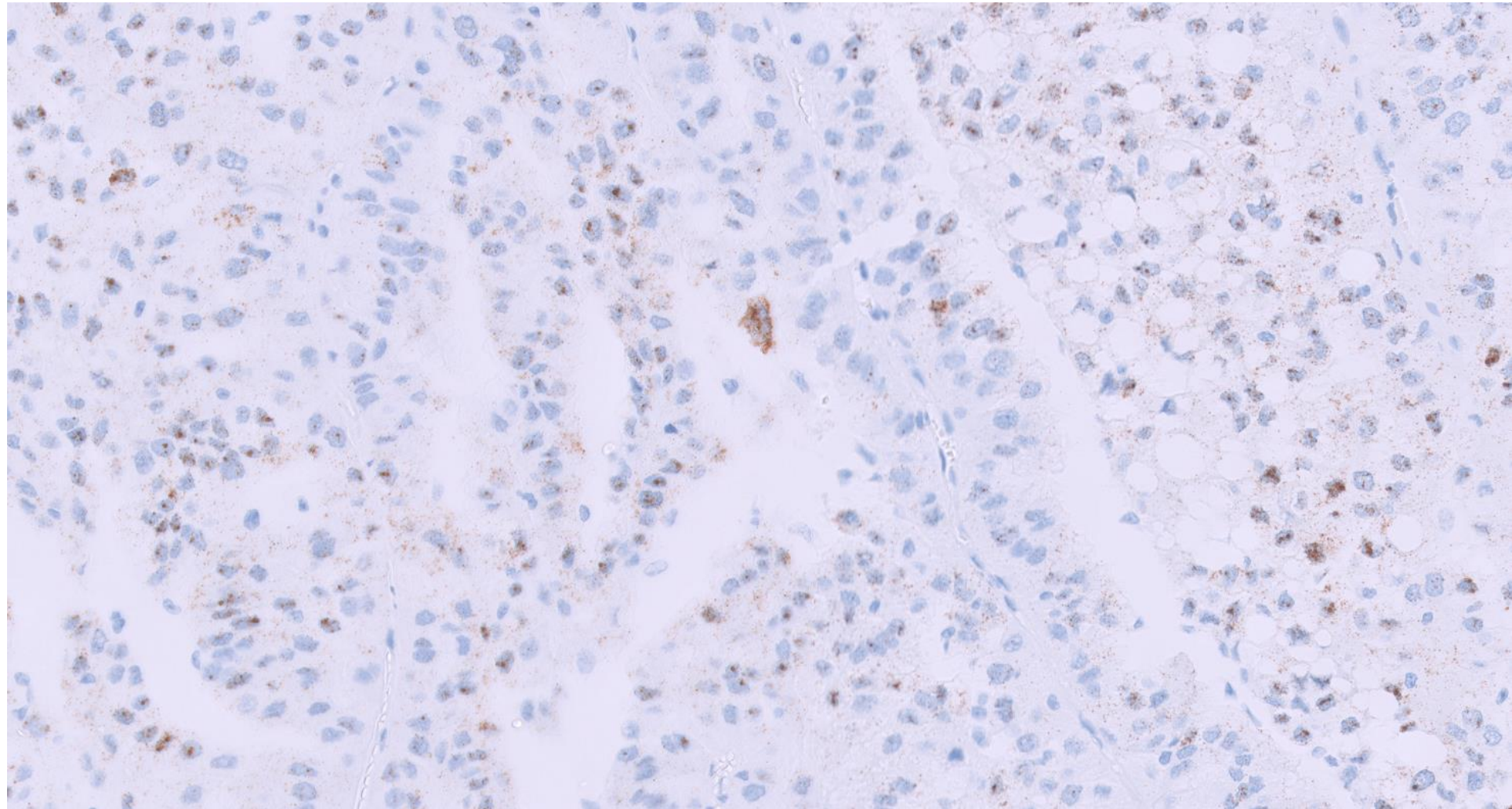






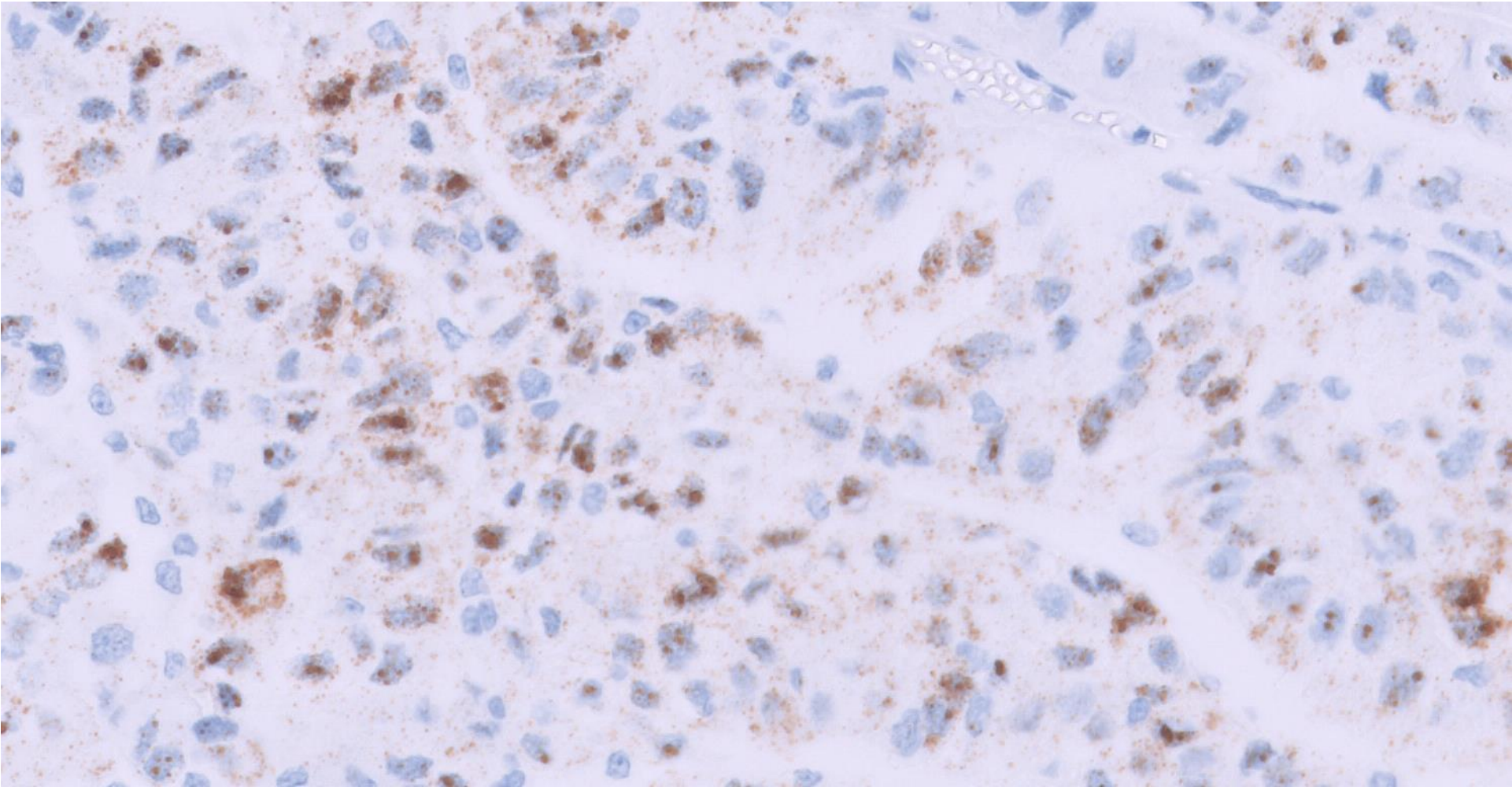
**TRIM63 ISH**





**TRIM63 ISH**







**TRIM63 ISH**

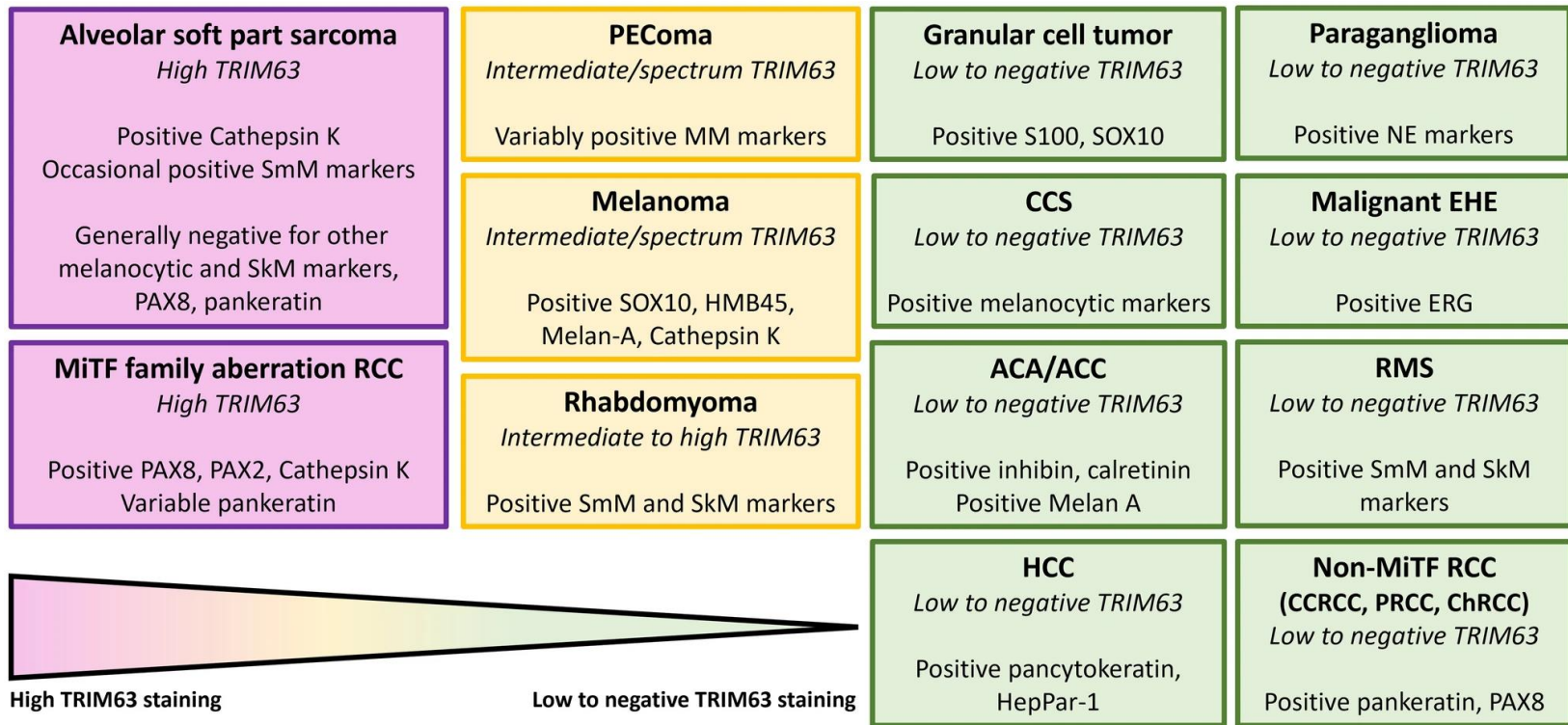




## ***TRIM63* is a sensitive and specific biomarker for MiT family aberration-associated renal cell carcinoma**

Xiao-Ming Wang<sup>1,2</sup> · Yuping Zhang<sup>2</sup> · Rahul Mannan <sup>2</sup> · Stephanie L. Skala<sup>1,3</sup> · Roshni Rangaswamy<sup>2</sup> · Anya Chinnaiyan<sup>2</sup> · Fengyun Su<sup>2</sup> · Xuhong Cao<sup>2</sup> · Sylvia Zelenka-Wang<sup>1,2</sup> · Lisa McMurry<sup>1</sup> · Hong Xiao<sup>1</sup> · Daniel E. Spratt<sup>4</sup> · Ankur R. Sangoi<sup>5</sup> · Lina Shao<sup>1</sup> · Bryan L. Betz<sup>1</sup> · Noah Brown<sup>1</sup> · Satish K. Tickoo<sup>6</sup> · Jesse K. McKenney<sup>7</sup> · Pedram Argani<sup>8</sup> · Sounak Gupta<sup>9</sup> · Victor E. Reuter<sup>6</sup> · Arul M. Chinnaiyan<sup>1,2,3,10,11</sup> · Saravana M. Dhanasekaran<sup>1,2</sup> · Rohit Mehra <sup>1,2,3</sup>







# Additional Testing

*RBM10::TFE3* fusion identified by next generation sequencing



# Diagnosis

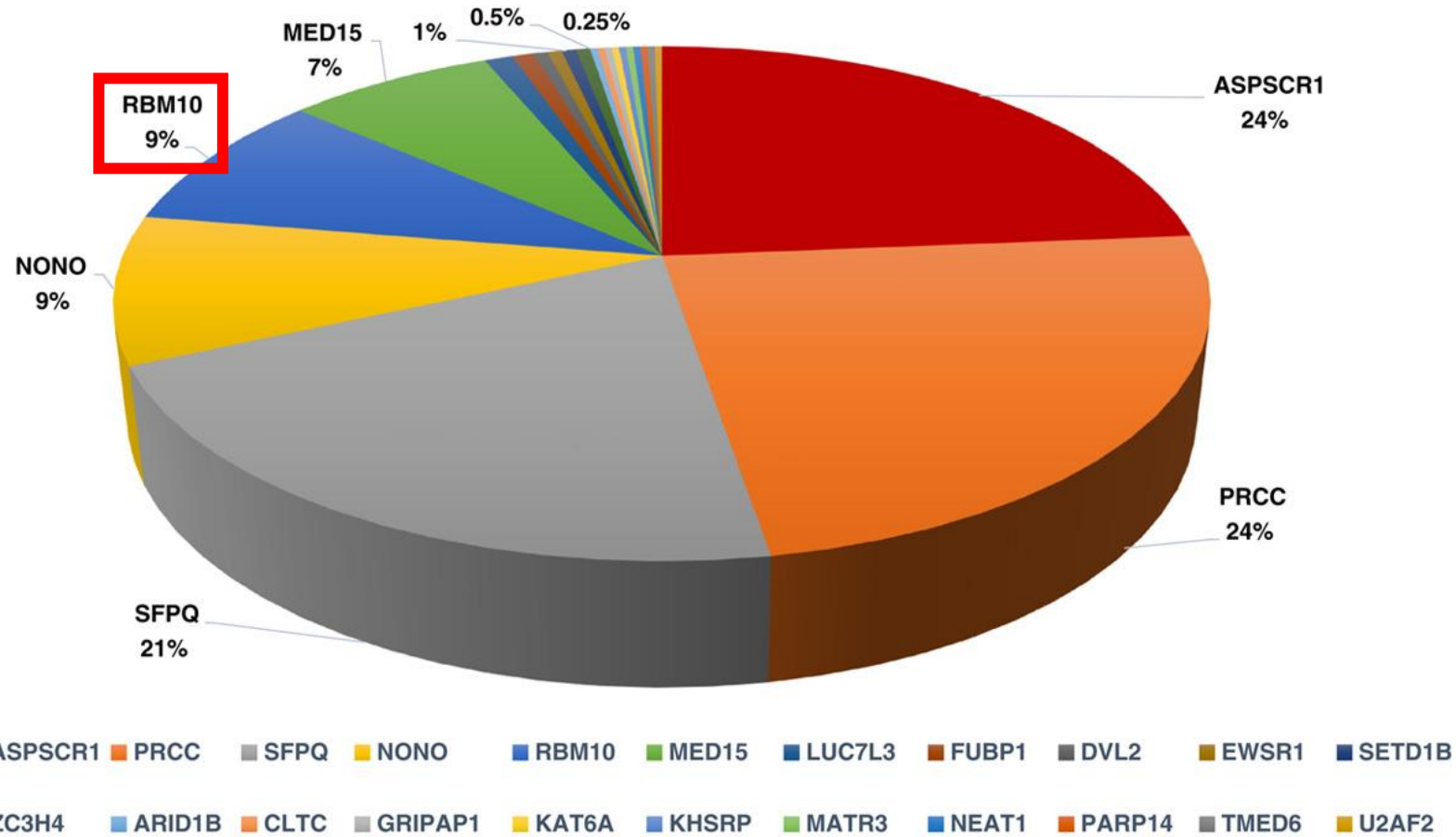
MiTF translocation renal cell carcinoma (*RBM10::TFE3*  
fusion)



# Translocation Renal Cell Carcinomas

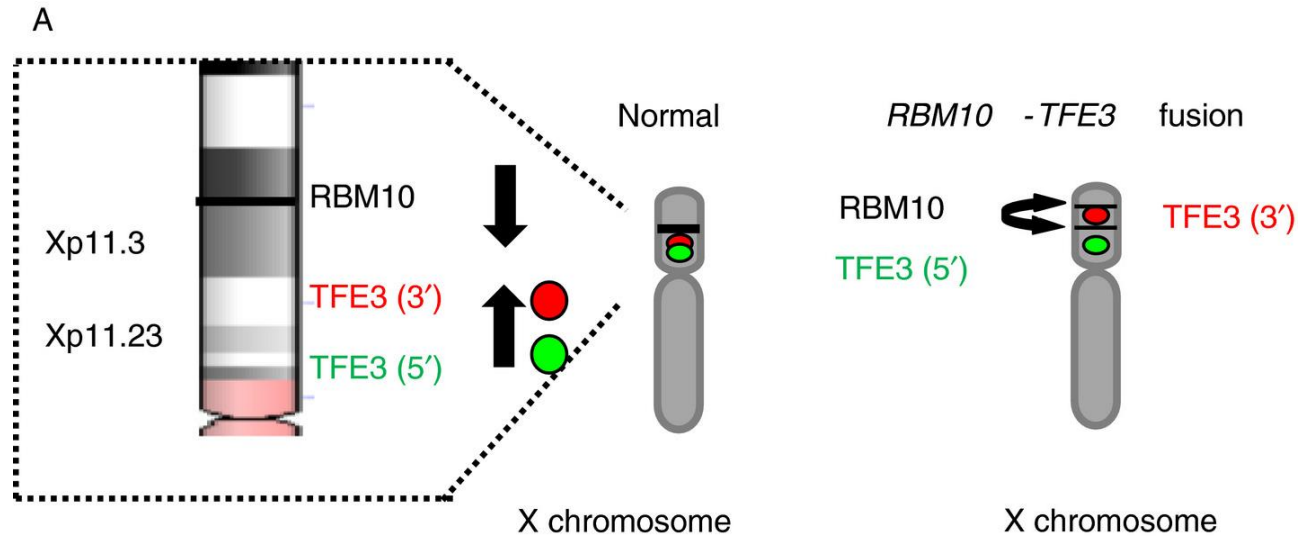


# Frequency of TFE3 fusion partners in 397 cases





# Pitfall!



- *TFE3/TFEB* FISH is considered the gold standard for diagnosis of MiTF-RCC
- FISH assays may show false-negative results in cases with intrachromosomal inversions involving *TFE3* and fusion patterners *RBM10*, *RBMX*, *NONO*, and *GRIPAP1*
- NGS can accurately identify these intrachromosomal inversion events



**TABLE 3 Comparison of IHC, FISH, RT-PCR, Karyotyping, and RNA-sequencing for TFE3-tRCC Diagnosis**

Ancillary Study	Advantages	Limitations	Current Recommendations (ISUP, GUPS) and Utilization
TFE3 IHC	High sensitivity and specificity if performed manually Low cost Quick TAT Positive results have prognostic value even in non-tRCC cases	Fixation and processing artifacts (weak, patchy, tumor periphery only) Subjective interpretation High background Variability in antibody performance (RTU vs. concentrate) or when automated	First line diagnostic tool  Adding IHC panel If inconclusive, FISH should be performed
DNA FISH (break-apart)	High specificity Quantitative Relatively short TAT  Can detect low copy gain and amplification	Fixation/cutting artifacts No validated commercial probes False negative: inversions, intrachromosomal fusions ( <i>NonO</i> , <i>RBM10</i> , <i>GRIPAP1</i> ) Inability to detect break-points, cryptic fusions or partner genes	Gold standard for TFE3-tRCC diagnosis
Karyotyping	Good reimbursement rate Global information Knowledge of anticipated anomaly not necessary  Relatively high specificity	Required fresh viable cells Difficulties of cell culturing (multiple days, low density, necrosis, stromal overgrowth, etc.) Unable to identify cryptic abnormalities Complex karyotypes, suboptimal morphology Low resolution	Not recommended for routine practice
RT-PCR	Relatively low cost	Custom designed primers Works for known breakpoints only	Not recommended for routine practice
RNA-seq	Low input FFPE (20 ng)  Multiple genes in a single assay Quantitative, high-resolution Detection of fusion partners (known and novel), precise break-point, functional domains and amplifications	High cost and low reimbursement rate  Slightly longer than FISH TAT Custom designed gene panels Not suitable for old FFPE tissues (>2y.o.), decalcified tissues or after prolonged fixation	Utilized by major institutions for challenging cases or research

FFPE indicates formalin fixed paraffin embedded; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; RTU, ready-to-use; TAT, turn-around-time.



# Morphologic Clues

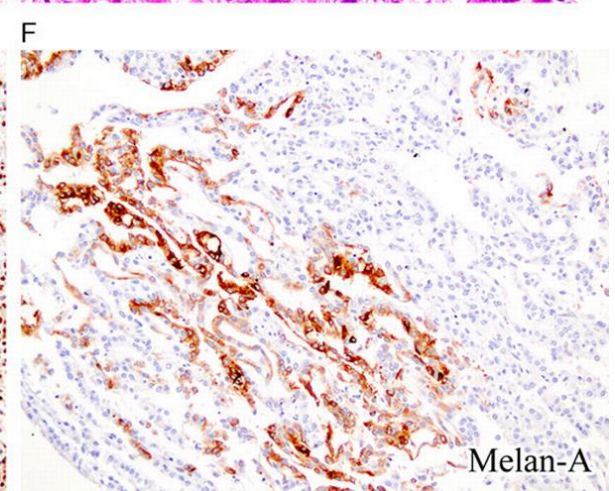
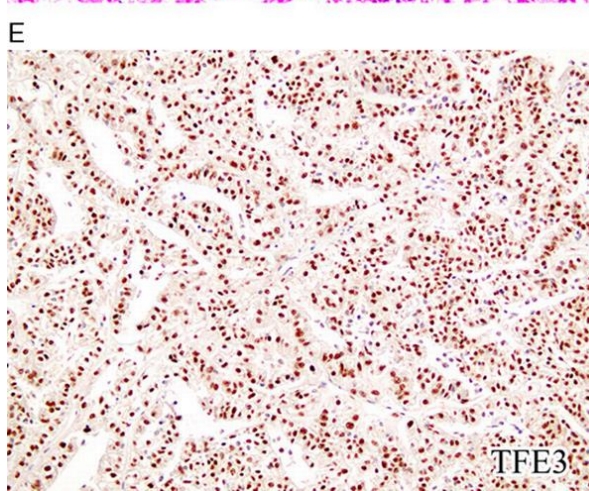
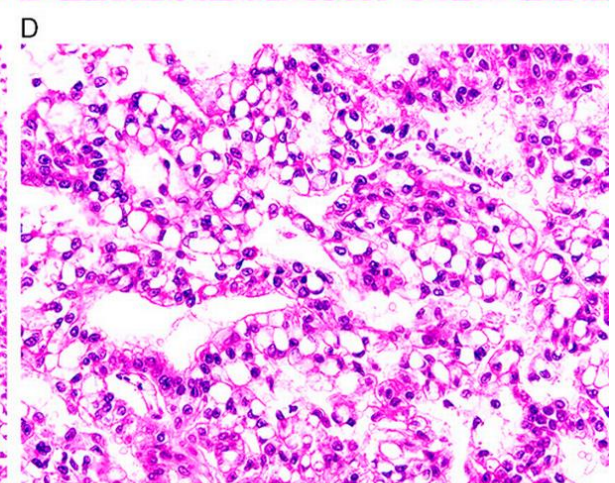
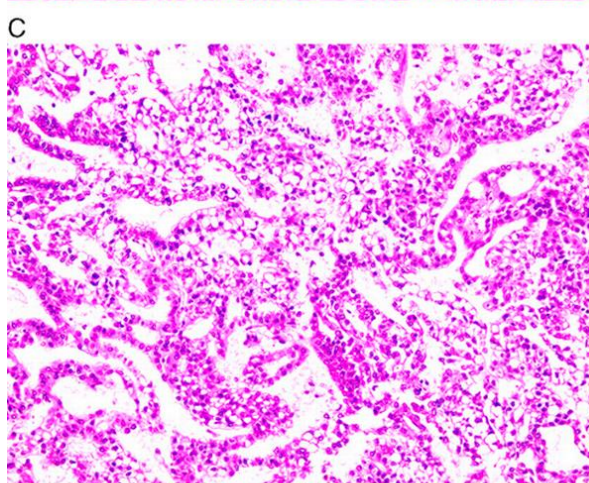
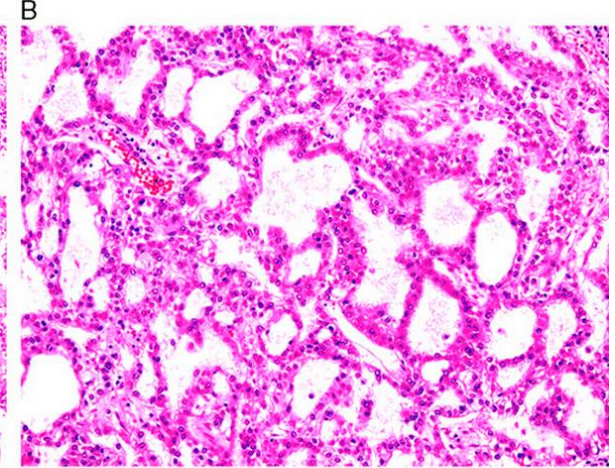
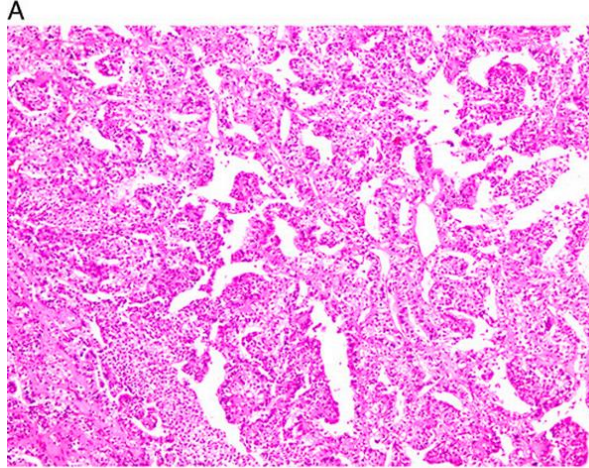
- Classic morphologic triad for translocation renal cell carcinomas:
  - Papillary architecture
  - Large pale or clear cells with prominent nucleoli
  - Frequent psammoma bodies



**TABLE 3.** Comparison of Subtypes of *TFE3* Translocation RCCs and t(6;11) RCCs

	<i>RBM-TFE3</i> RCCs <sup>13-15</sup>	<i>NONO-TFE3</i> RCCs <sup>10,20</sup>	<i>ASPSCR1-TFE3</i> RCCs <sup>2,10</sup>	<i>PRCC-TFE3</i> RCCs <sup>3,10</sup>	<i>SFPQ-TFE3</i> RCCs <sup>4,10</sup>	t(6;11) RCCs <sup>22-25</sup>
Morphology feature	A biphasic morphology overlapping with t(6;11) RCCs: mixed areas of sheets, nests and papillary patterns of epithelioid cells and pseudorosette-like architecture. Cytoplasmic vacuolization and nuclear grooves were usually observed	A biphasic pattern: sheets of epithelial cells and glandular/tubular or papillary architecture mimicking secretory endometrioid gland or clear cell papillary RCC	Nested to papillary architecture, voluminous clear to eosinophilic cytoplasm, and abundant psammoma bodies	Compact nested to papillary architecture, clear to eosinophilic cytoplasm, and fewer psammoma bodies	Nested or papillary architecture and predominantly clear cytoplasm. Subnuclear vacuoles similar was usually seen. Occasionally present pseudorosette-like architecture	The most distinctive pattern of the t(6;11) RCCs is of a biphasic neoplasm, composed of nests of larger epithelioid cells and smaller cells clustered around basement membrane material
Psammoma bodies	Often present	Usually present	Usually present	Sometimes present	Sometimes present	Often present
Pigment	Occasionally present	Absent	Absent	Absent	Absent	Often present
IHC findings	Positive: TFE3, Cathepsin K and Melan-A (focally expressed) Negative: TFEB, HMB45	Positive: TFE3 Negative: Cathepsin K, Melan-A and HMB45	Positive: TFE3 Negative: Cathepsin K, Melan-A and HMB45	Positive: TFE3, Cathepsin K Negative: Melan-A and HMB45	Positive: TFE3 Negative: Cathepsin K, Melan-A and HMB45	Positive: TFEB, Cathepsin K, HMB45 and Melan-A Negative: TFE3
FISH findings	“False negative” for <i>TFE3</i> (split signals with a distance < 1 signal diameter) Negative for <i>TFEB</i>	Equivocal results for <i>TFE3</i> (split signals with a distance of nearly 2 signal diameters) Negative for <i>TFEB</i>	Positive for <i>TFE3</i> Negative for <i>TFEB</i>	Positive for <i>TFE3</i> Negative for <i>TFEB</i>	Positive for <i>TFE3</i> Negative for <i>TFEB</i>	Negative for <i>TFE3</i> Positive for <i>TFEB</i>





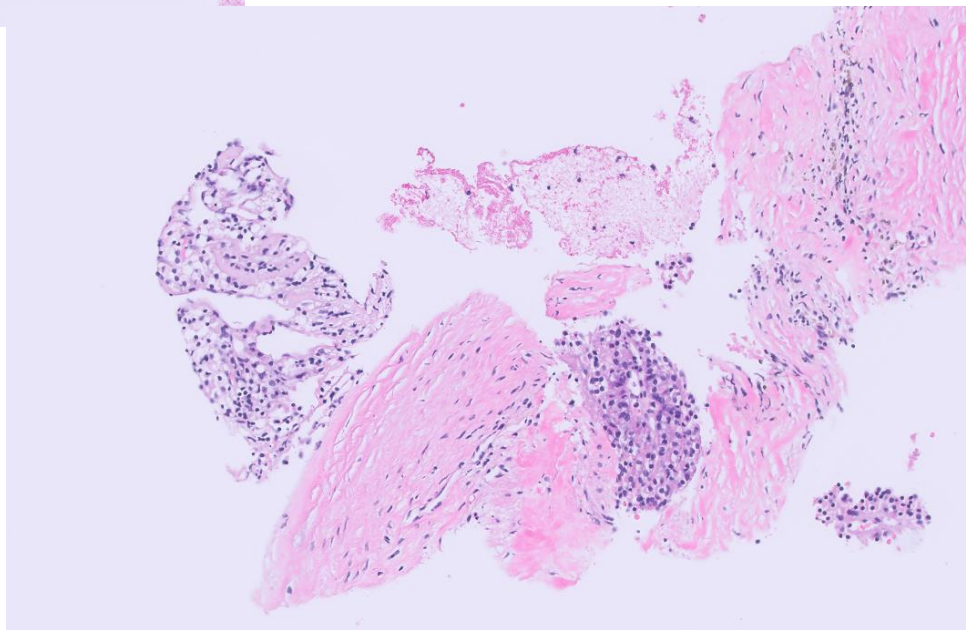
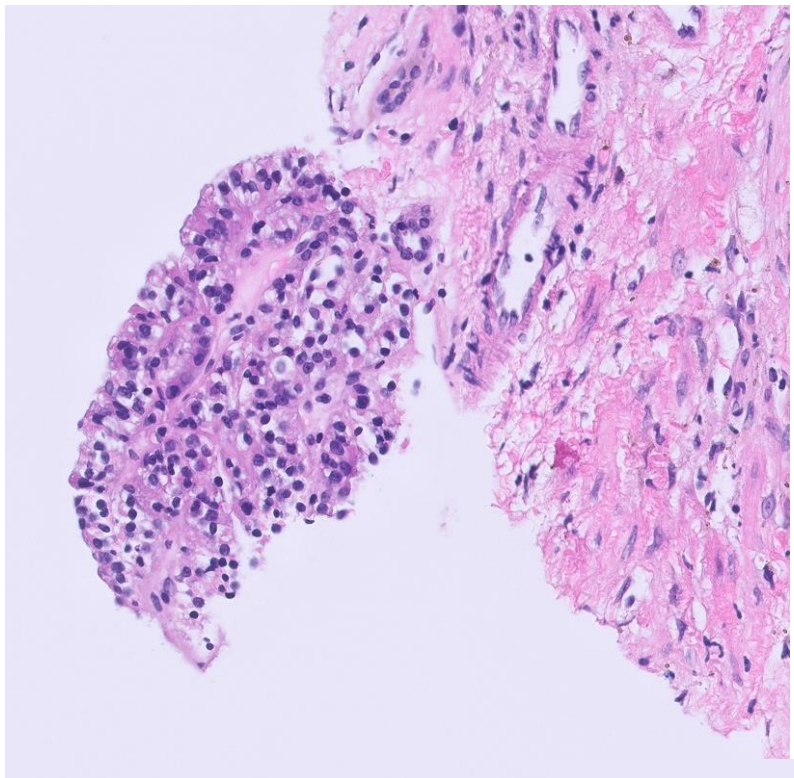


Another example: 61-year-old female patient presents with a left renal mass and undergoes biopsy and resection

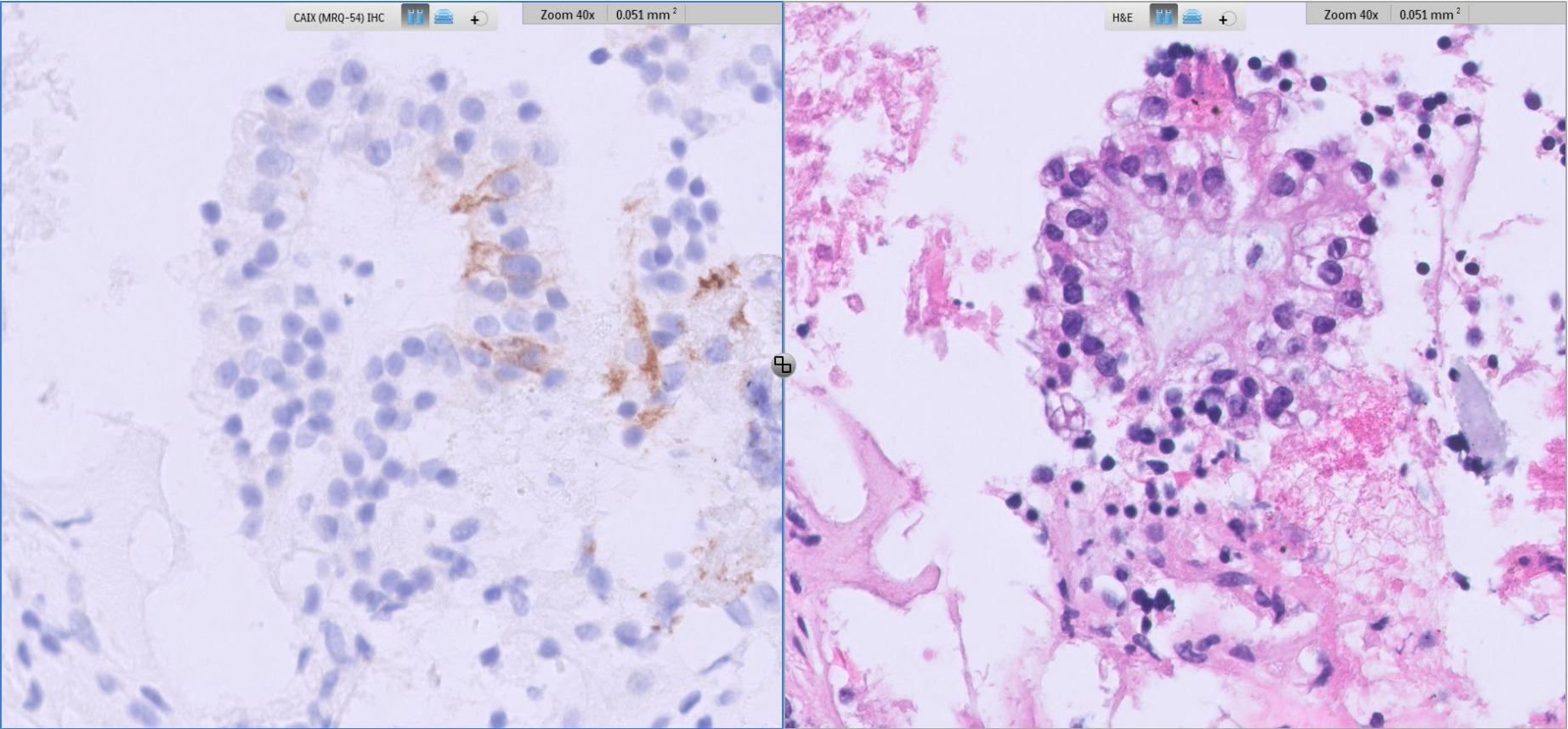




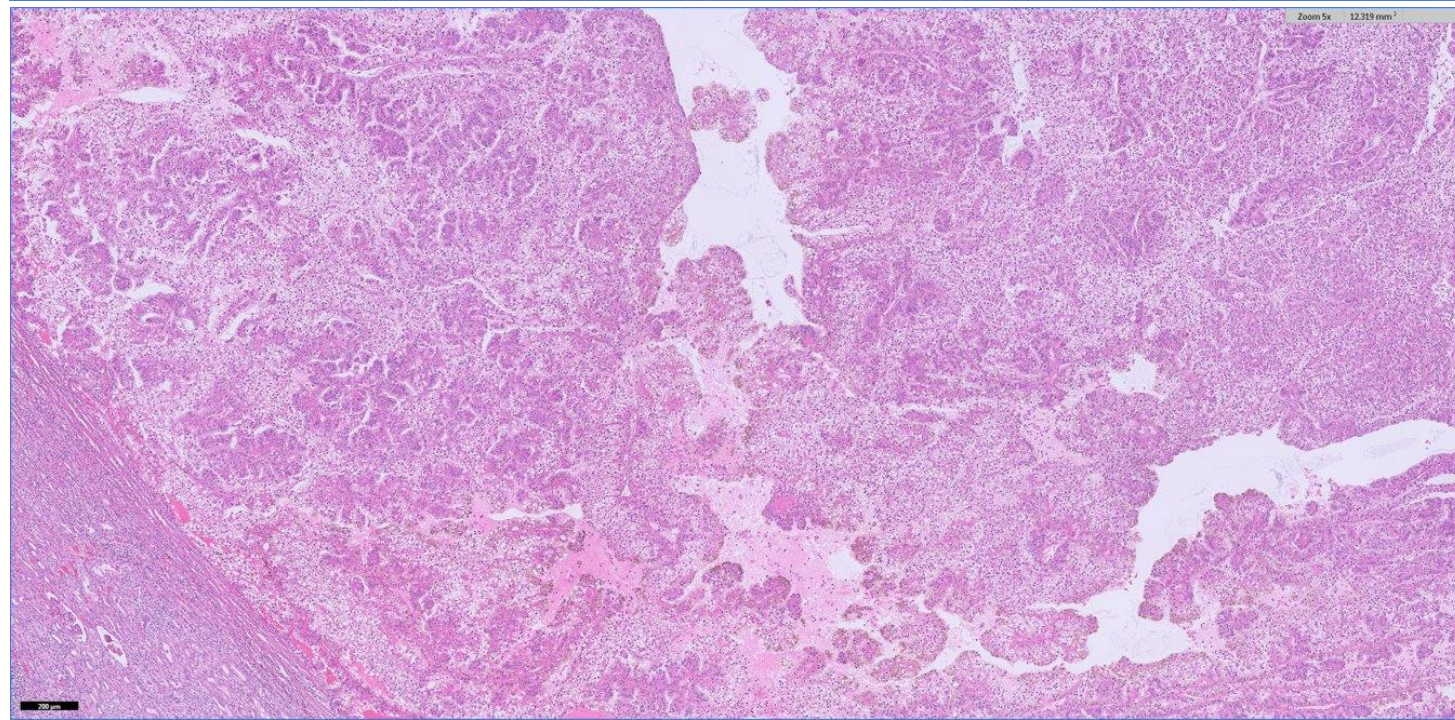
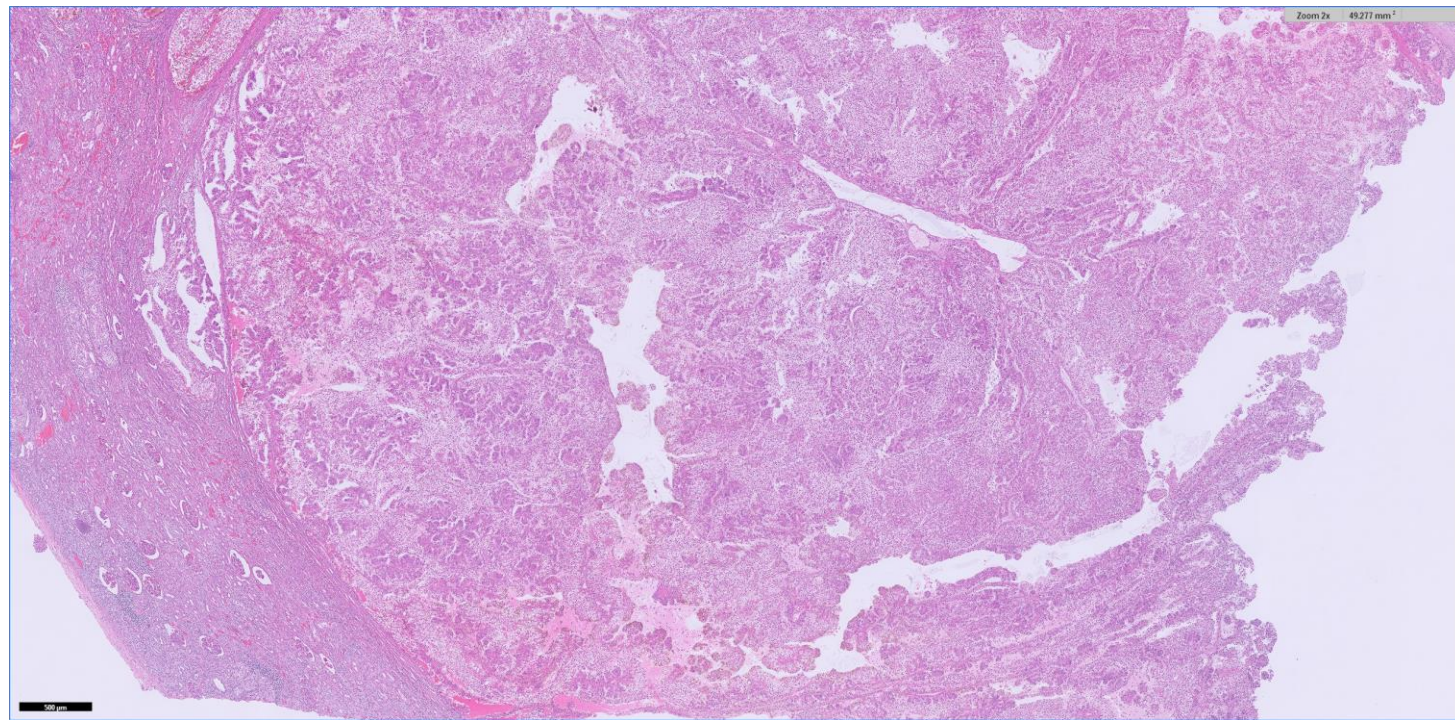




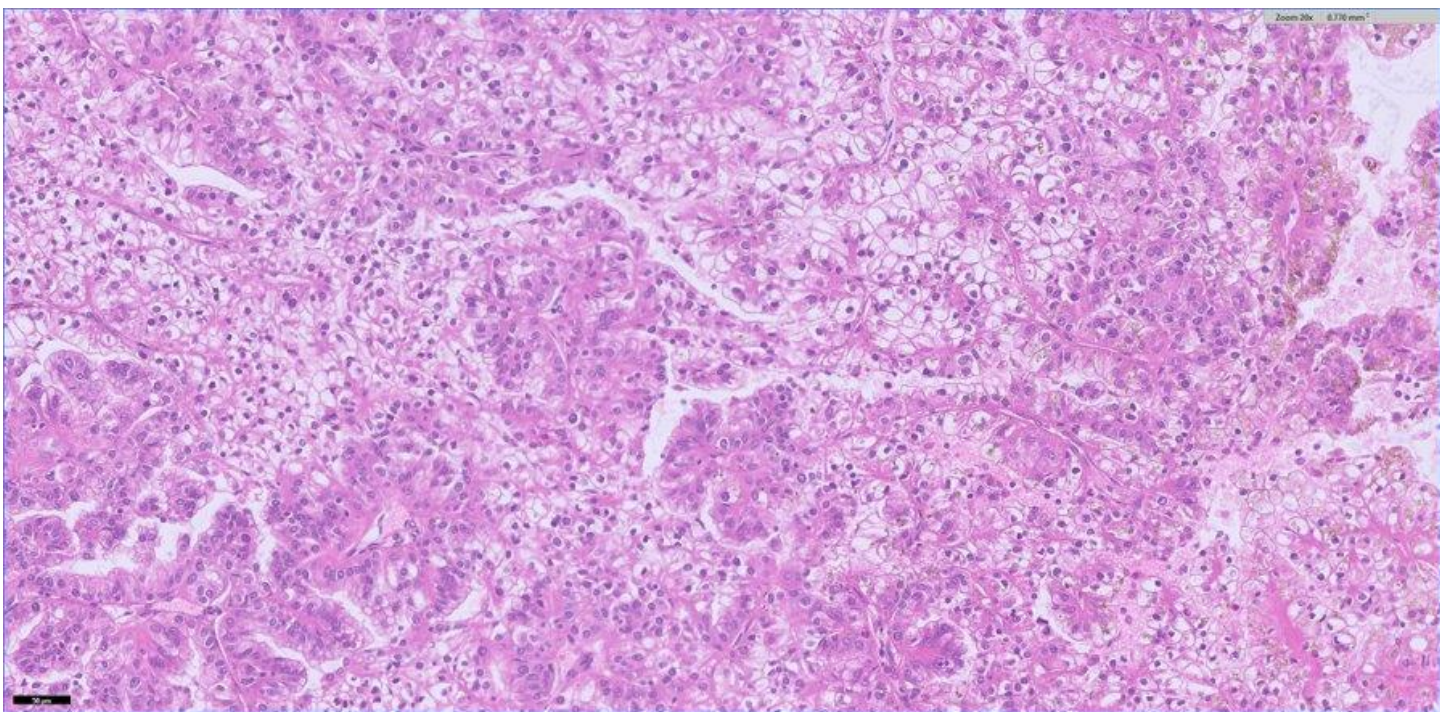
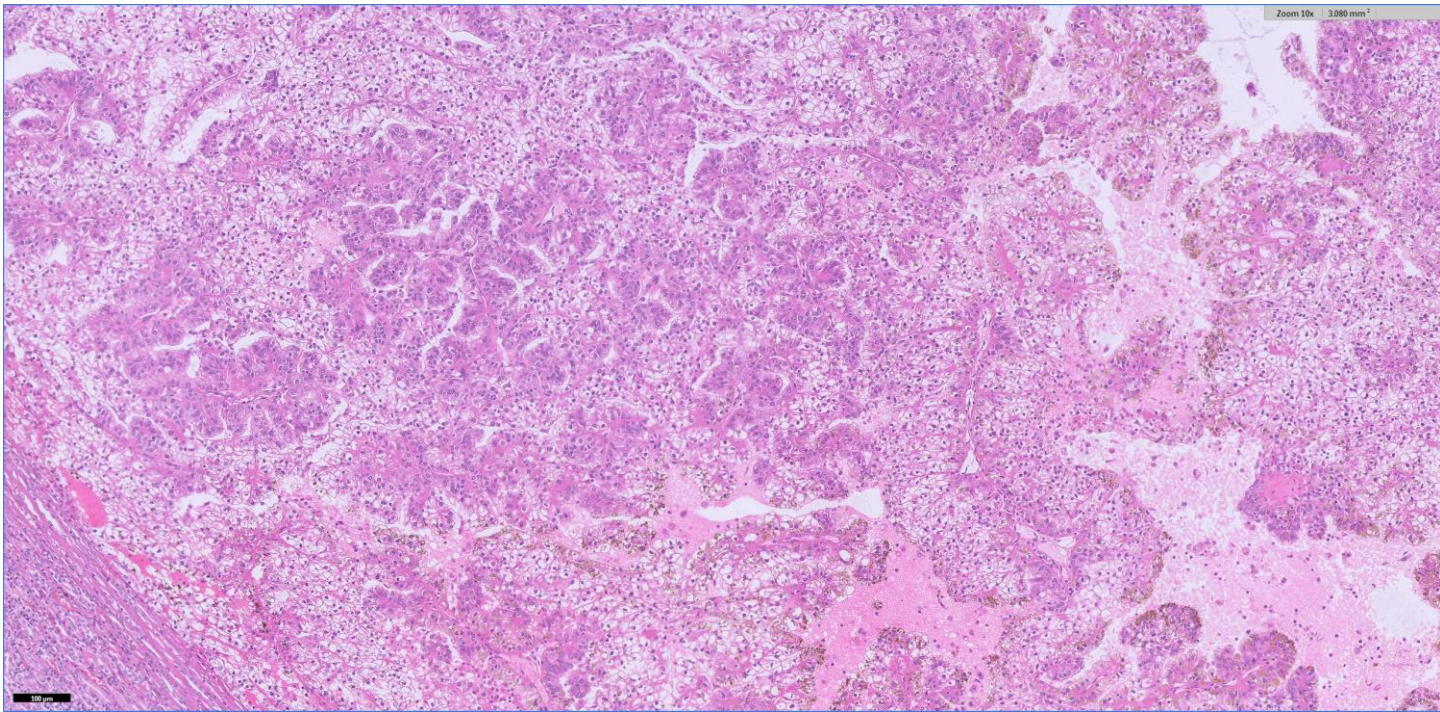




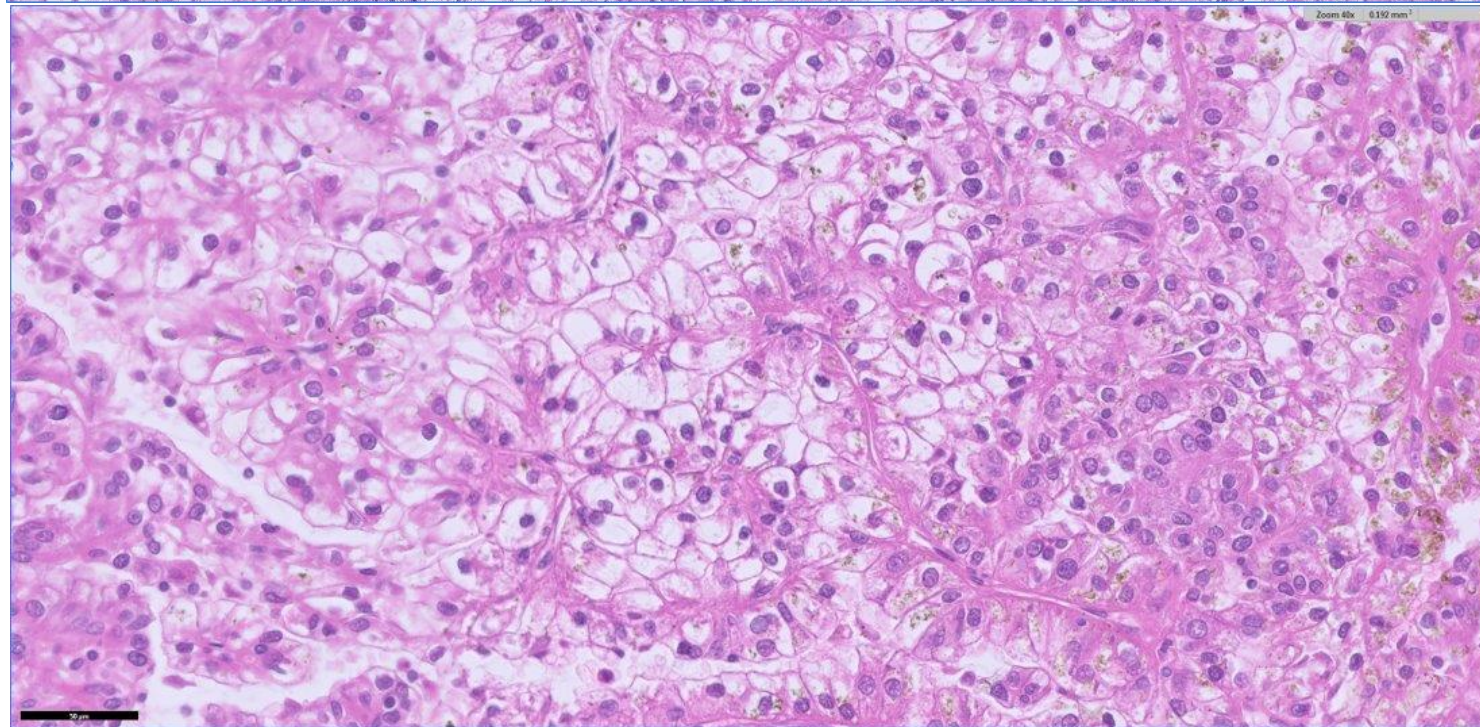
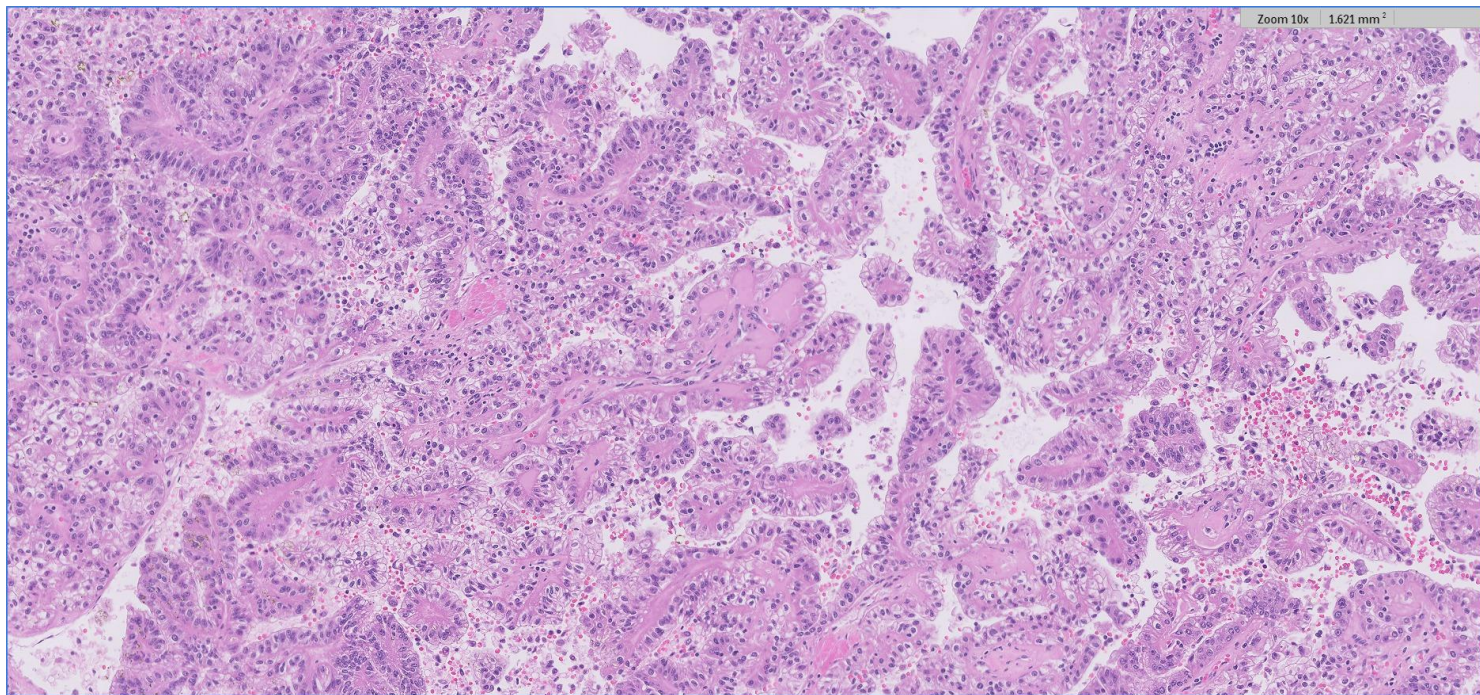














# Summary

## *RBM10::TFE3* translocation renal cell carcinoma

- Morphology:
  - Biphasic papillary and nested growth patterns with epithelioid cells and pseudorosette-like architecture
  - Cytoplasmic vacuolization and nuclear grooves
- IHC: Positive for TFE3, Cathepsin K, Melan A (focal)
- TRIM63 RNA ISH positive
- Ancillary testing
  - *TFE3* FISH: May show false negative result
  - Fusion can be detected by RNA sequencing



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# Financials from Dean

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