



THE UNIVERSITY
of EDINBURGH



Slide Seminar

C Simon Herrington

Edinburgh Cancer Research Centre

Institute of Genetics and Cancer

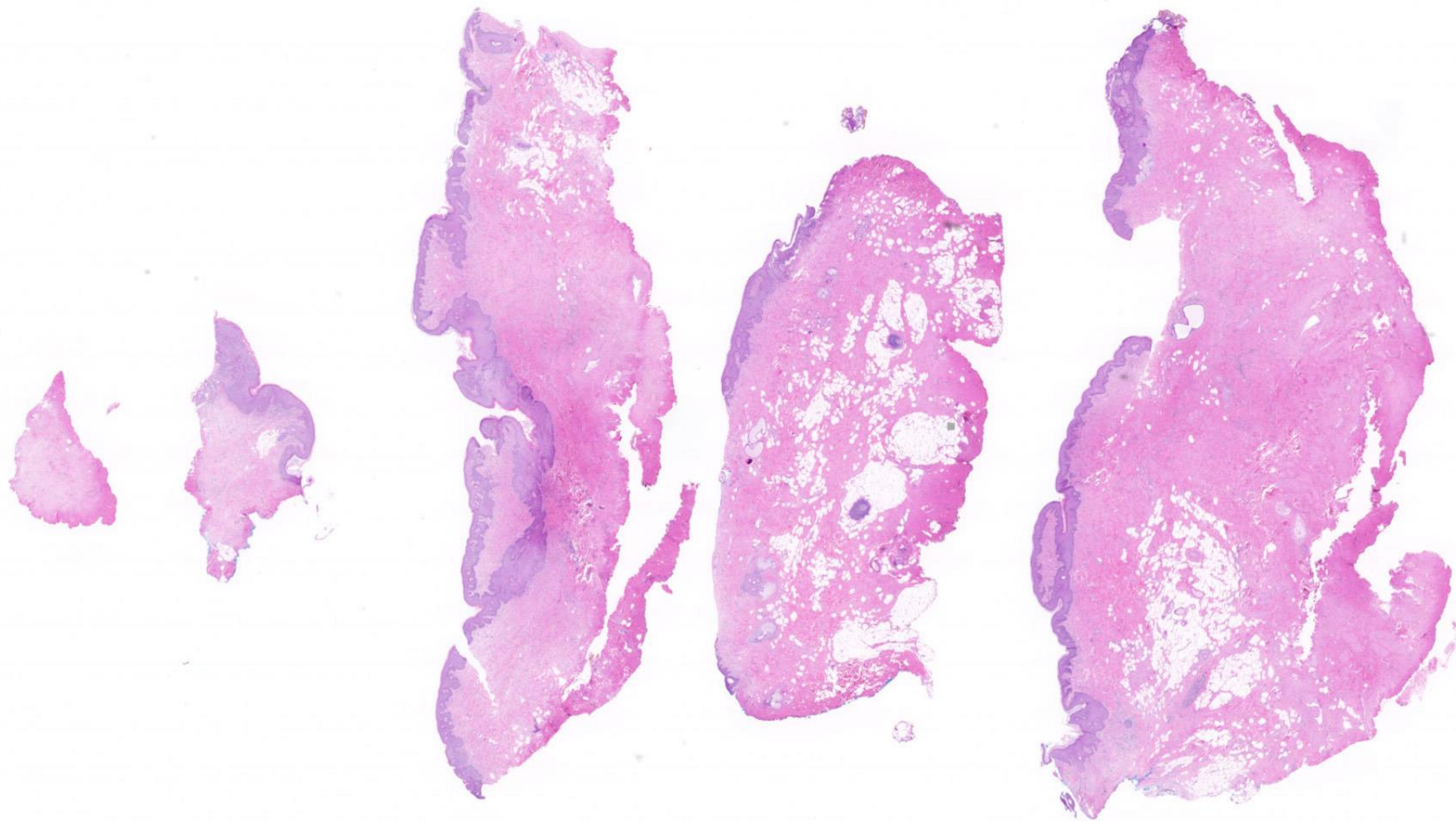
University of Edinburgh

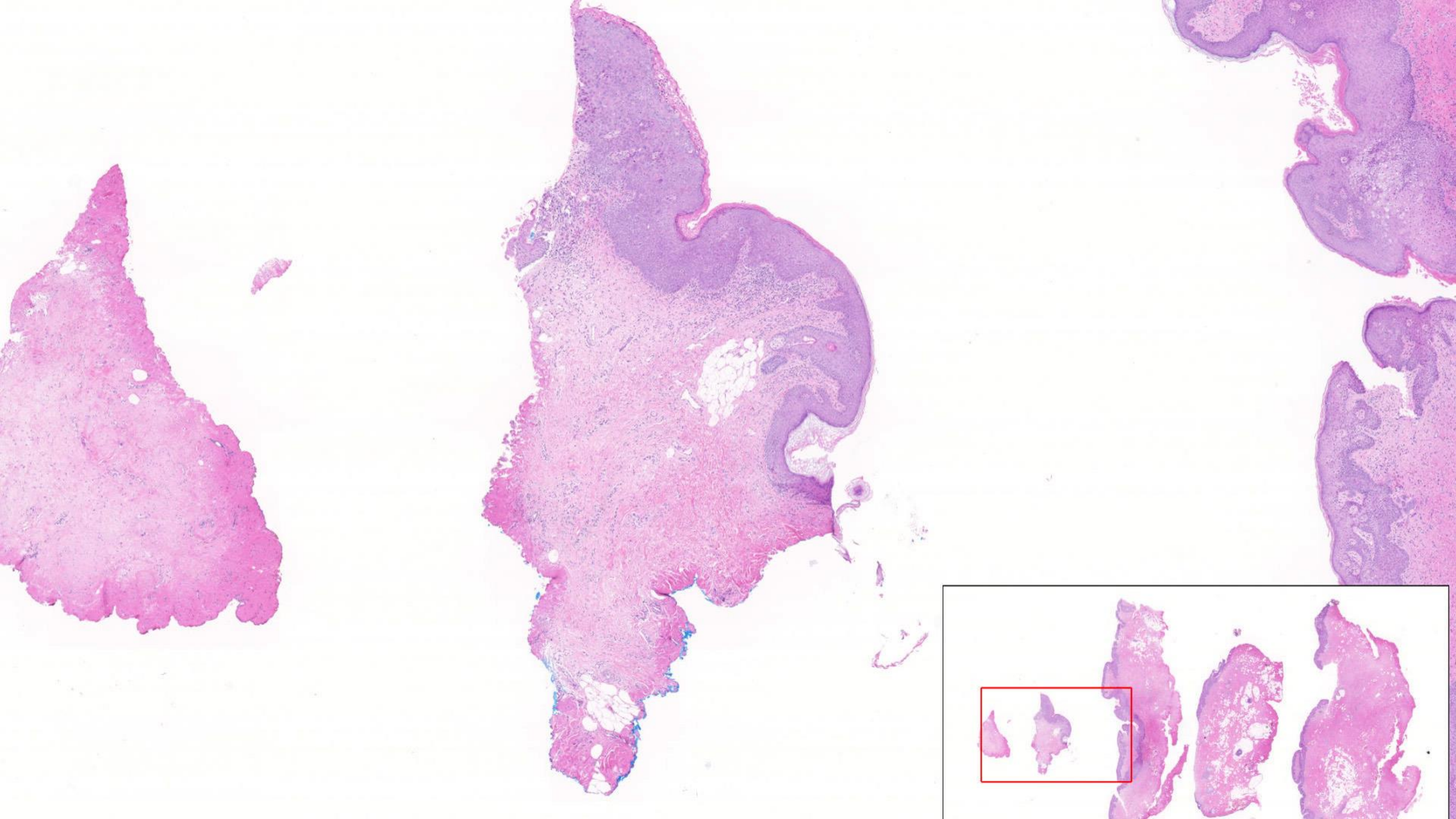
Western General Hospital

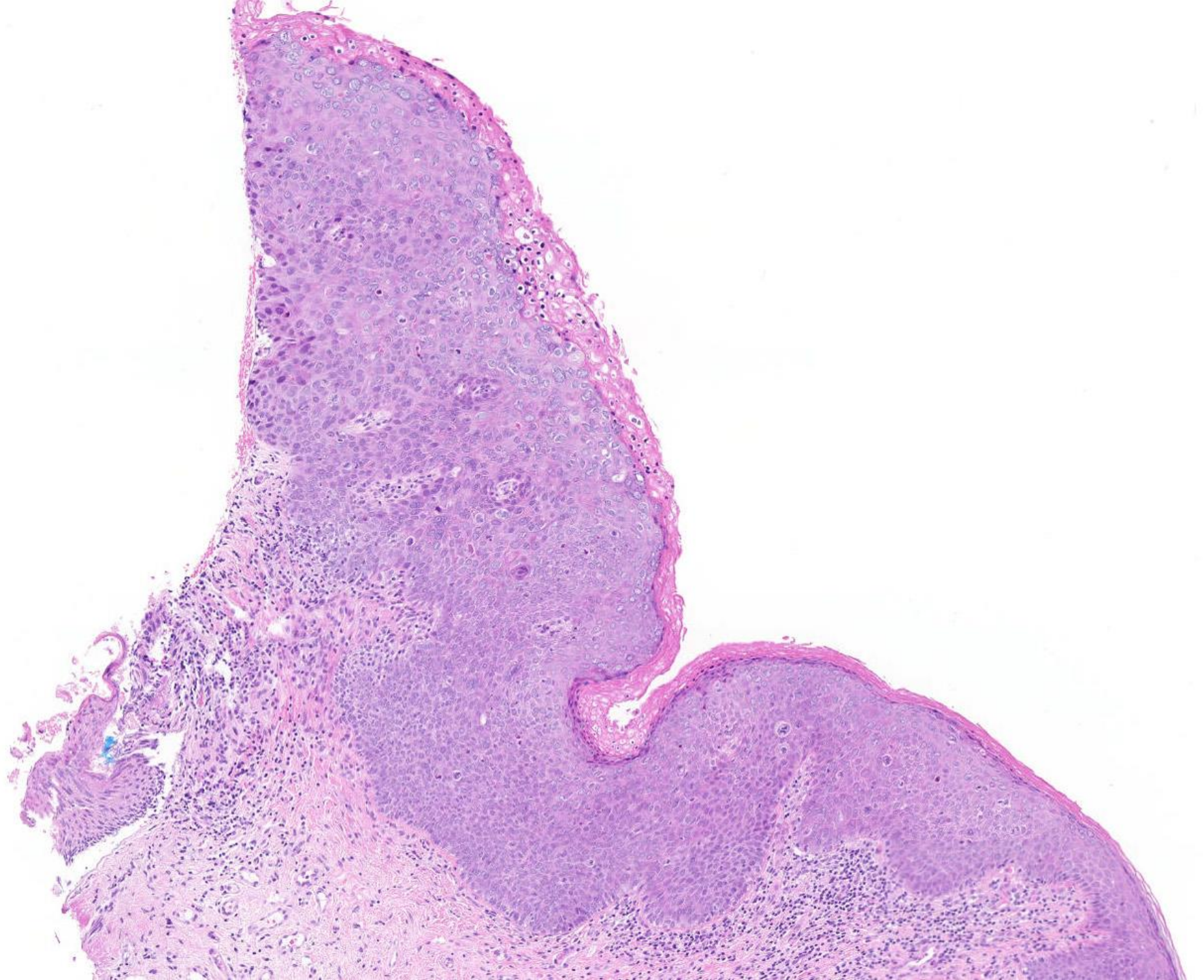
Edinburgh, UK

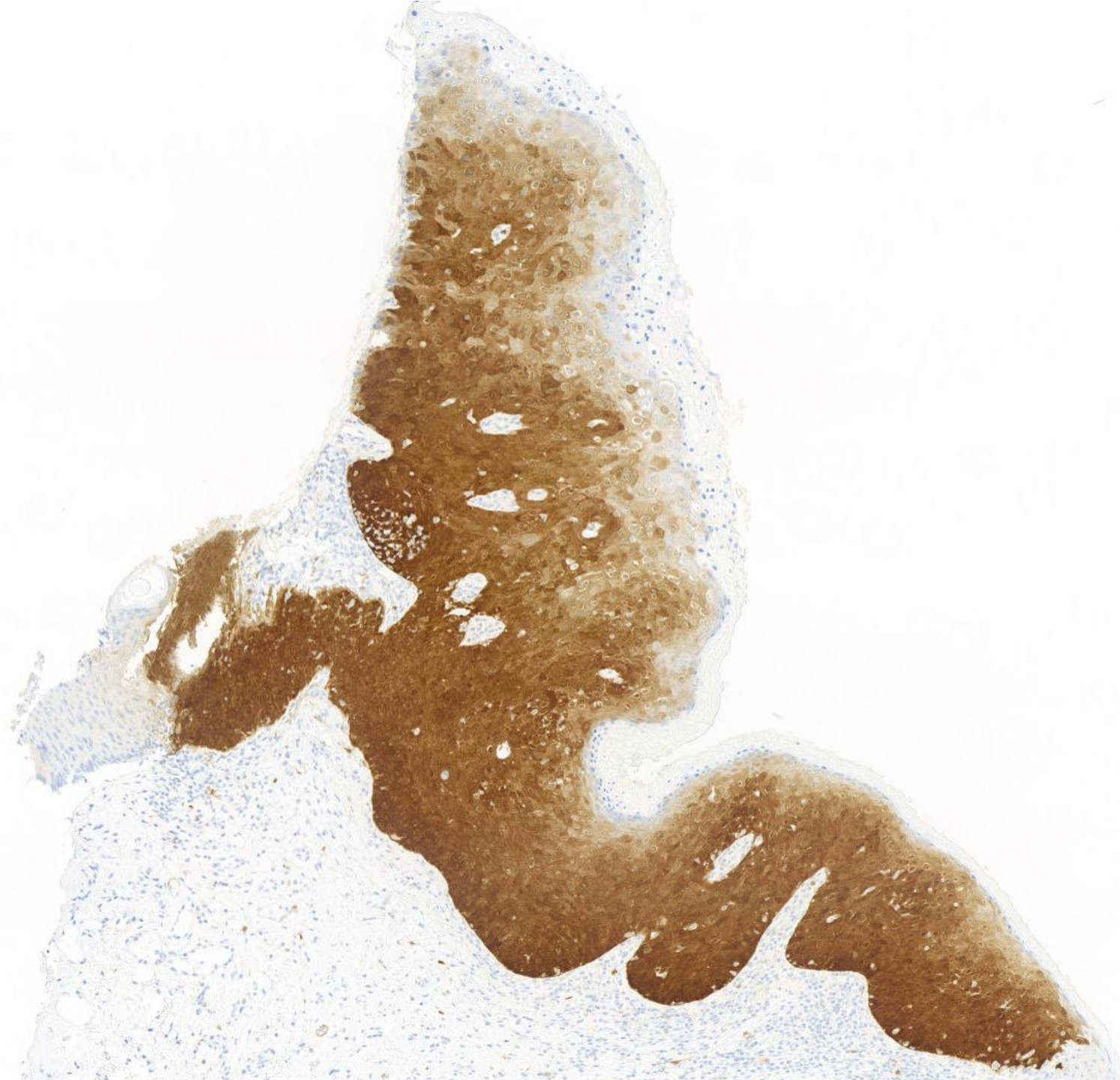
Case 1

- 64 year old female with a history of VIN 3 / HSIL
- New lesions on left and right side of vulva. Macroscopically the biopsies had an irregular skin surface
- The slides are from right (A) and left (B) vulval lesions

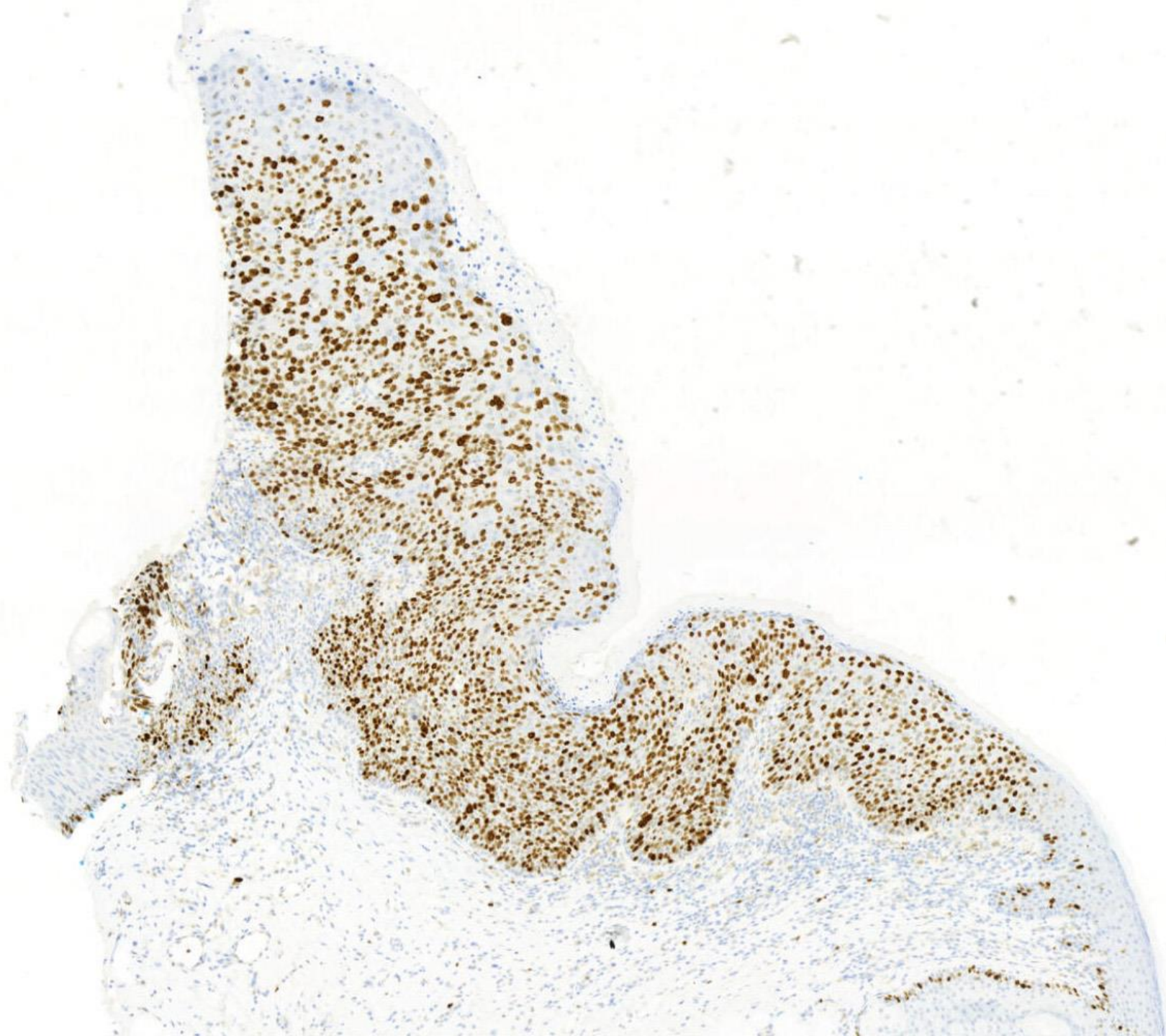




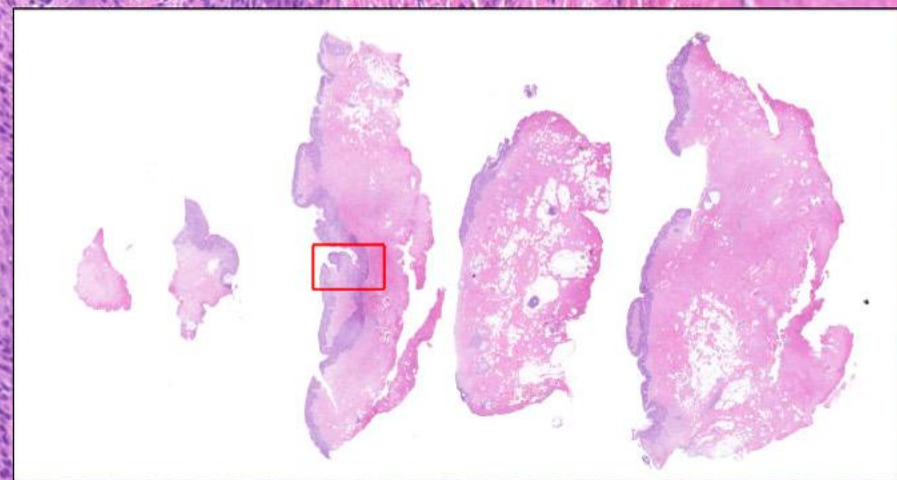
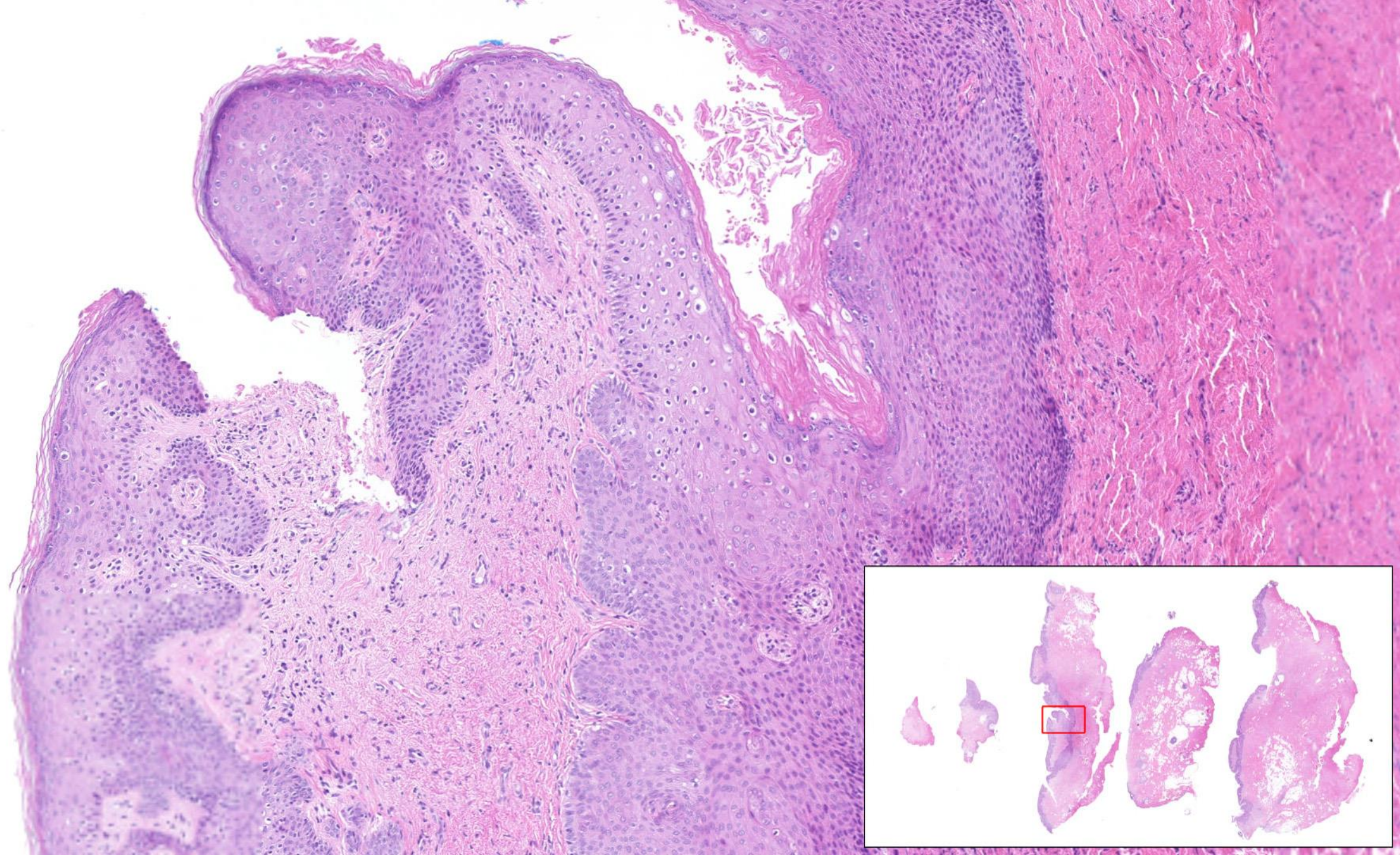


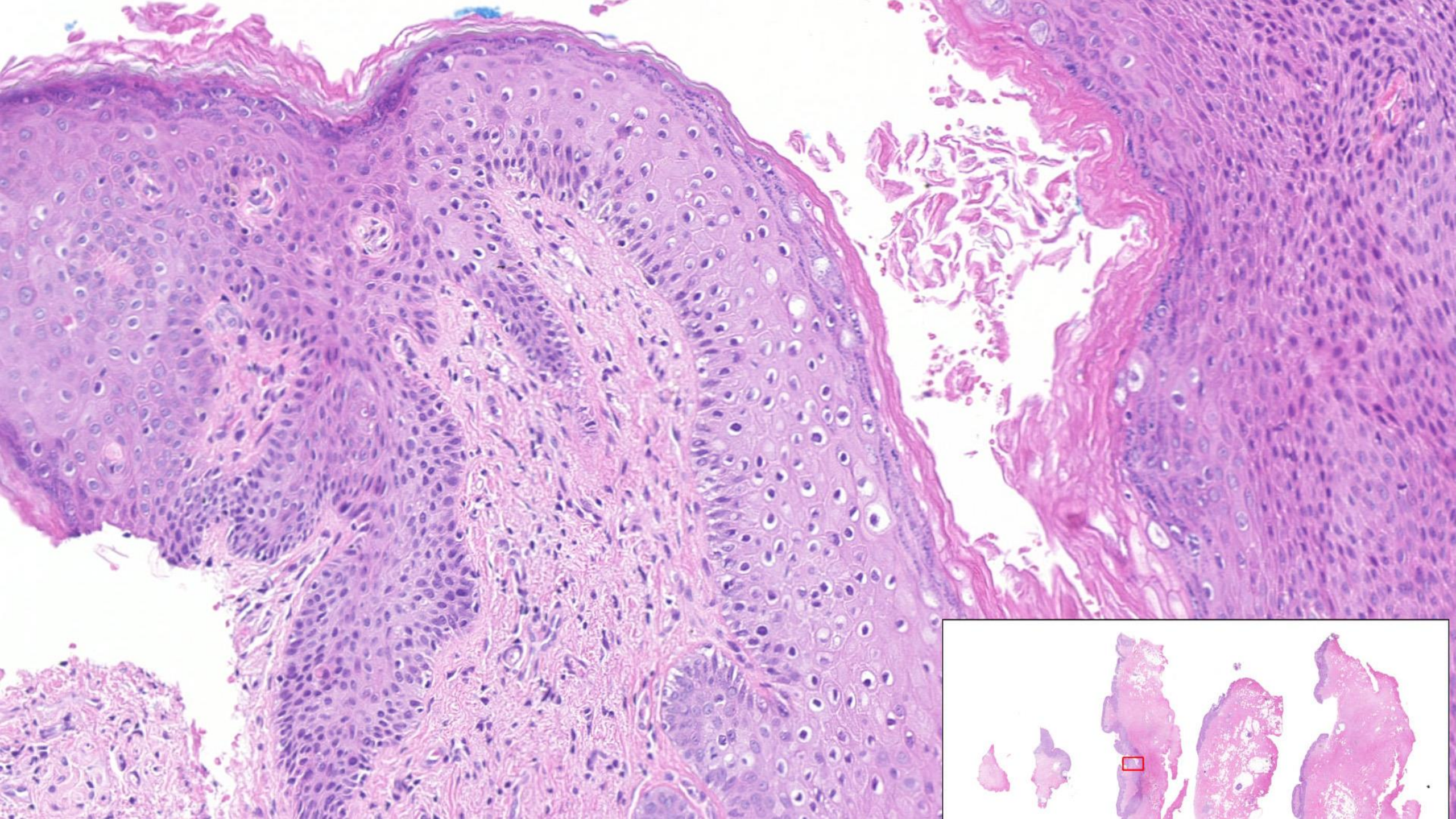


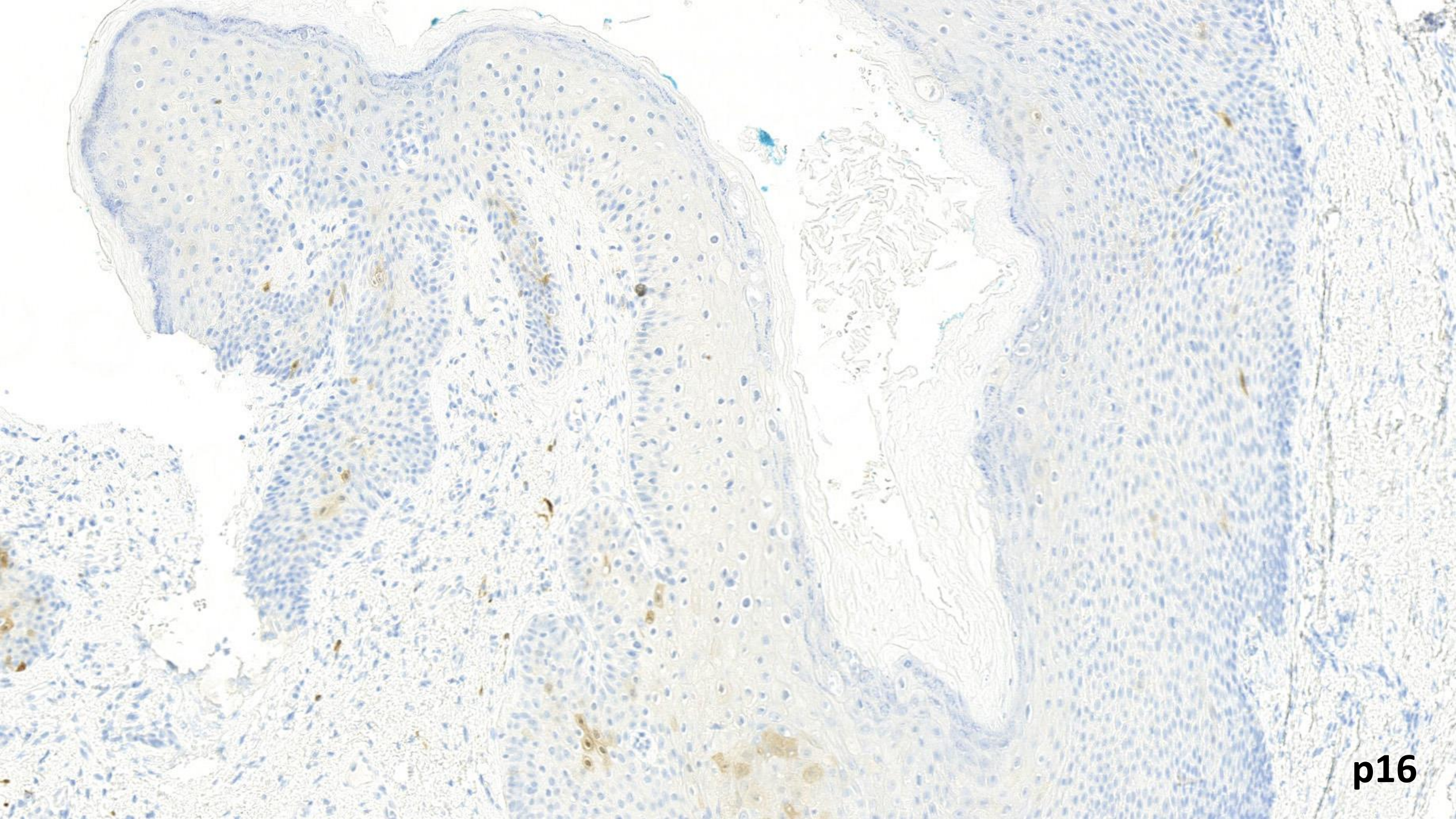
p16



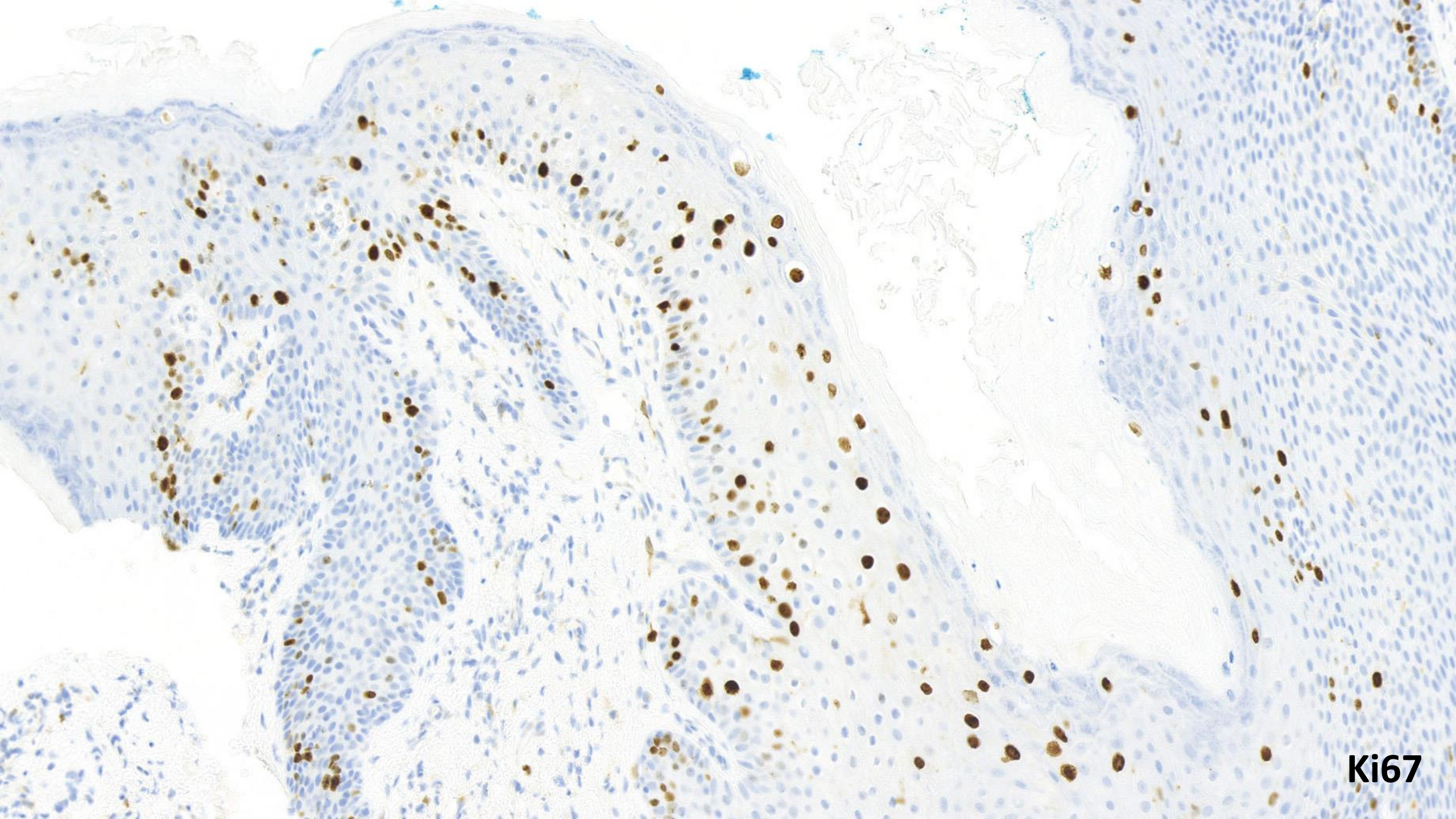
Ki67



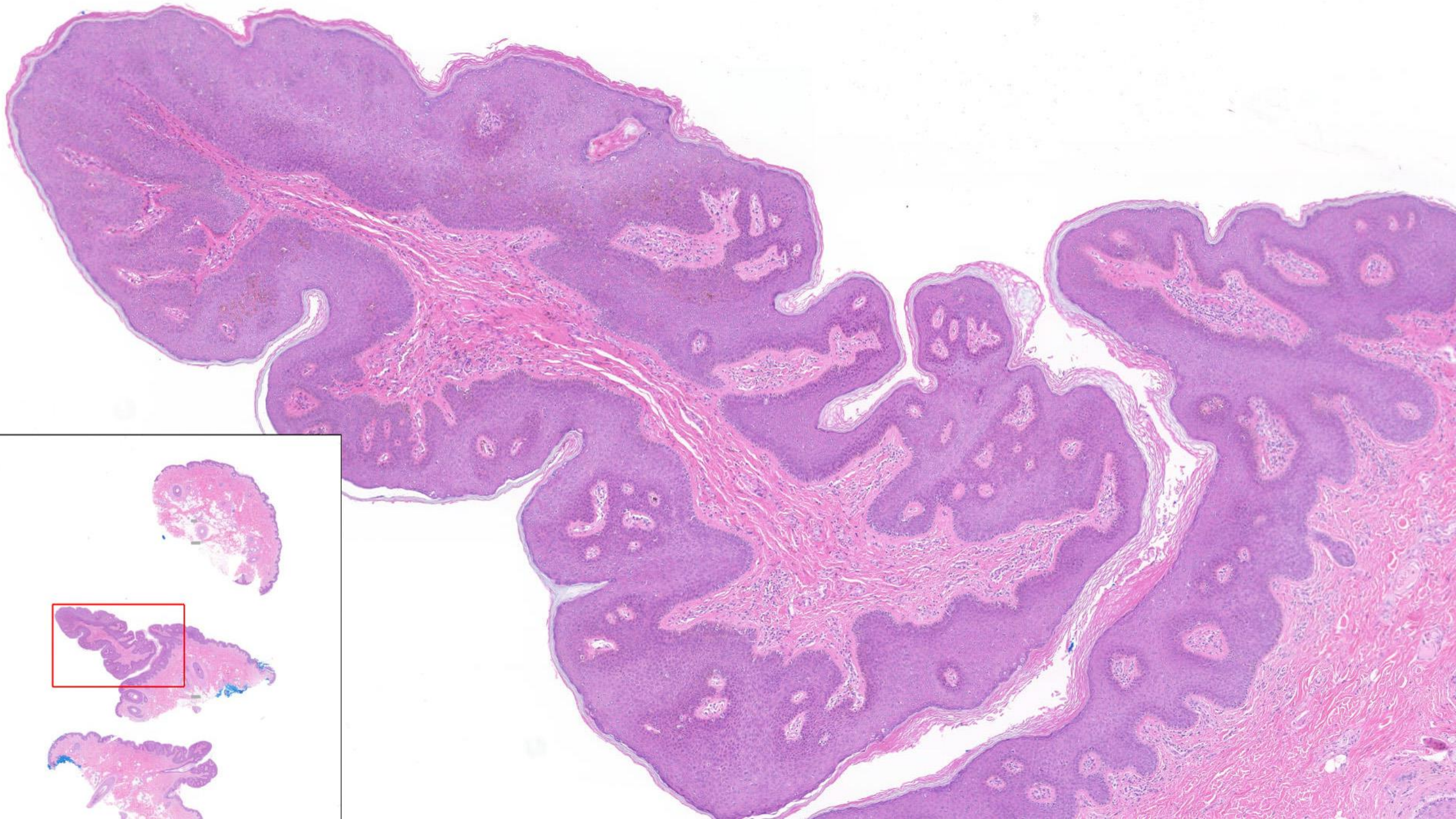




p16

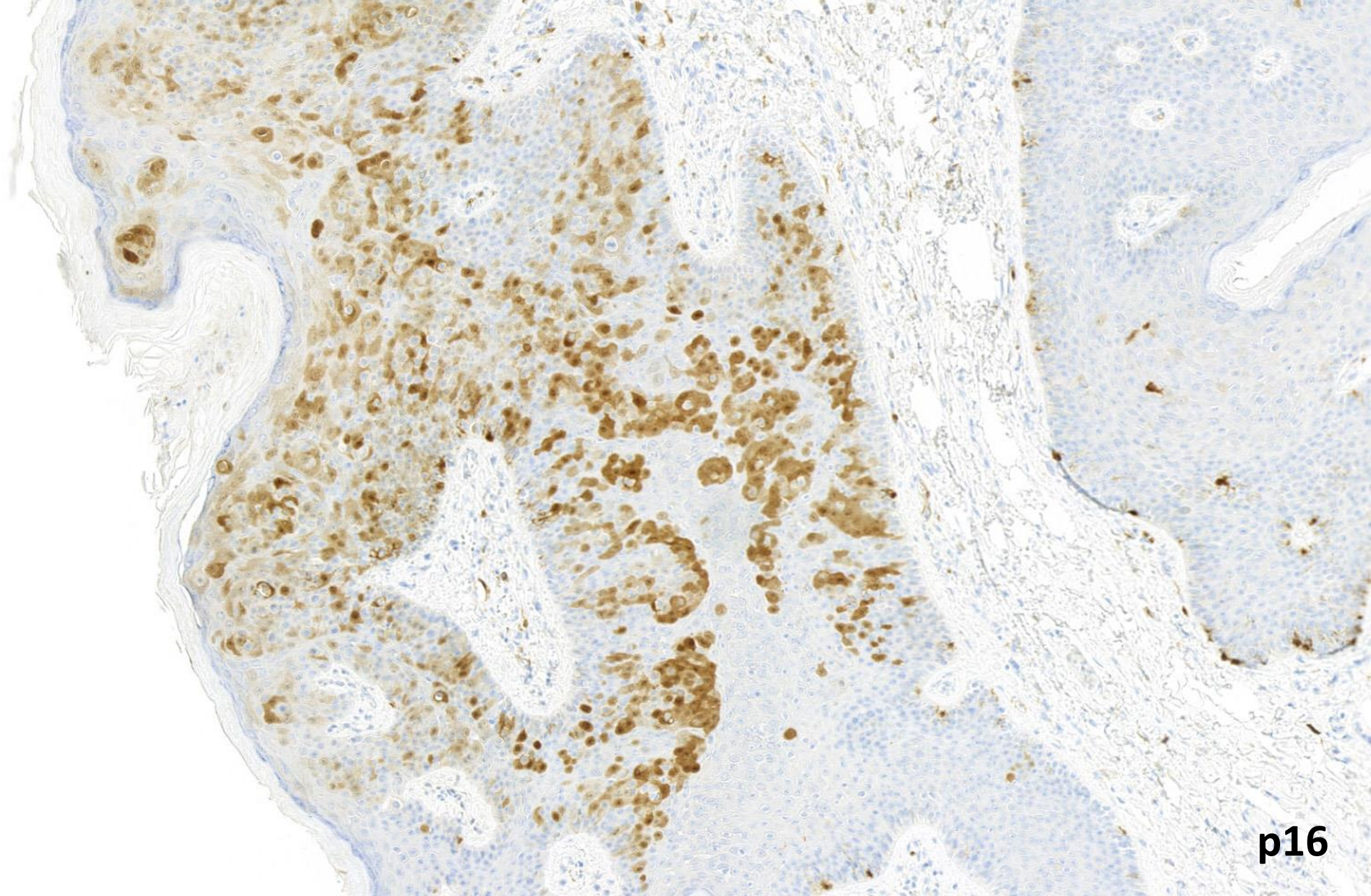


Ki67

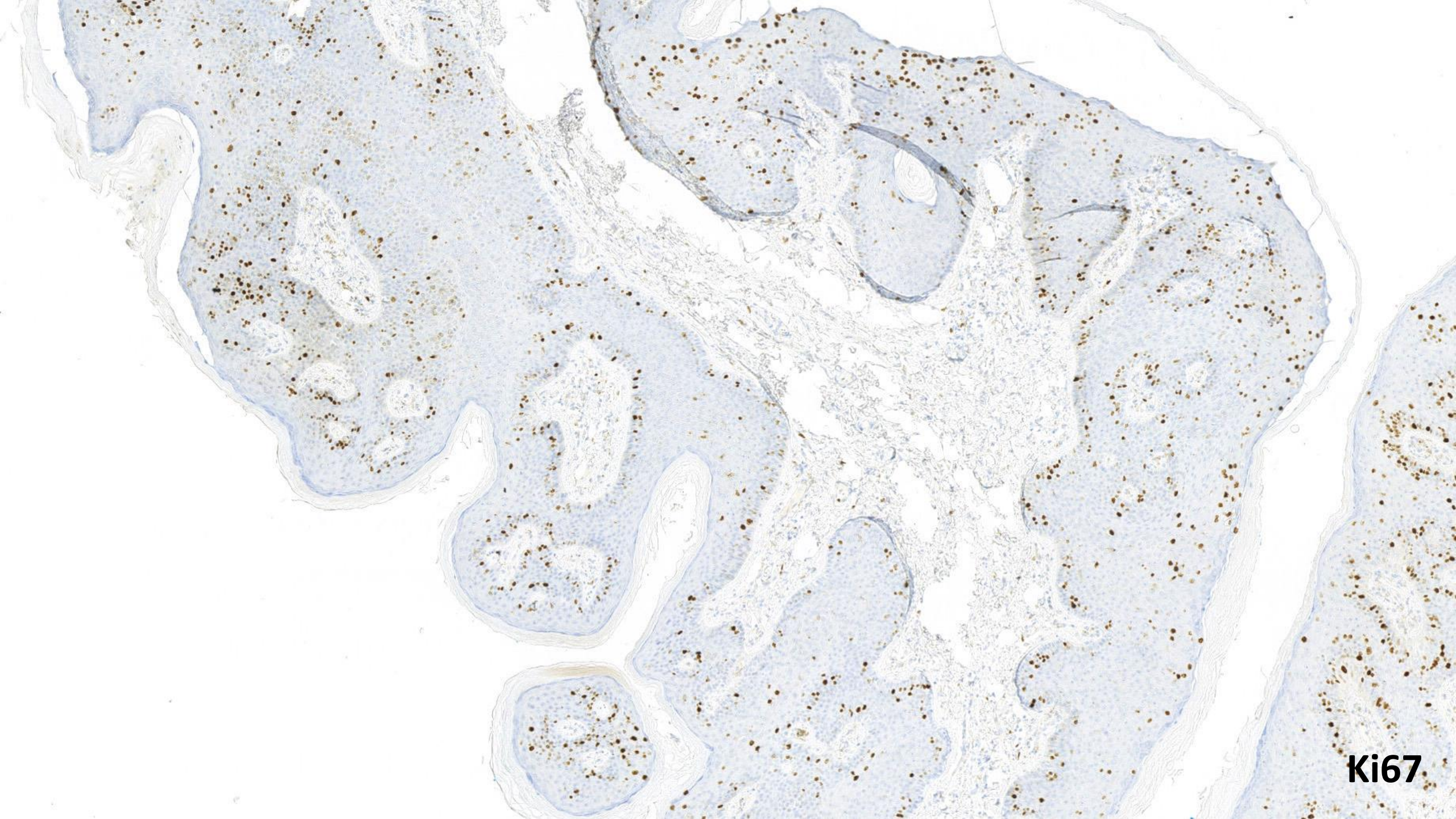




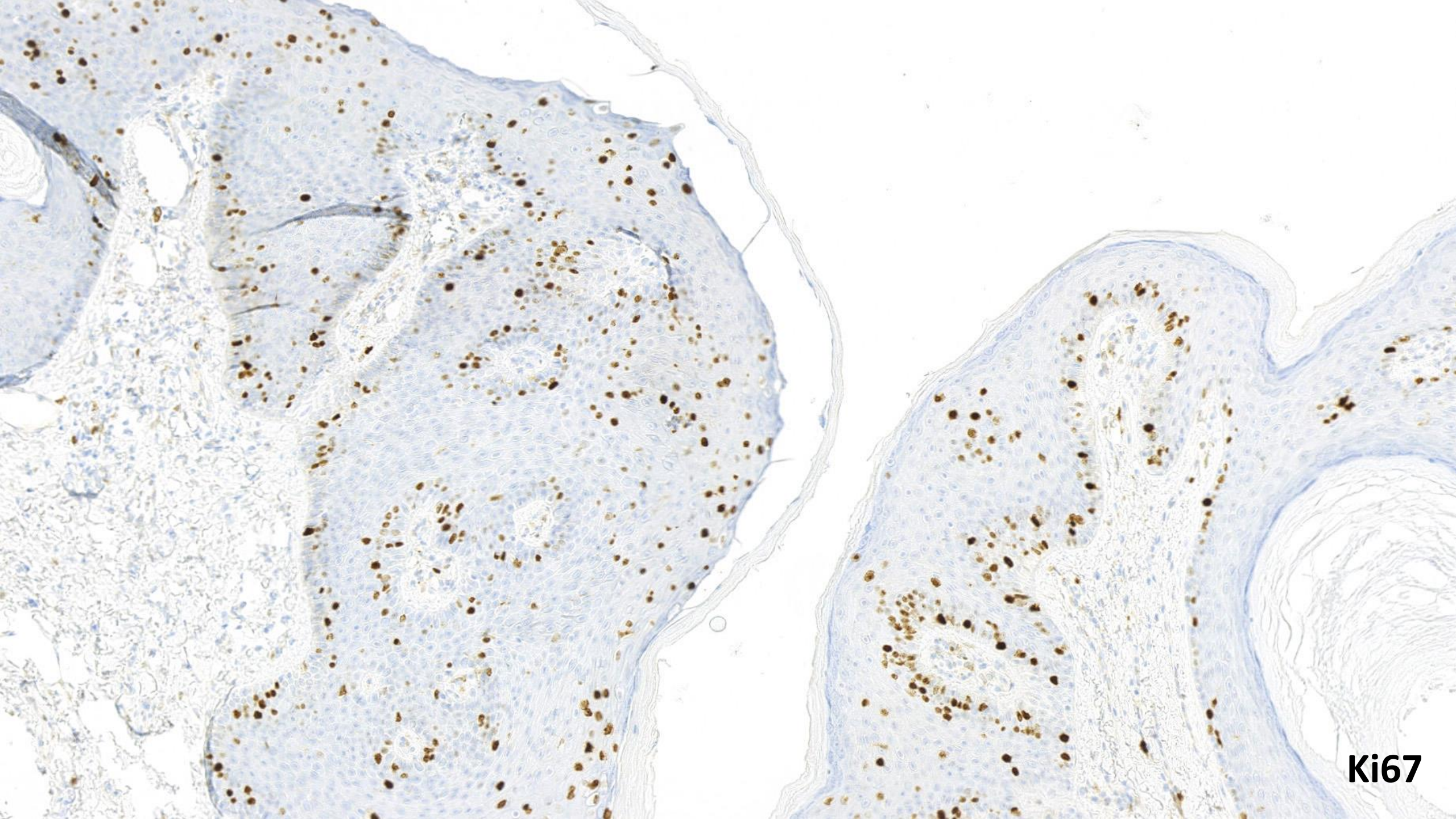
p16



p16



Ki67



Ki67

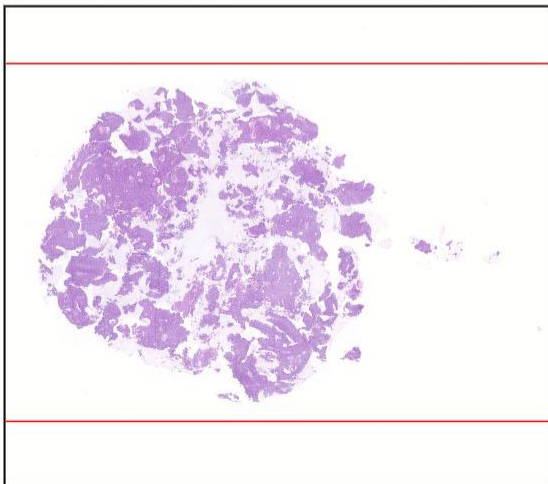
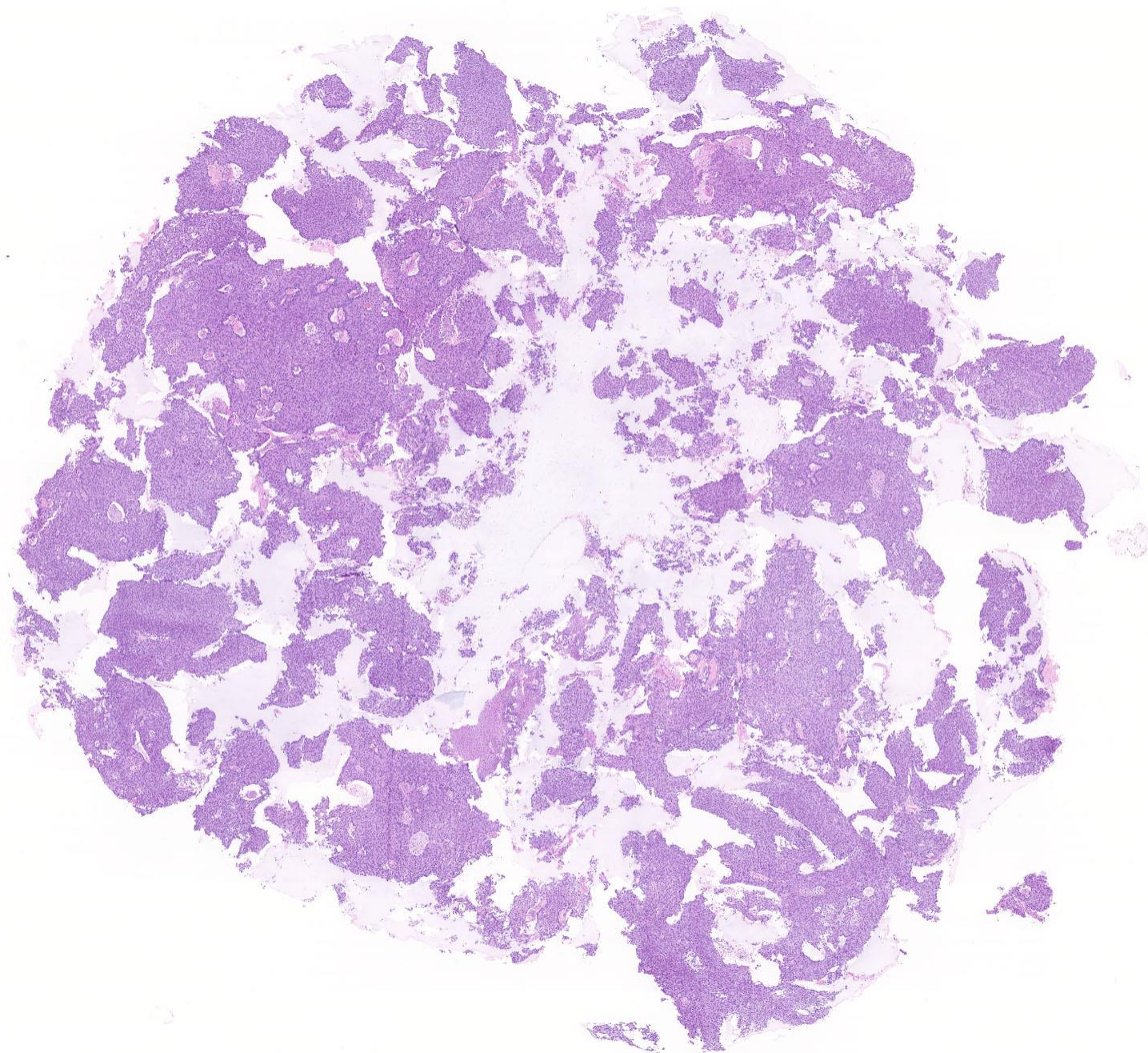
Diagnosis

Combined HSIL and Squamous cell papillomata (LSIL)

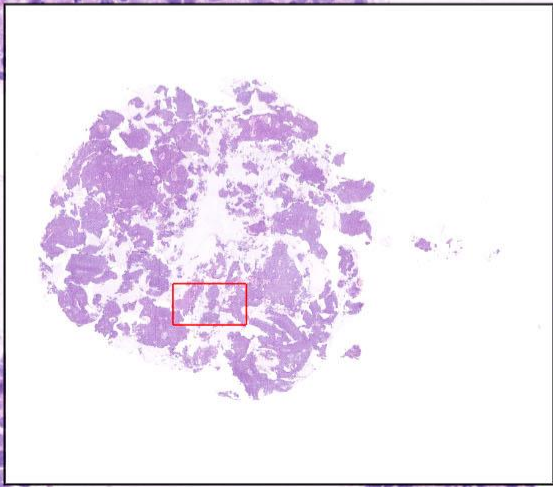
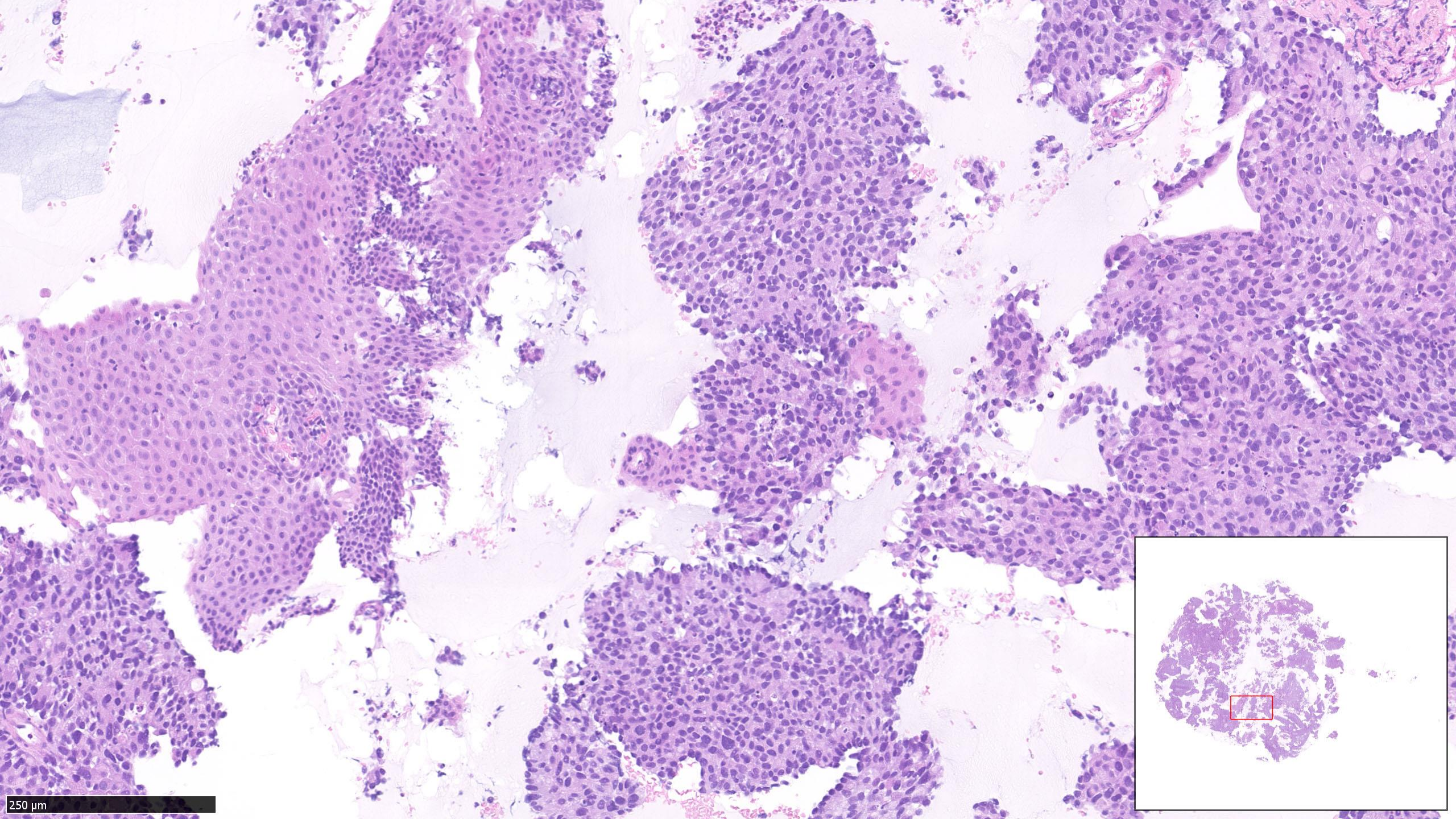
Mixed p16 staining pattern, with suprabasal Ki67 positivity in both areas, consistent with mixed high-risk and low-risk HPV infection

Case 2

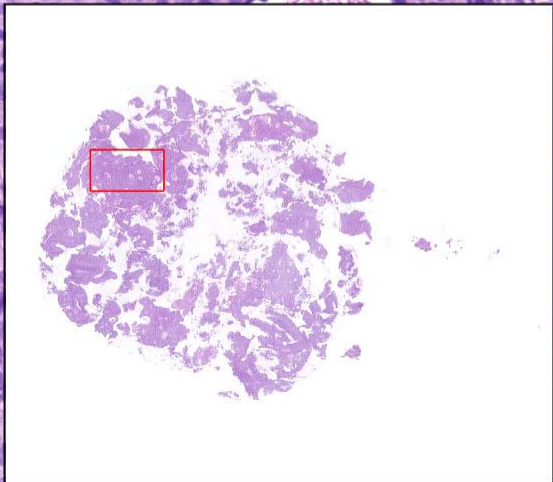
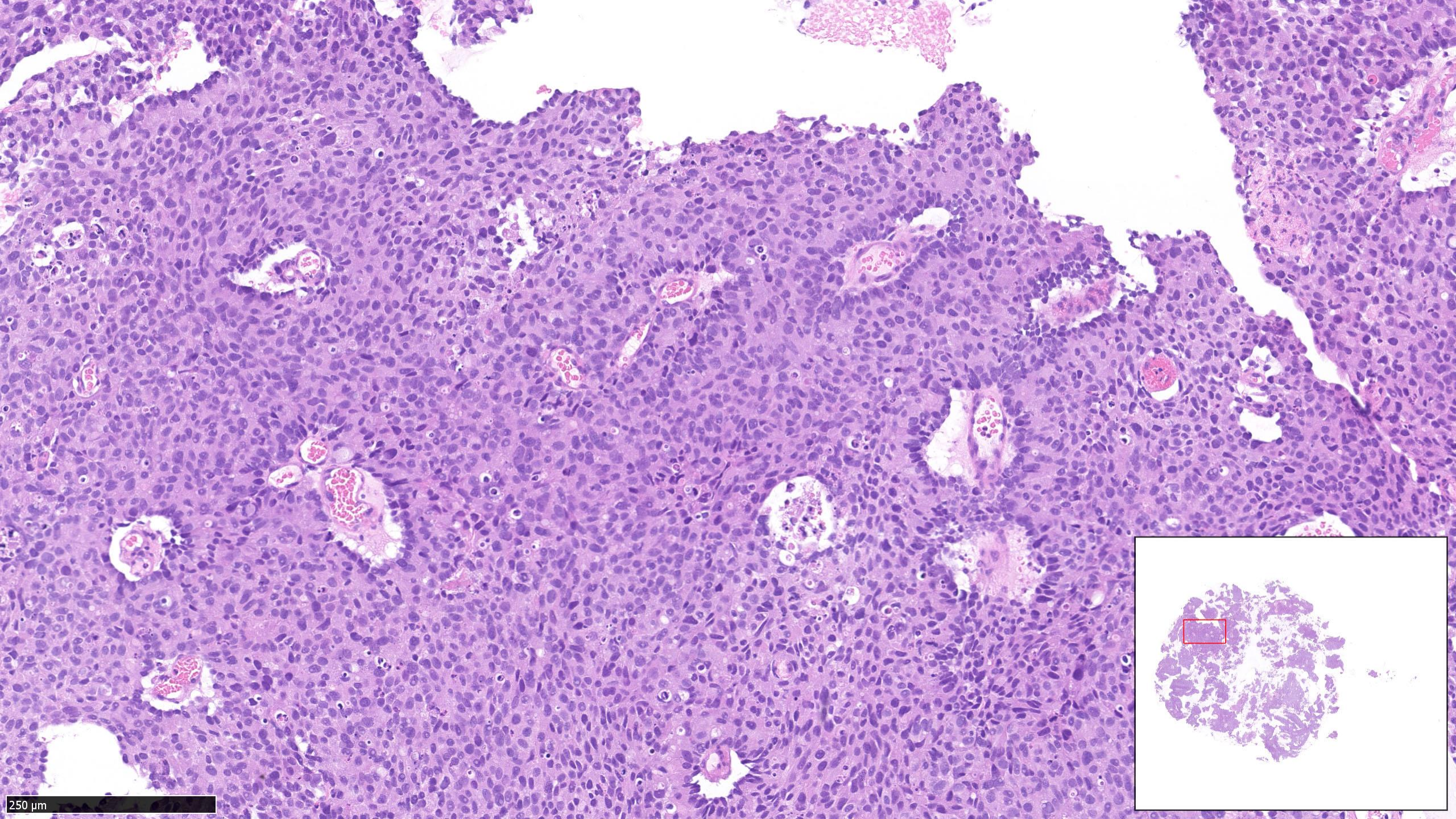
- Female aged 54
- Previously treated HSIL (CIN 2/CIN 3)
- 2 months of postcoital bleeding
- Mass in vagina, suspicious of malignancy
- Vaginal biopsy and subsequent LETZ of cervix



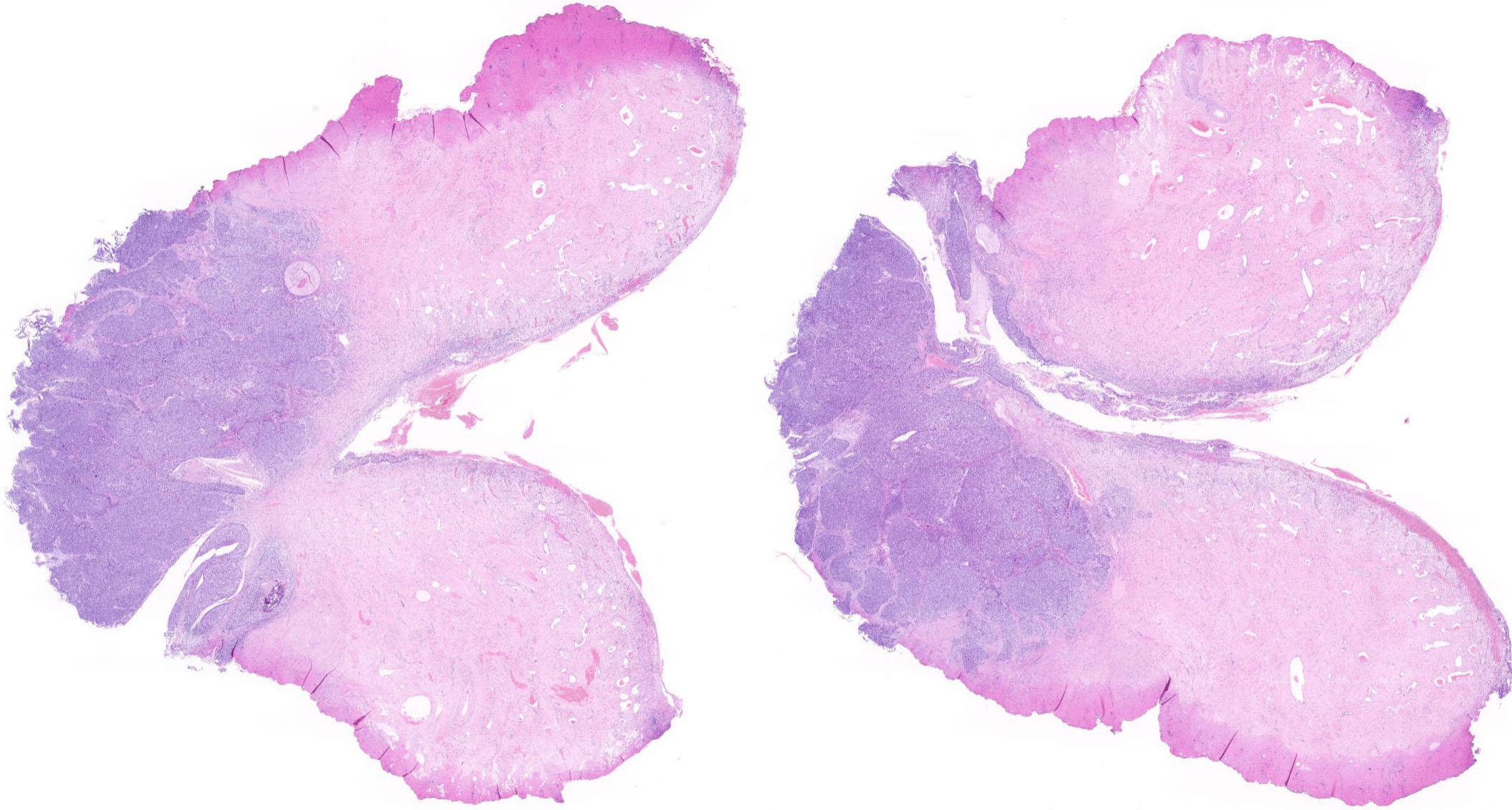
2.5 mm

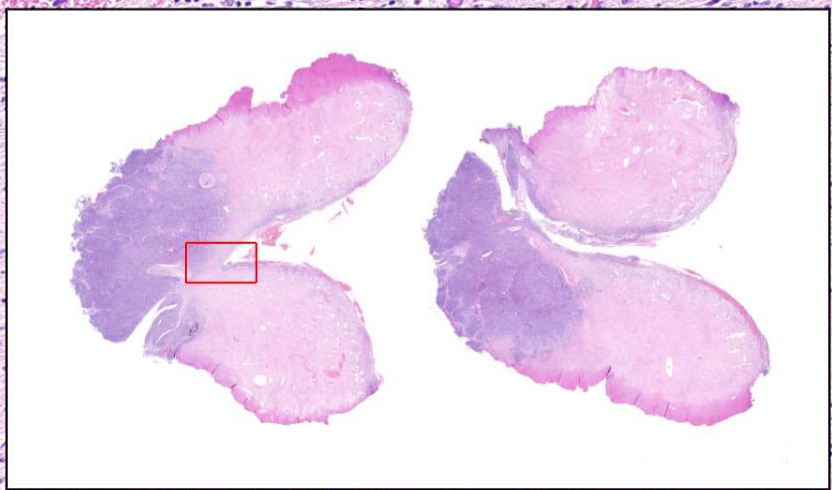
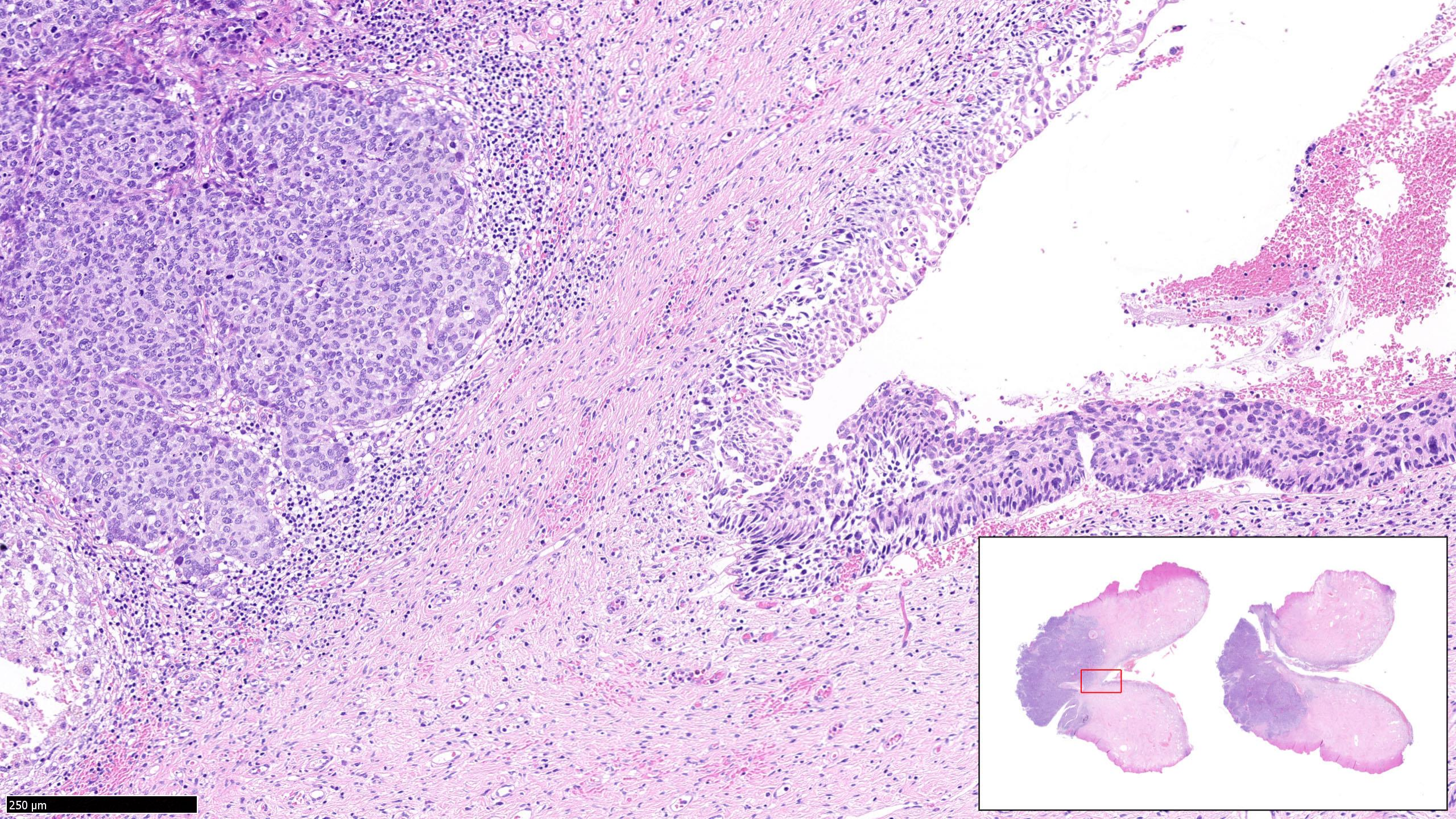


250 μ m

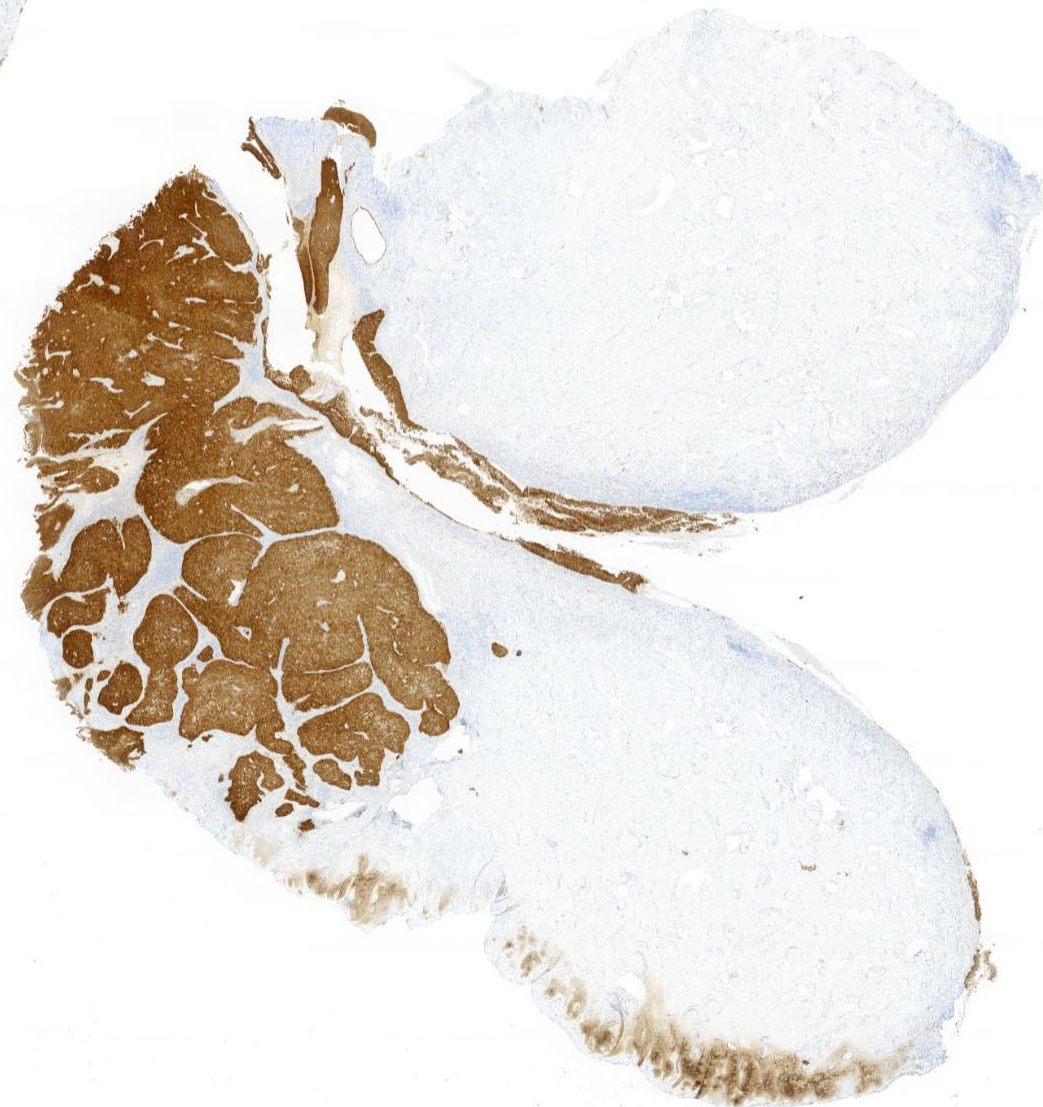
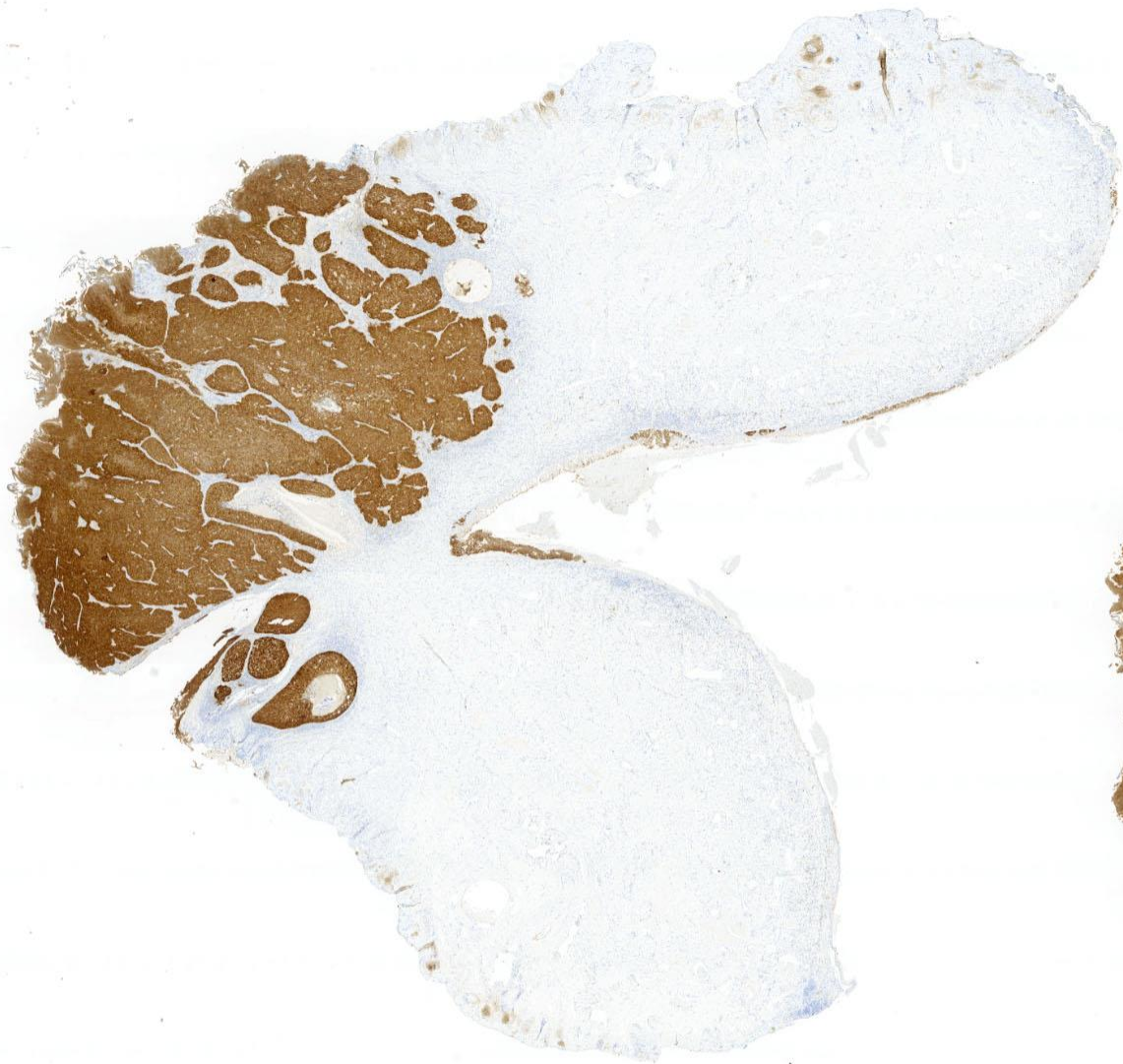


250 μ m

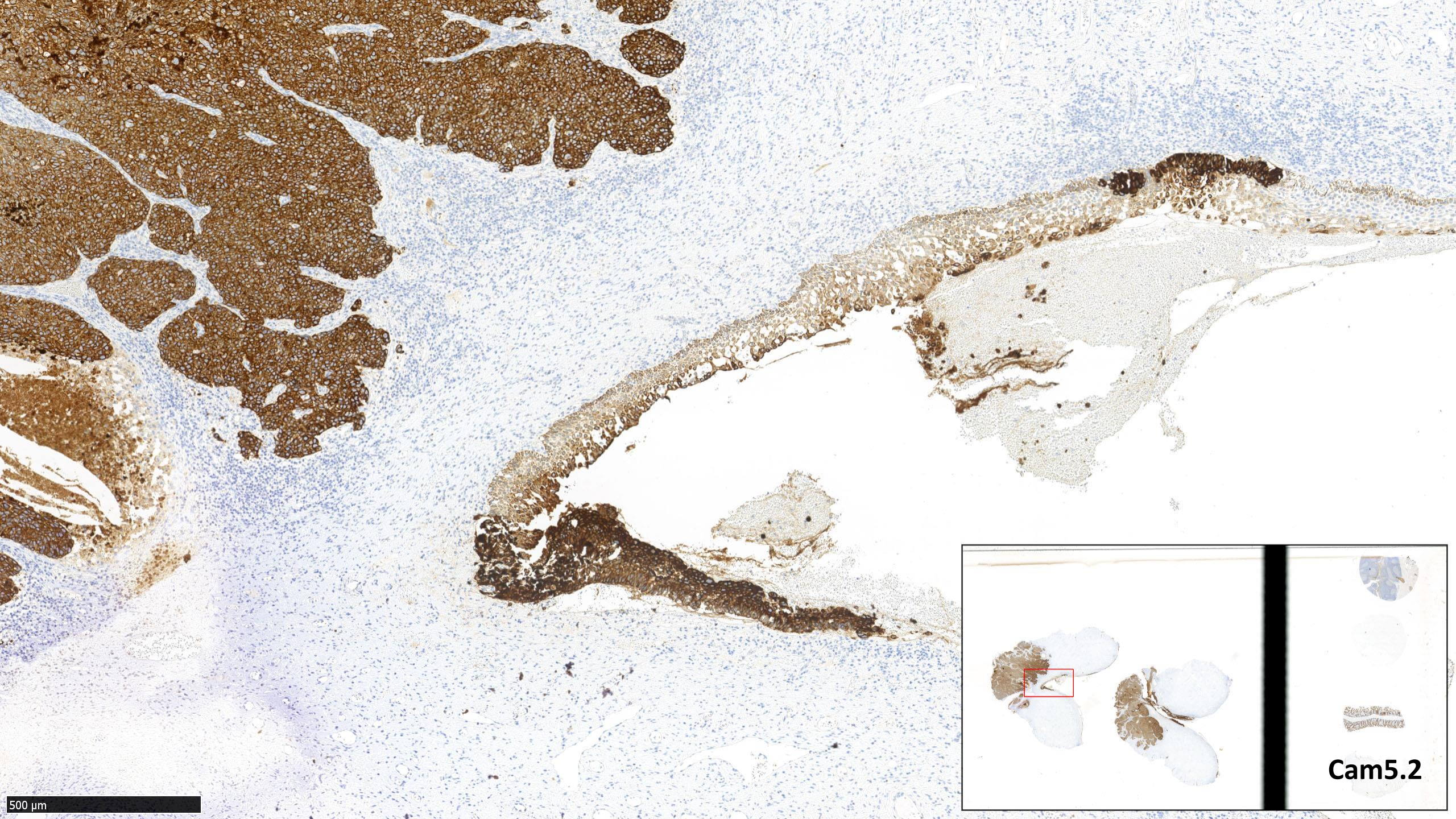




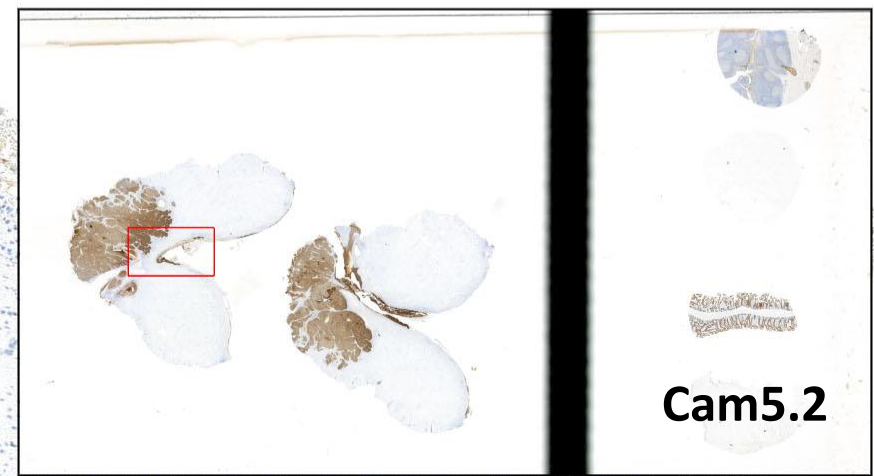
250 μ m



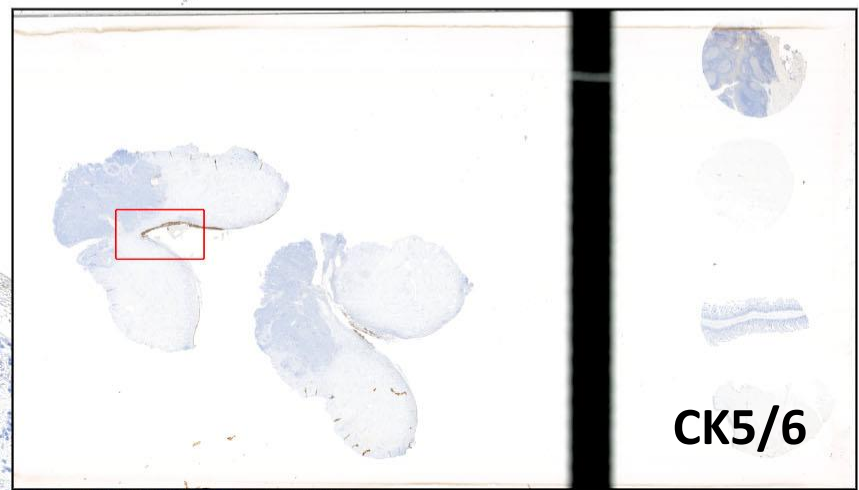
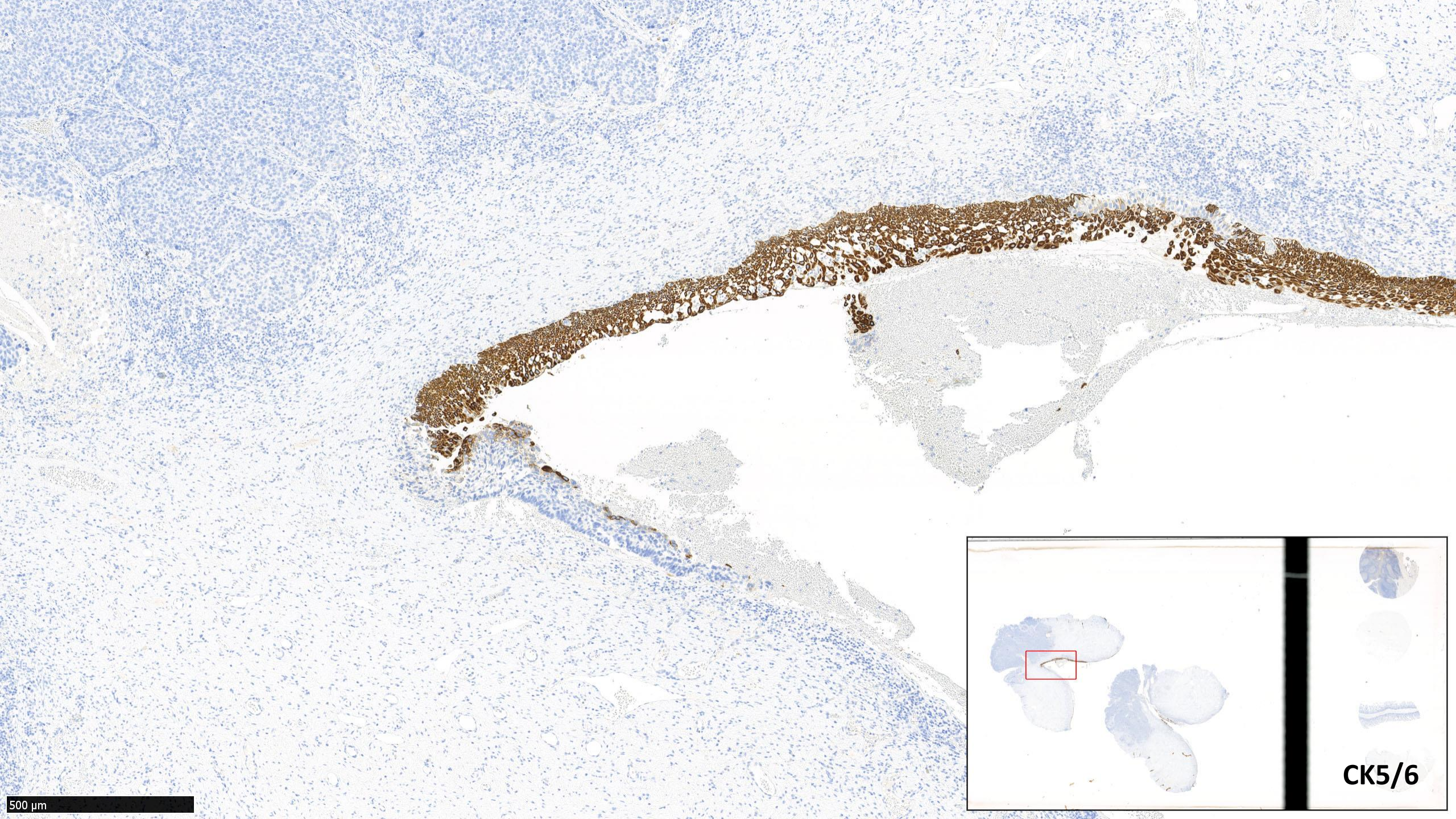
p16



500 μ m

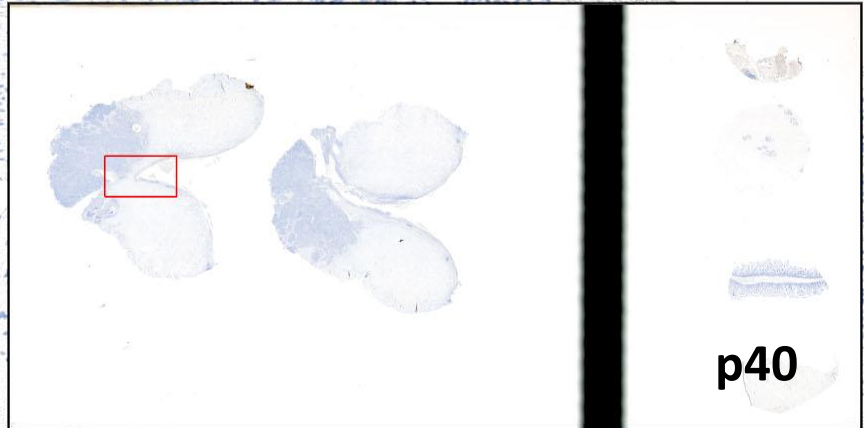
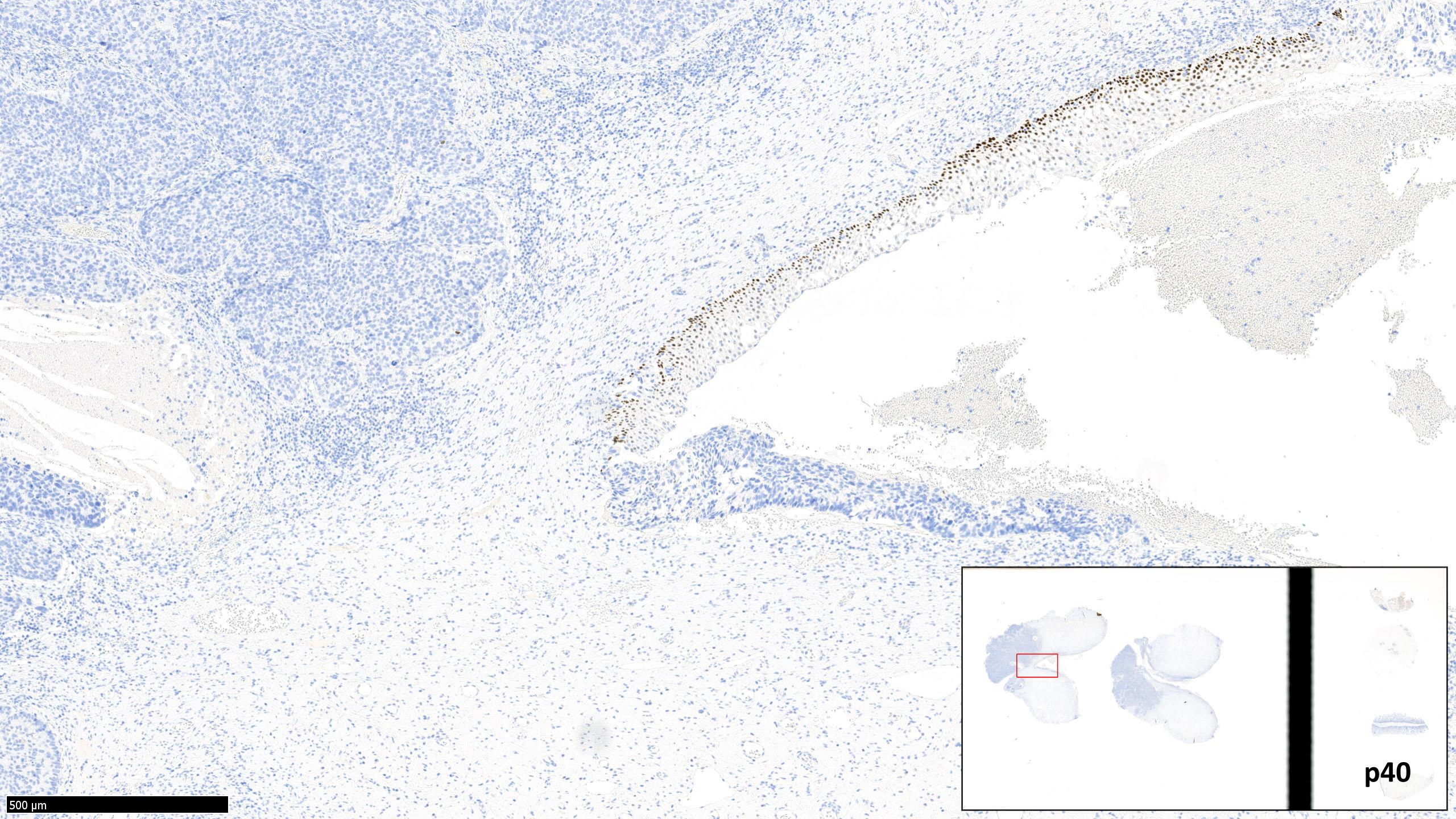


Cam5.2



CK5/6

500 μ m



500 μ m

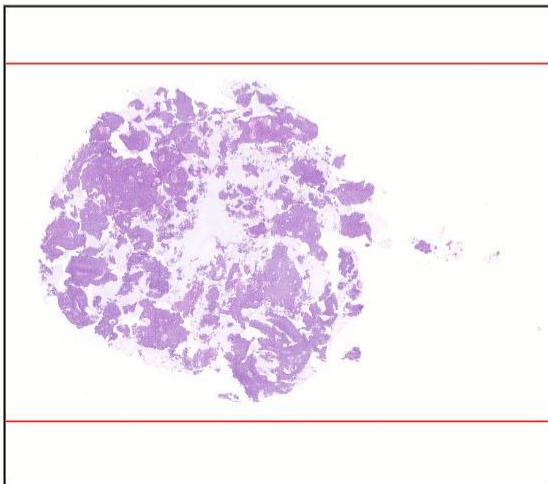
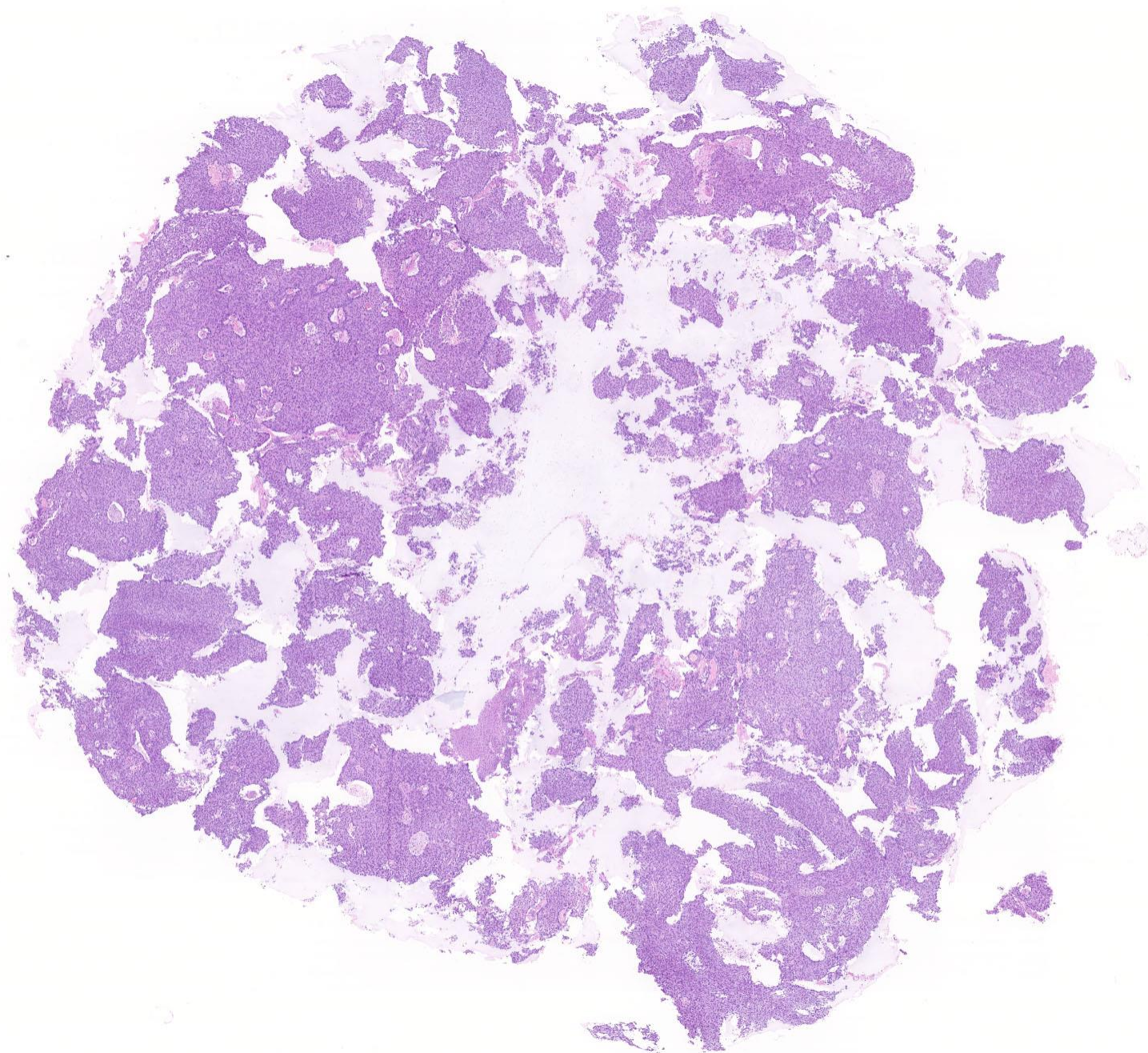
p40

Diagnosis

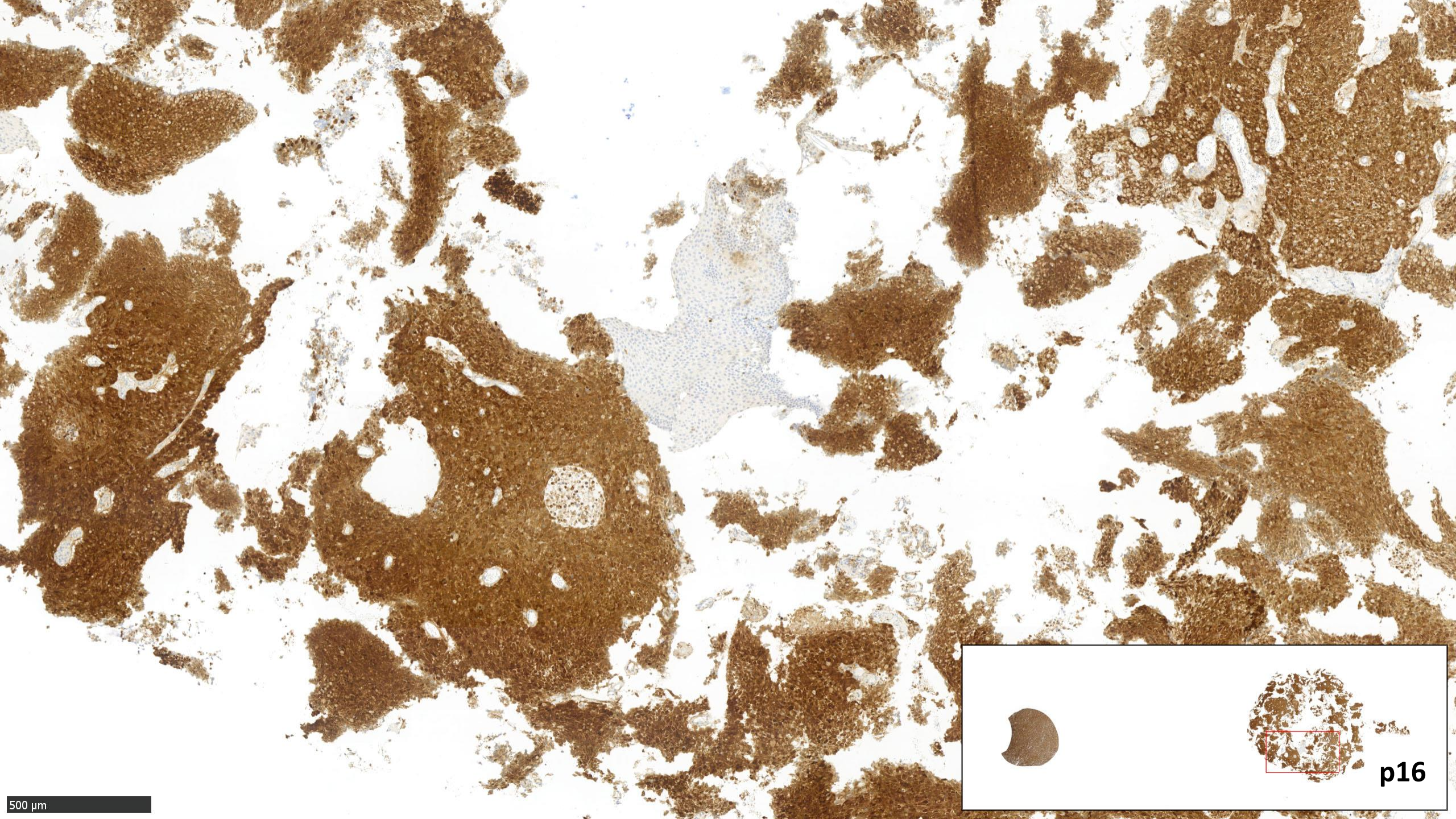
Invasive Stratified Mucin-producing Carcinoma and
Stratified Mucin-producing Intraepithelial Lesion (SMILE)

Lastra R et al Am J Surg Pathol. 2016; 40:262–9

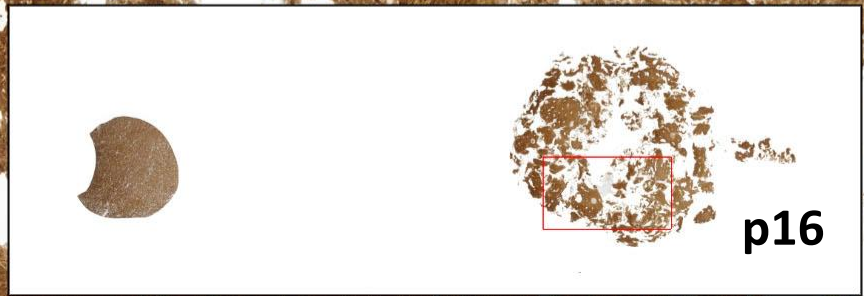
Onishi J et al Hum Pathol. 2016 55:174–81



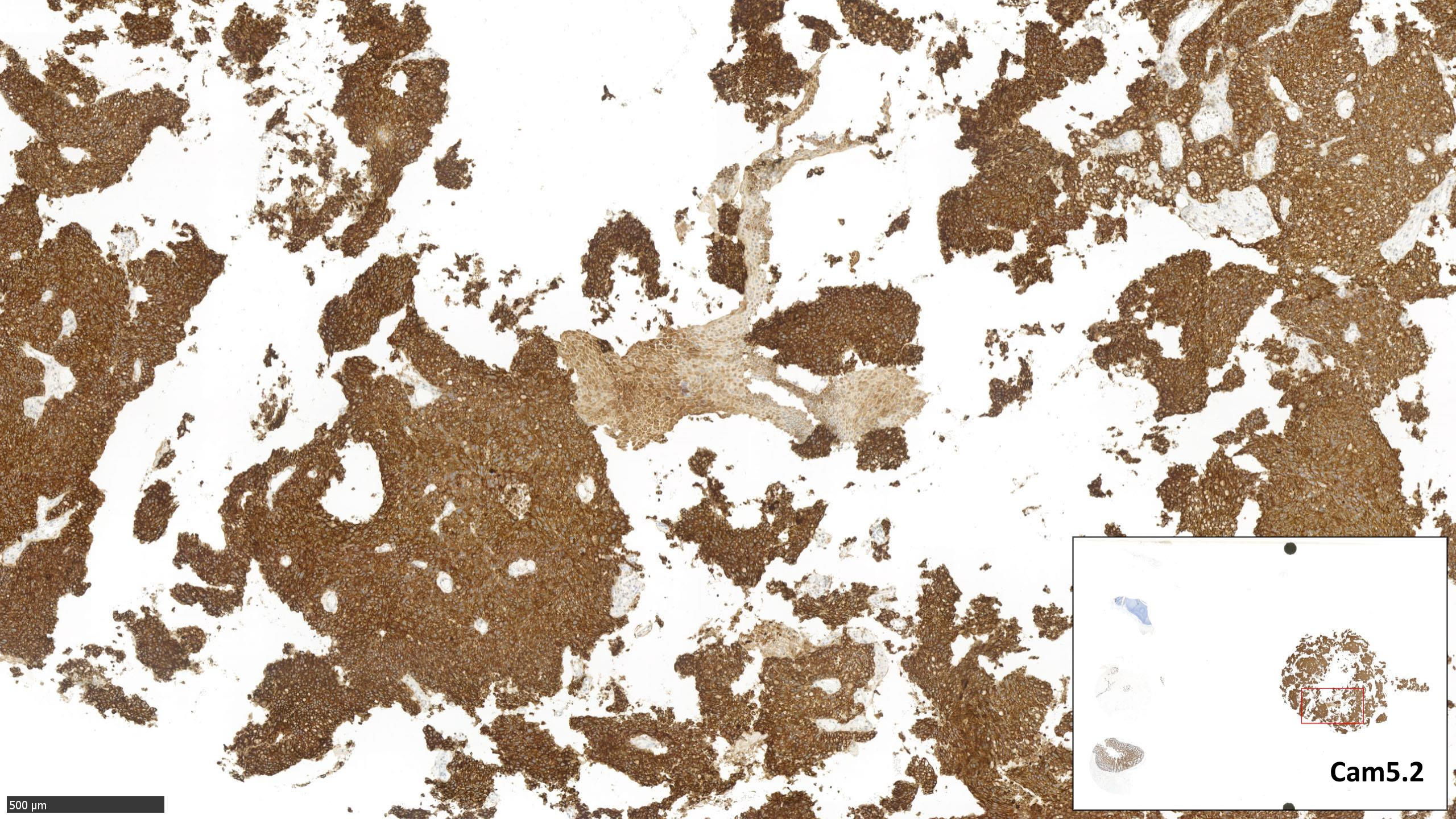
2.5 mm



500 μ m

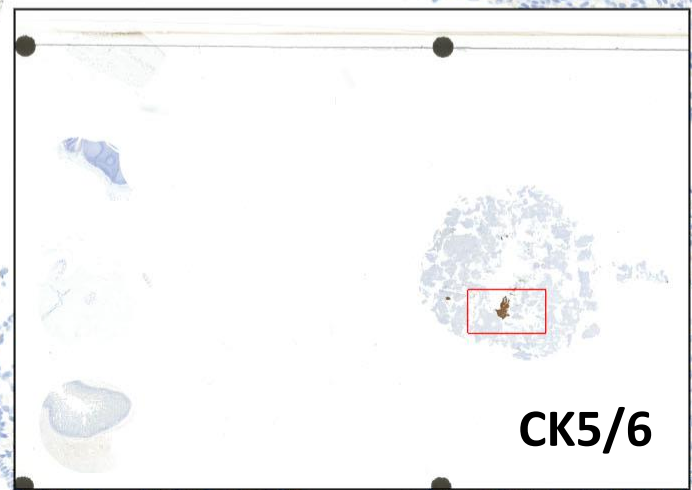
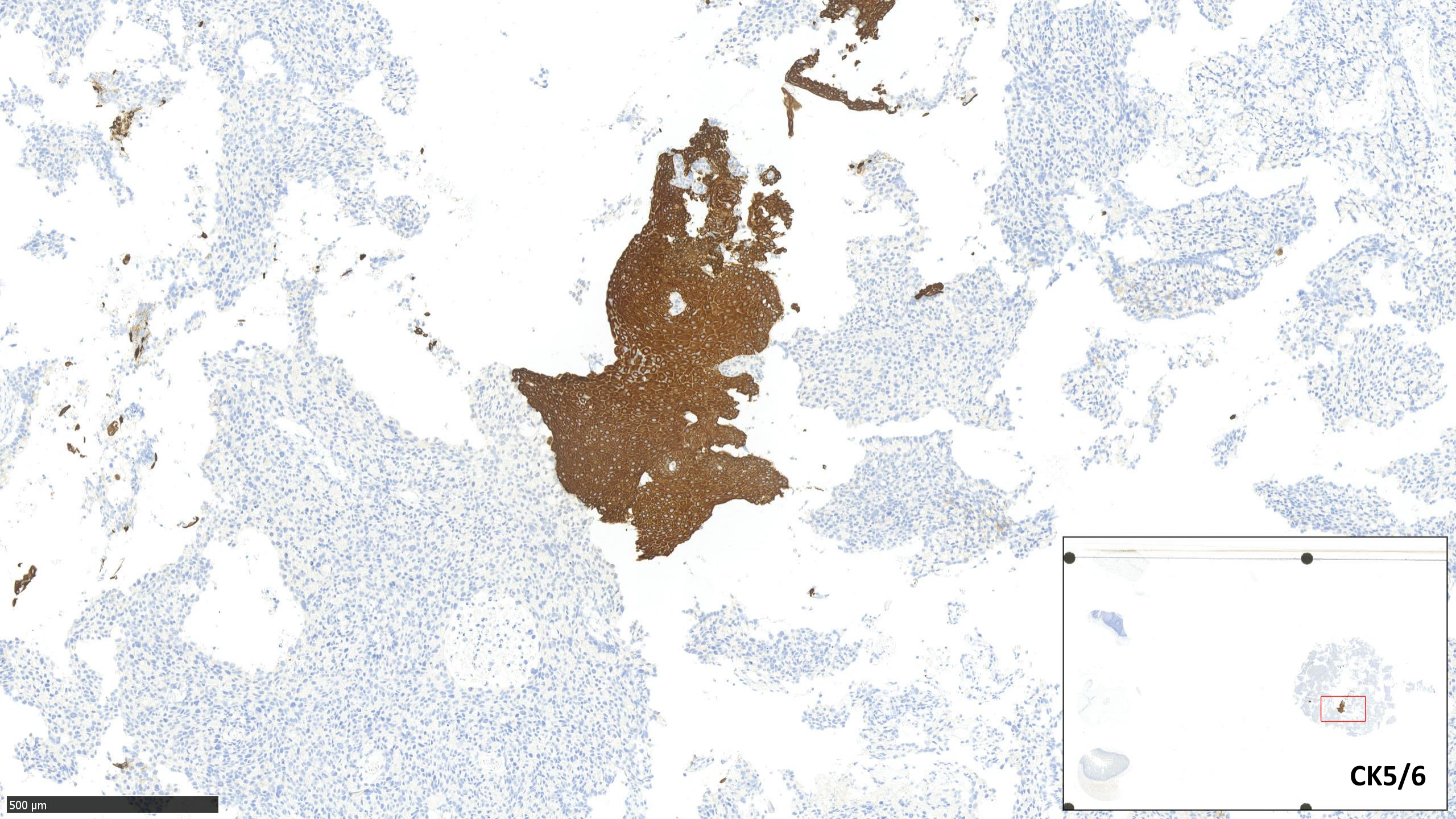


p16



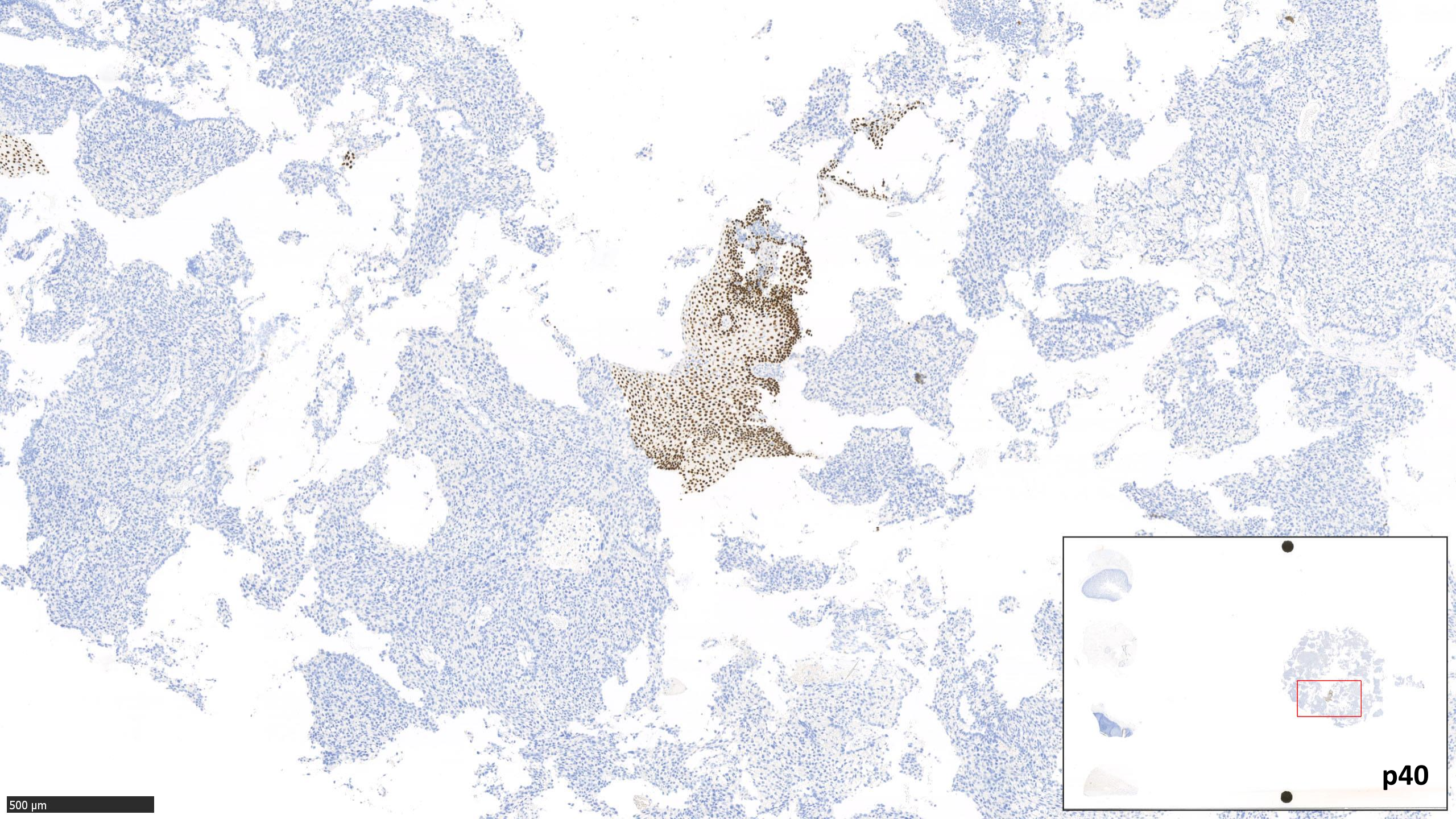
Cam5.2

500 μ m

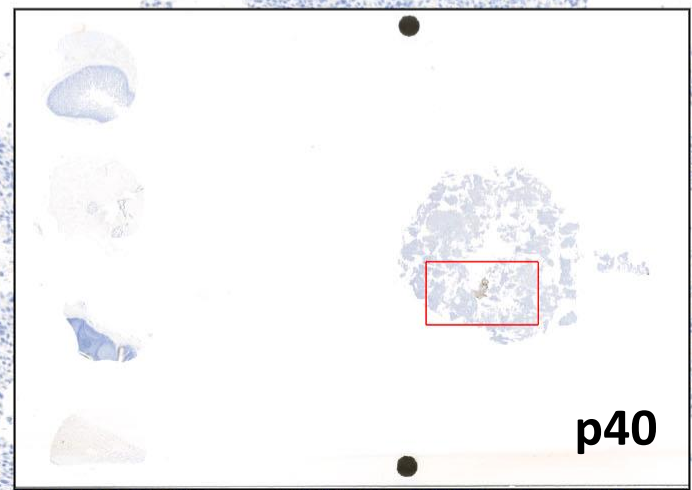


CK5/6

500 μm



500 μ m



p40

SMILE and ISMC

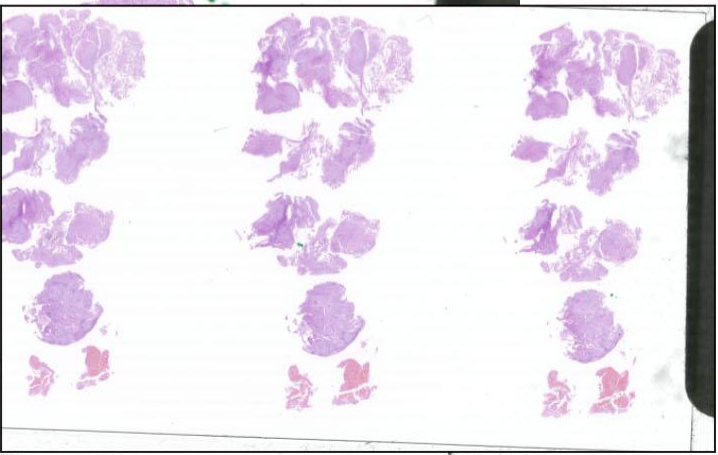
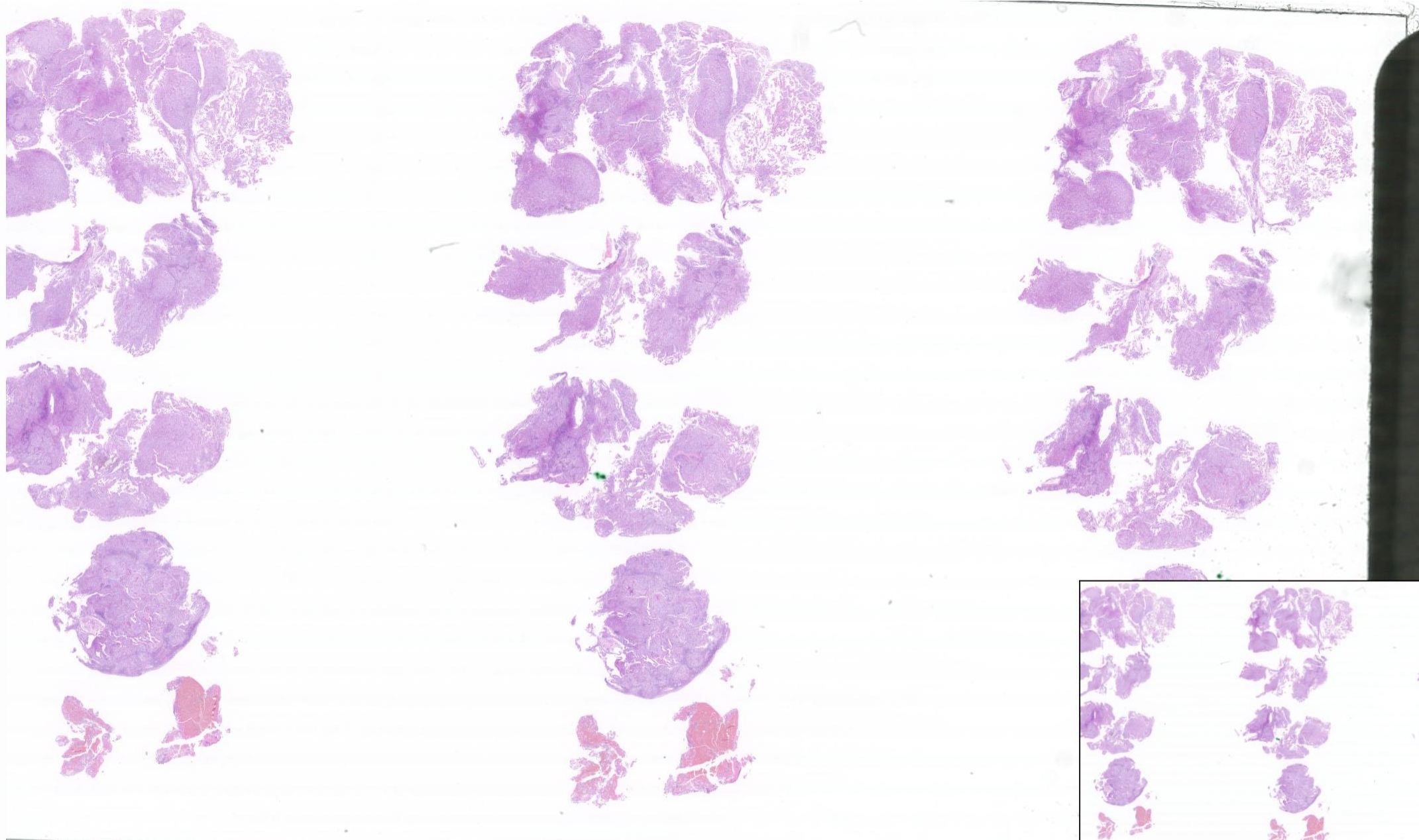
- Variant patterns of adenocarcinoma in situ, HPV-associated and adenocarcinoma, HPV-associated, mucinous type
- SMILE consists of stratified epithelium with cells containing mucin in the form of discrete vacuoles or as cytoplasmic clearing throughout all cell layers
- Nuclear atypia, hyperchromasia, mitoses and apoptotic bodies are usually present
- p16 immunohistochemistry is positive and there is a high Ki-67 proliferation index
- Often occurs in association with HSIL and/or AIS but may rarely appear as an isolated finding

SMILE and ISMC

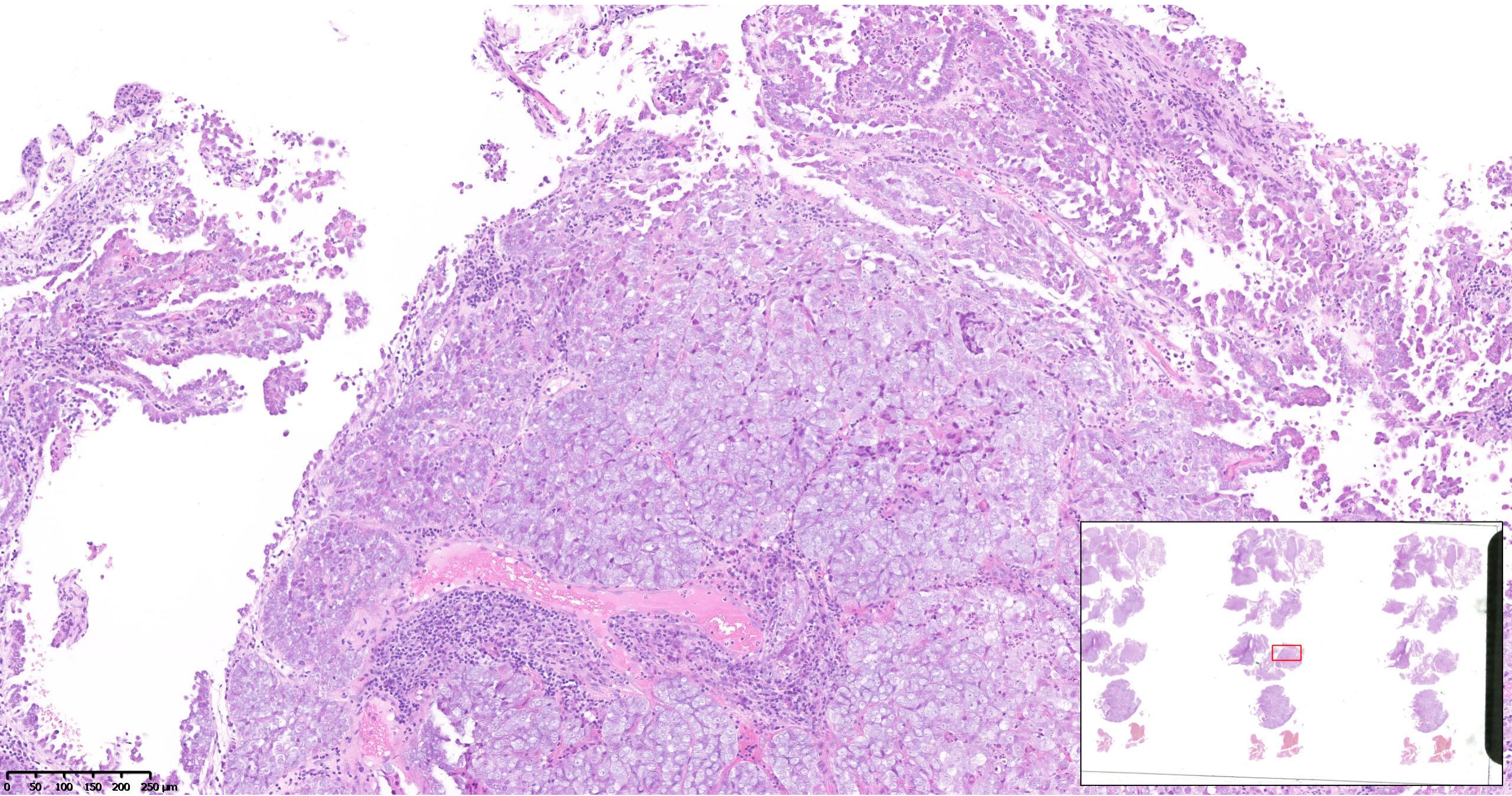
- 445 patients with HSIL, AIS, SMILE or invasive carcinoma
- 250 had only intraepithelial lesions, 195 invasive carcinomas
- 12 cases of SMILE identified
- 9 had associated carcinoma, 3 of these ISMC
- Immunoprofile (both SMILE and ISMC)
 - Cam5.2 positive – diffuse
 - p16 positive – diffuse
 - IMP3 positive – focal
 - p63 – ‘almost negative or only focally positive’

Case 3

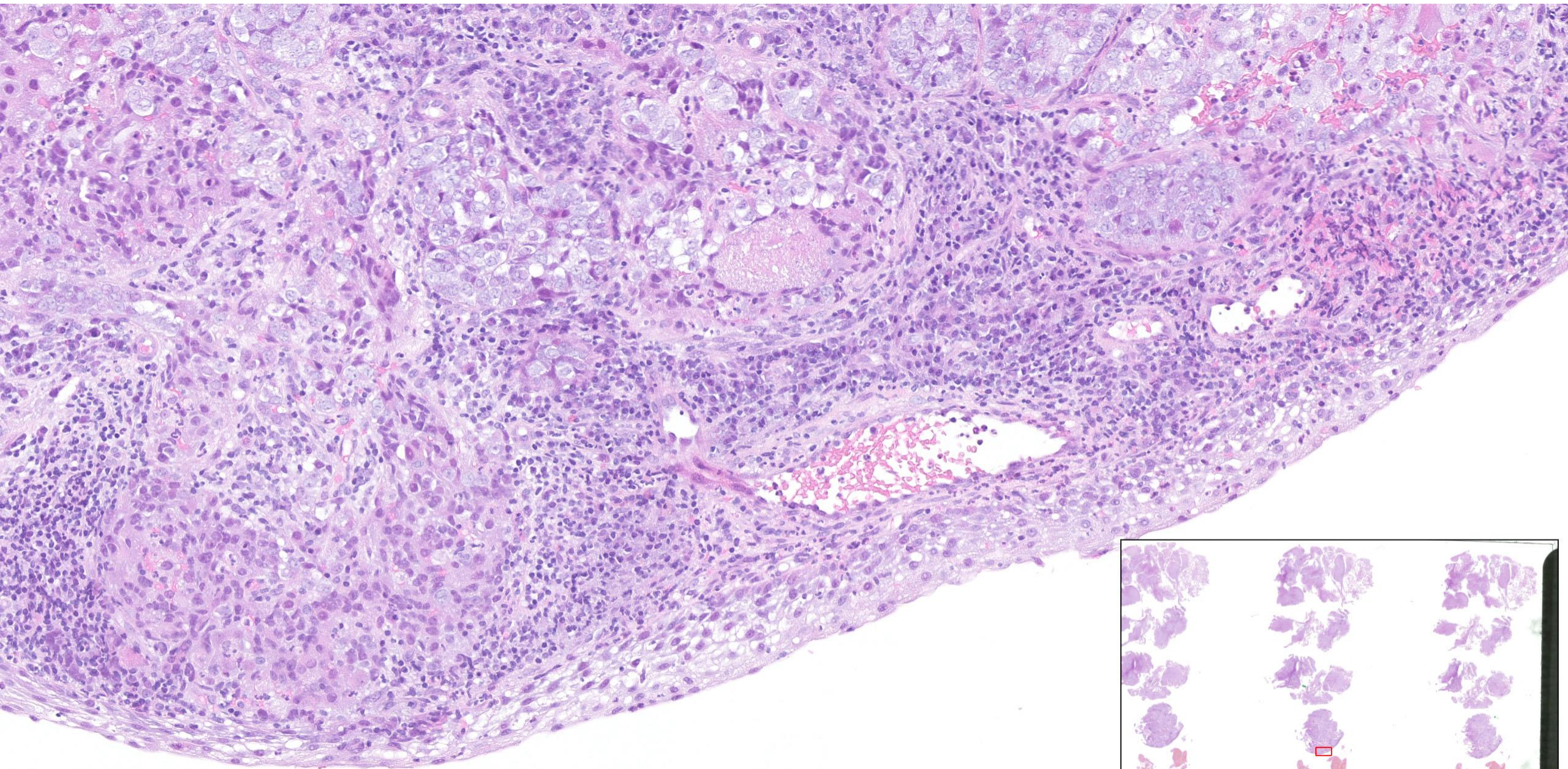
- Female aged 49
- Intermenstrual bleeding
- Smear negative
- Friable growth on cervix, 2 cm, bleeds easily on touch
- Cervical biopsies x 3



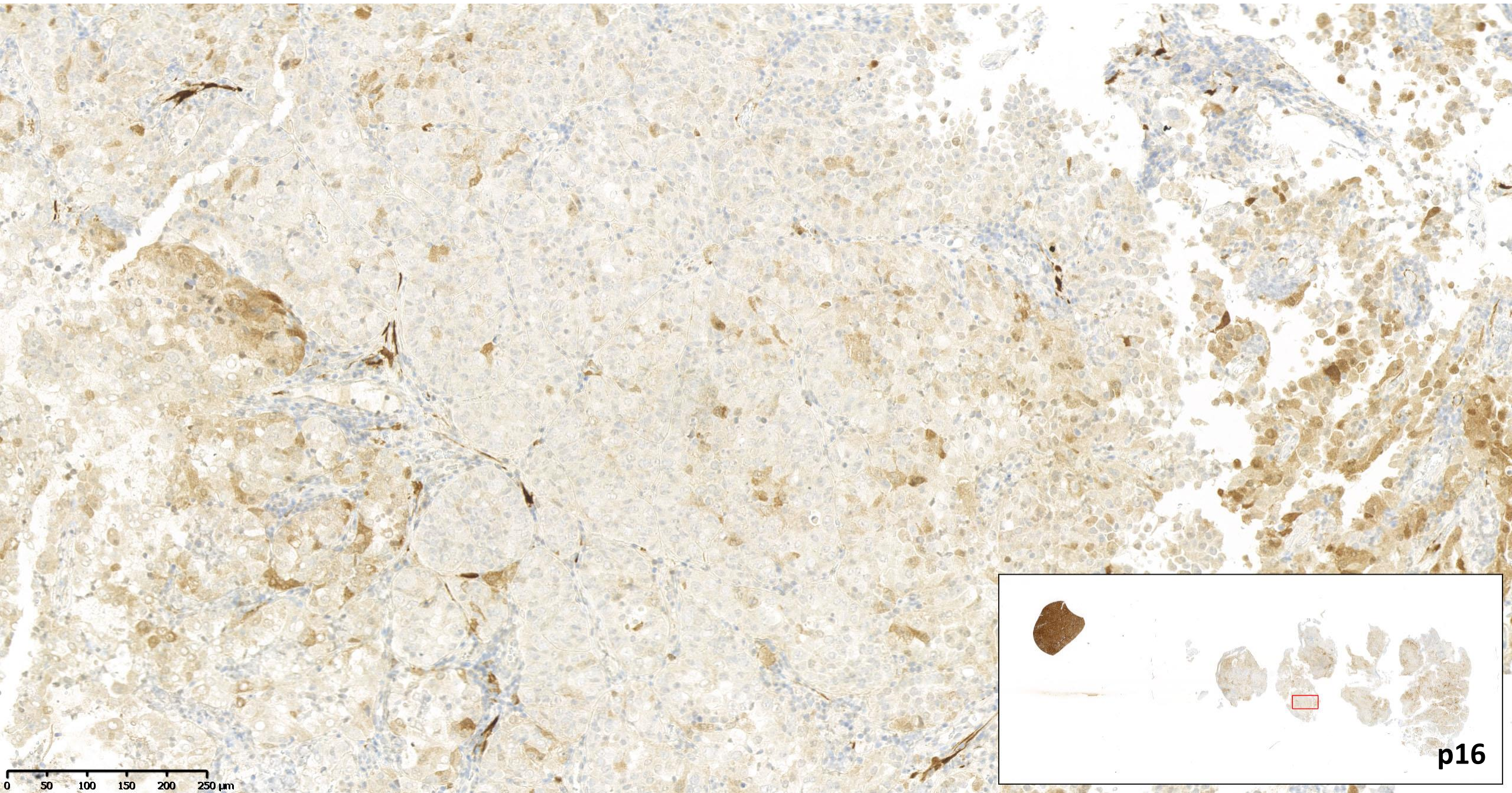
0 1 2 3 4 5 mm



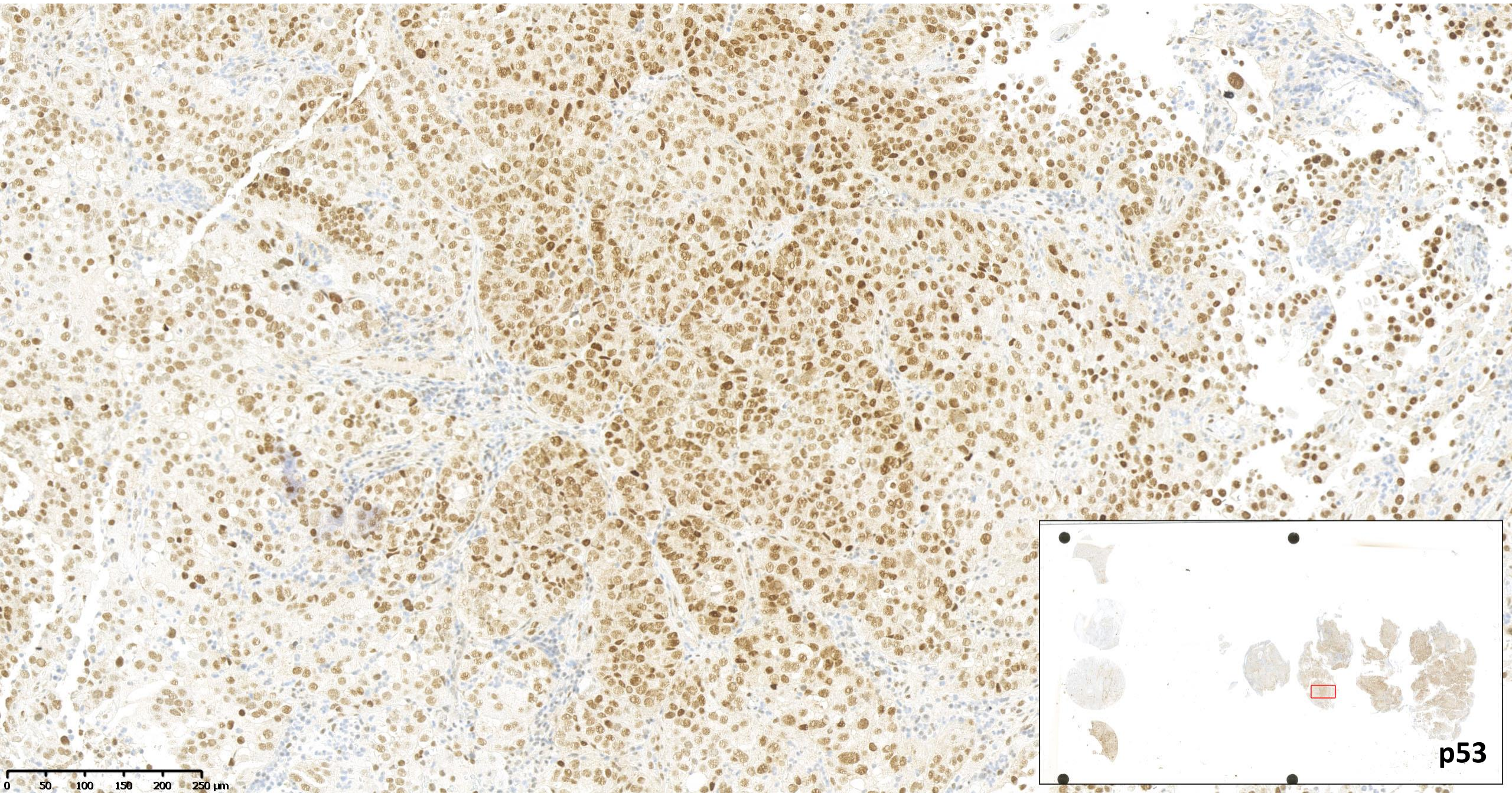
0 50 100 150 200 250 μm

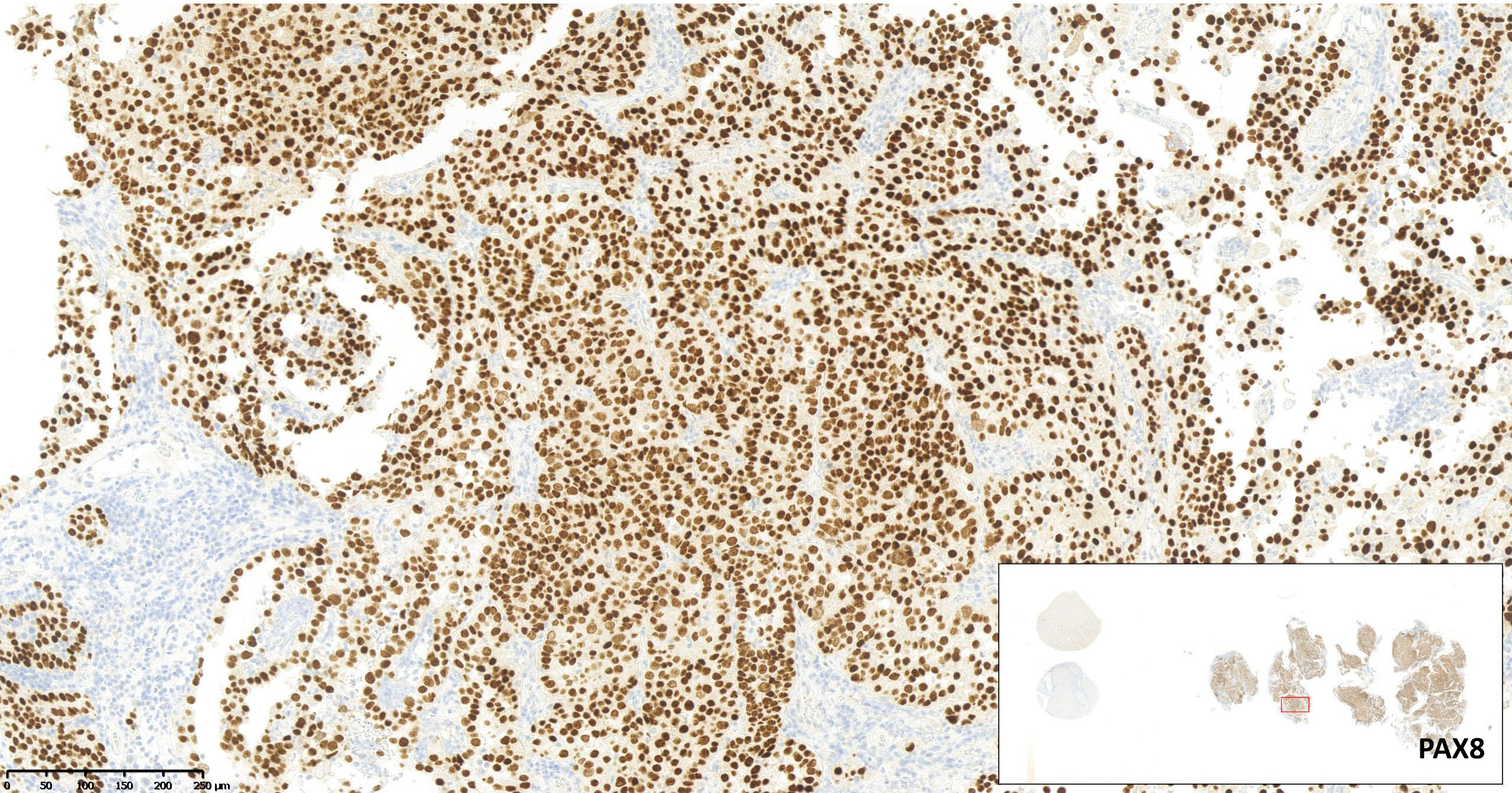


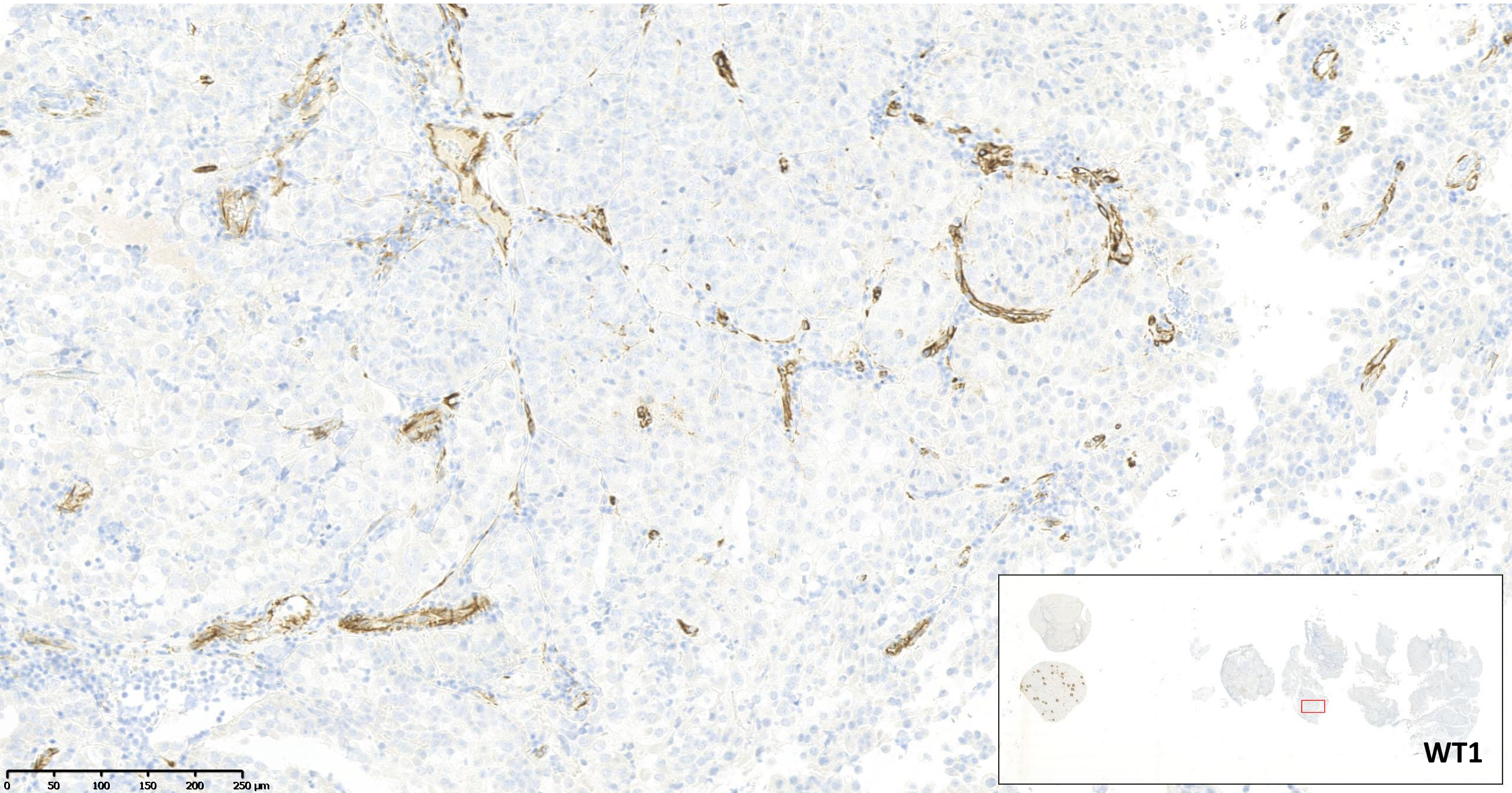
0 50 100 150 200 250 μm



p16







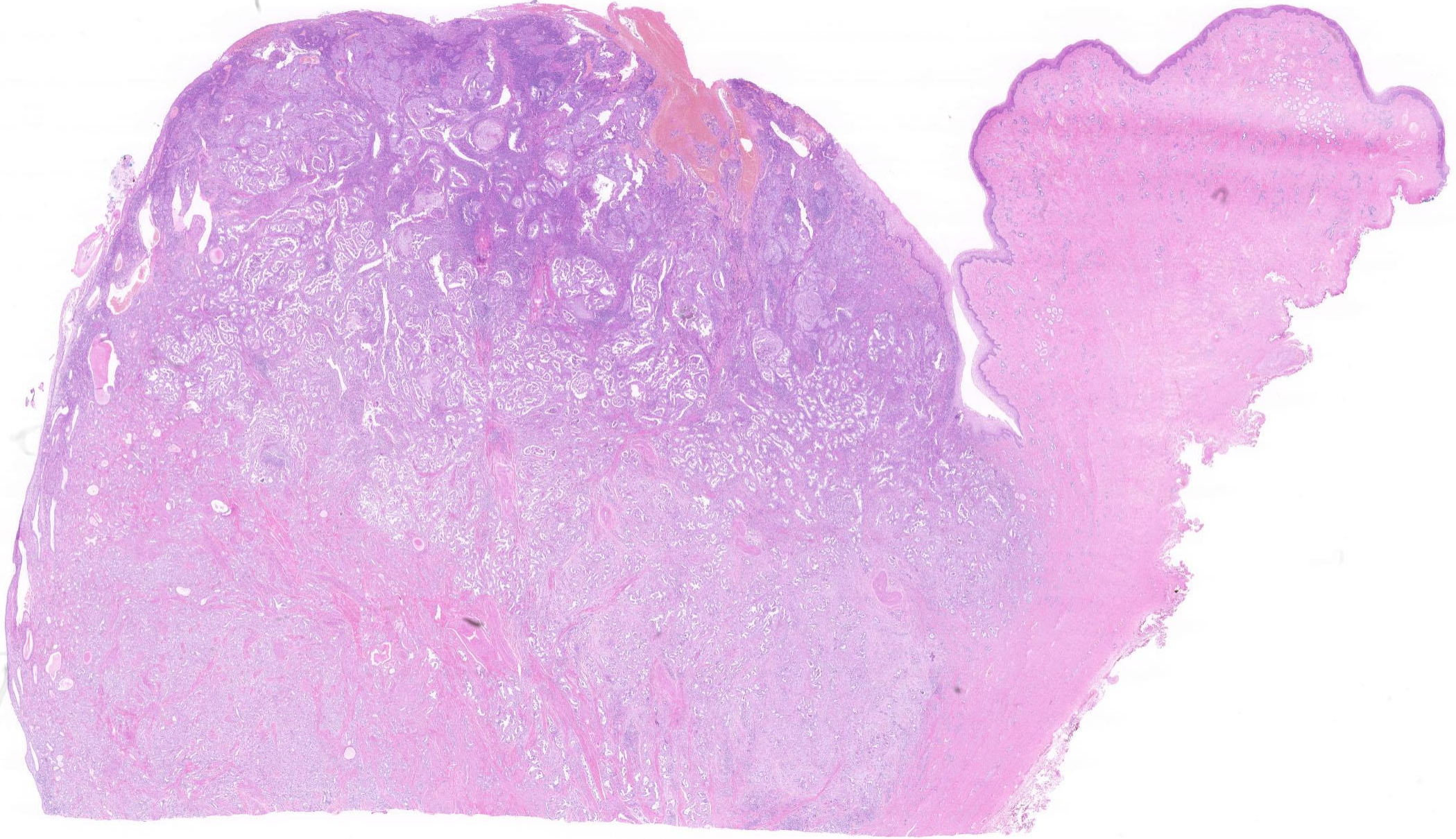
0 50 100 150 200 250 μm



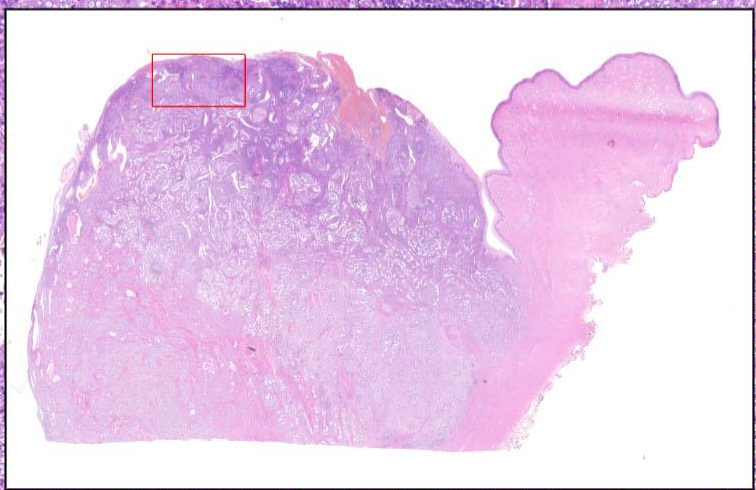
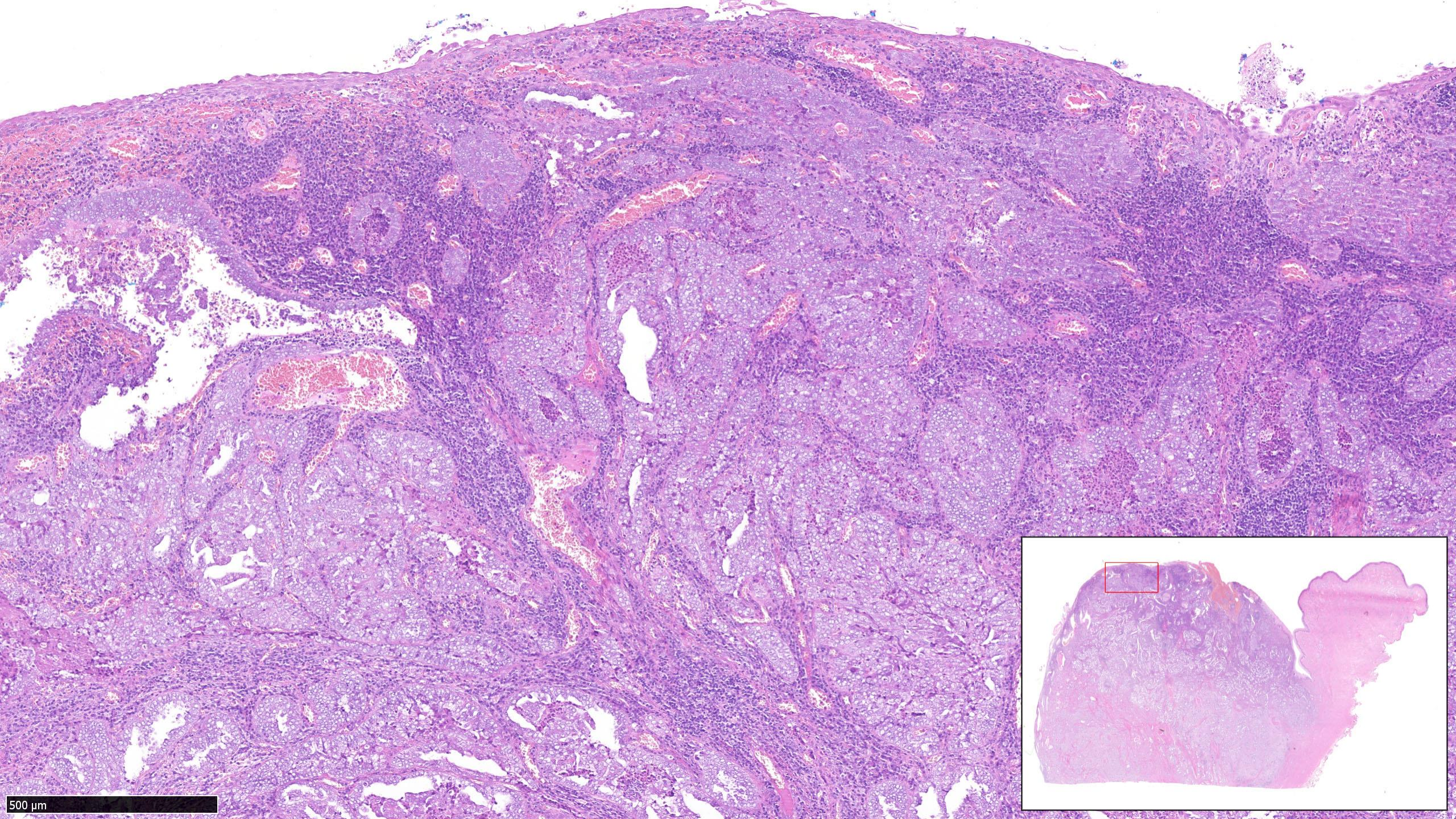
WT1

Subsequent operation

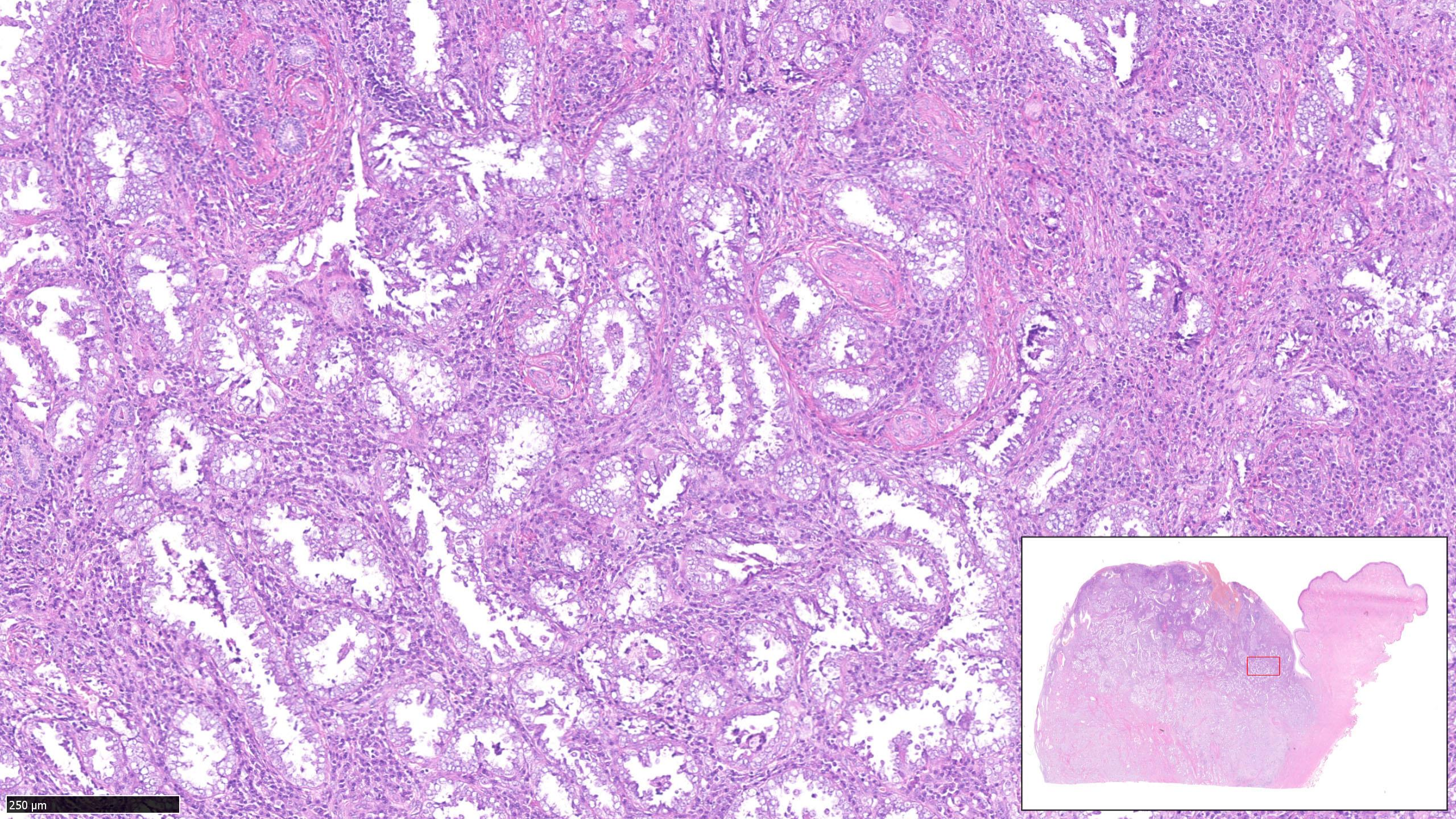
- Wertheim's hysterectomy
- Pelvic and para-aortic lymph node dissection
- Omental biopsy
- Findings
 - Cervical tumour 29 mm in diameter
 - Lymph nodes negative
 - Omentum negative



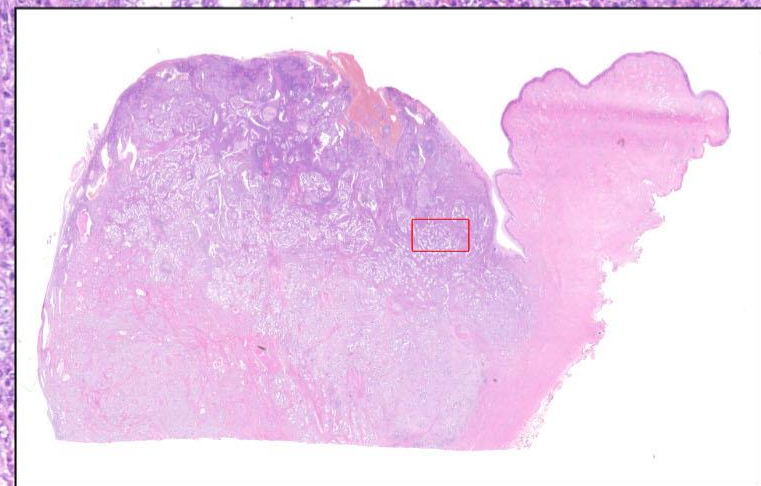
2.5 mm

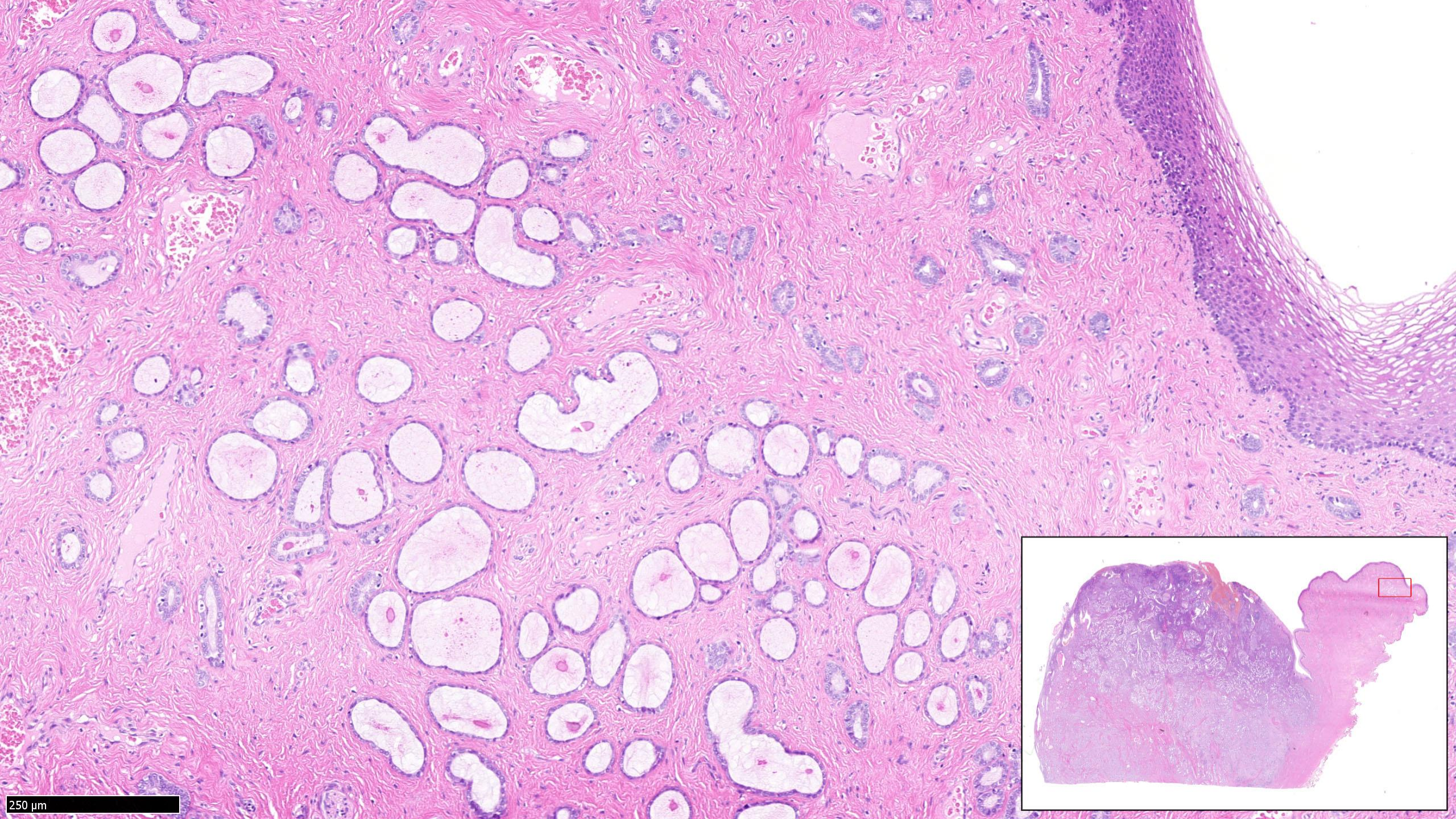


500 μ m

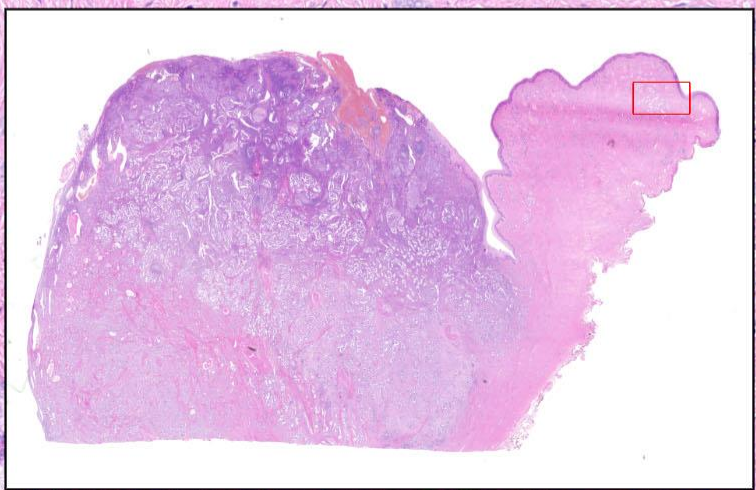


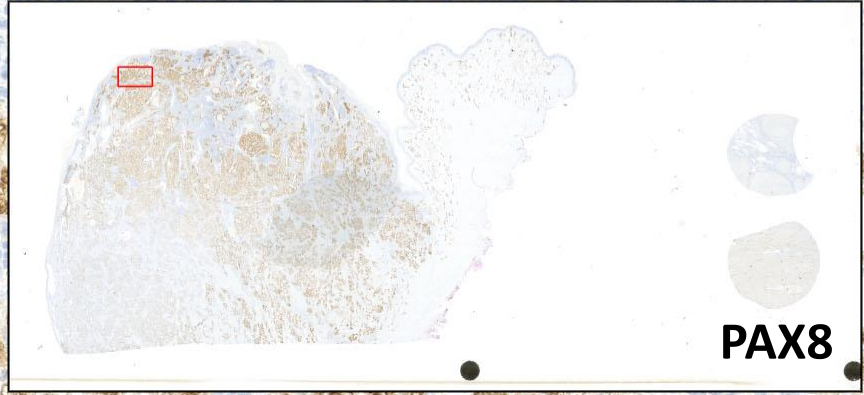
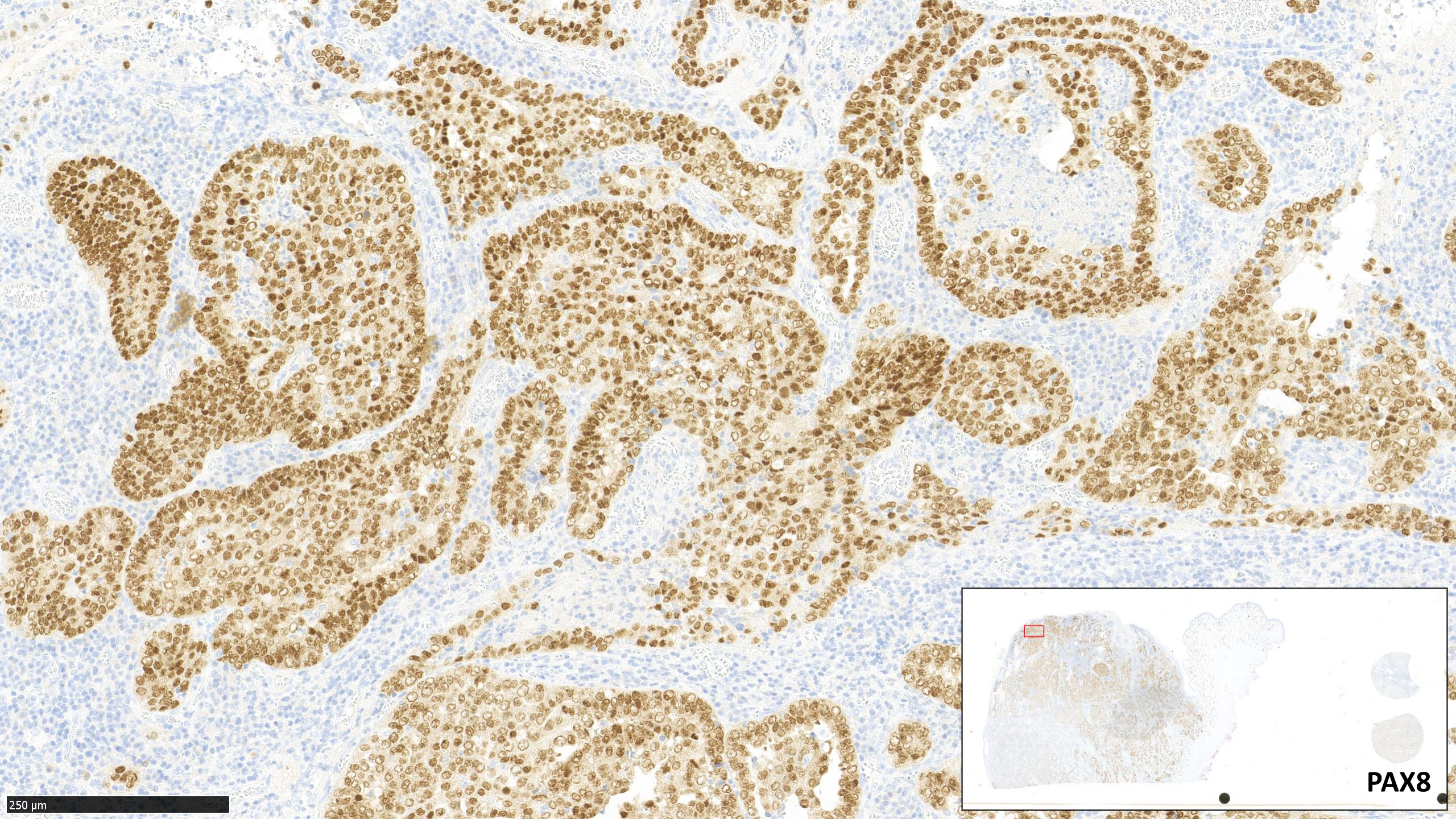
250 μ m





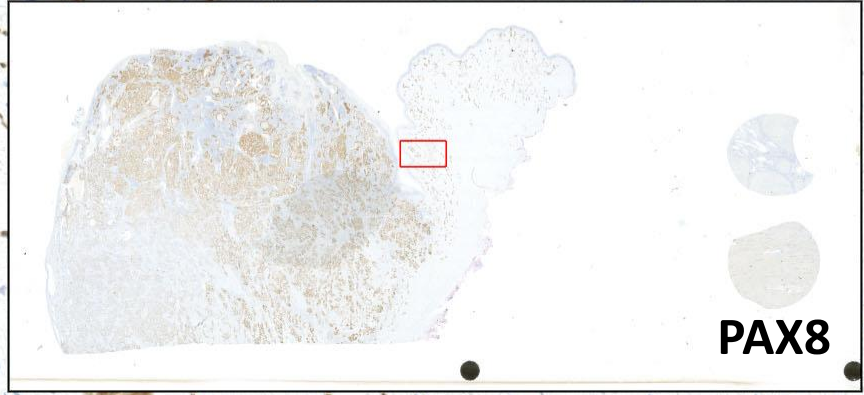
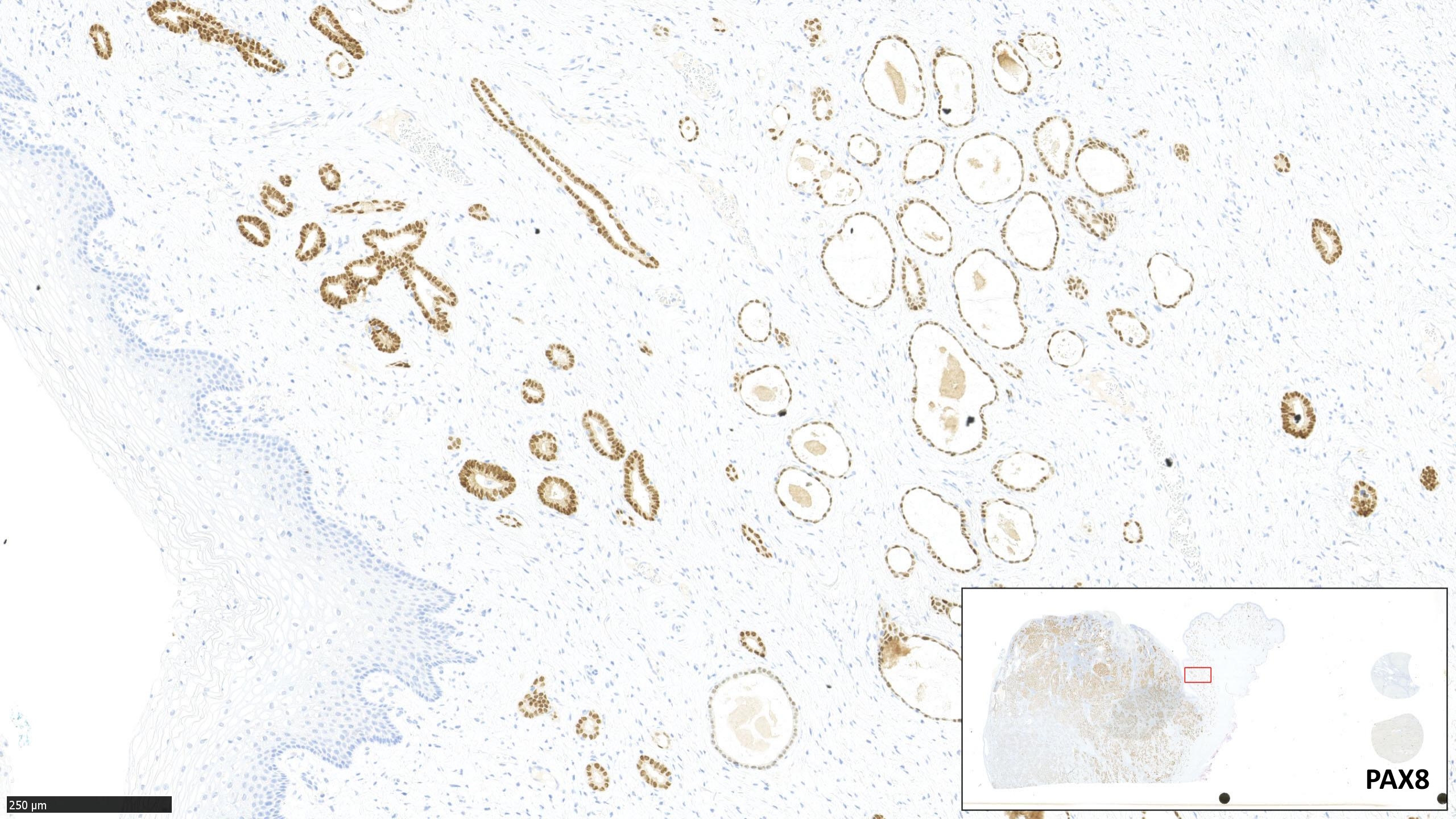
250 μm





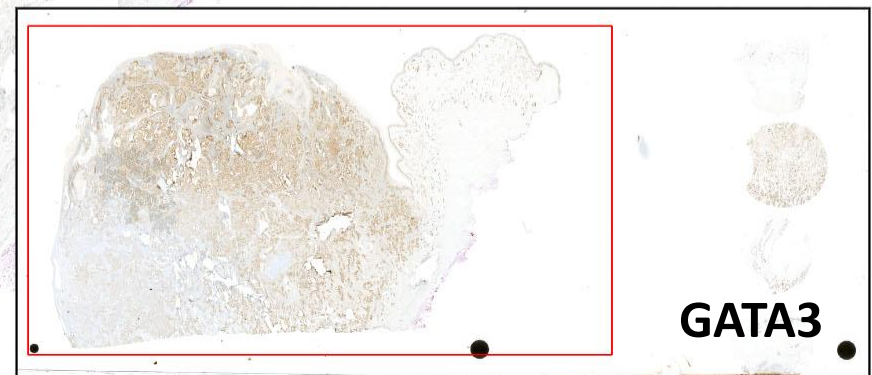
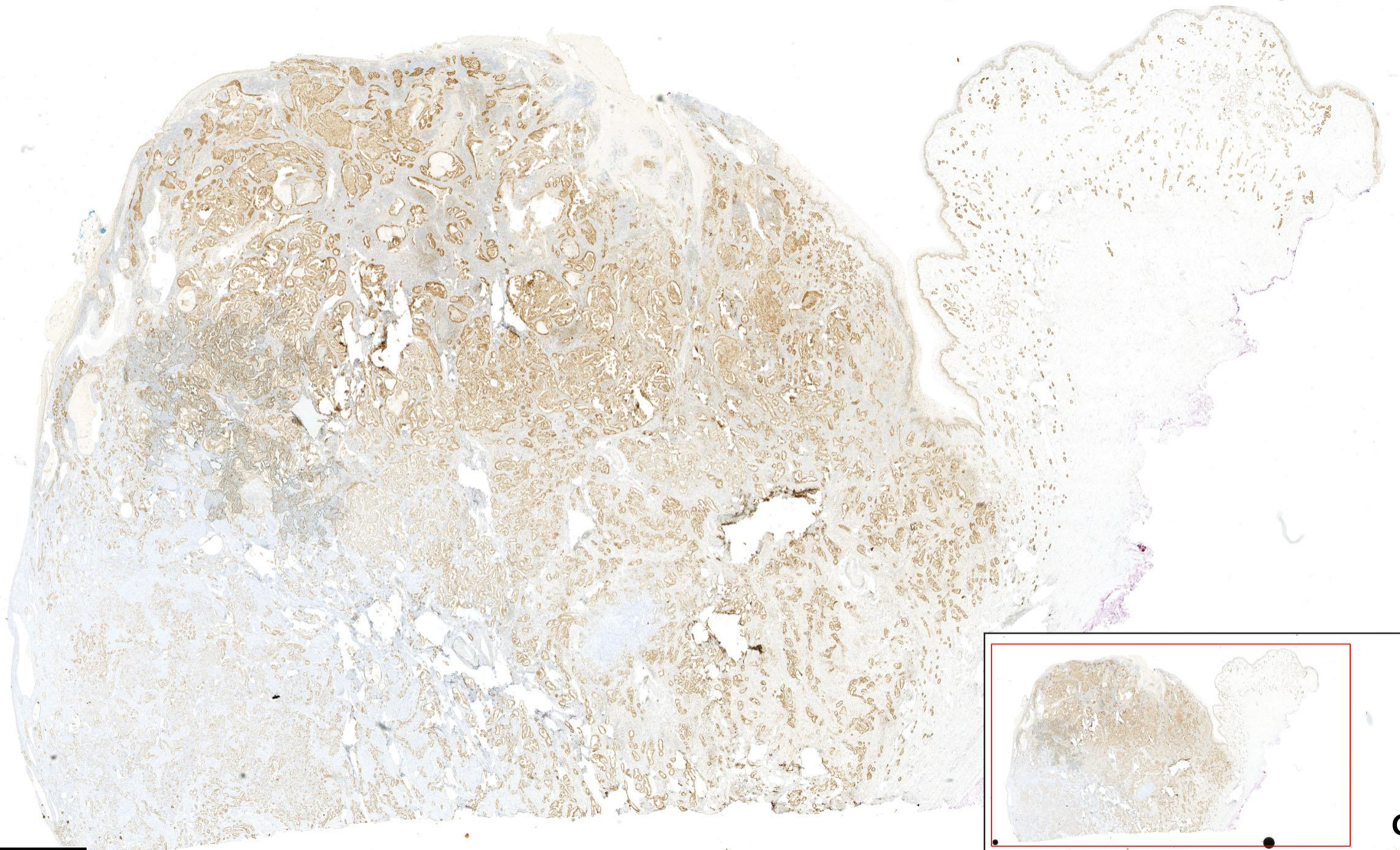
PAX8

250 μ m



PAX8

250 μm



GATA3

2.5 mm

Diagnosis

Mesonephric Carcinoma of the Cervix

Mesonephric Lesions of the Cervix

- Mesonephric duct remnants
- Mesonephric hyperplasia
 - Lobular
 - Diffuse
- Mesonephric carcinoma
- Malignant mixed mesonephric tumour

Mesonephric Lesions of the Cervix

- Typically GATA3 positive
 - But 20% (23/113) carcinosarcomas also stain
- Calretinin, CD10 and p16 less useful
- Typically TTF1 negative

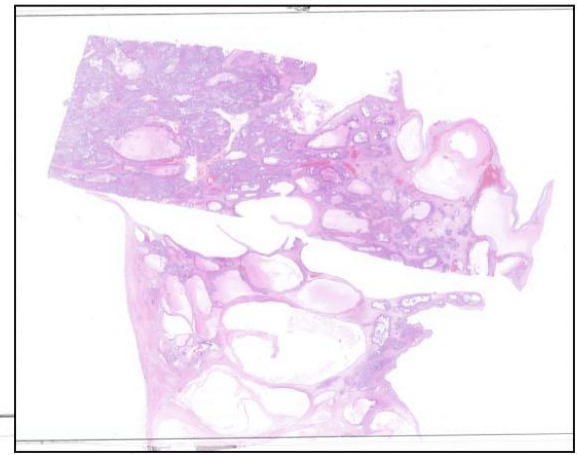
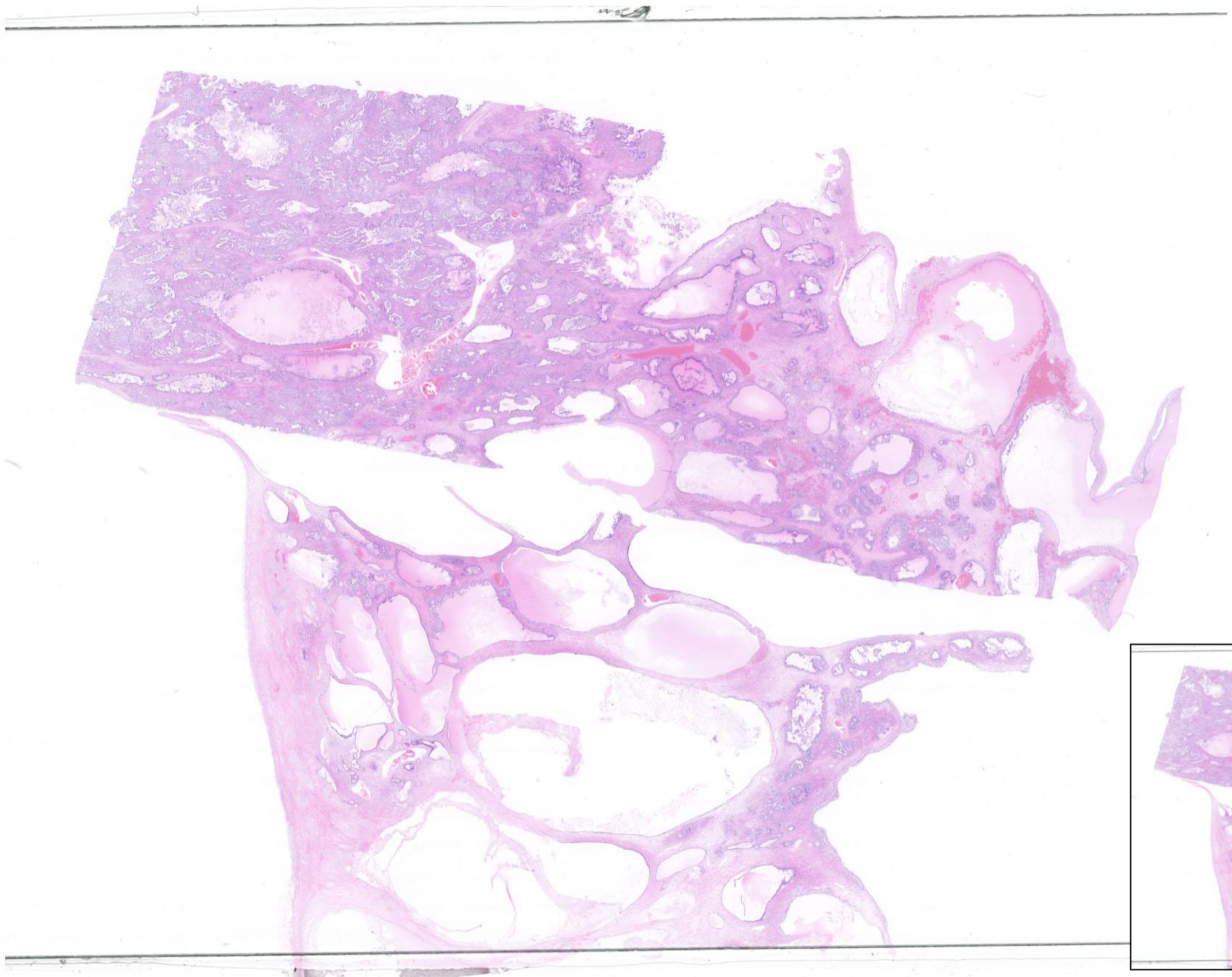
Howitt BE et al Am J Surg Pathol 2015; 39: 1411-9

Roma AA et al Int J Gynecol Pathol 2015; 34: 480-6

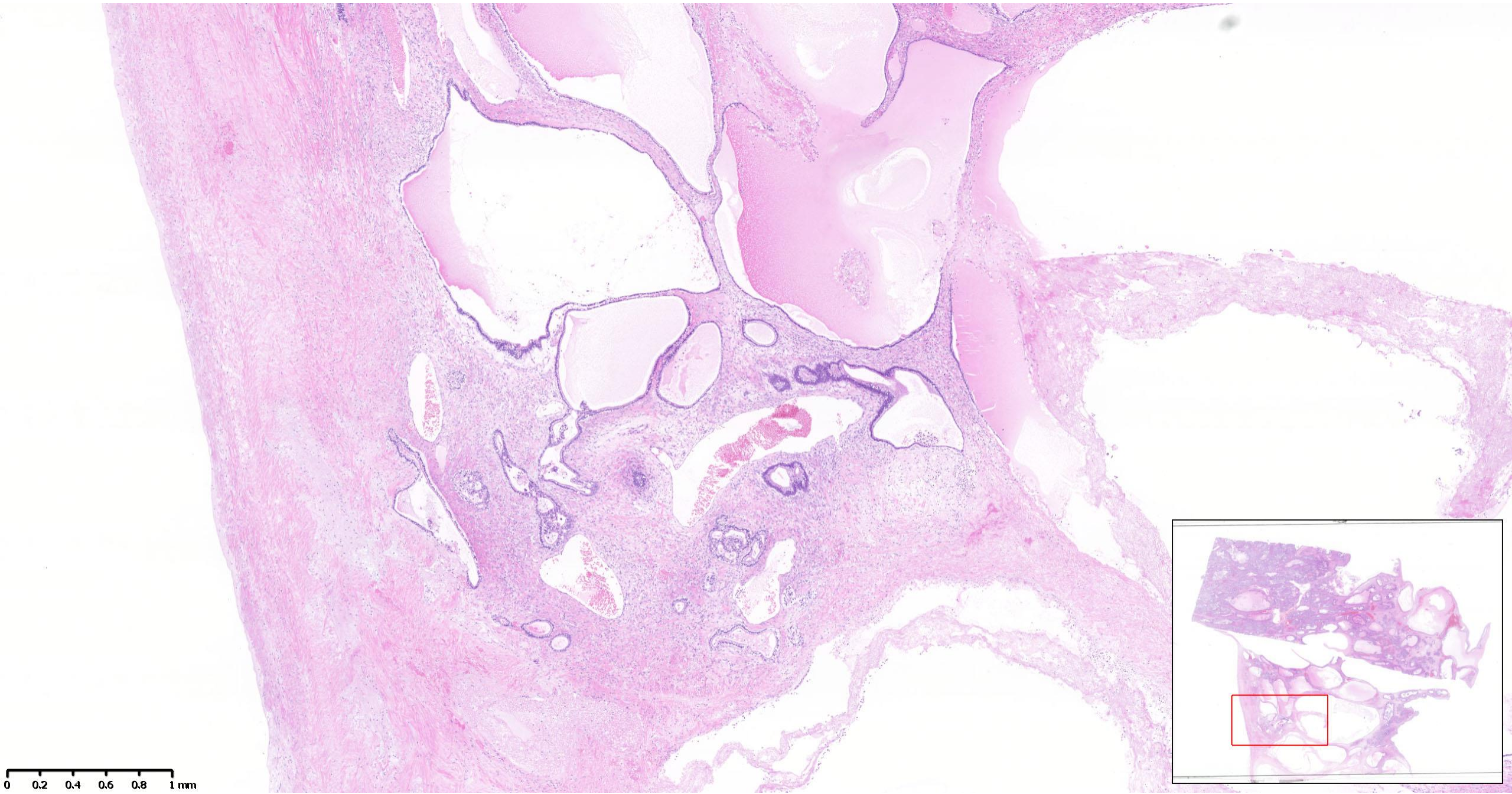
Pors et al Am J Surg Path 2018; 42: 1596-1606

Case 4

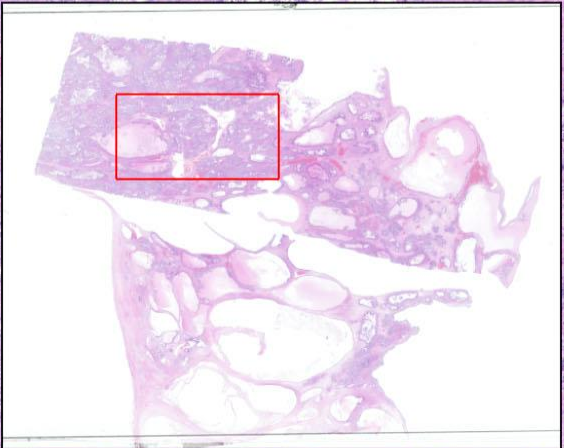
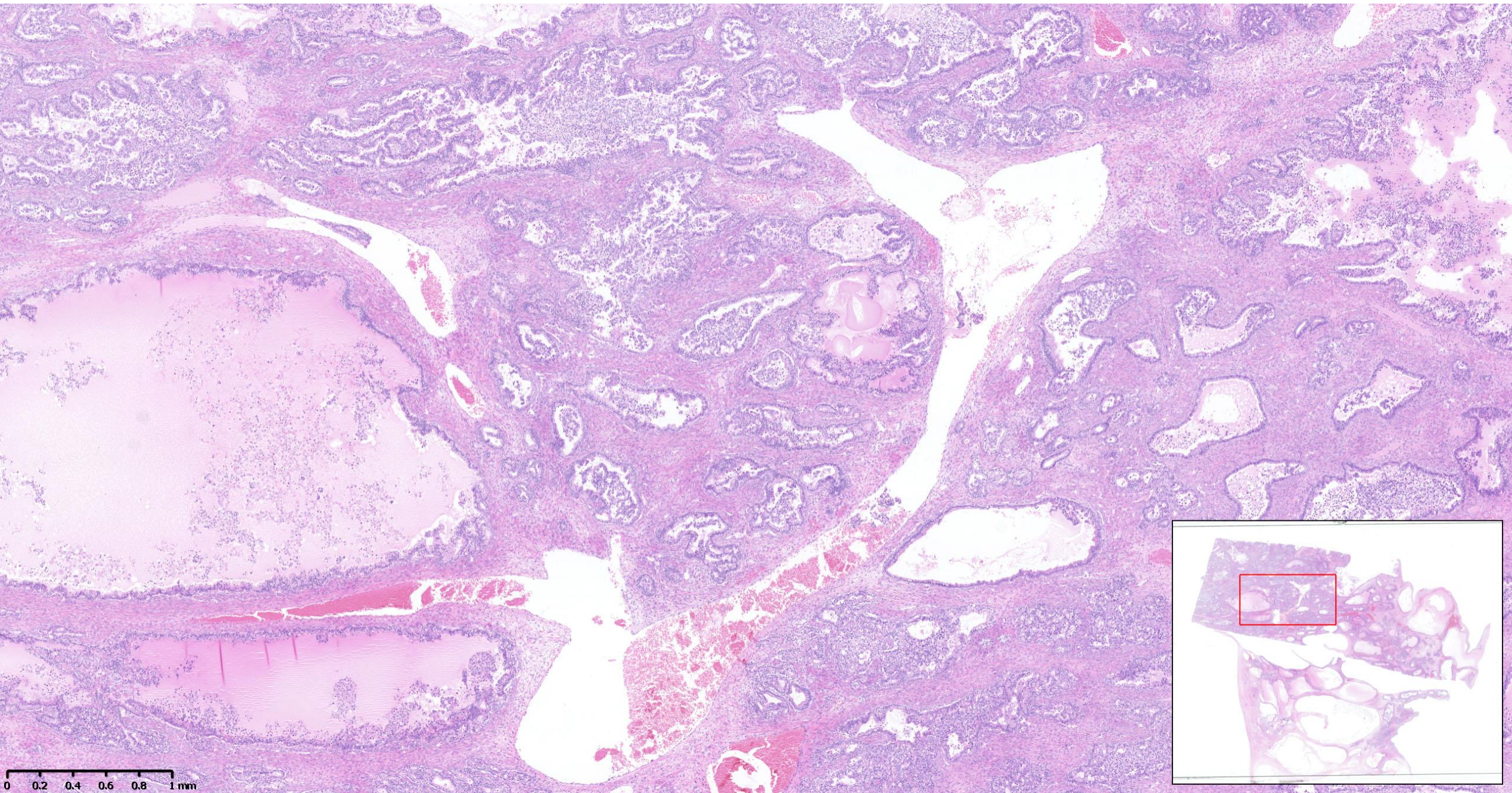
- Female aged 78
- BSO and omental biopsy
- CA125 increased to 130.
- Previous radical radiotherapy for cervical cancer
- Multicystic right ovarian mass 190 x 120 x 80 mm, weighing 620g



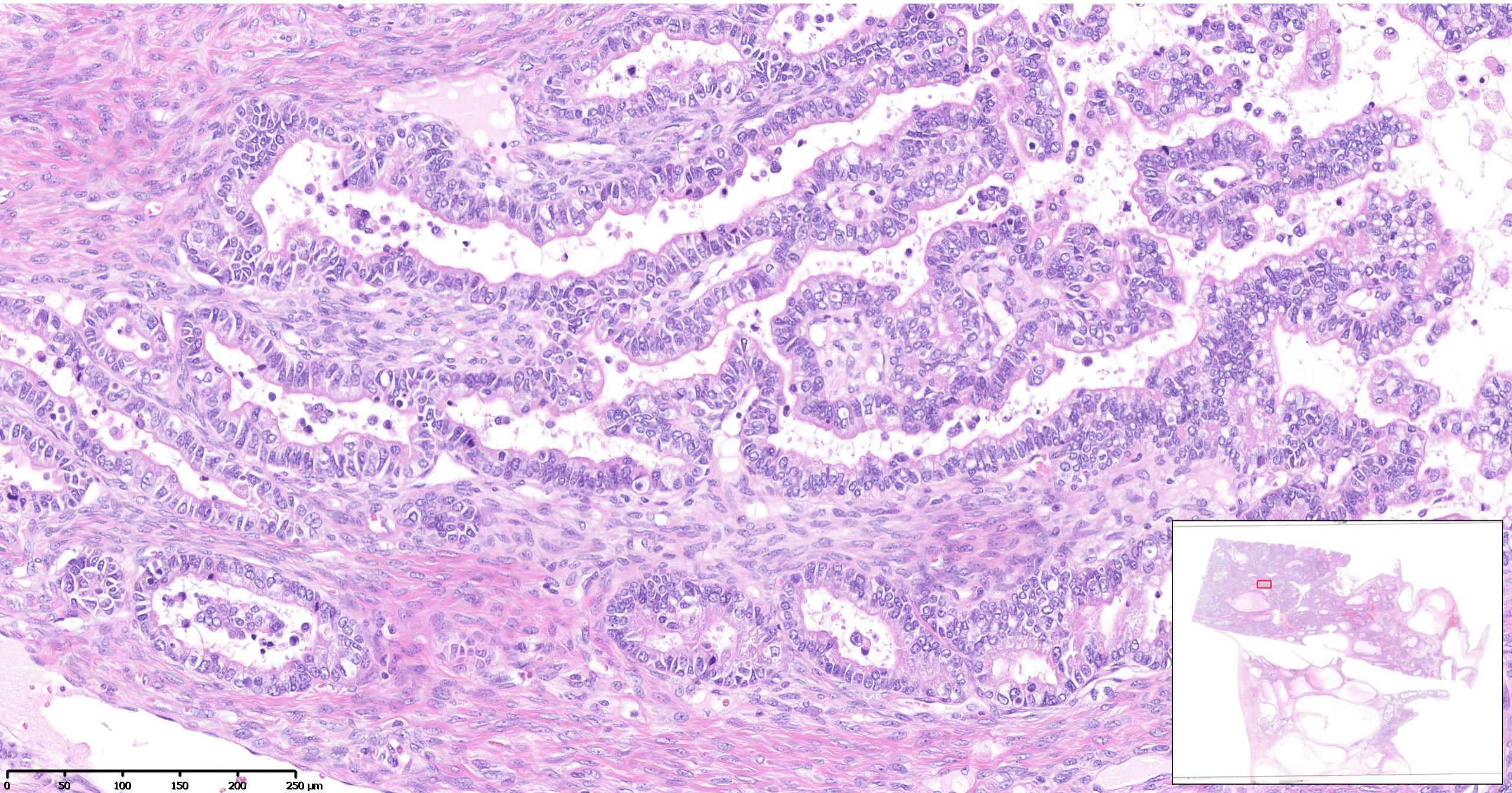
0 1 2 3 4 5 mm



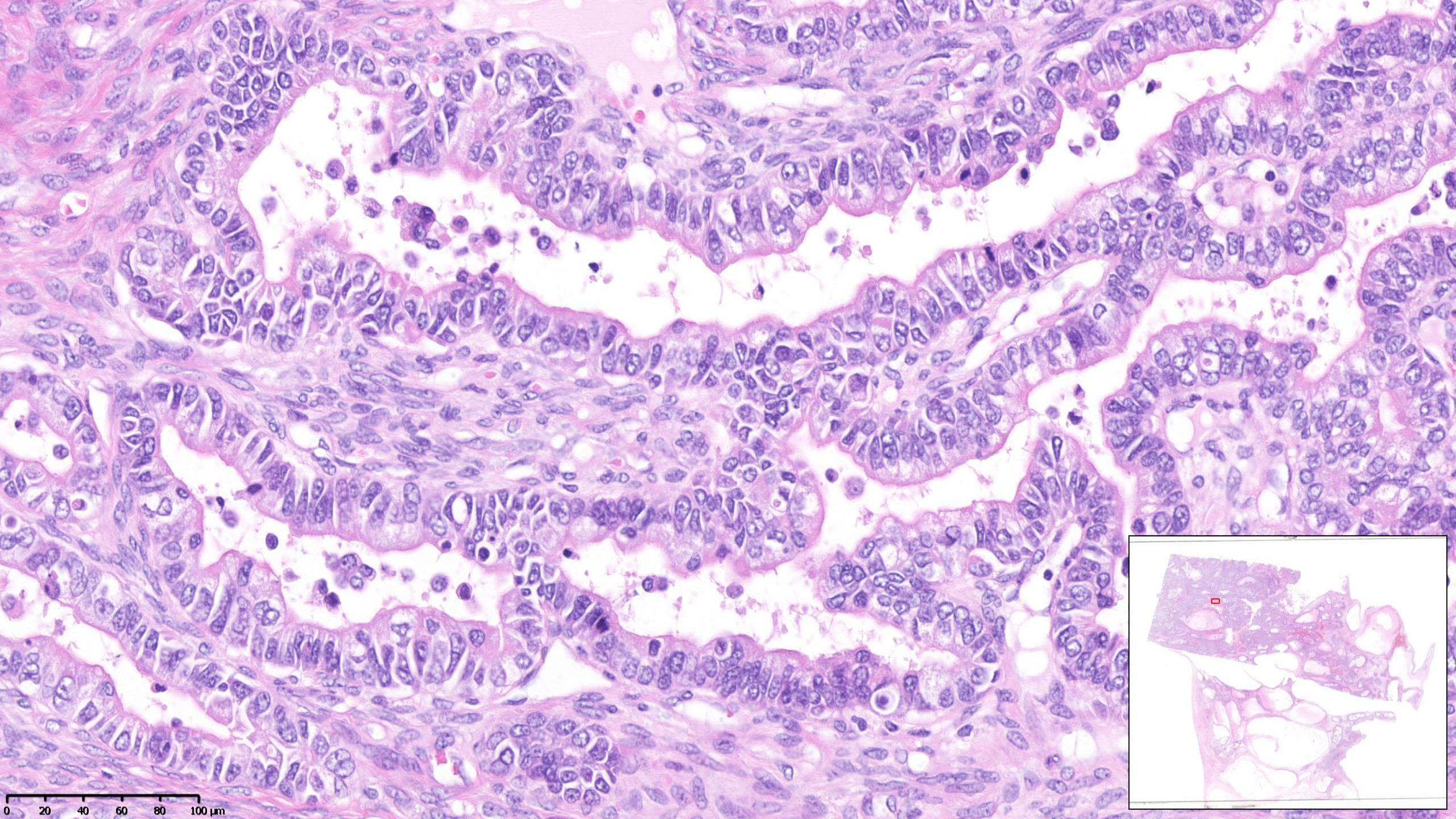
0 0.2 0.4 0.6 0.8 1 mm



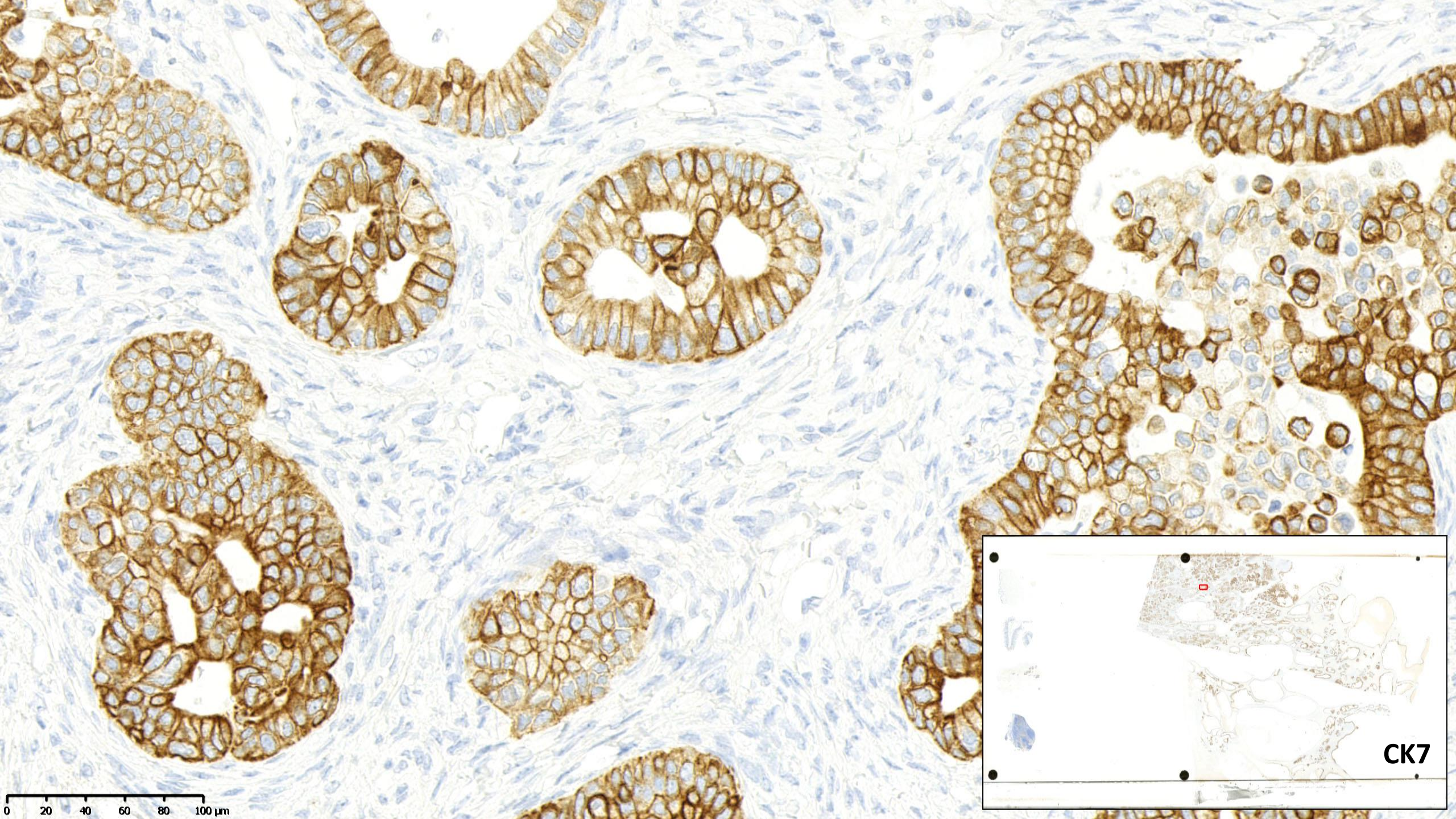
0 0.2 0.4 0.6 0.8 1 mm



0 50 100 150 200 250 μm

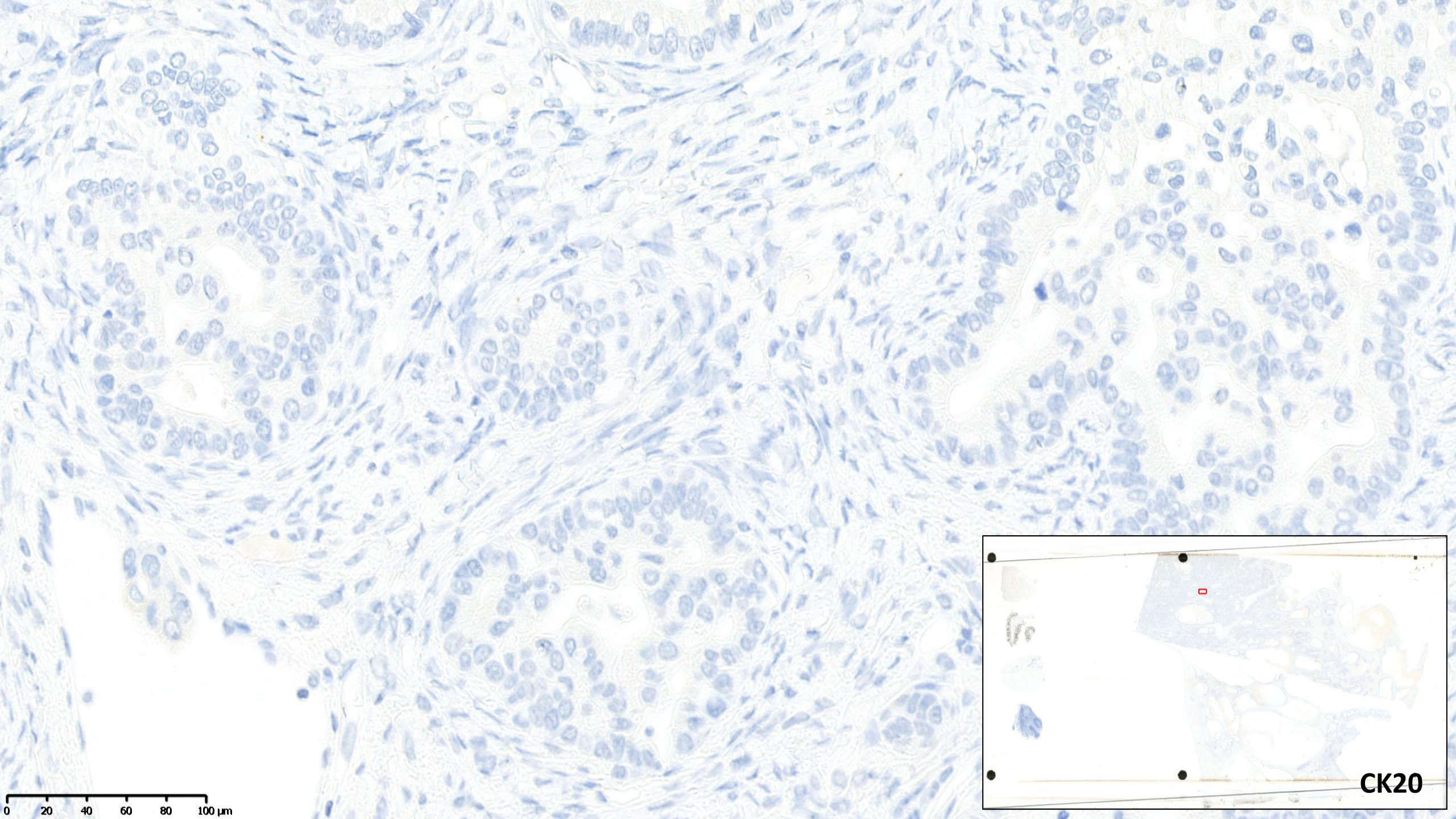


0 20 40 60 80 100 μm



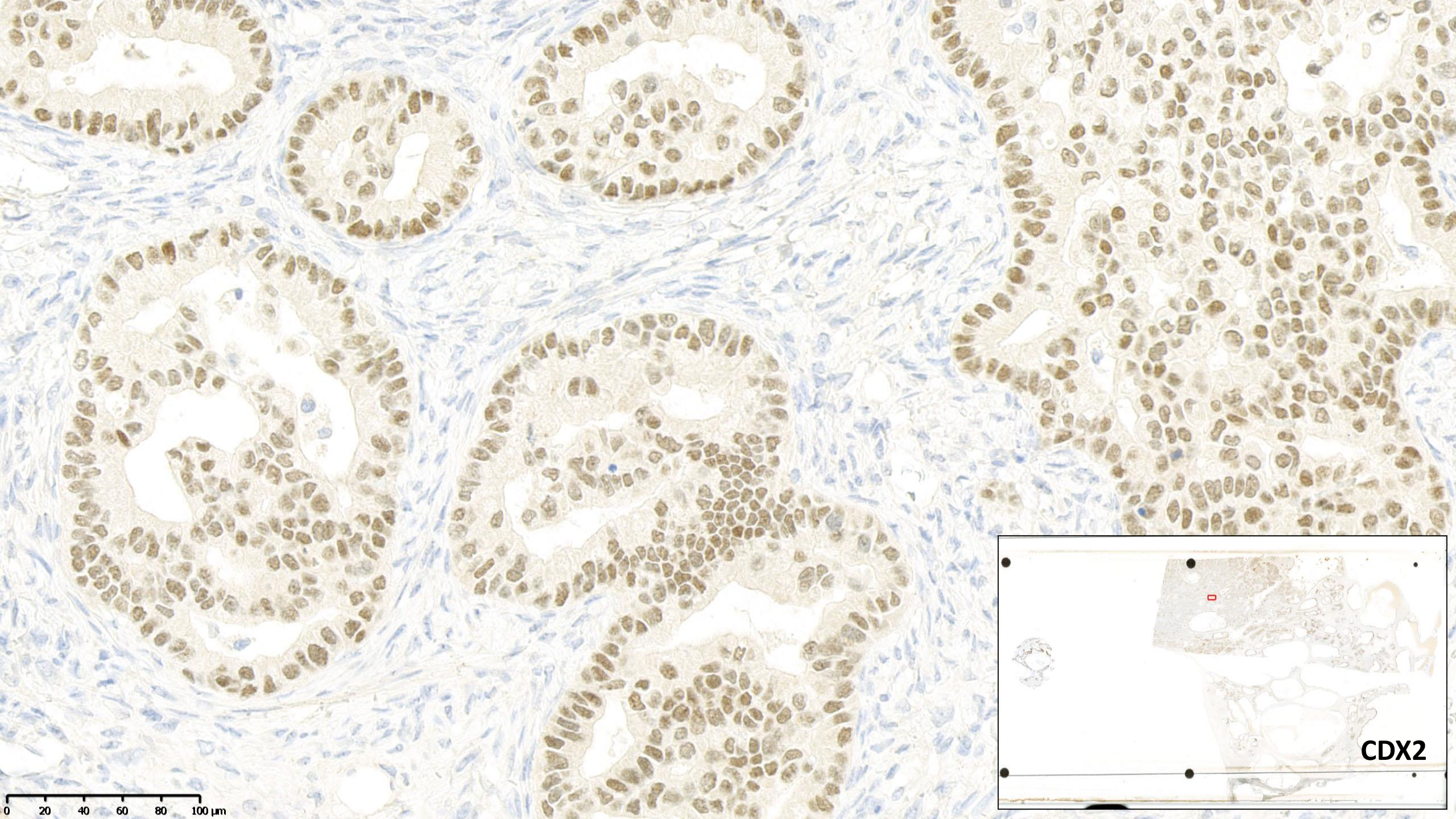
CK7

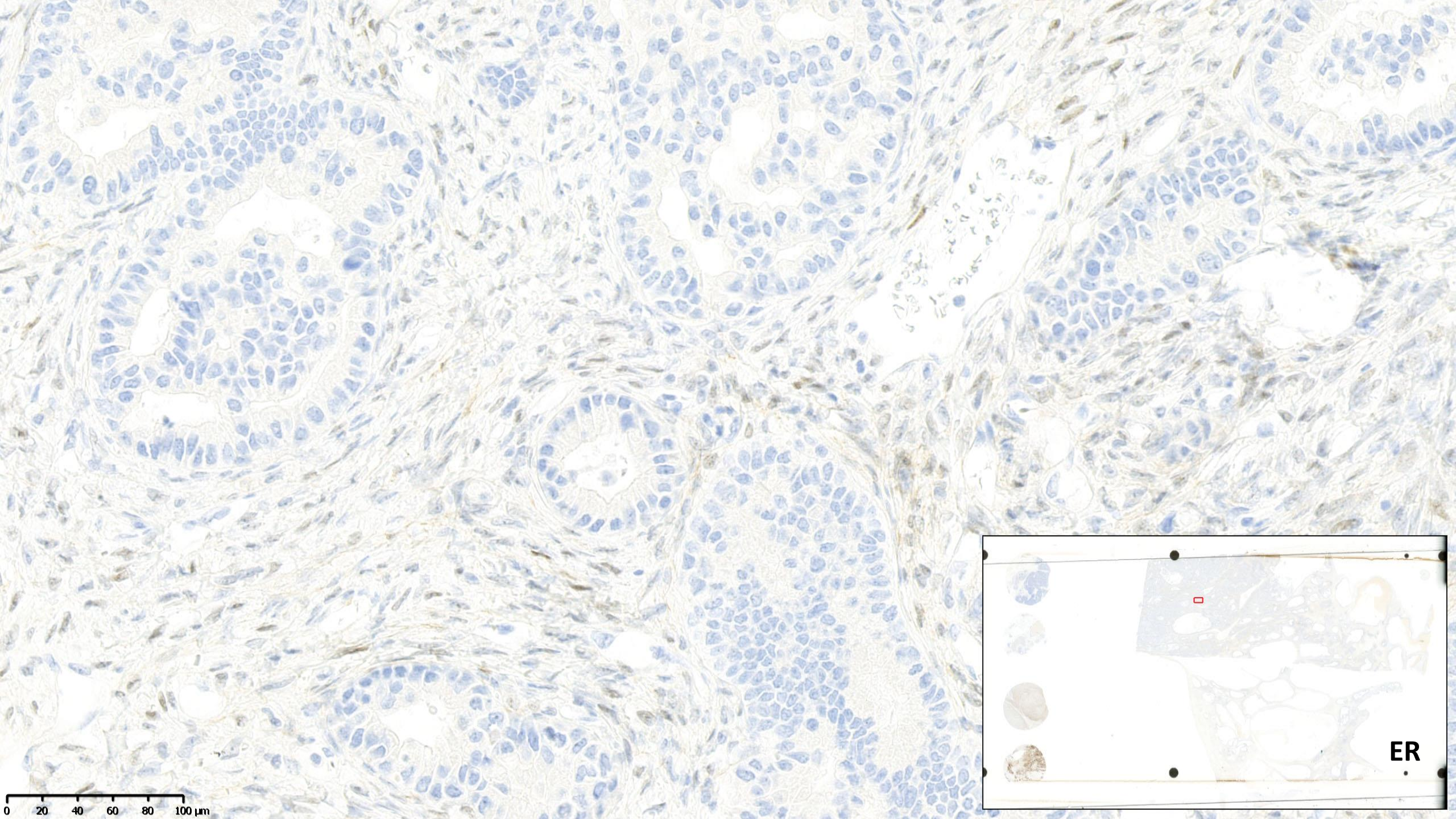
0 20 40 60 80 100 µm



CK20

0 20 40 60 80 100 μ m

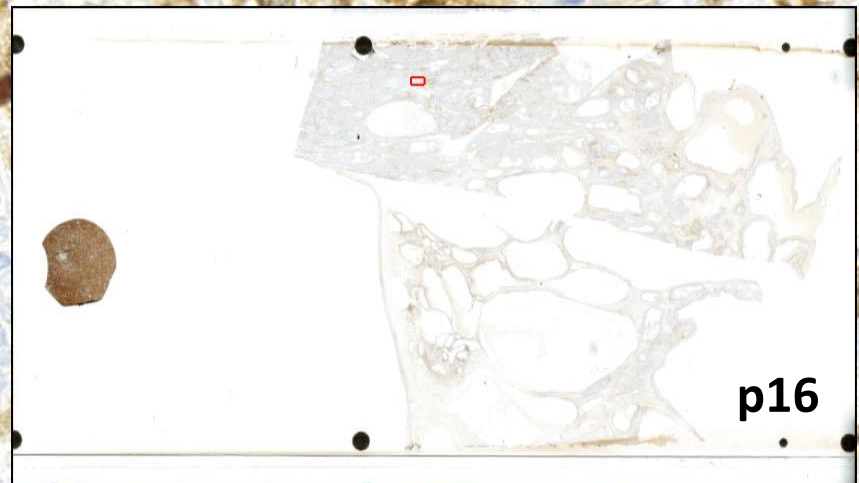
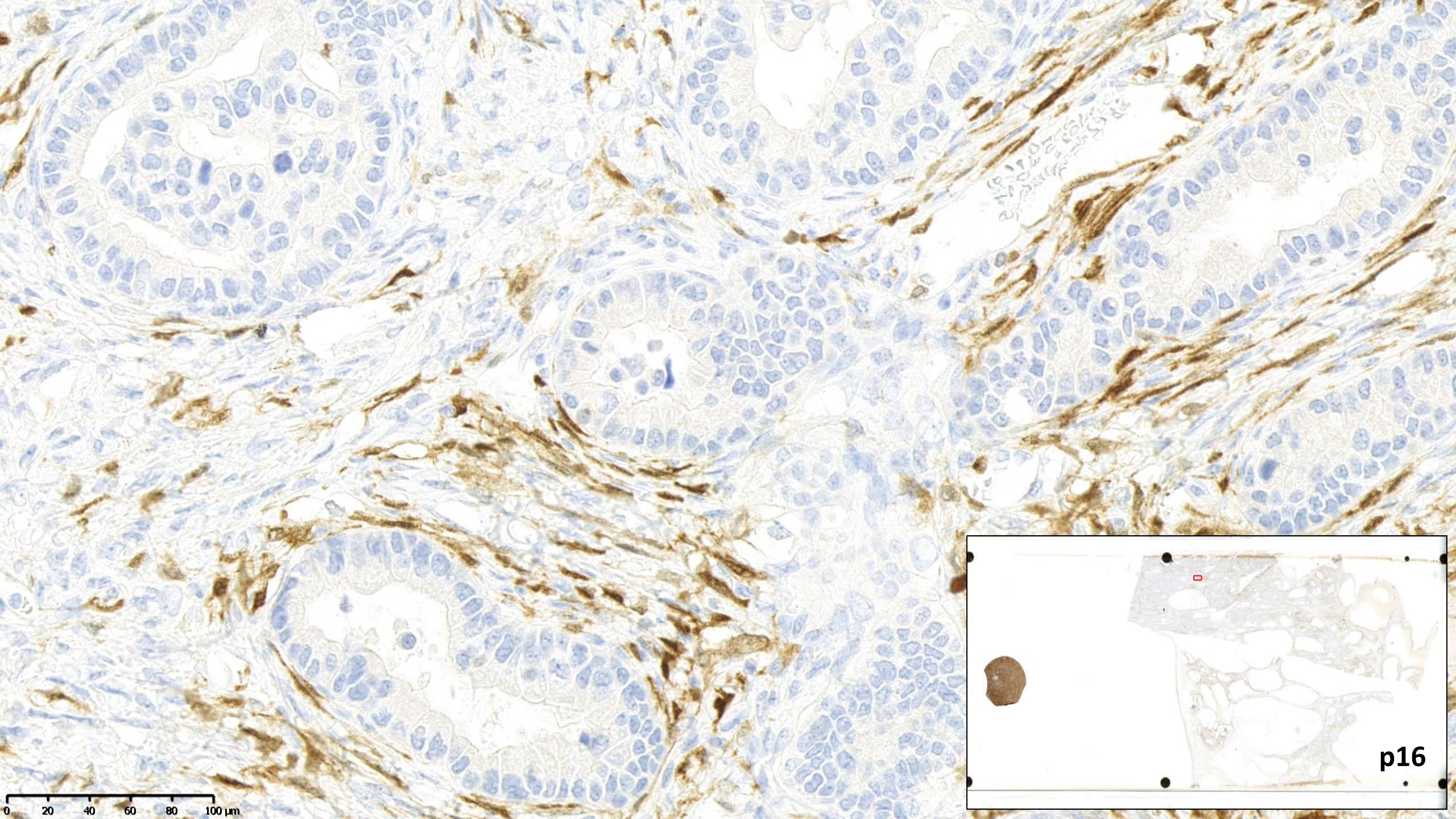




0 20 40 60 80 100 μm



ER



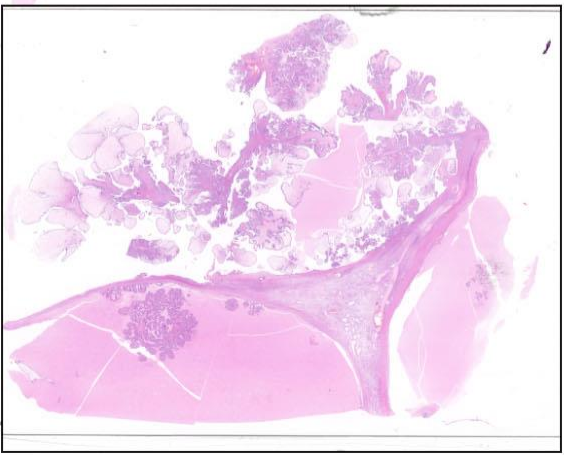
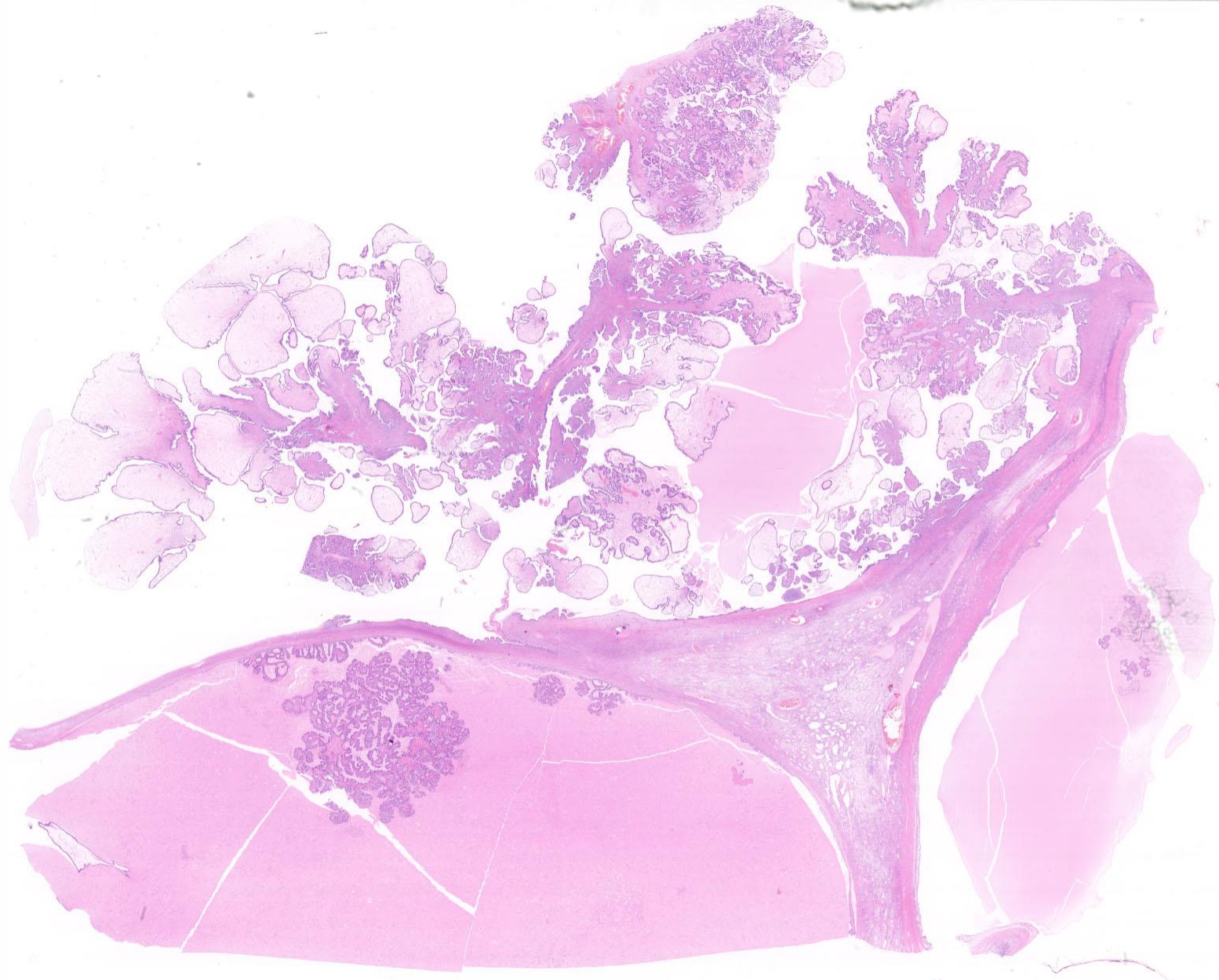
0 20 40 60 80 100 μm

Diagnosis

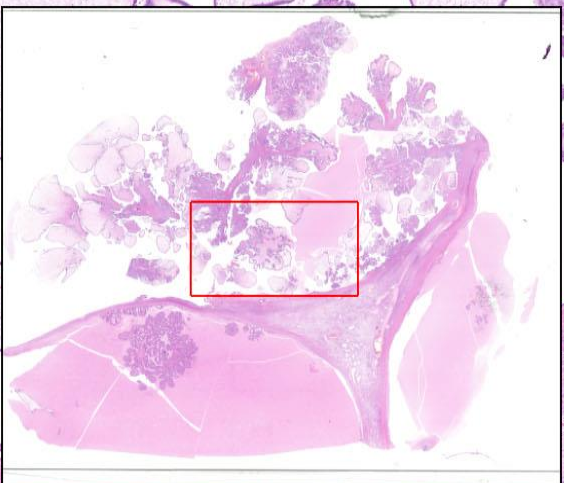
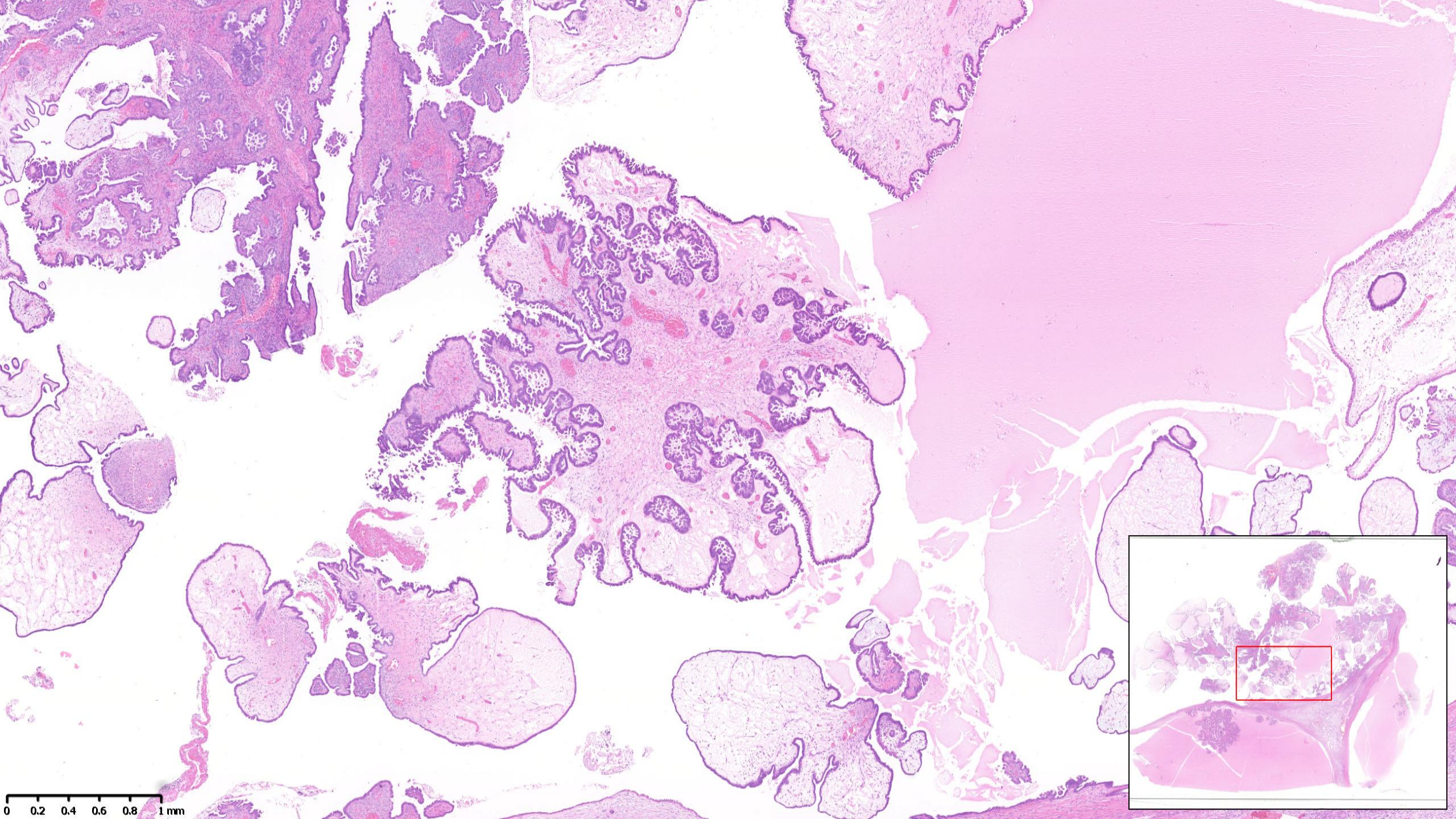
Metastatic Gastric-Type Adenocarcinoma
of the Cervix

Case 5

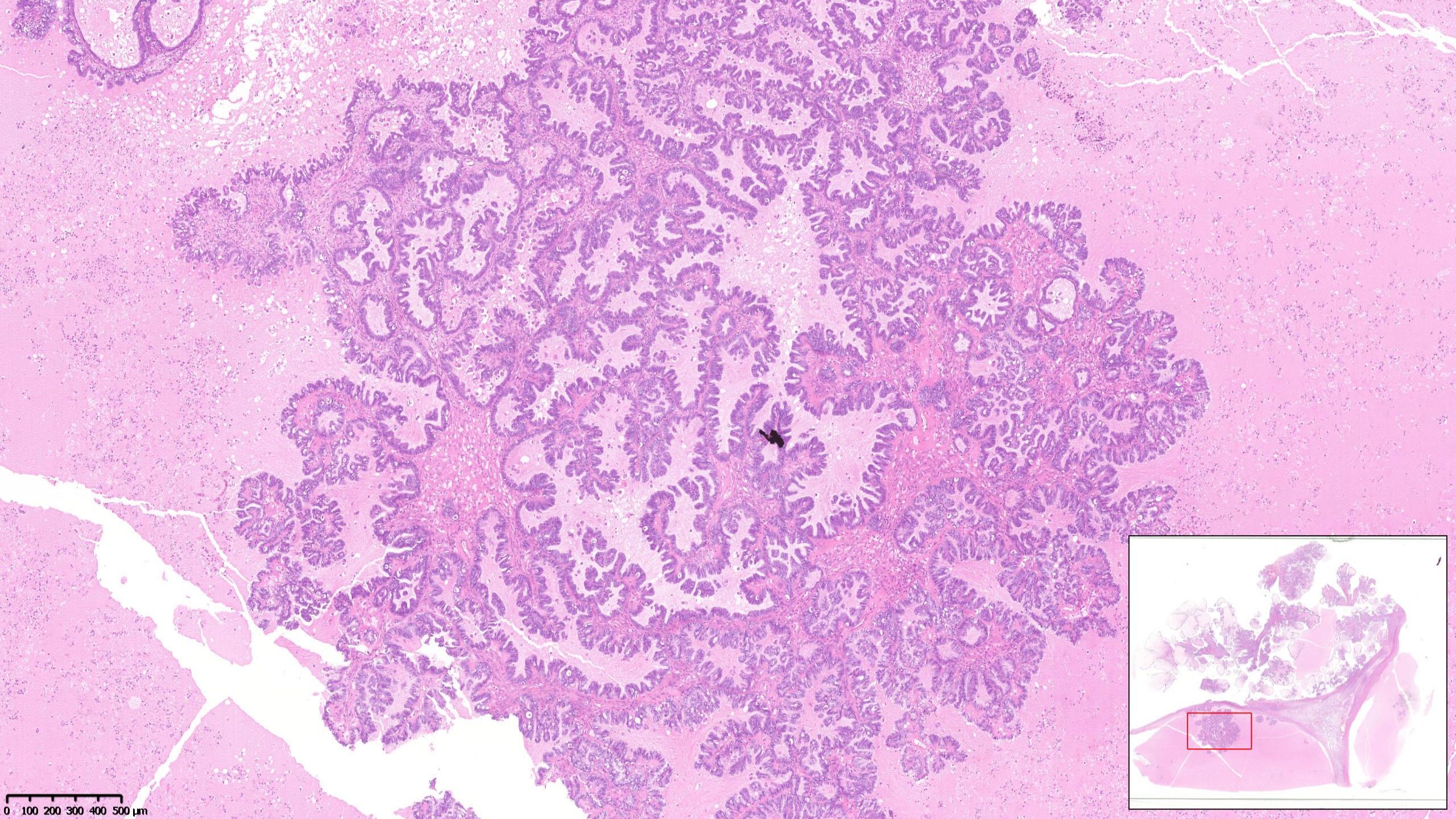
- Female aged 45
- Emergency admission with abdominal pain
- CT suggested dermoid cyst
- At laparotomy, disease involving uterus and colon
- Received TAH, BSO, omentum, sigmoid colon, peritoneal biopsy and washings
- Bilateral cystic ovarian masses 140 x 90 x 70 and 85 x 80 x 50 mm with surface papillary excrescences
- Sections from the (A) right ovarian tumour and (B) colon



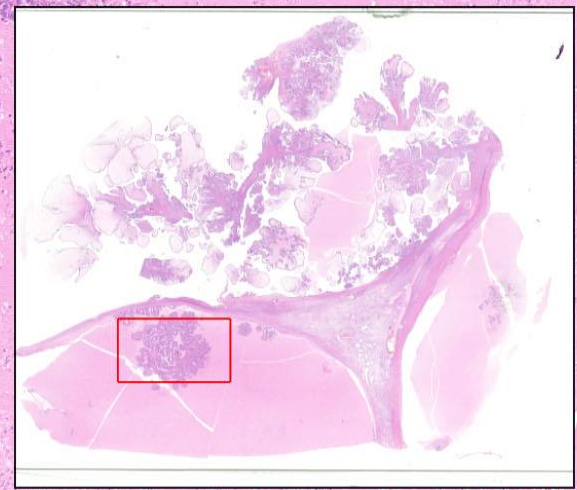
0 1 2 3 4 5mm

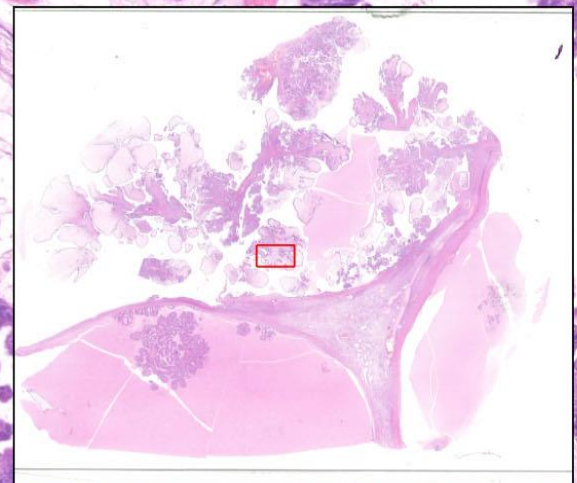
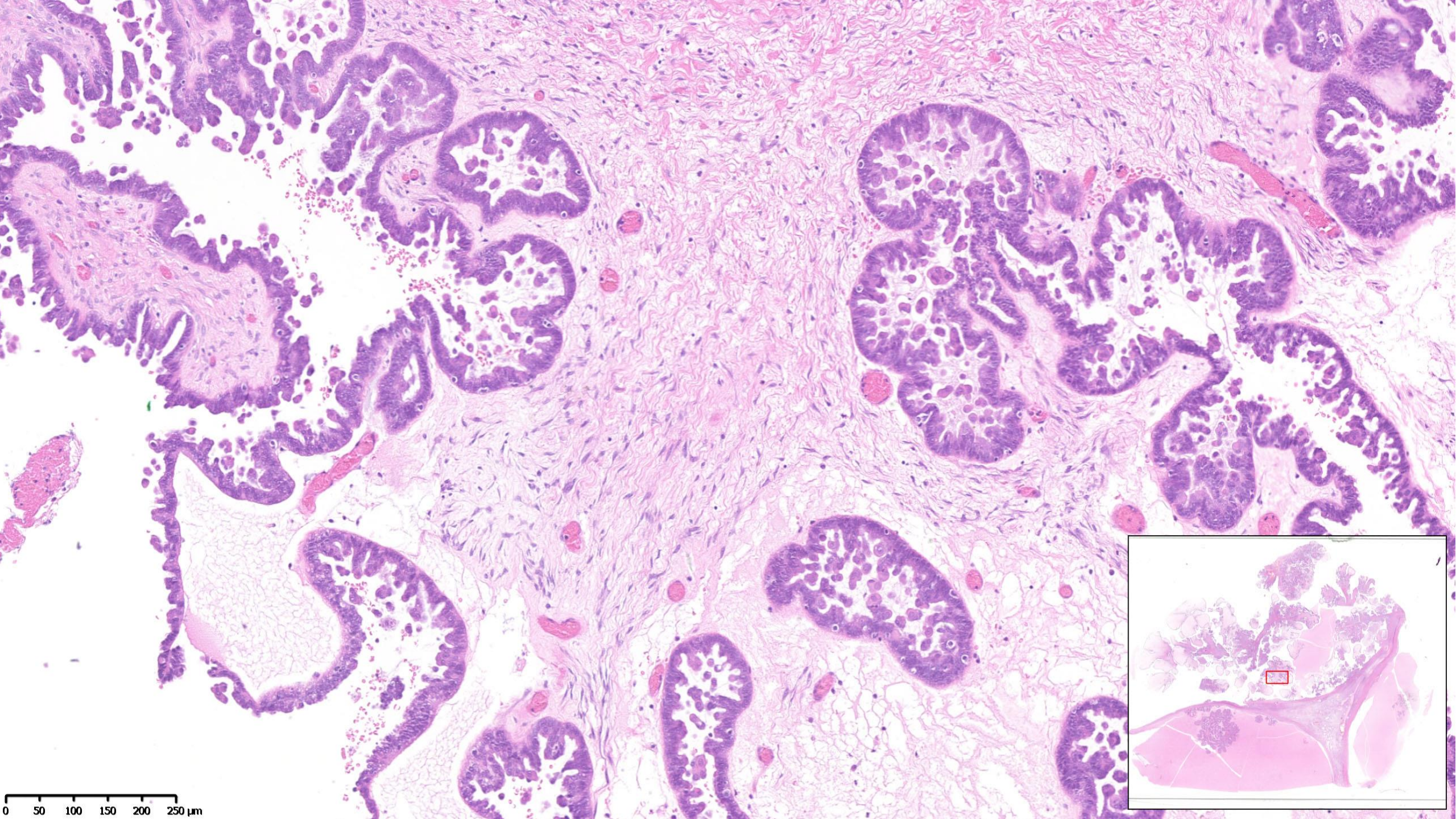


0 0.2 0.4 0.6 0.8 1mm

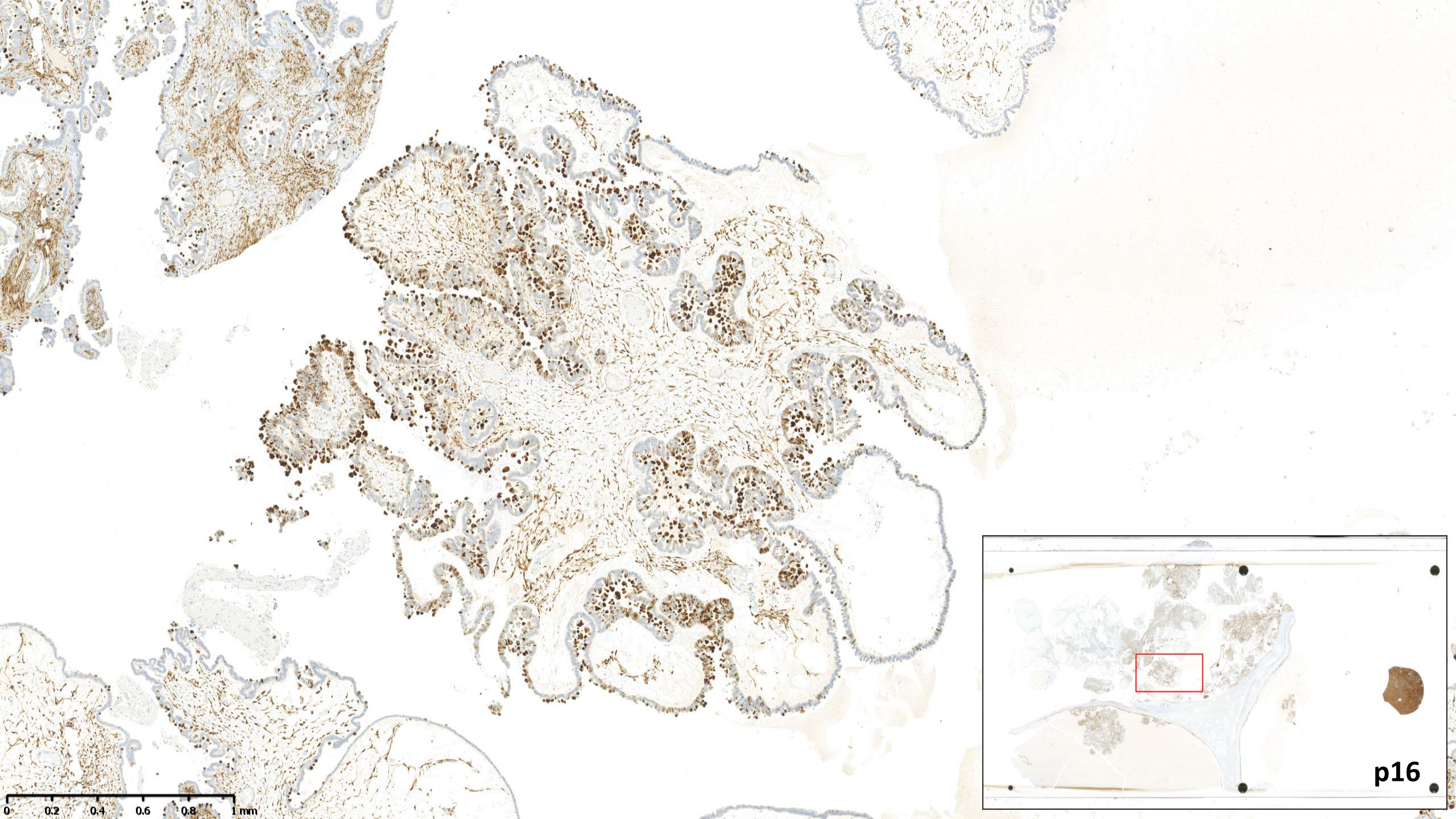


0 100 200 300 400 500 μm

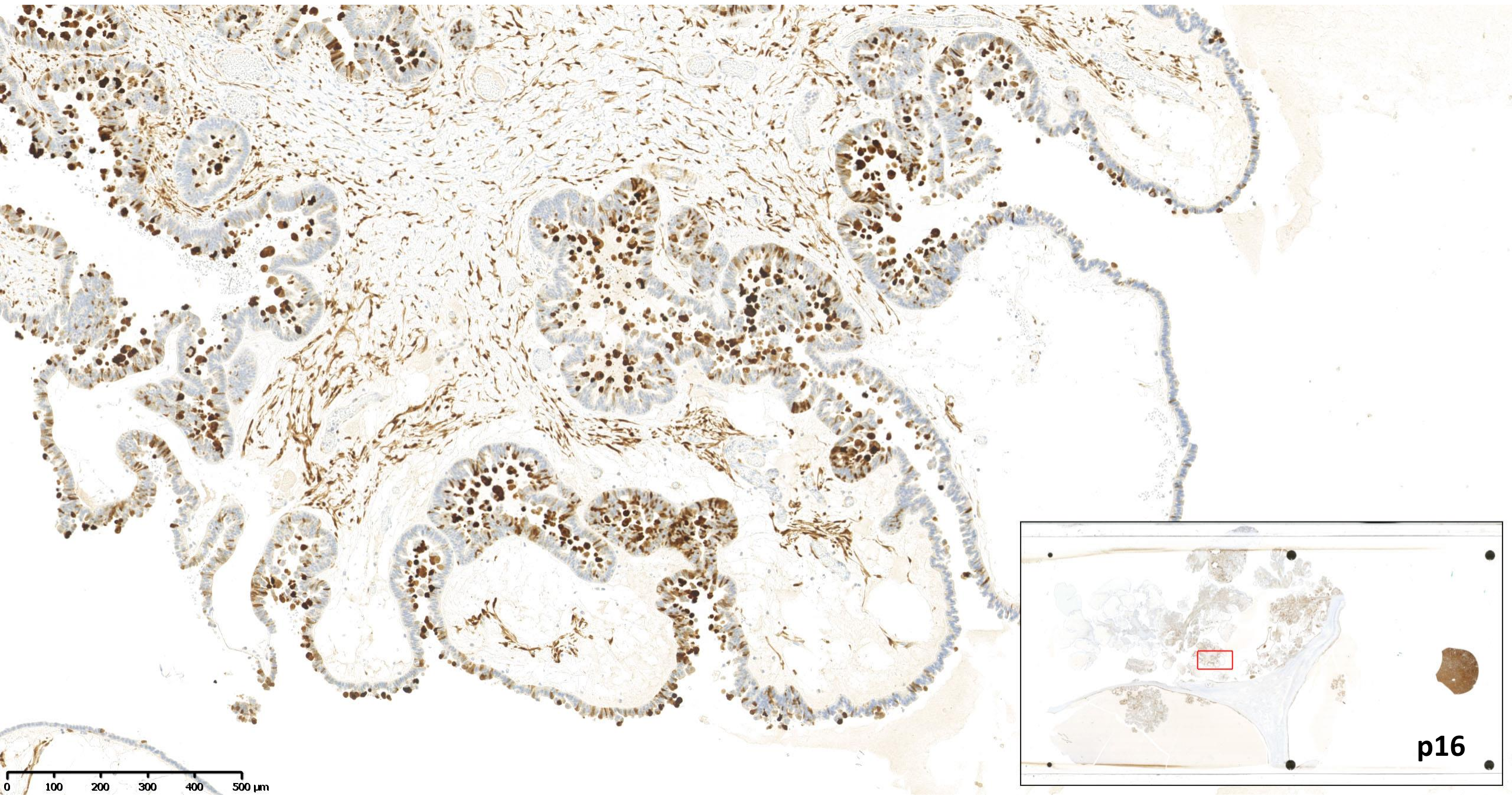


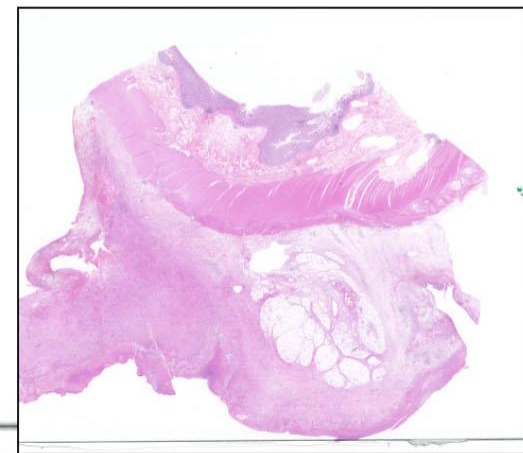
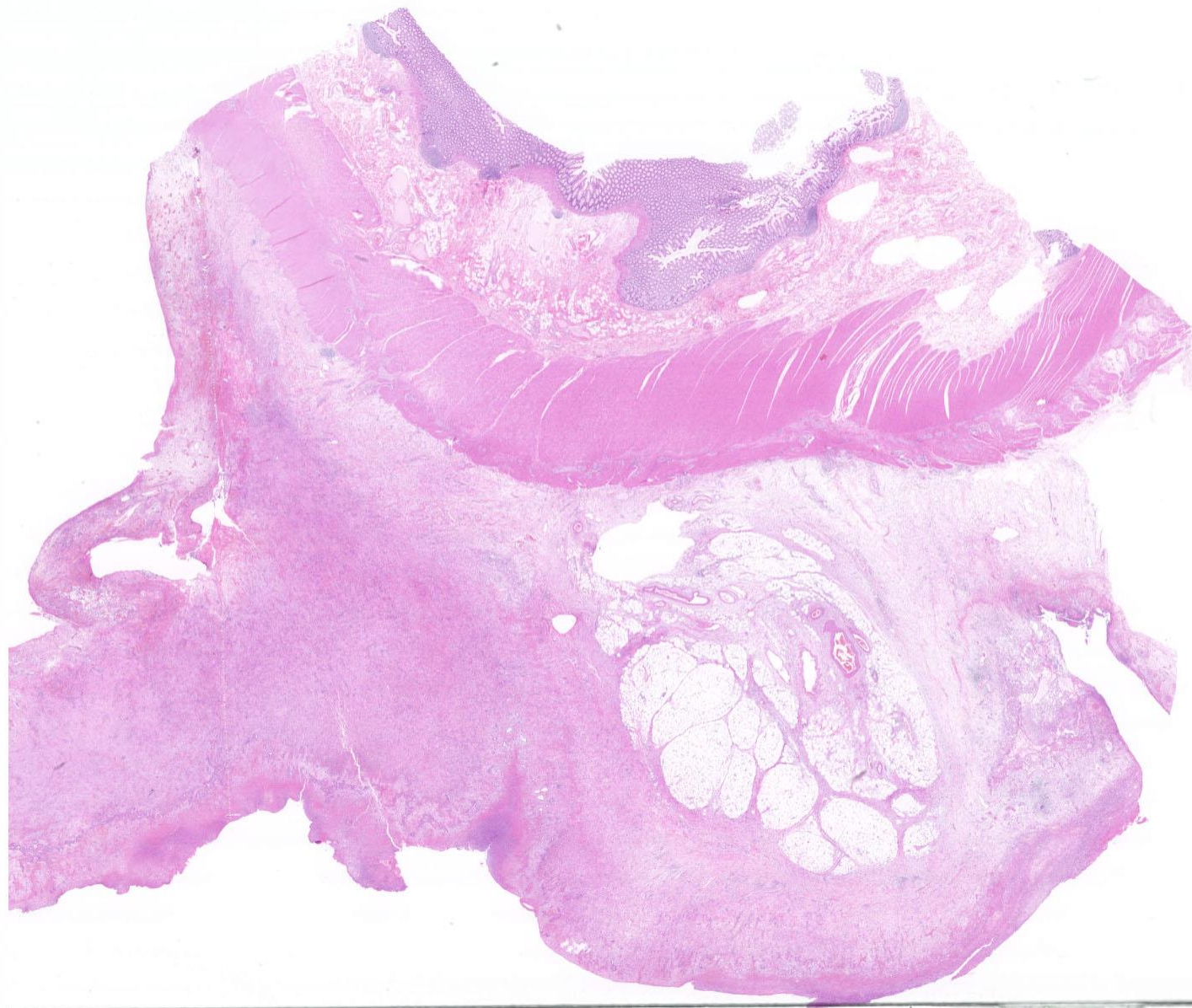


0 50 100 150 200 250 μm

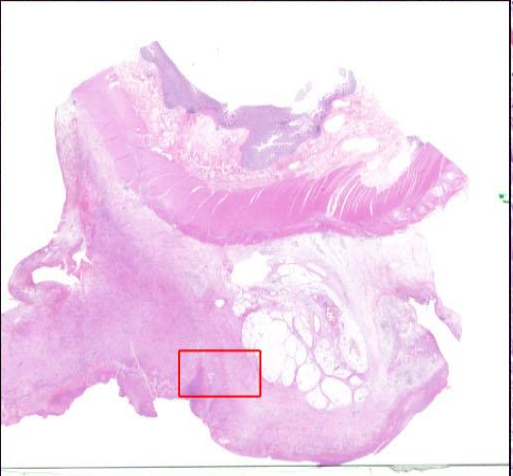
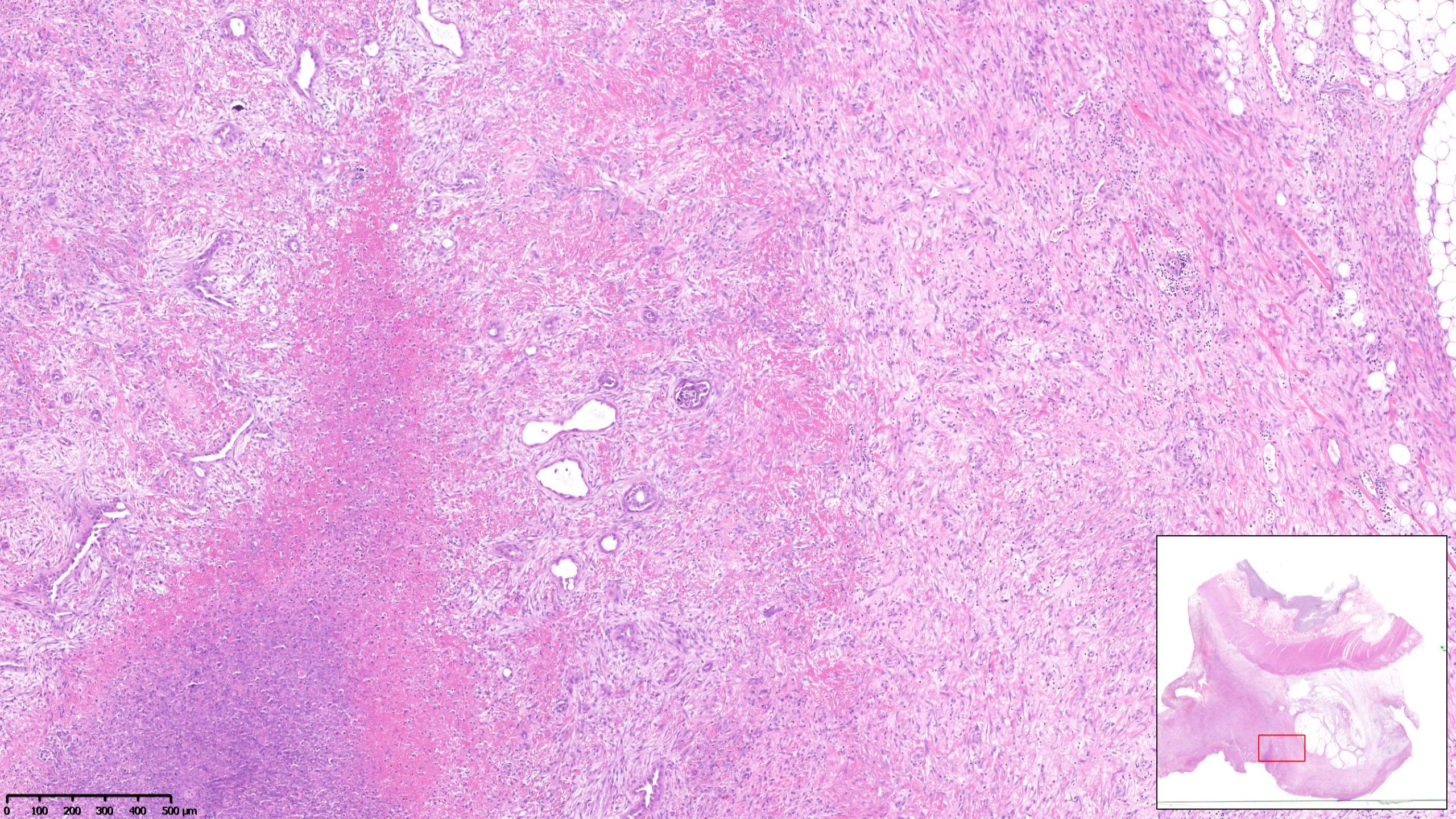


p16

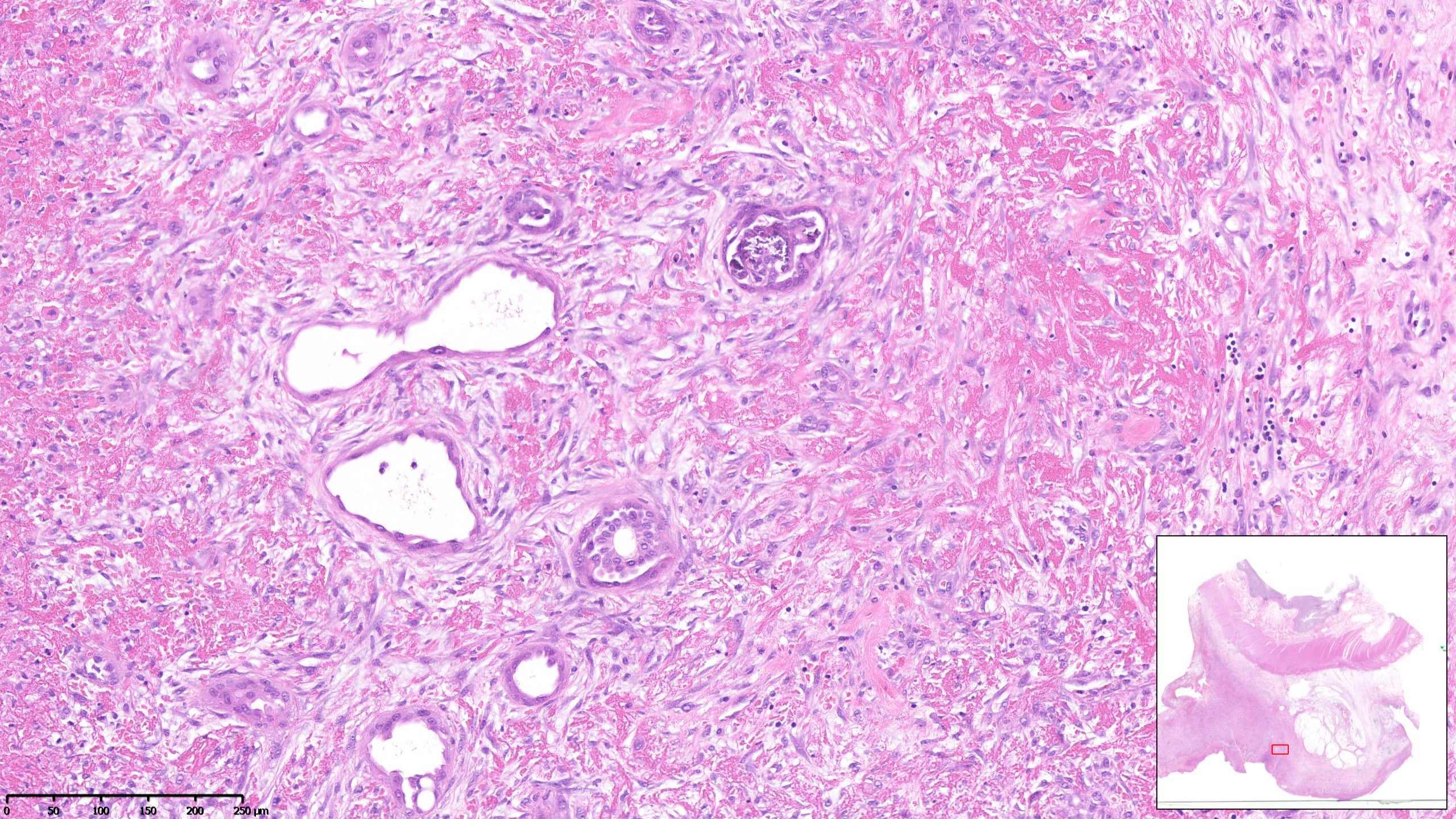




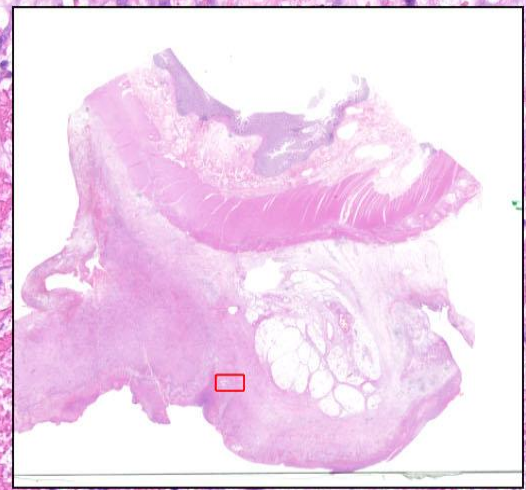
0 1 2 3 4 5 mm



0 100 200 300 400 500 μm



0 50 100 150 200 250 μm

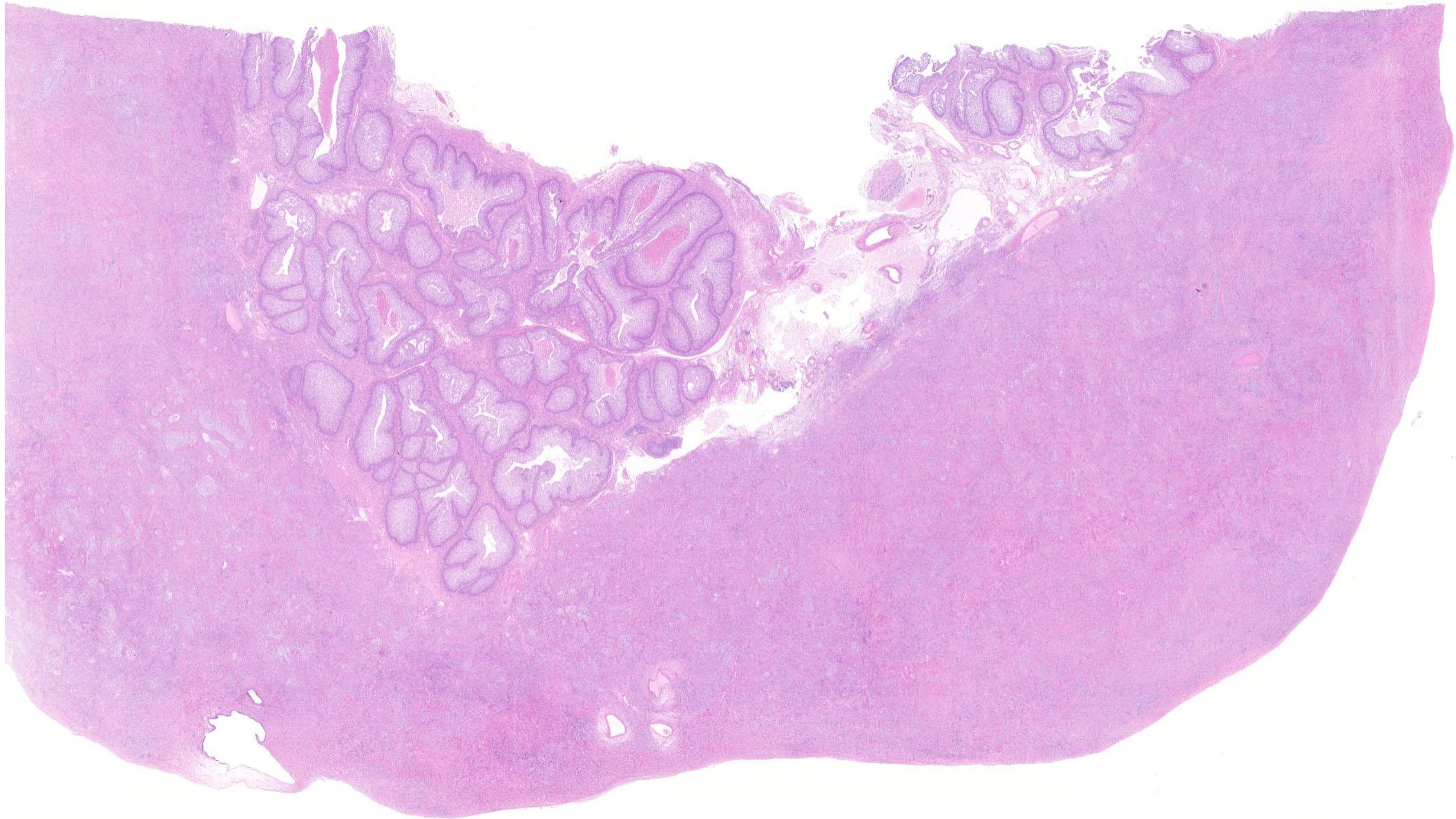


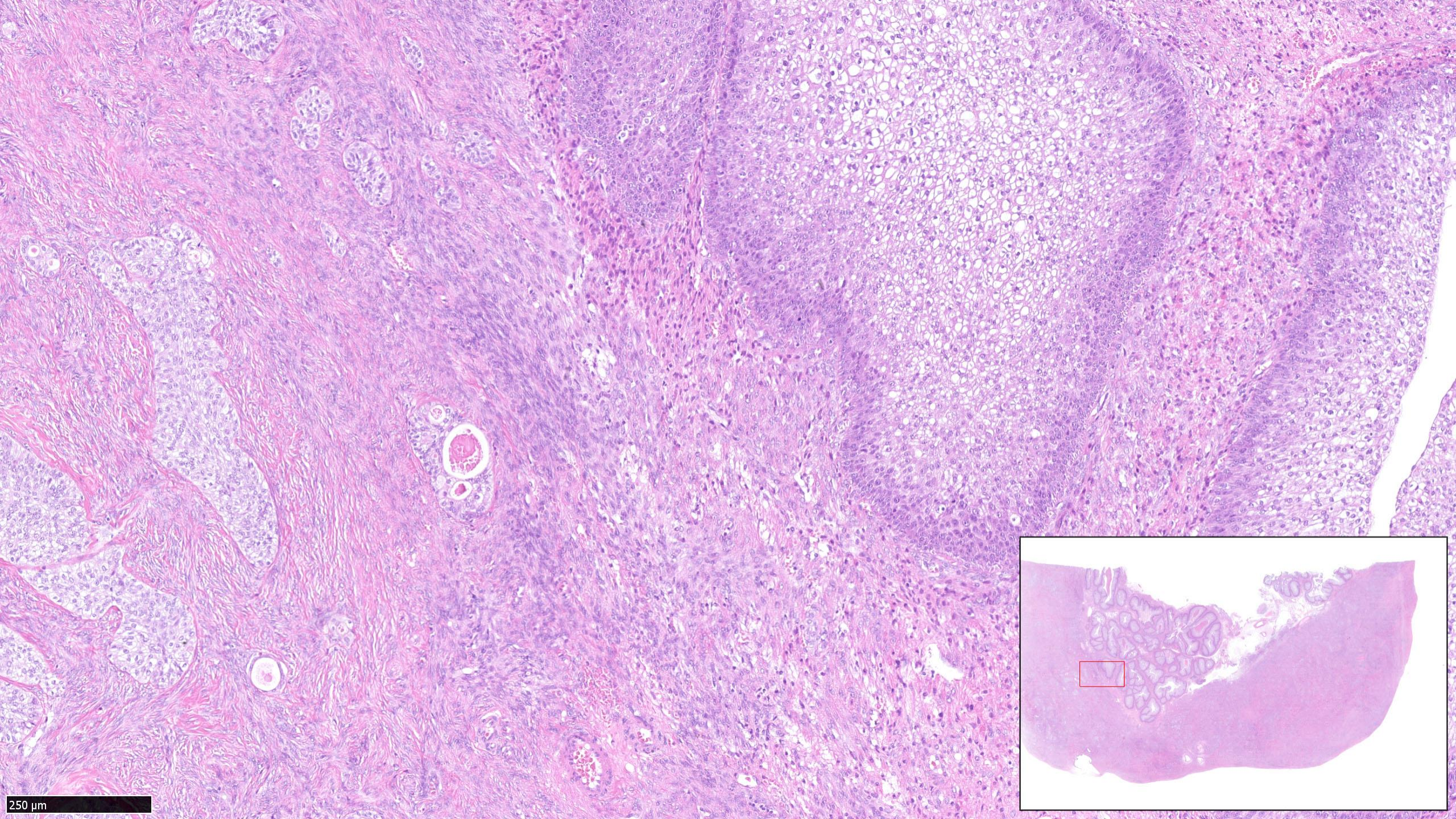
Diagnosis

Serous Borderline Ovarian Tumour with
Non-Invasive Desmoplastic Implants

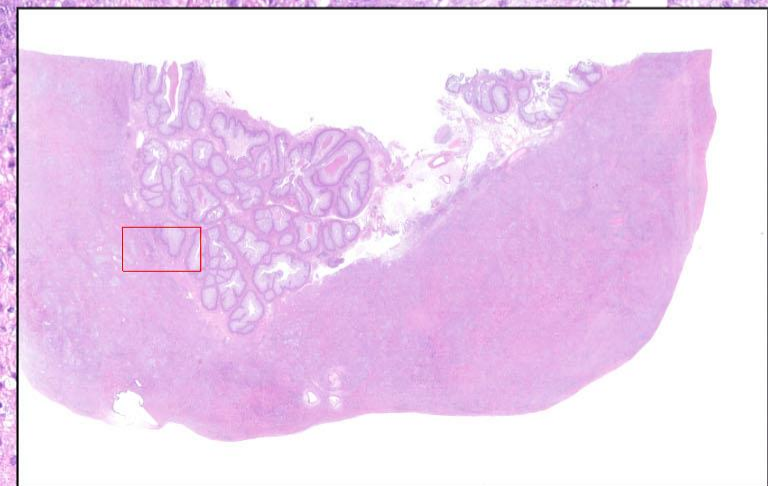
Case 6

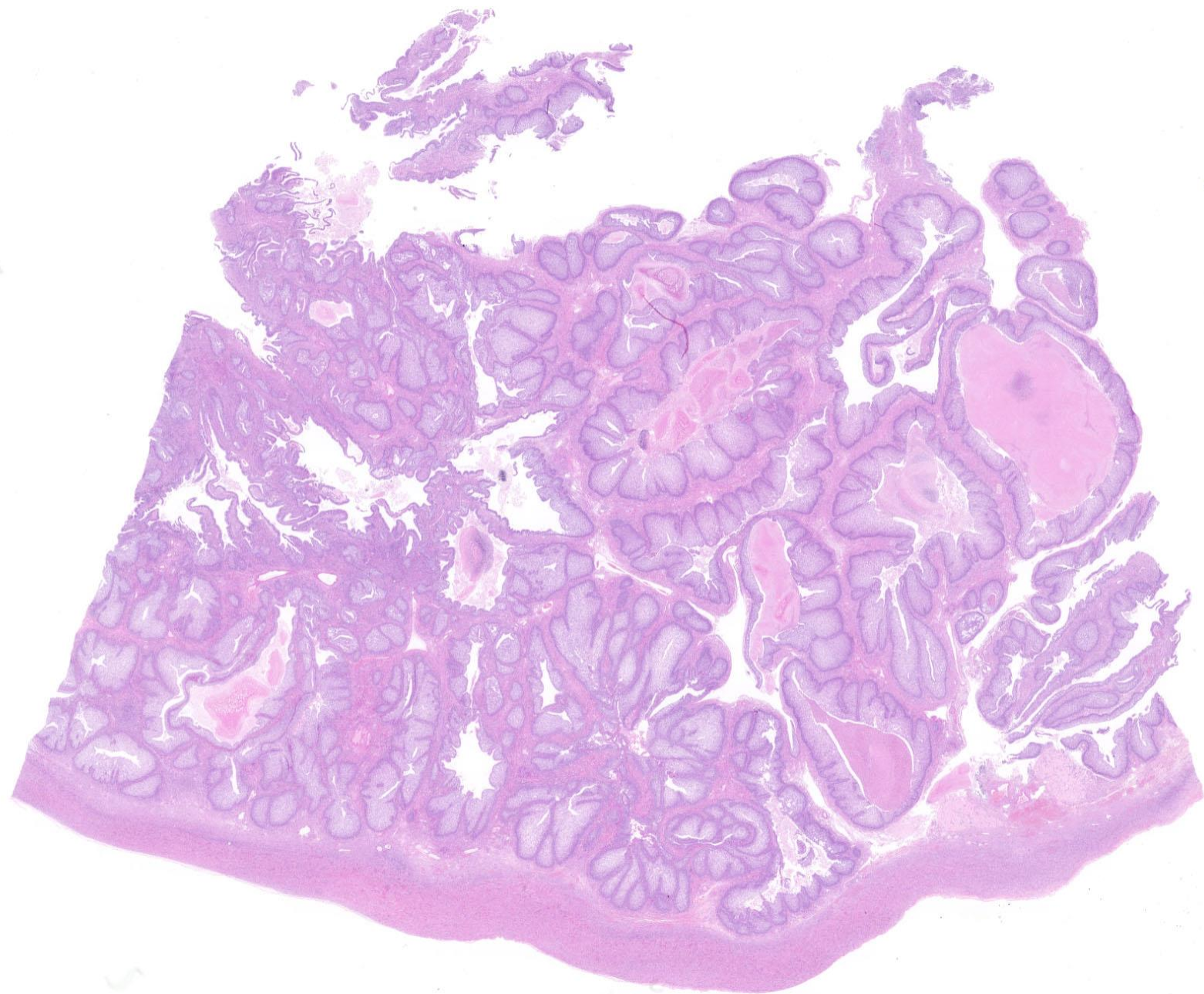
- Female aged 78
- Ovarian cyst
- Normal CA125
- Laparoscopic BSO
- Intact irregular white cyst measuring 75 x 35 x 30 mm
- On sectioning, some areas have a firm 'fibromatous' appearance but elsewhere there is friable tissue

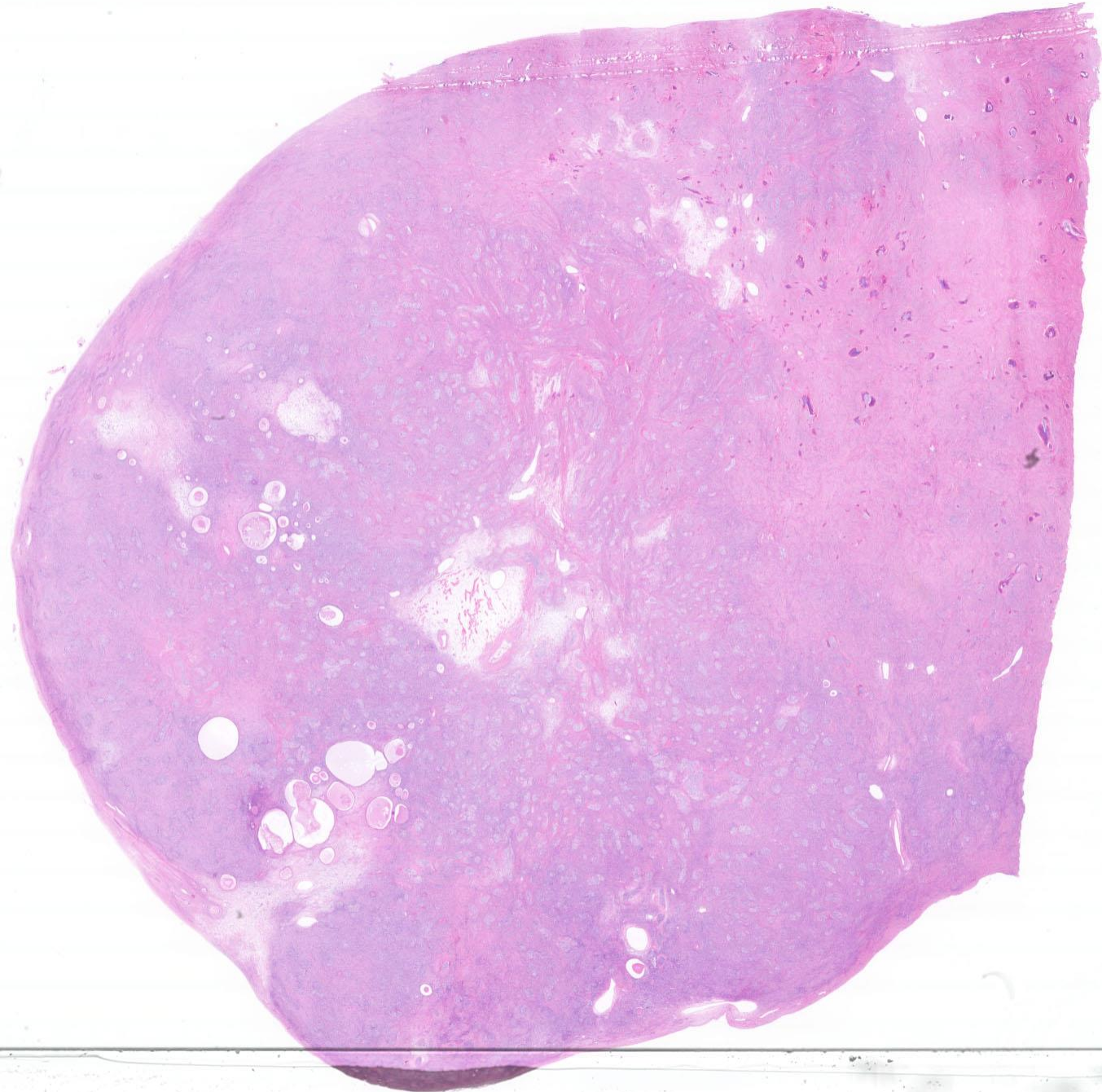




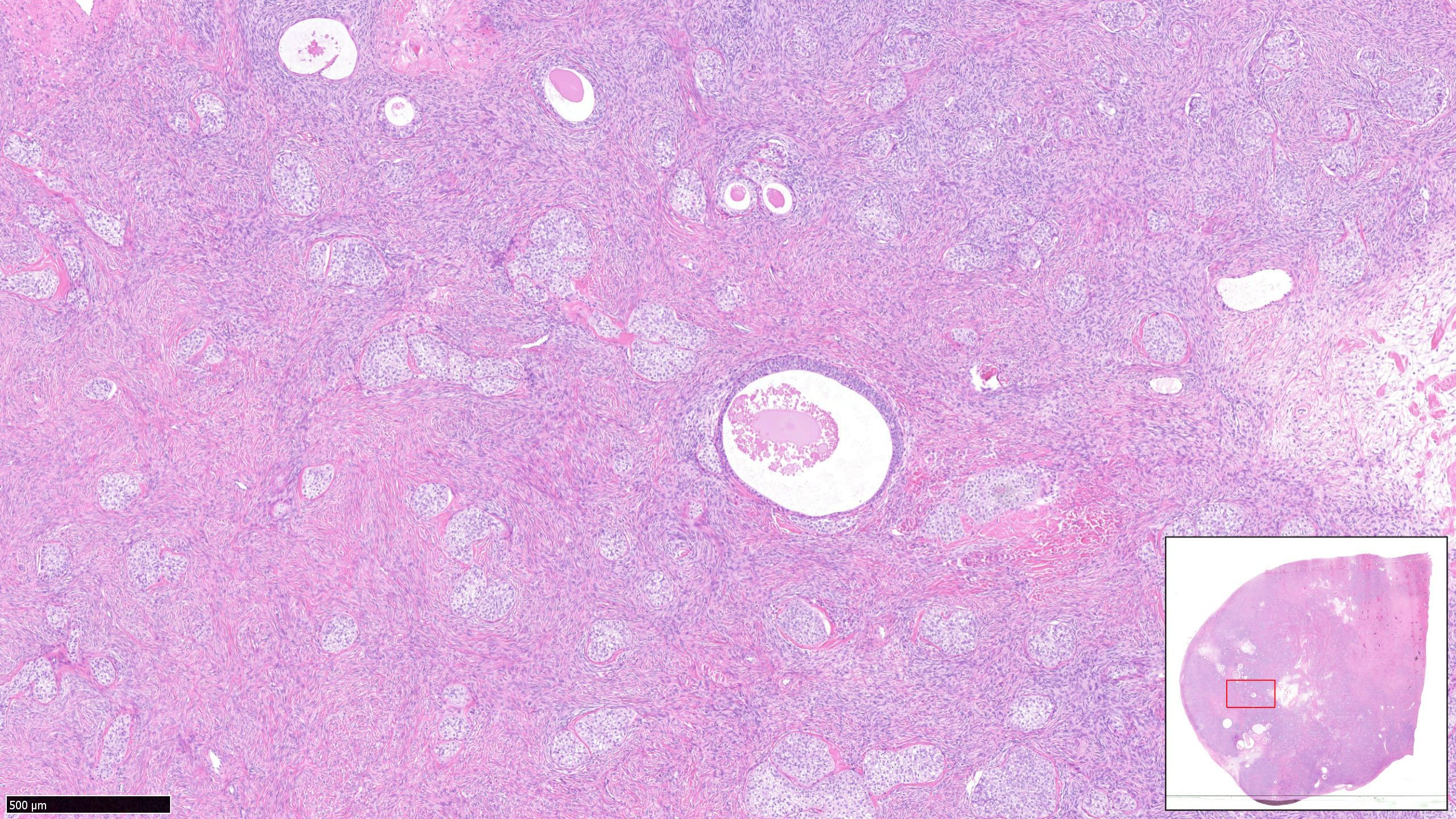
250 μ m



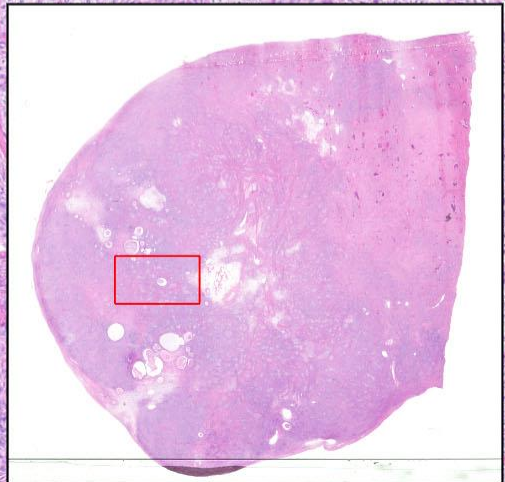




5 mm



500 μ m



Diagnosis

Borderline Brenner Tumour