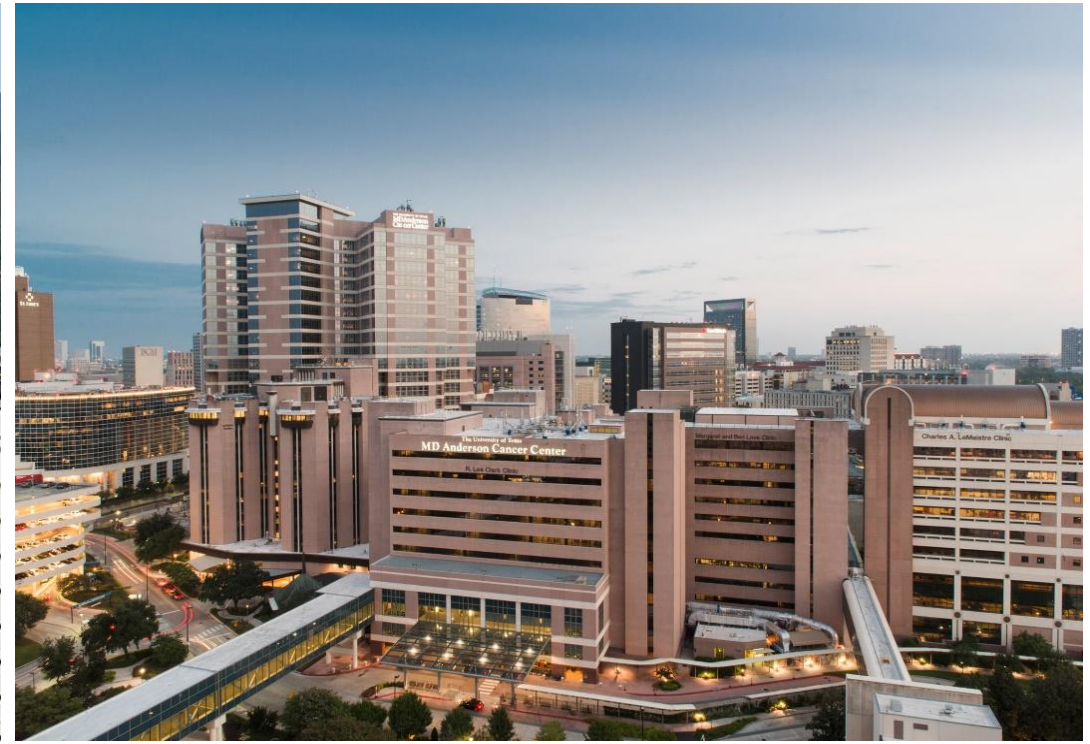




Ovarian Epithelial Tumors, Do Not Get Stumped

The International Academy of Pathology

Hong Kong Division

Anaís Malpica, M.D.

Professor

Department of Pathology

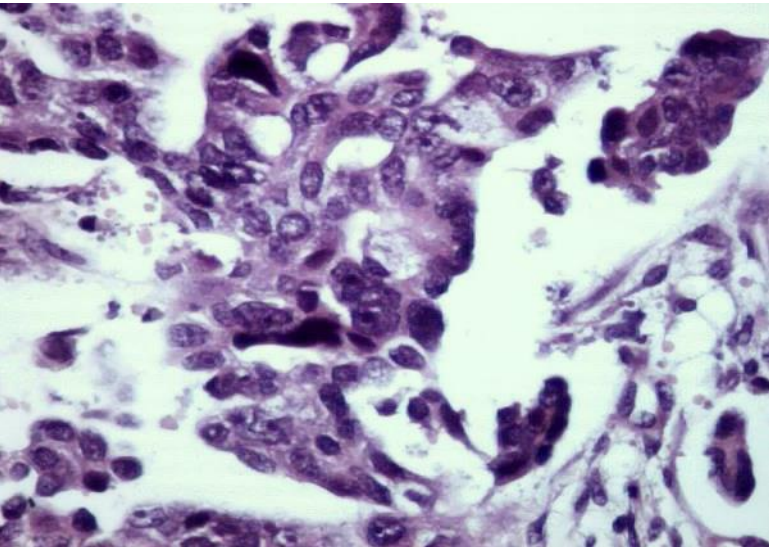
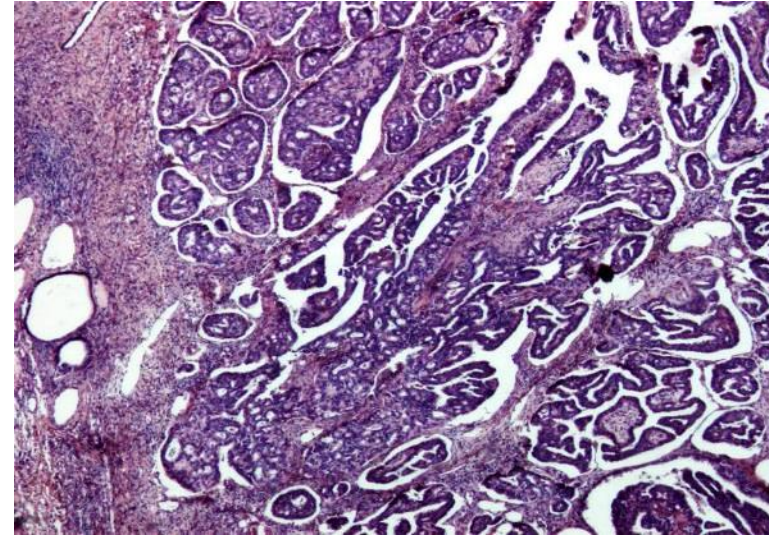
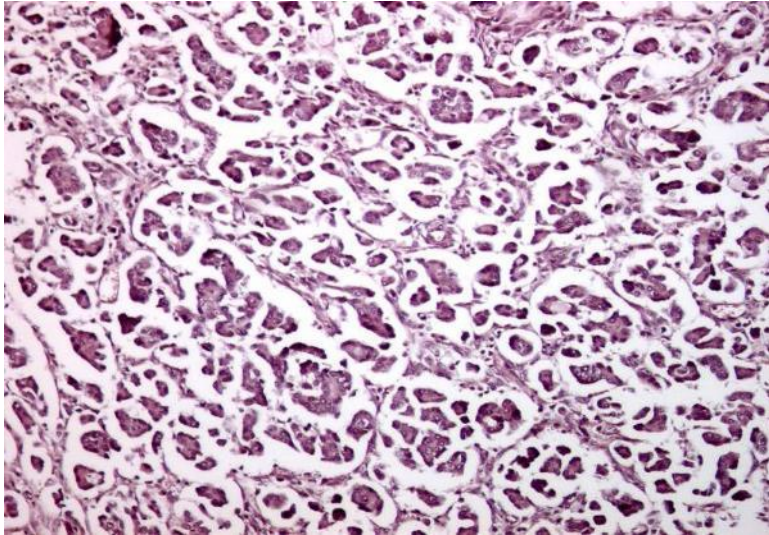
THE UNIVERSITY OF TEXAS
MD Anderson
~~Cancer~~ Center
Making Cancer History®

No conflicts of interest

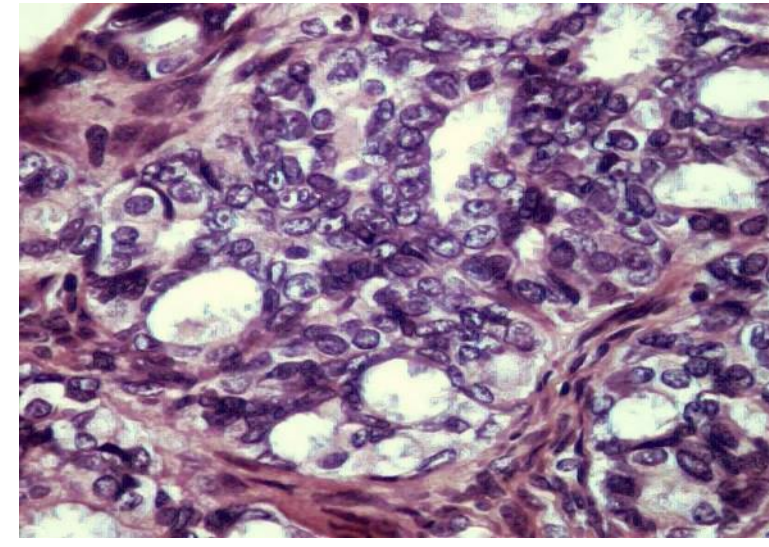
High Grade Serous Ca, Issues

- Using the architecture and not paying attention to the degree of atypia to assign the grade
- Tumor heterogeneity
- A wide variety of patterns and appearances
- Recurrence has a different histotype
 - Carcinosarcoma —undersampling vs. lack of recognition vs. dedifferentiation
 - Sarcoma —undersampling vs. lack of recognition vs. dedifferentiation
 - Neuroendocrine Ca — lack of recognition

Pathologist does not follow diagnostic criteria



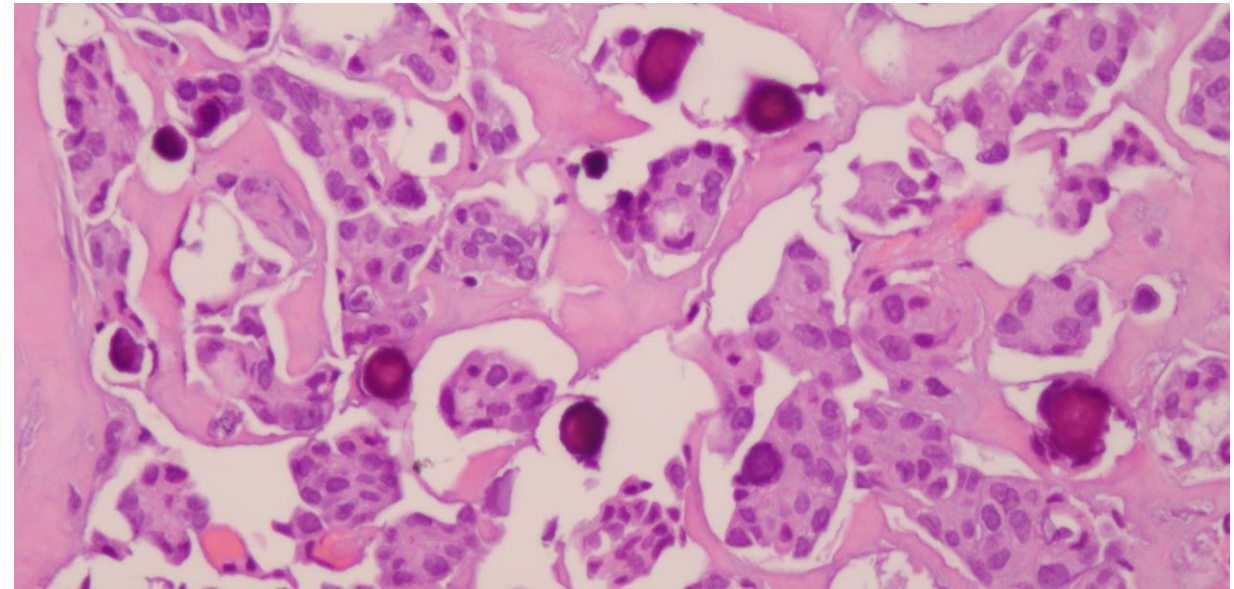
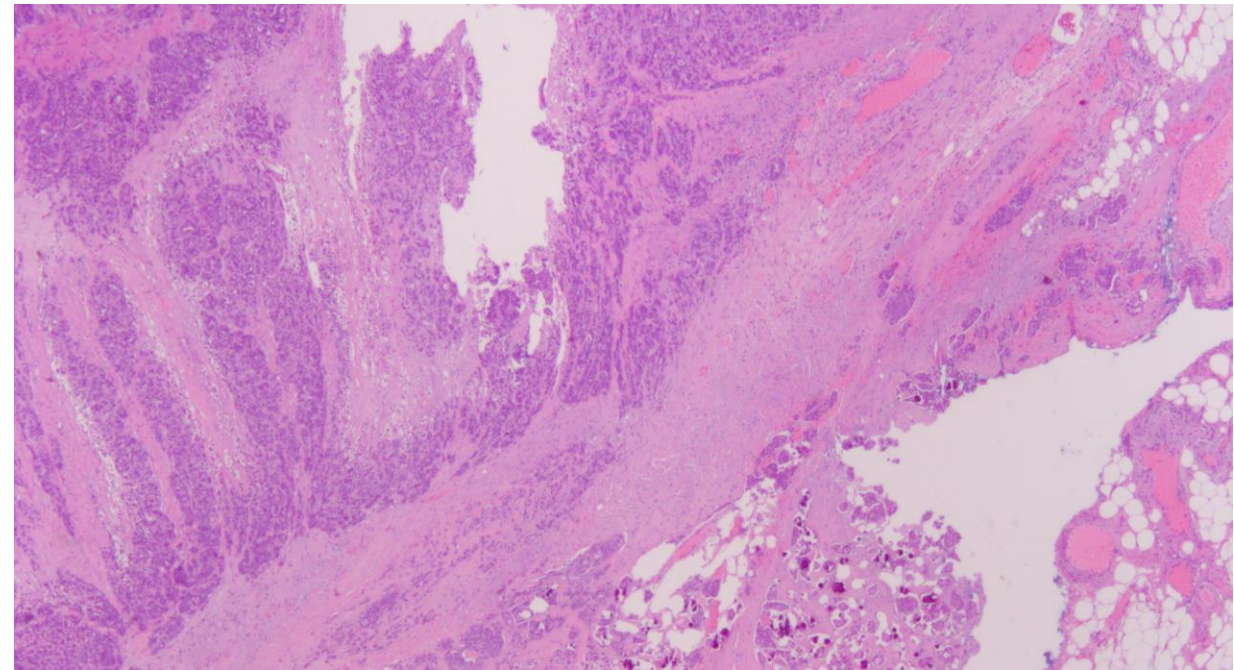
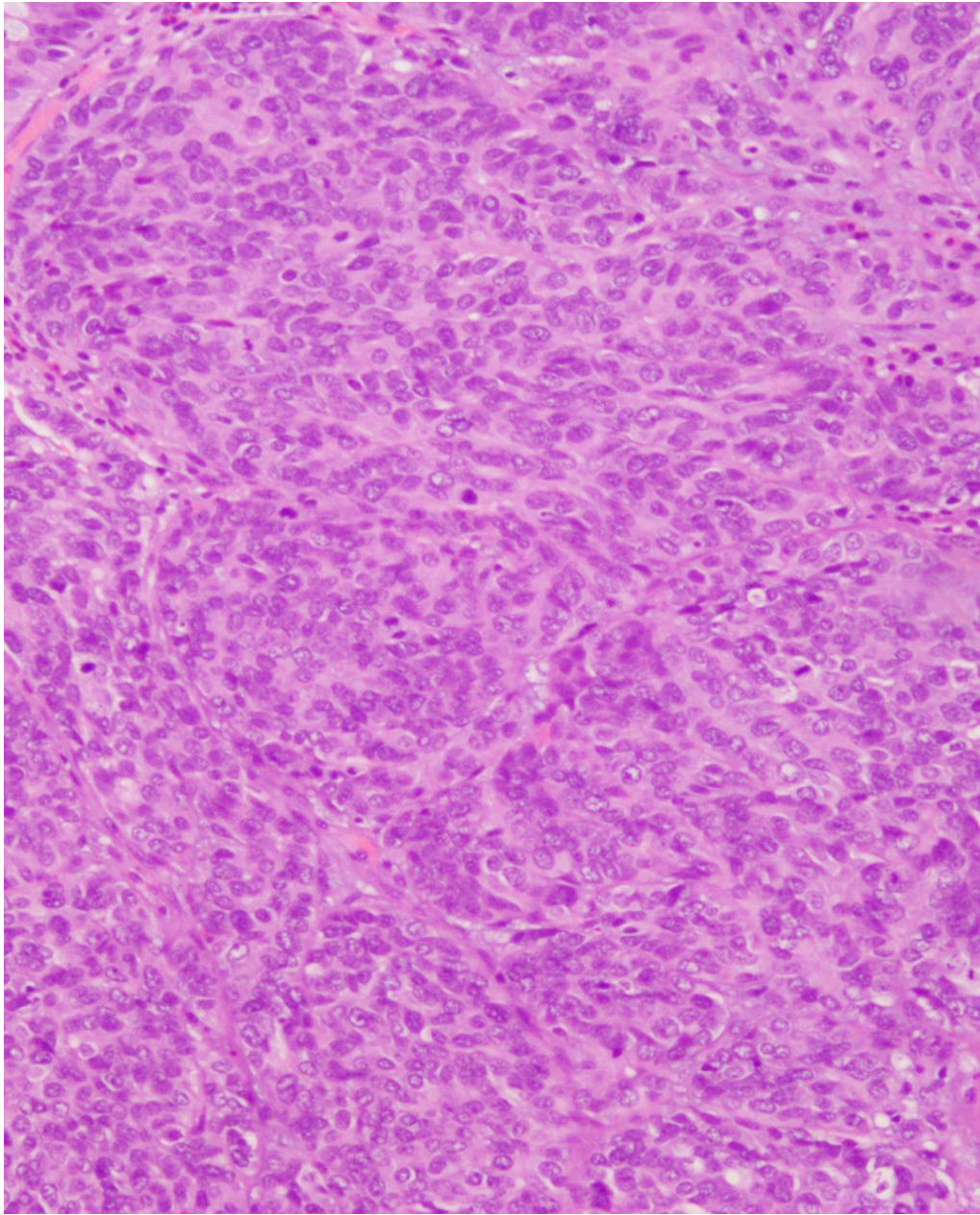
High grade serous Ca, interpreted
as low grade



Low grade serous Ca, interpreted
as high grade

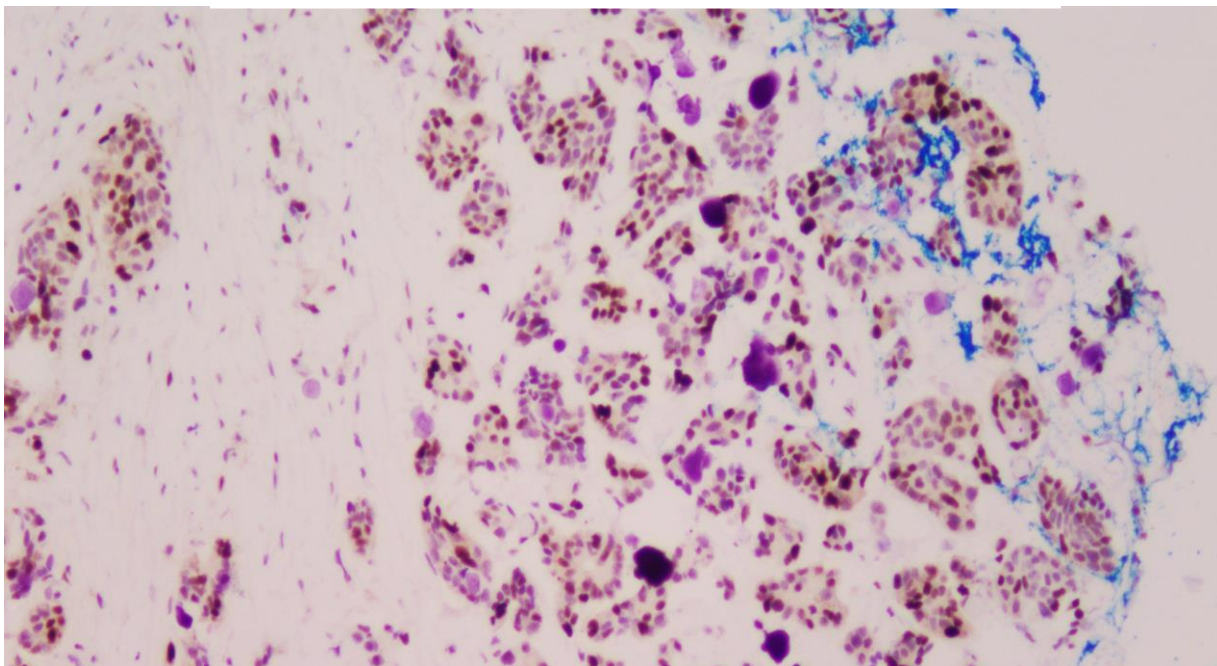
Serous Carcinoma, Tumor Heterogeneity, Low Grade and High Grade

- Uncommon
- Synchronous or metachronous phenomenon
- A problem when dealing with limited tissue

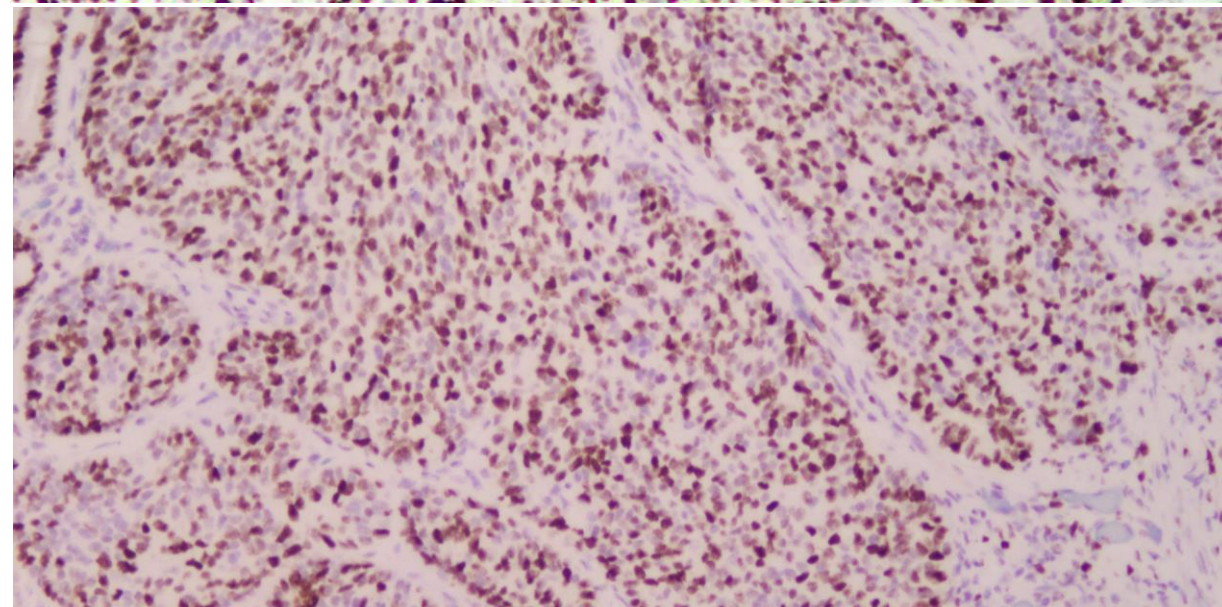
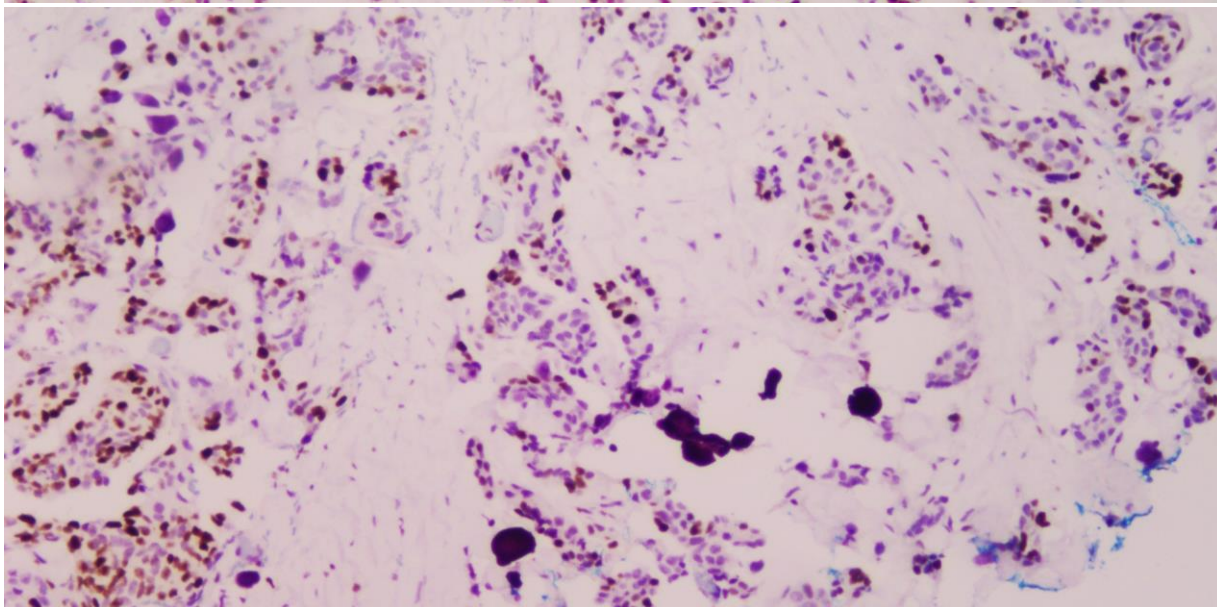
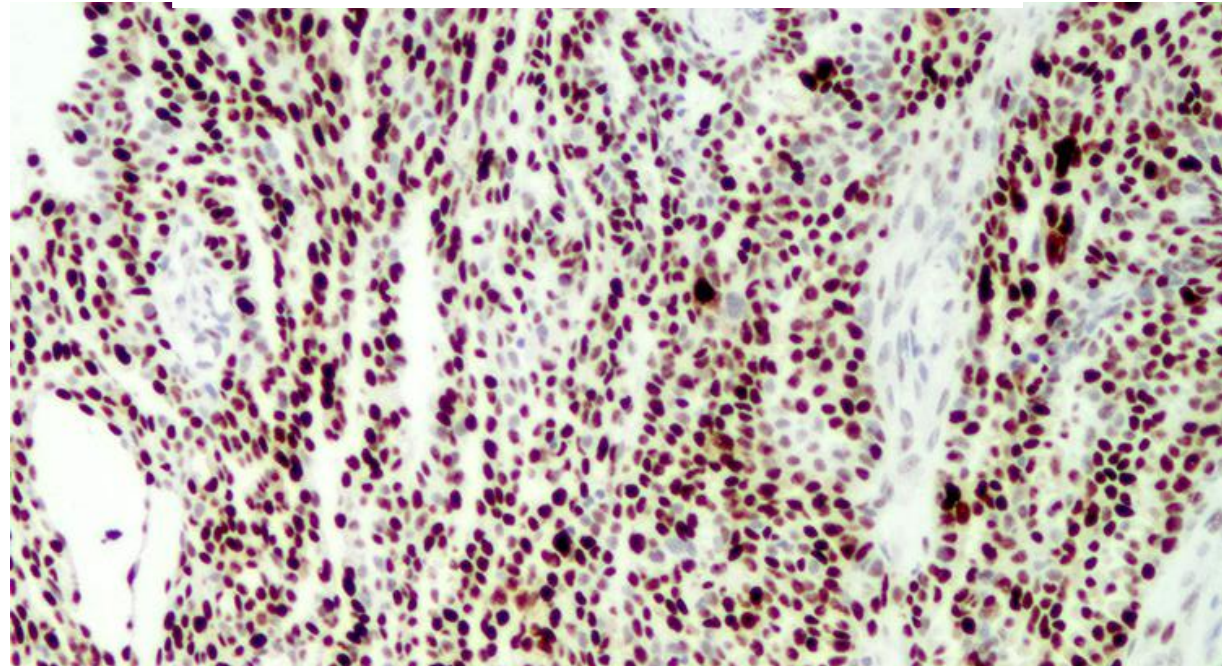


Serous Carcinoma, Tumor Heterogeneity, Low Grade and High Grade

Low Grade Serous Ca, p53 wild type



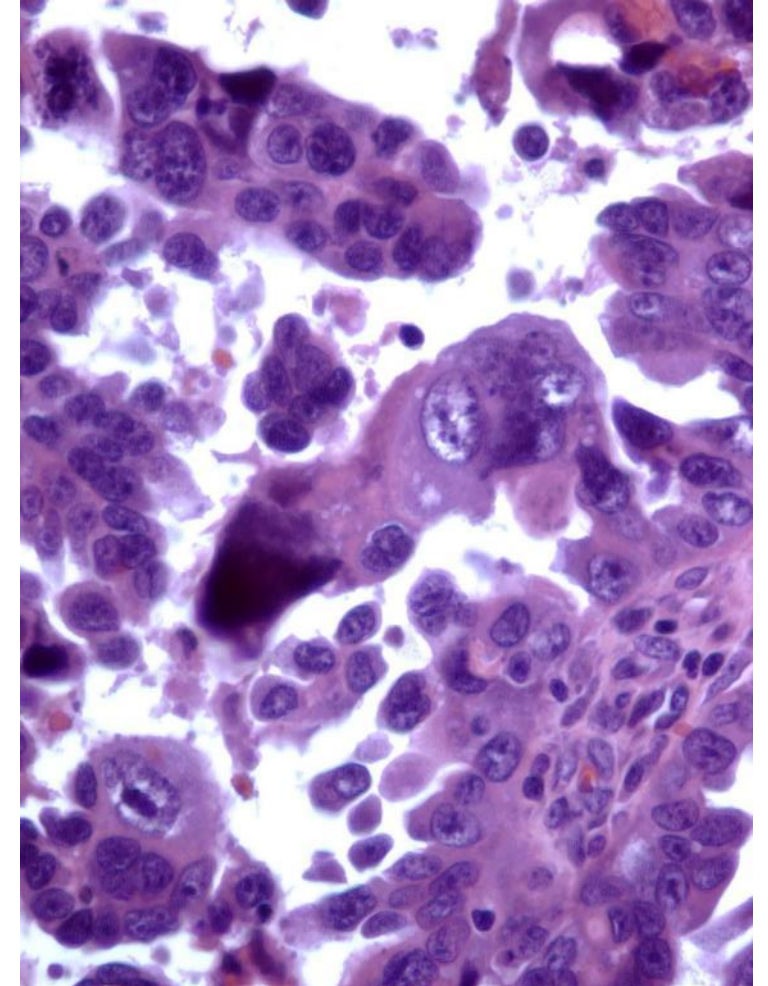
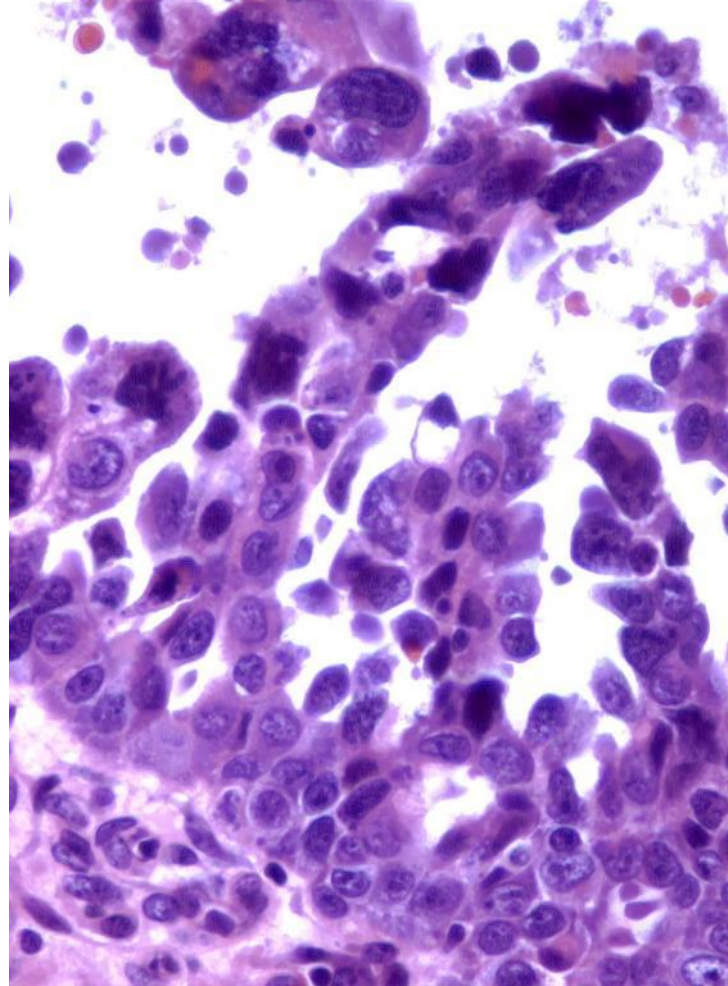
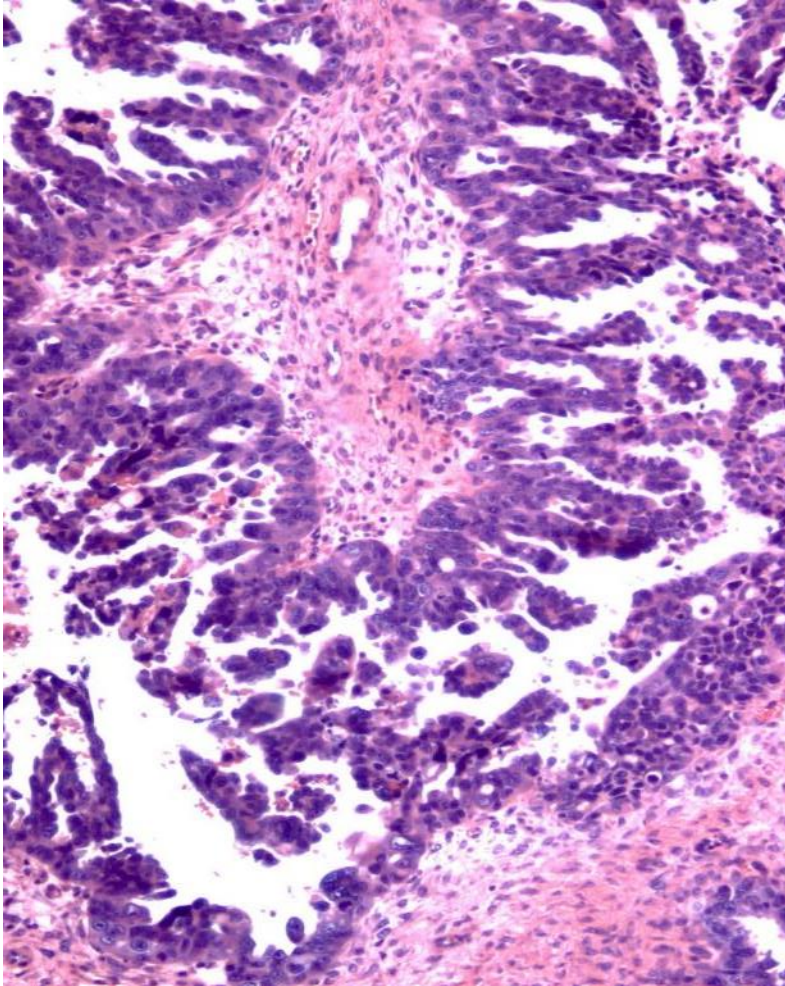
High Grade Serous Ca, aberrant p53



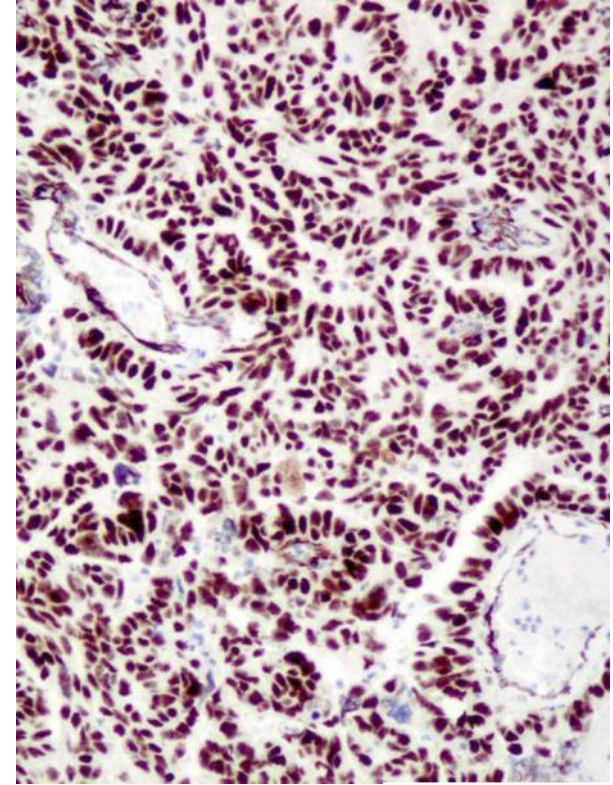
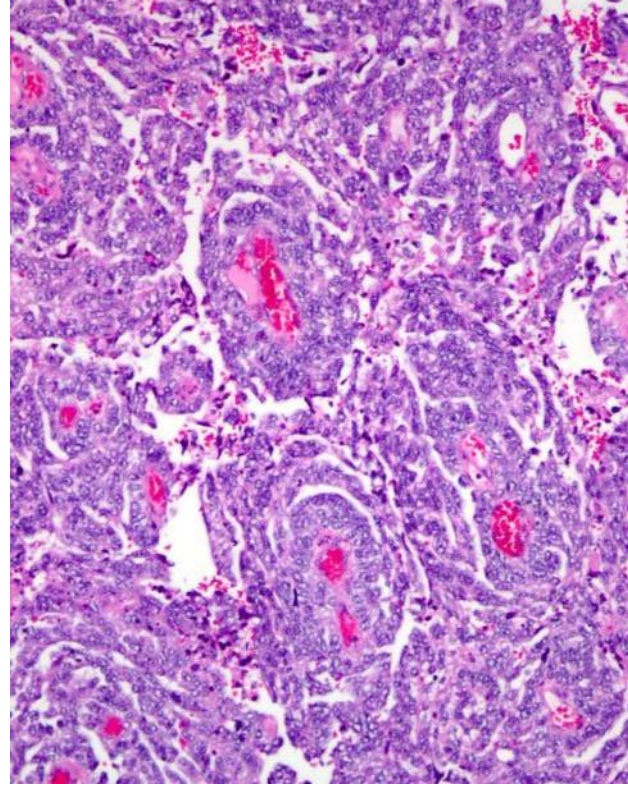
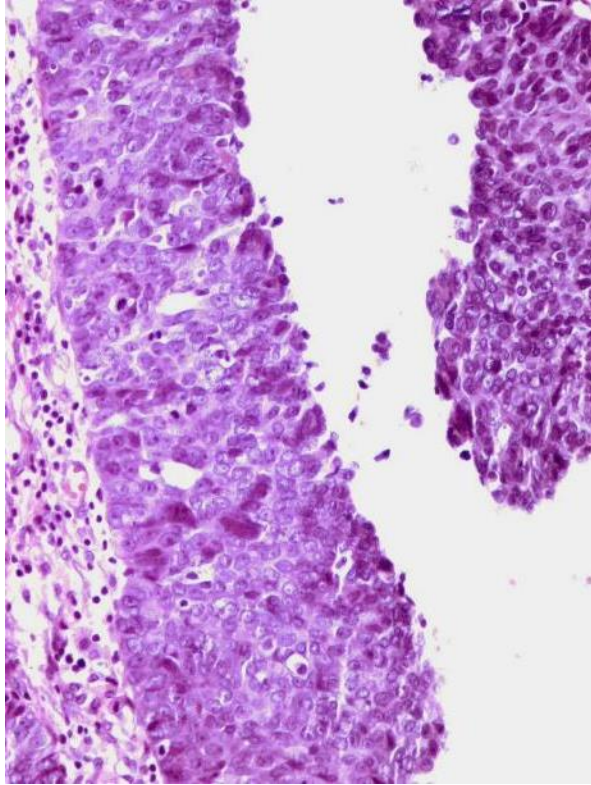
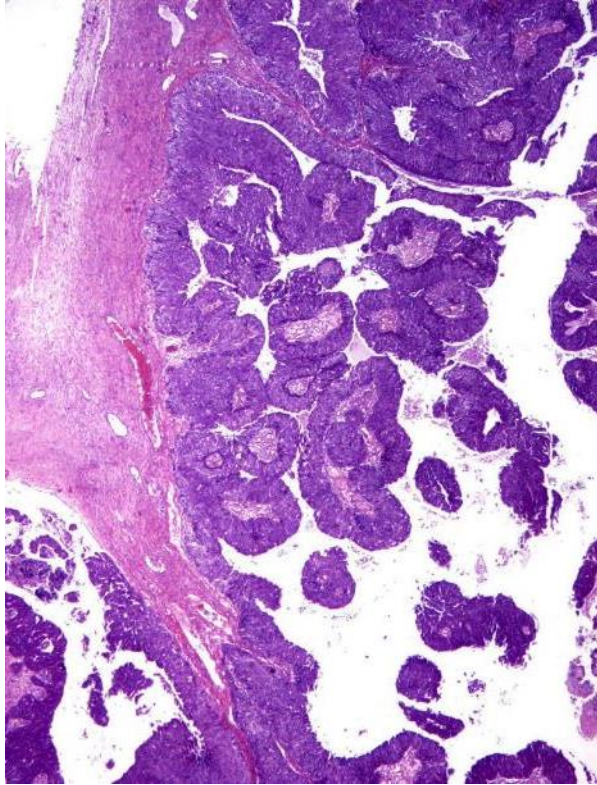
Low Grade Serous Ca, Ki-67

High Grade Serous Ca, Ki-67

High Grade Serous Ca, Papillary Pattern, Mimicking a Serous Borderline Tumor with a Micropapillary Pattern



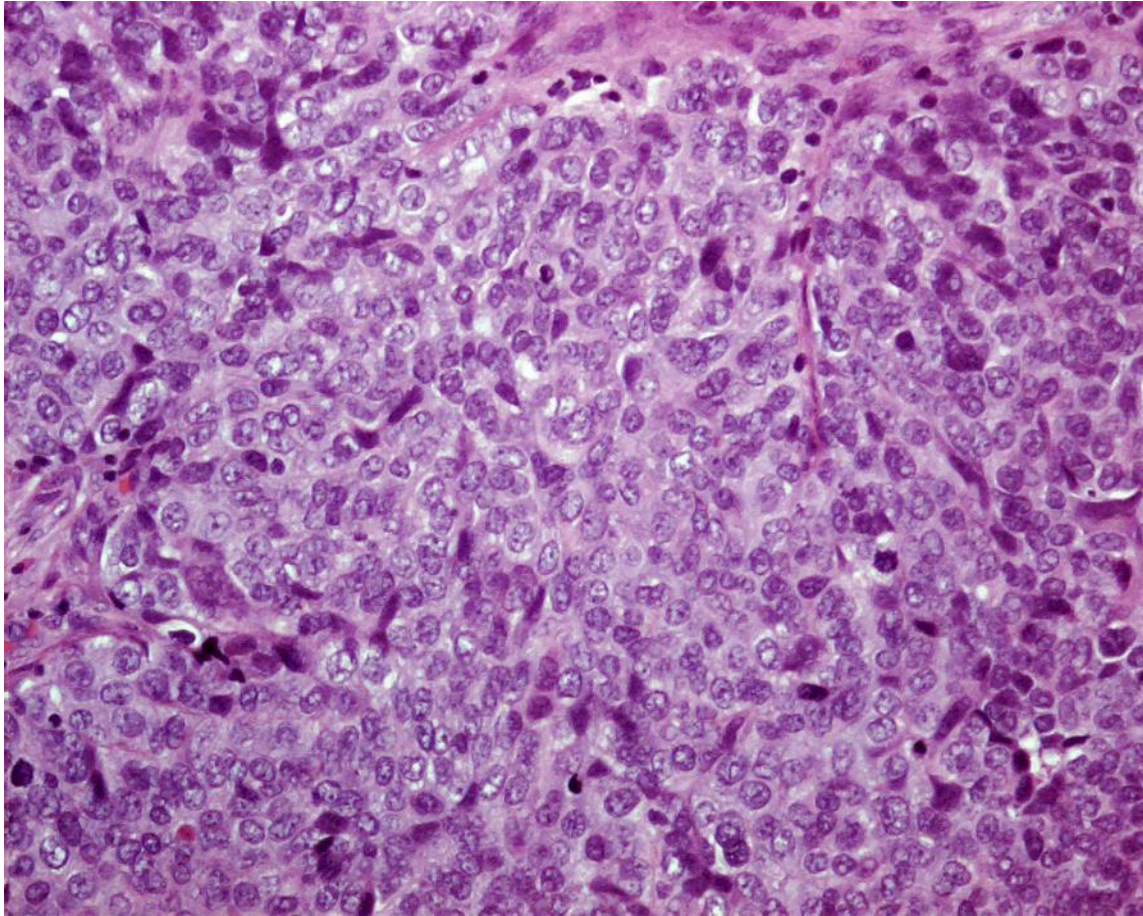
High Grade Serous Ca, Broad Base Papillae (TCC Pattern) and Papillae with Prominent Vessels



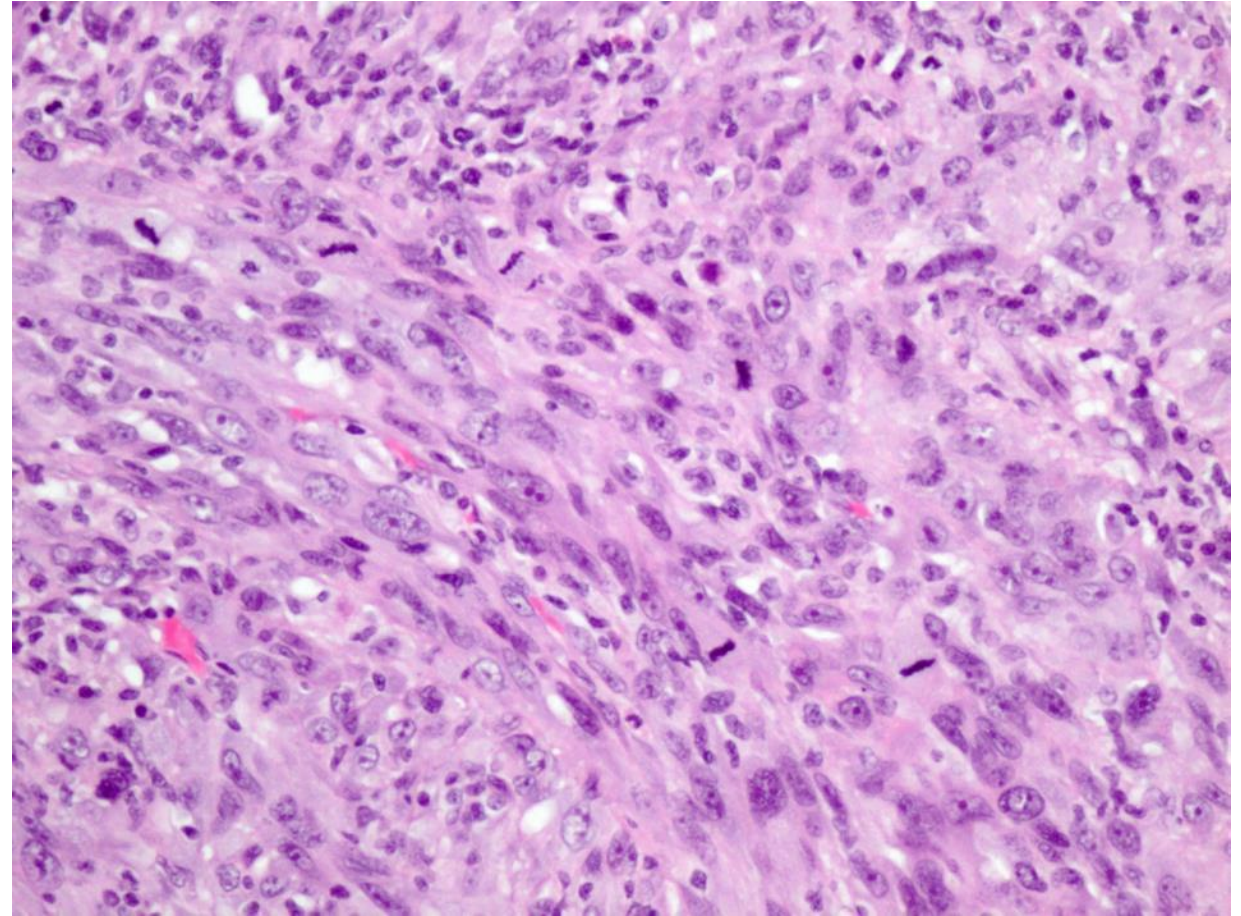
WT-1+

High Grade Serous Ca

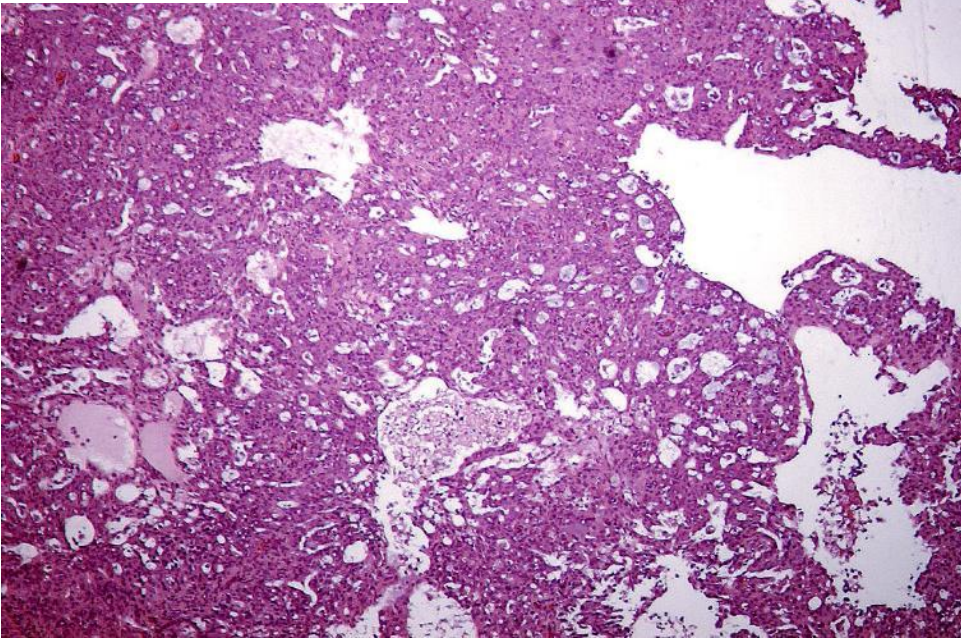
Solid pattern



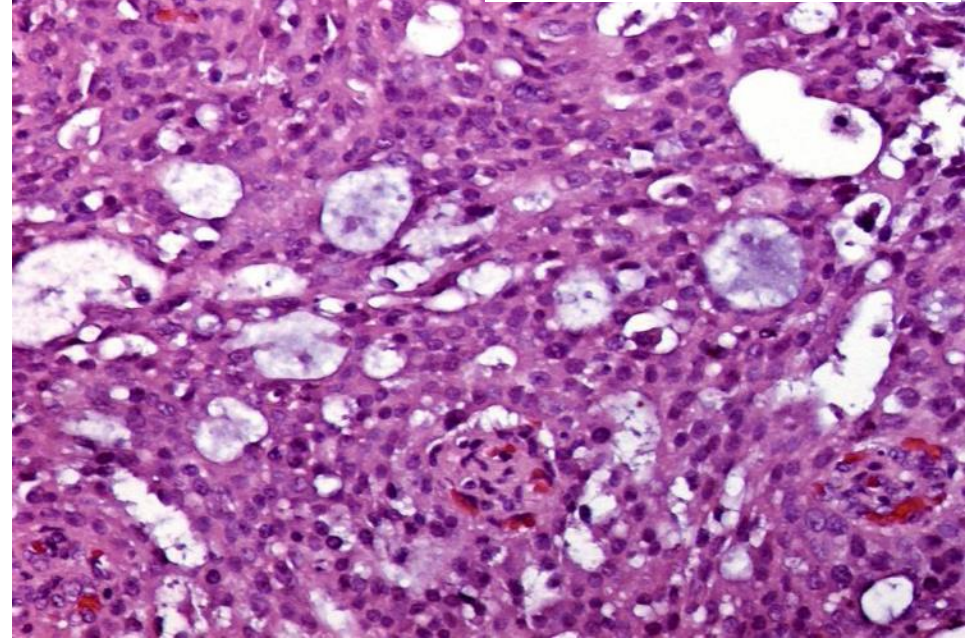
Spindle cells



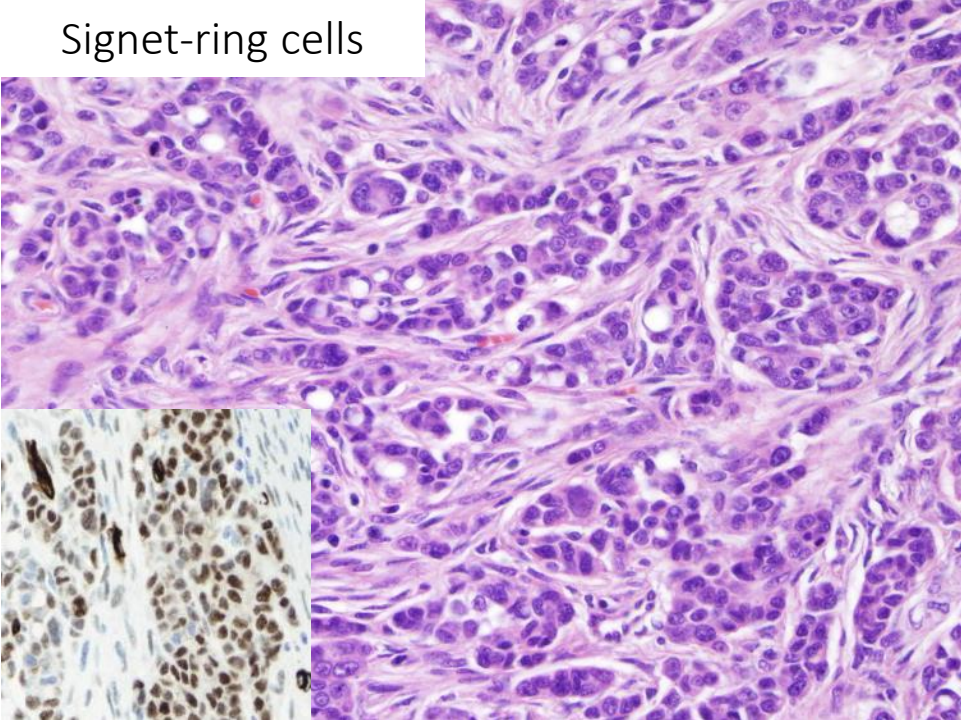
Microcystic pattern



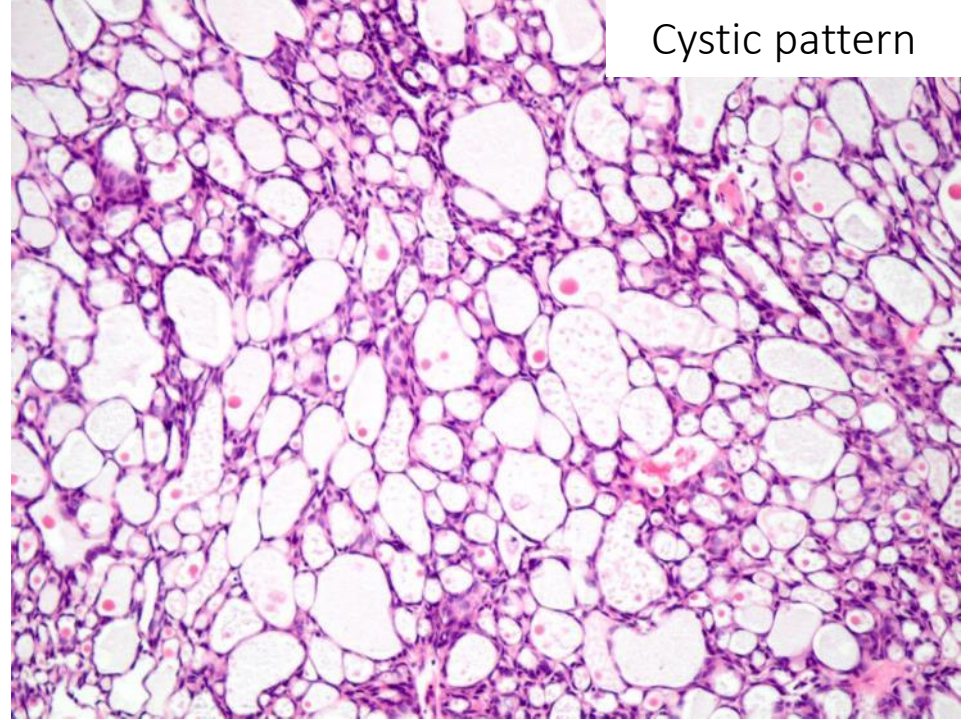
Microcystic pattern



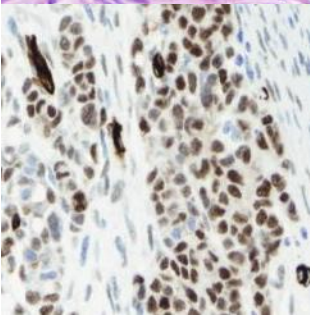
Signet-ring cells

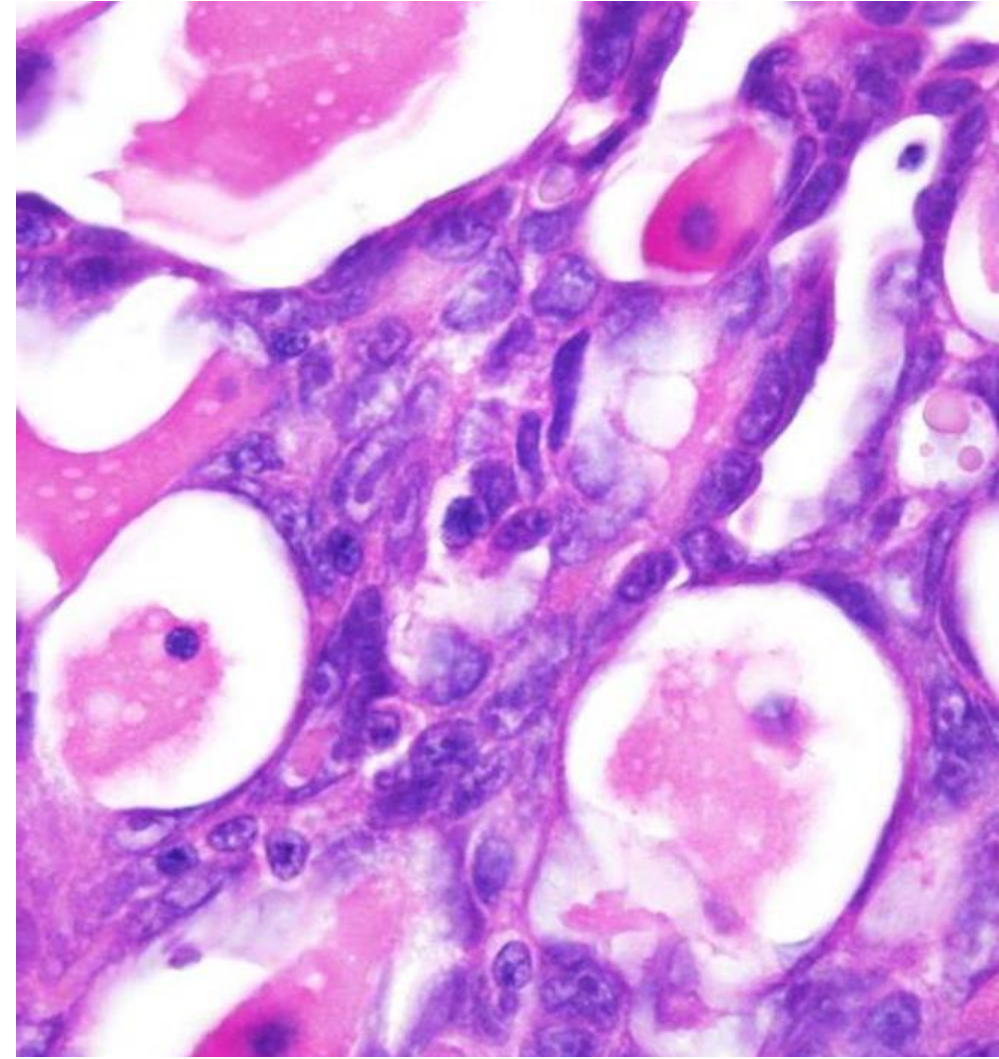
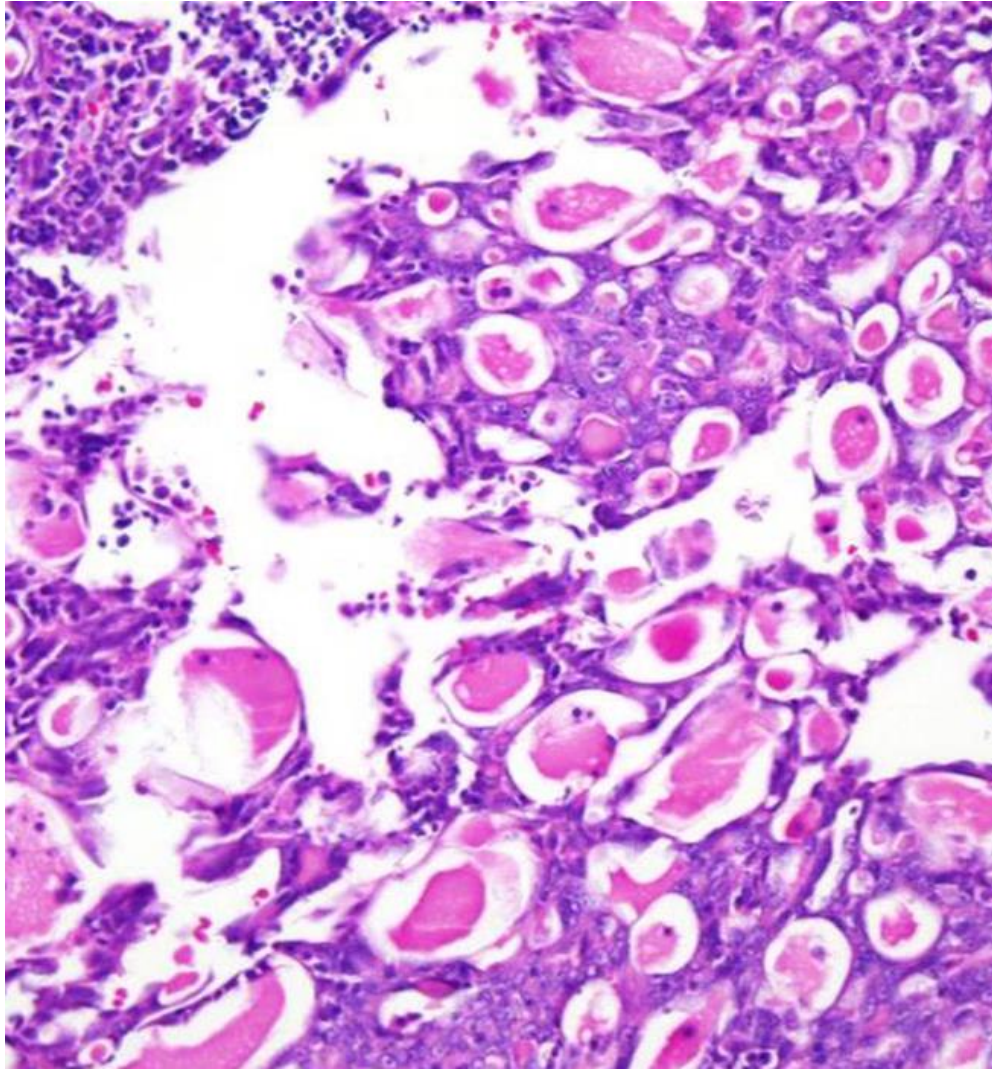


Cystic pattern



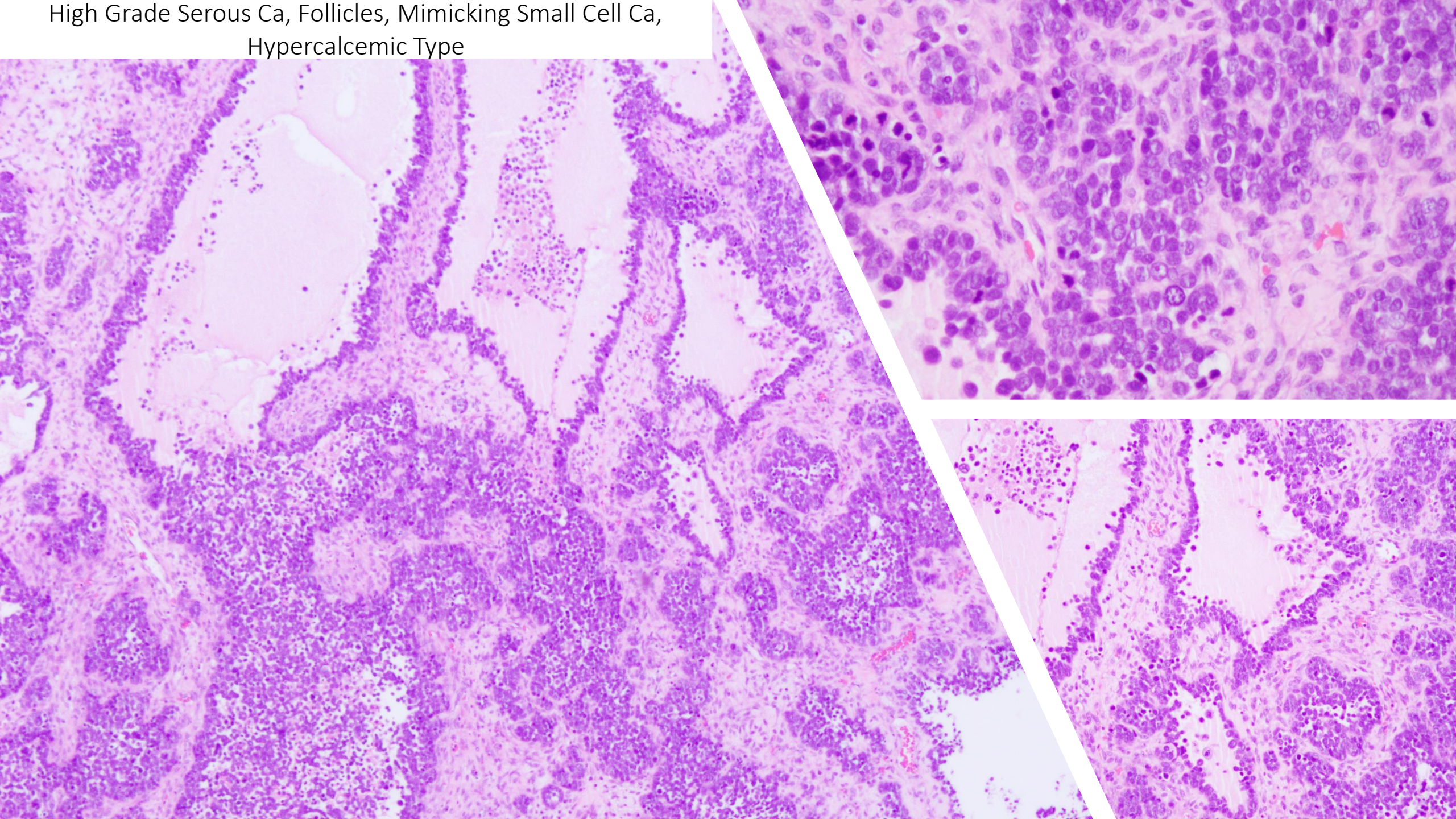
WT-1+



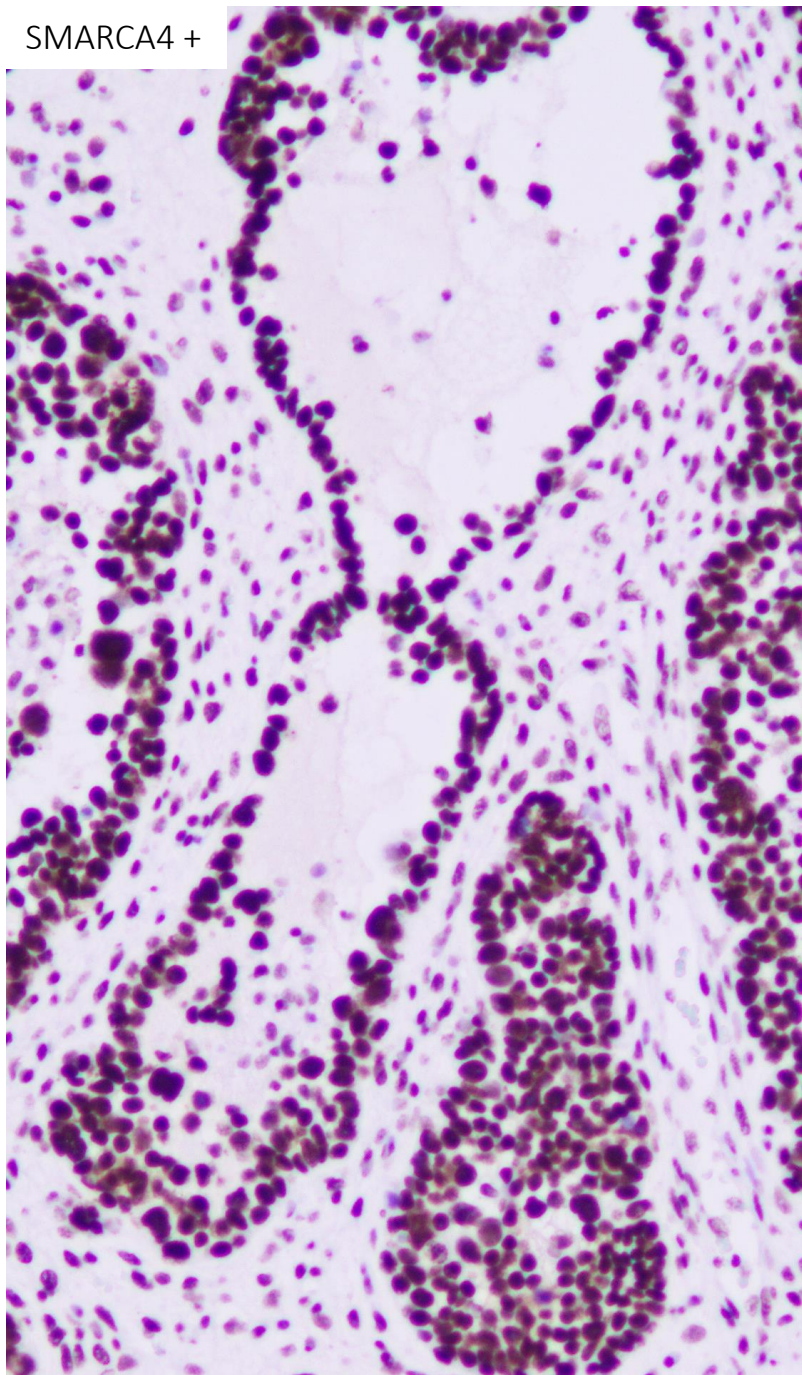


High Grade Serous Ca, Follicles, and Colloid-like Material

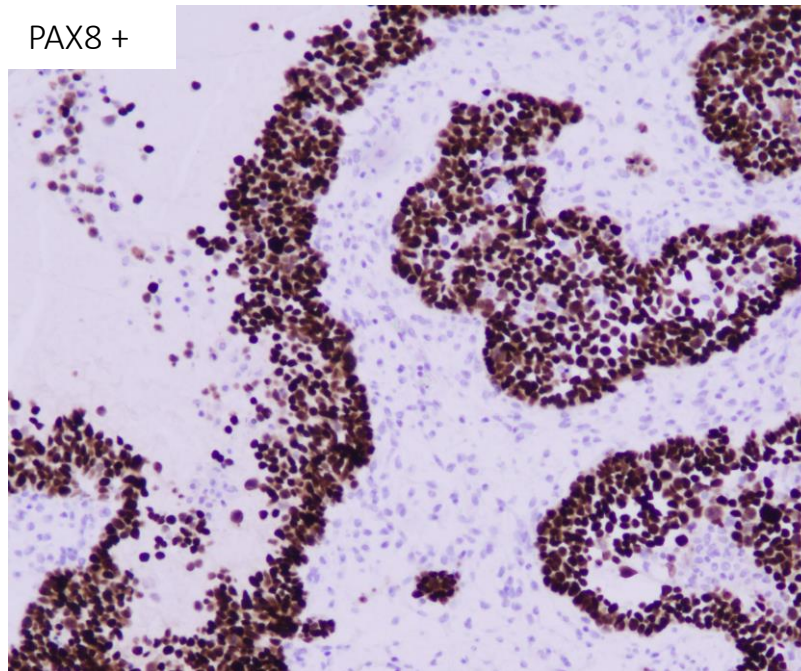
High Grade Serous Ca, Follicles, Mimicking Small Cell Ca,
Hypercalcemic Type



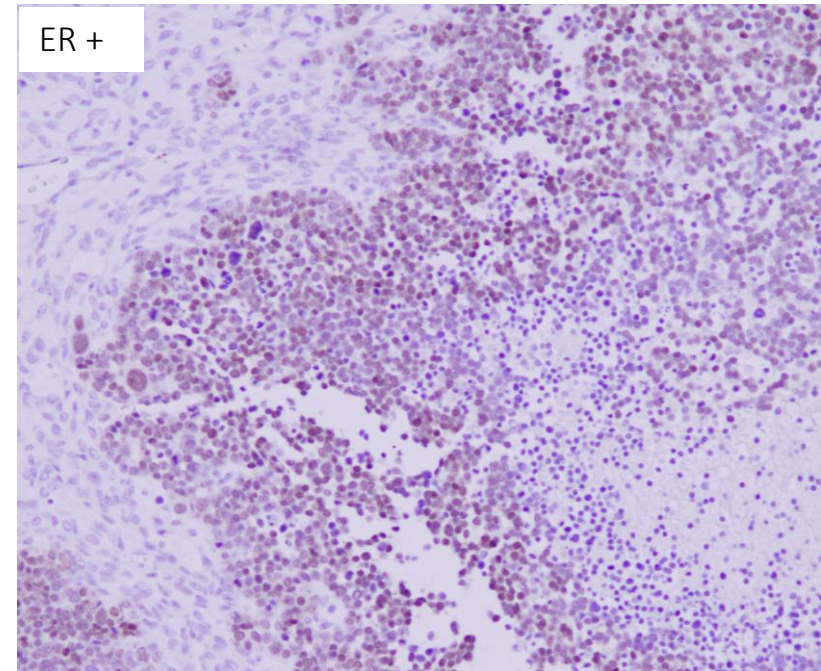
SMARCA4 +



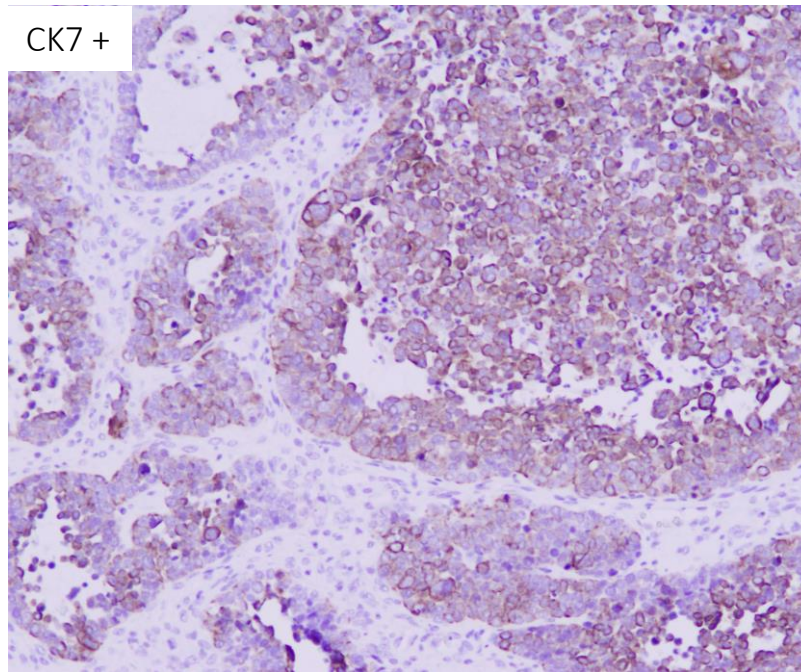
PAX8 +



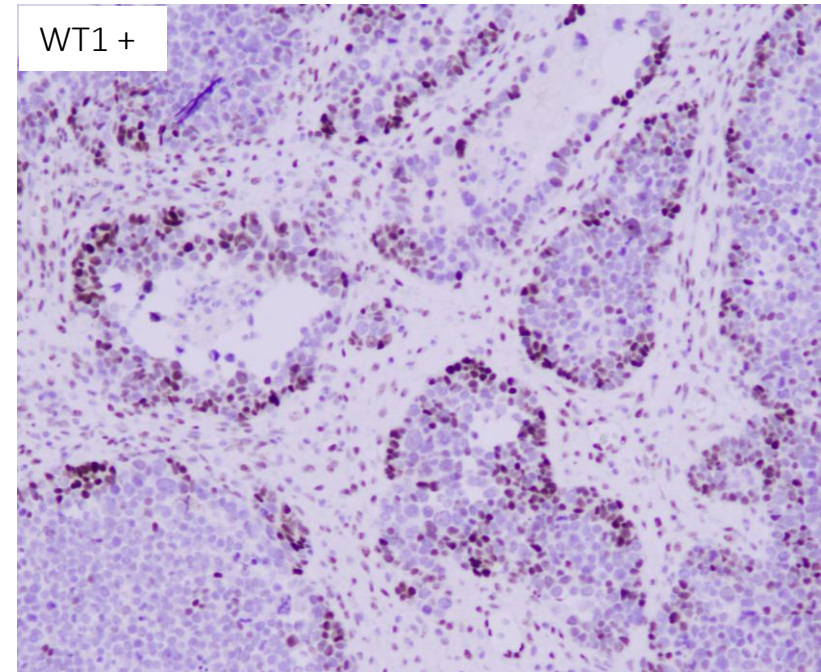
ER +



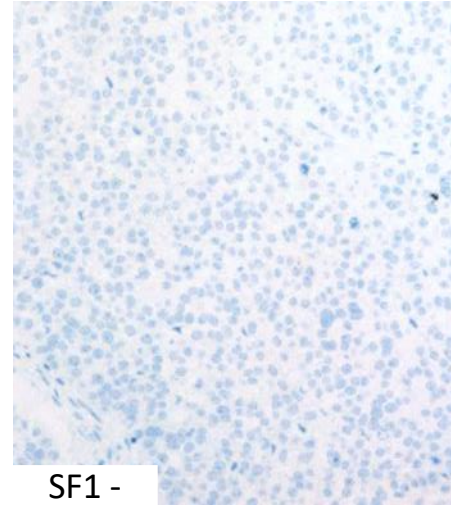
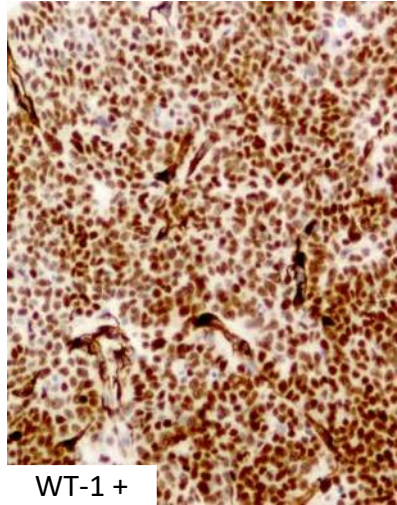
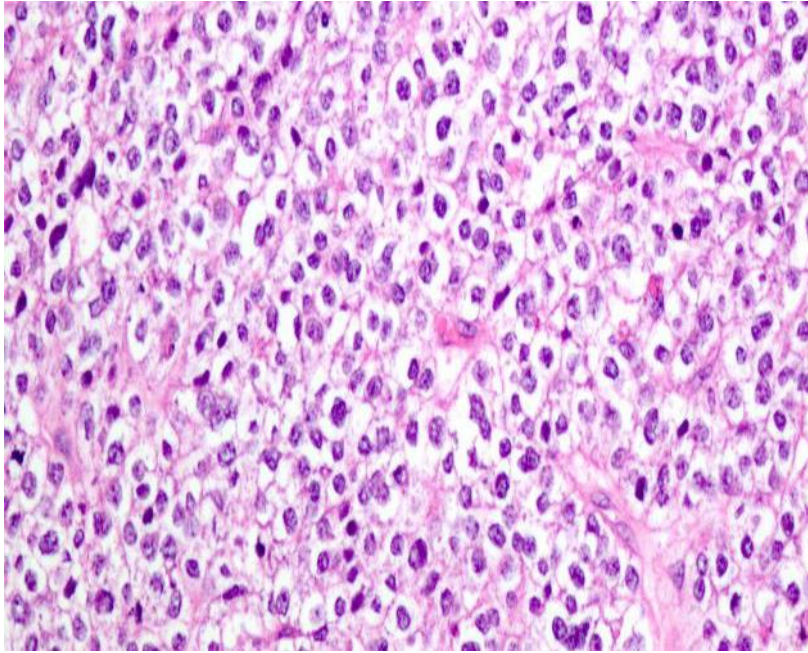
CK7 +



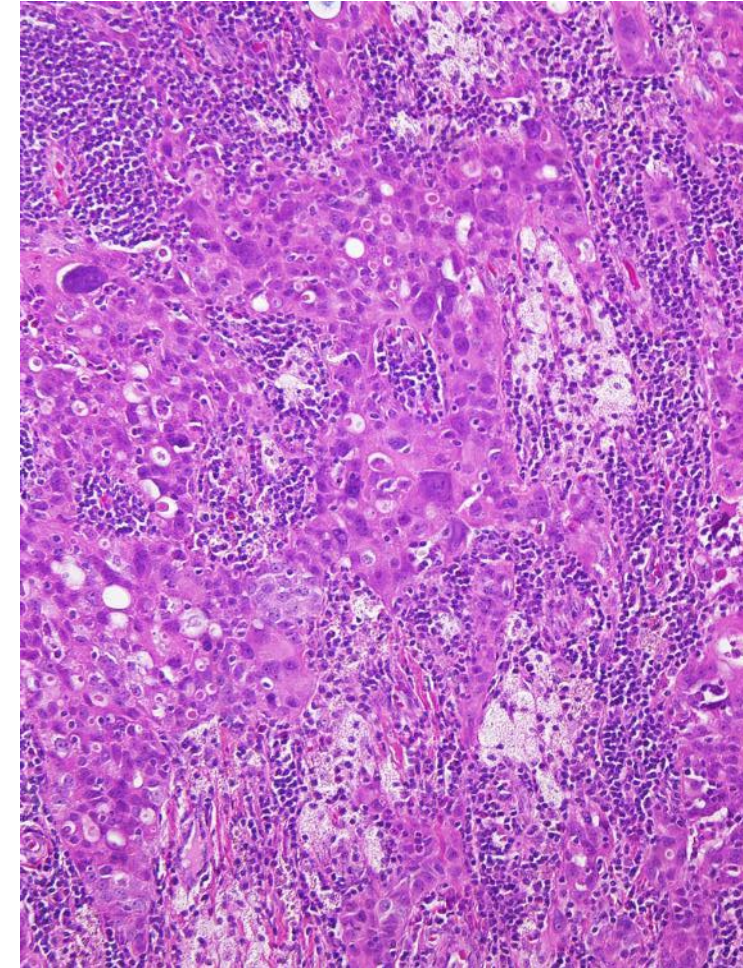
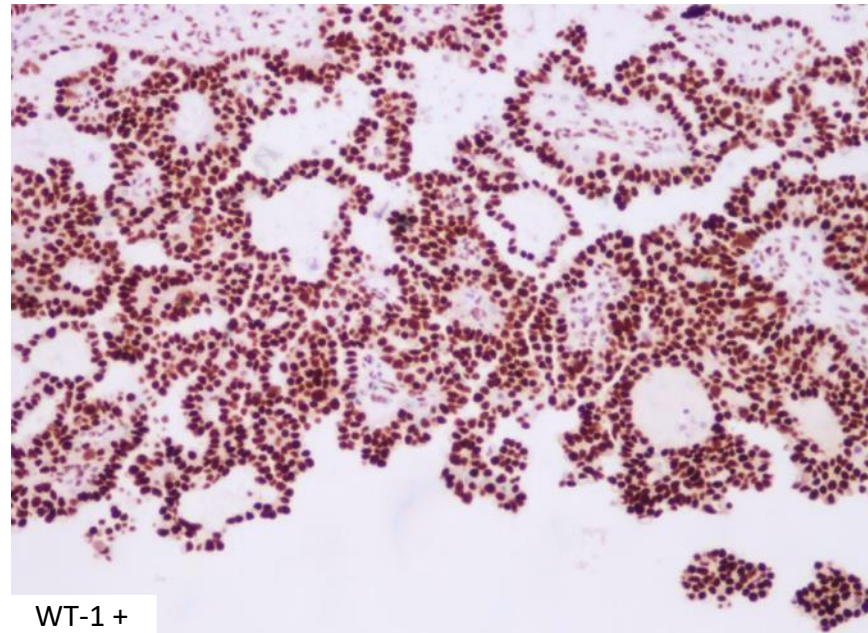
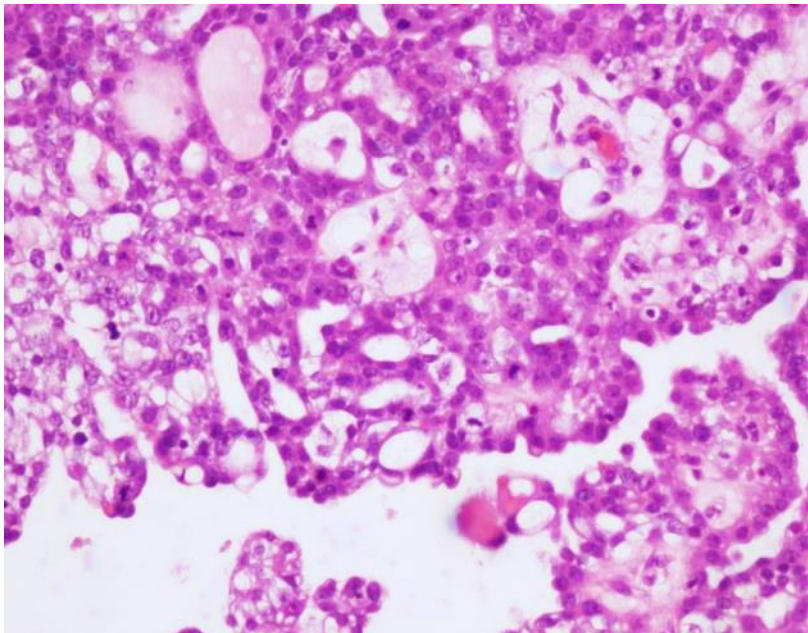
WT1 +



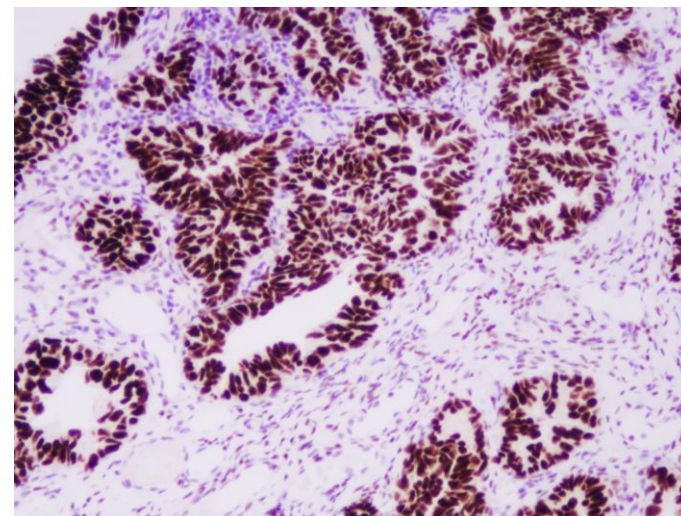
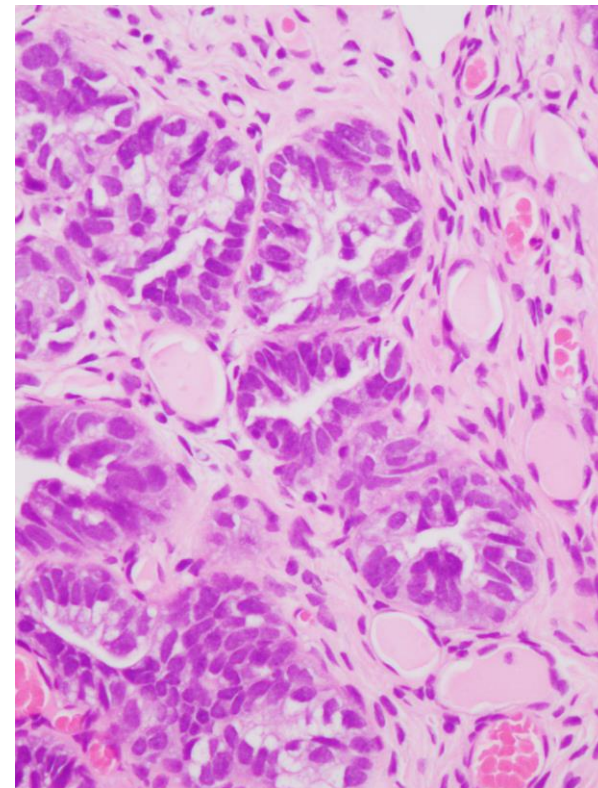
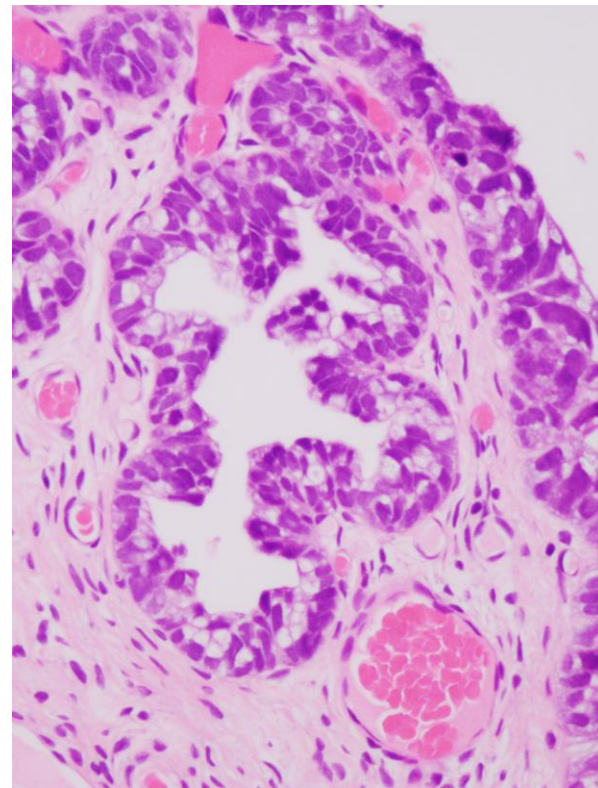
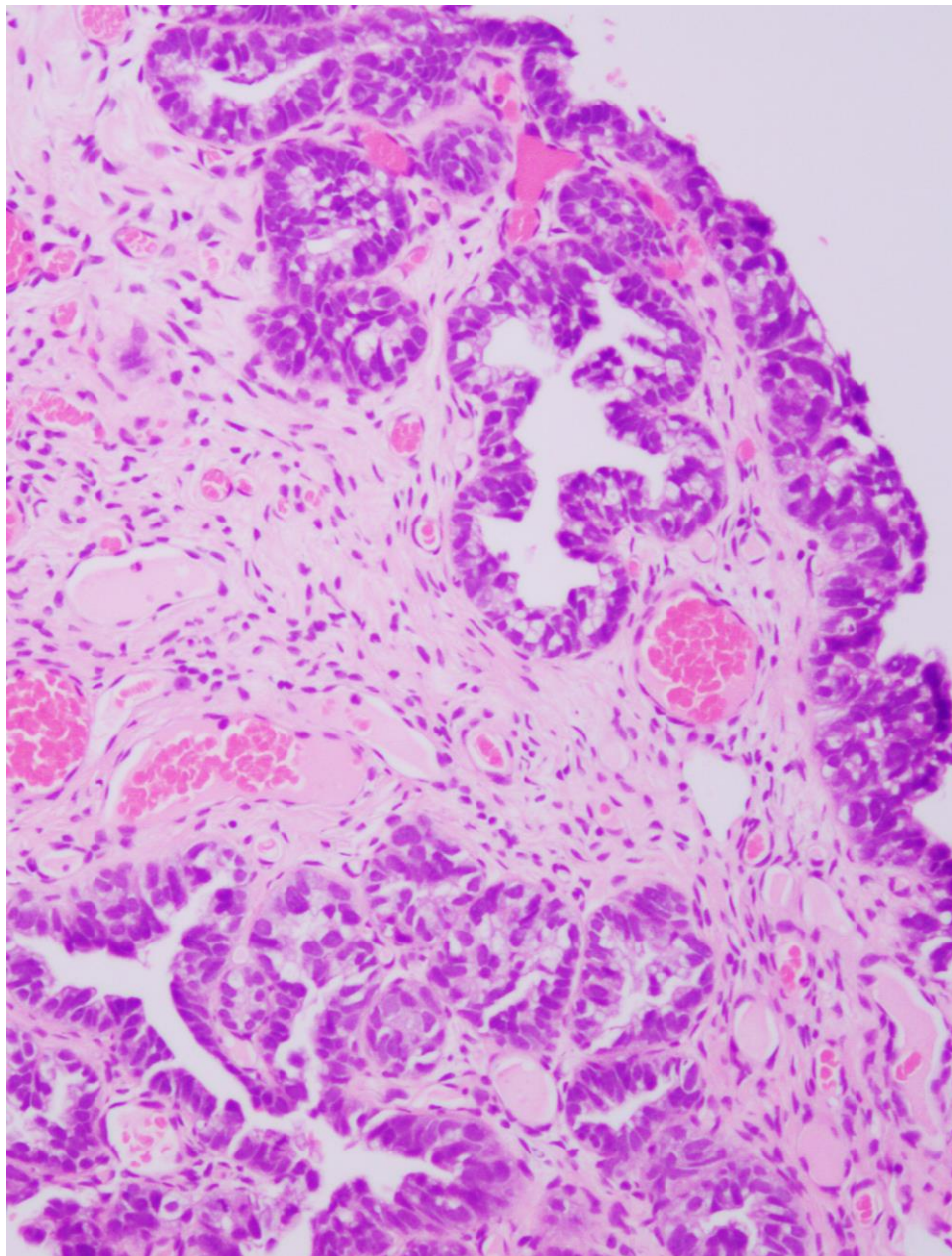
High Grade Serous Ca



Clear cells

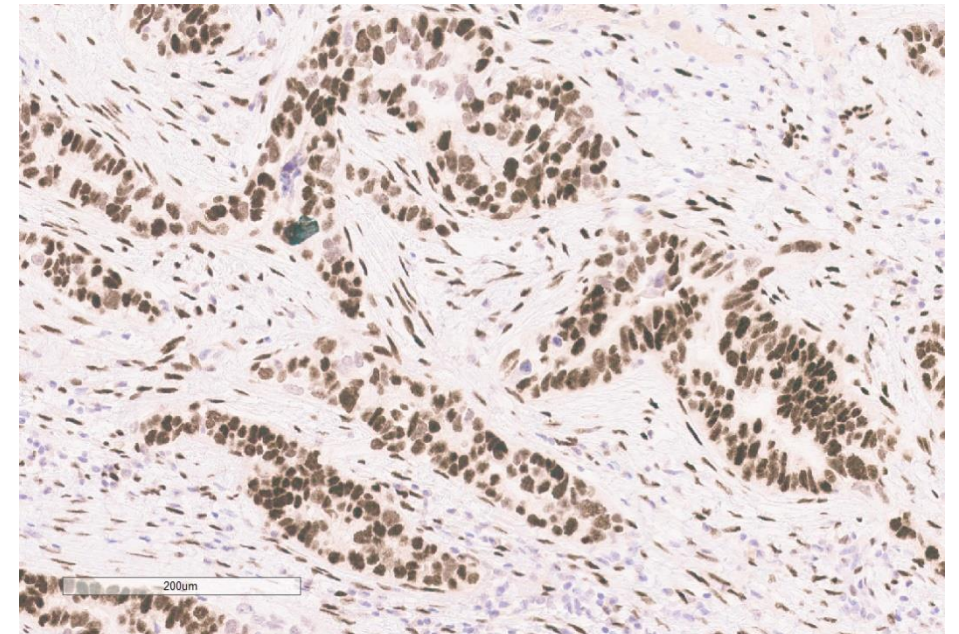
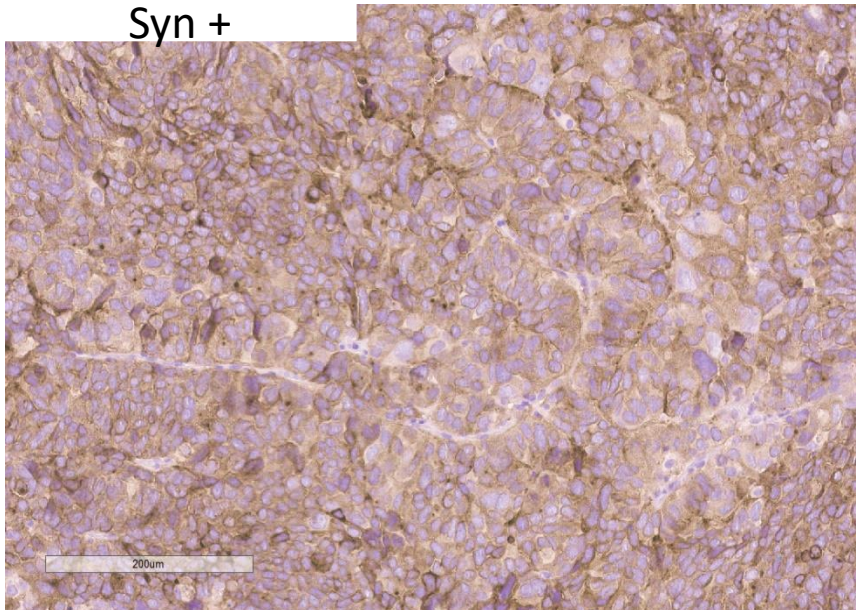
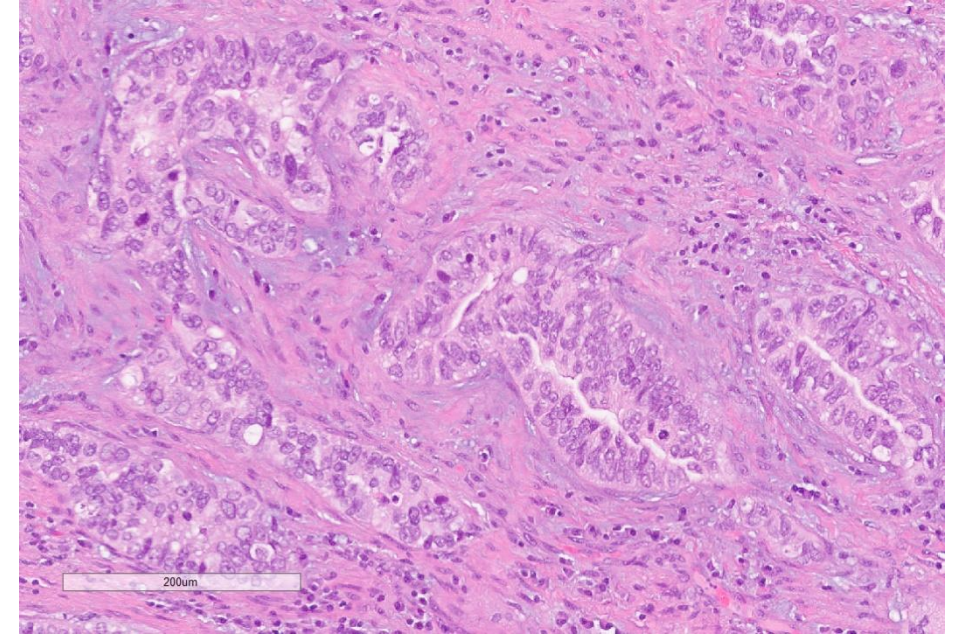
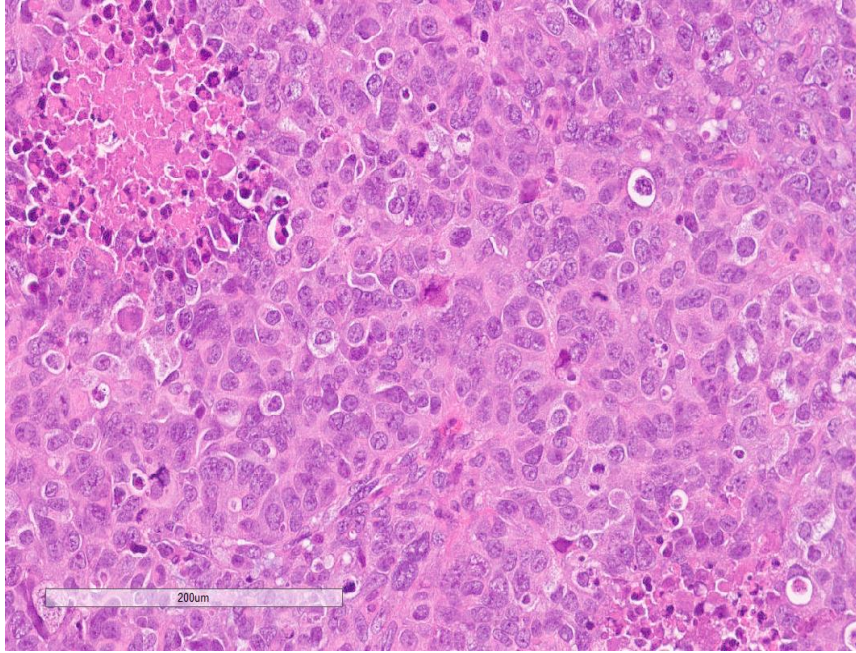


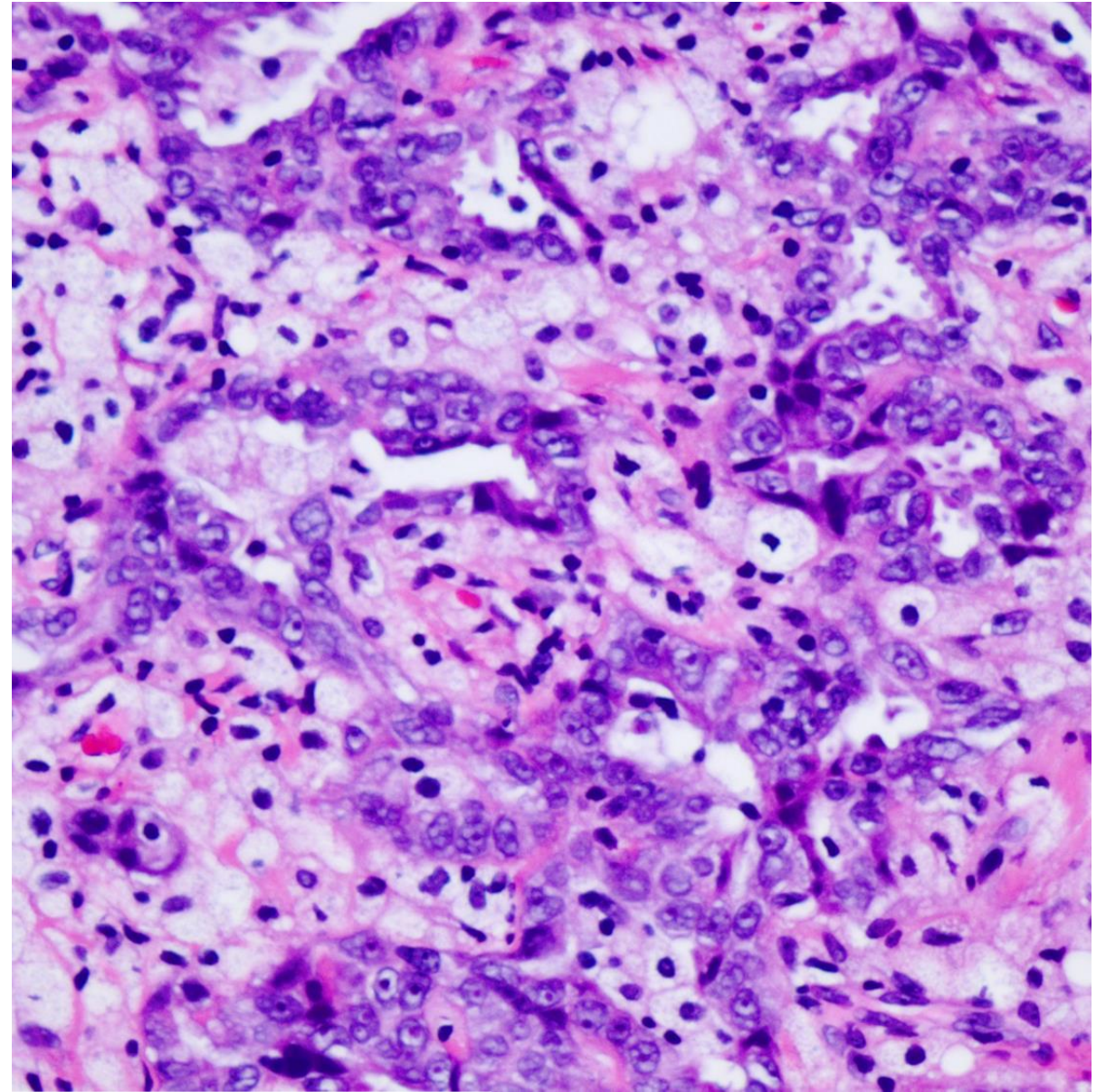
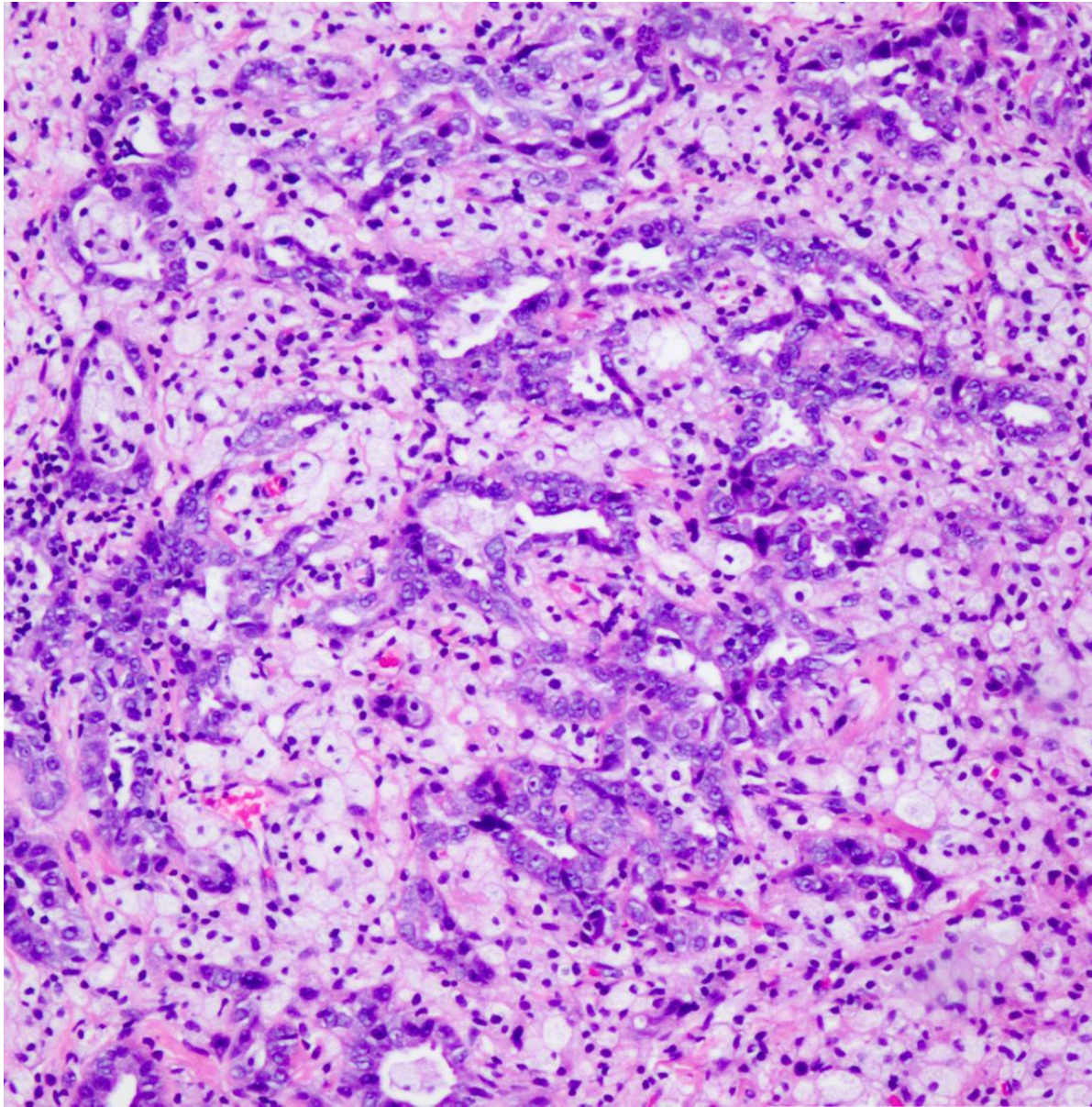
Adenosquamoid
appearance



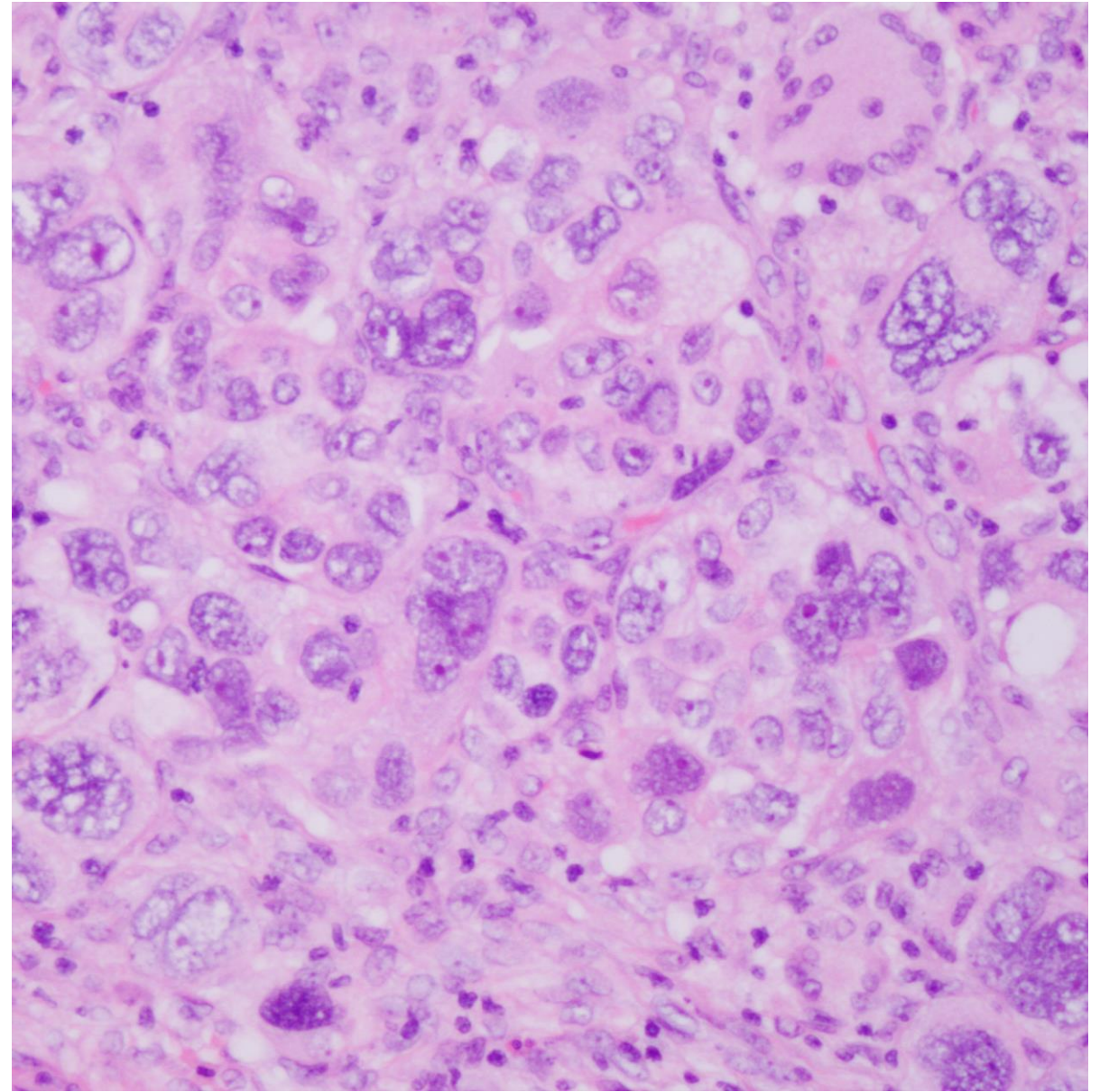
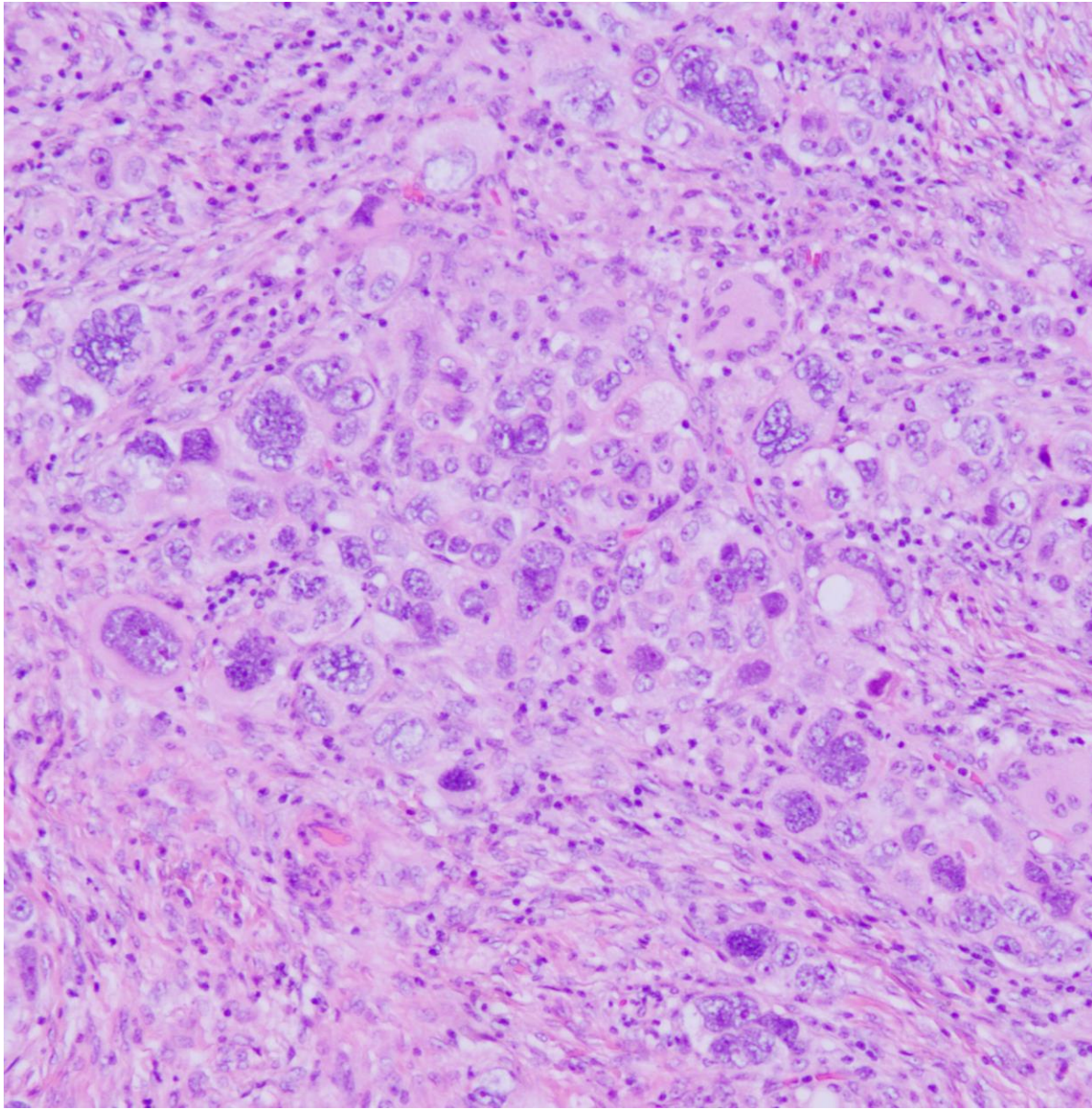
High Grade Serous Ca, vacuoles

Neuroendocrine Ca and HGSCa



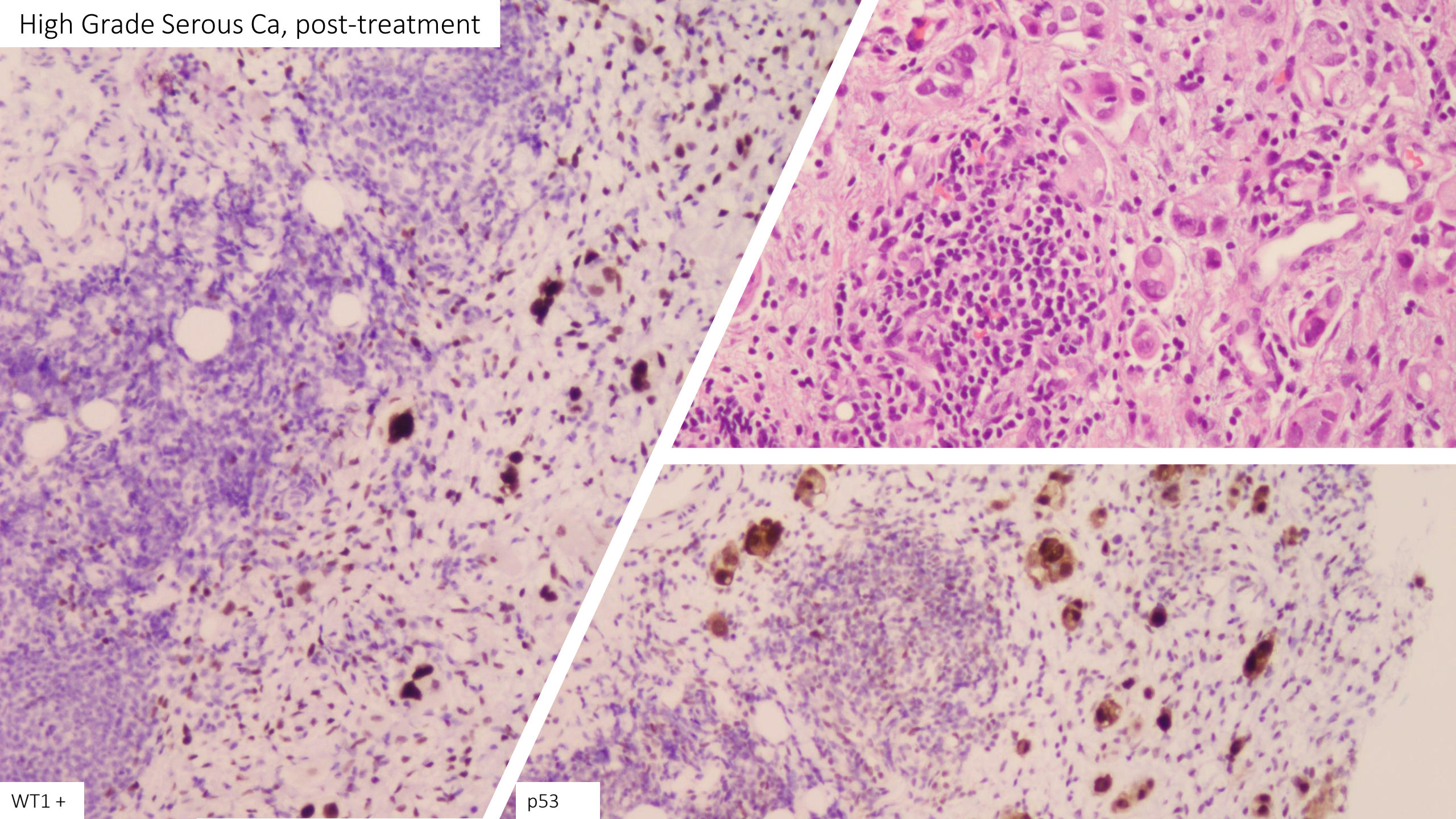


High Grade Serous Ca, post-treatment



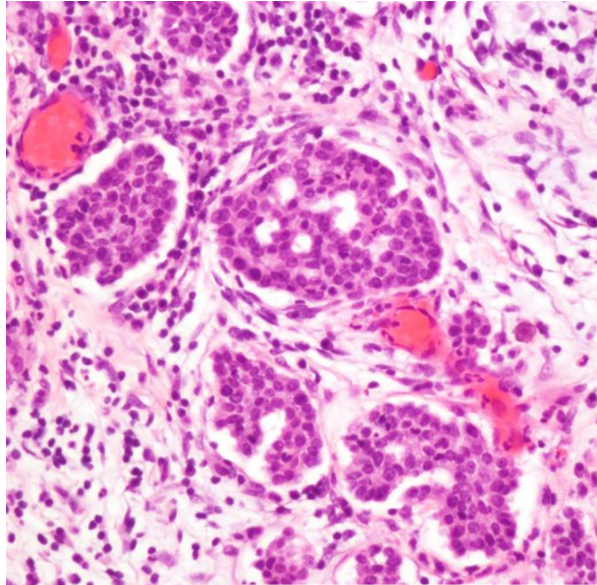
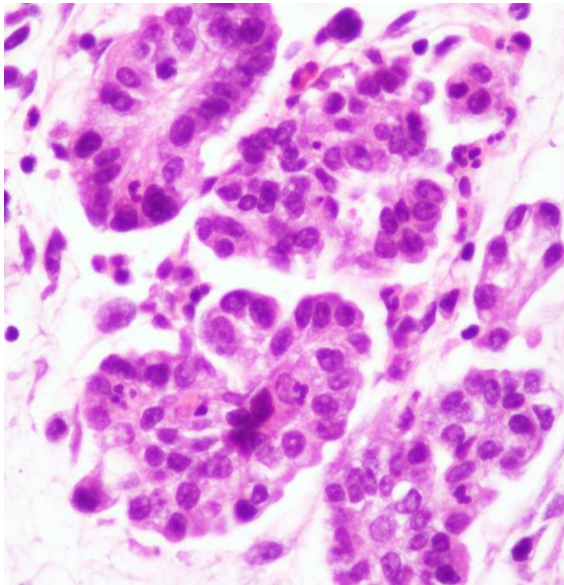
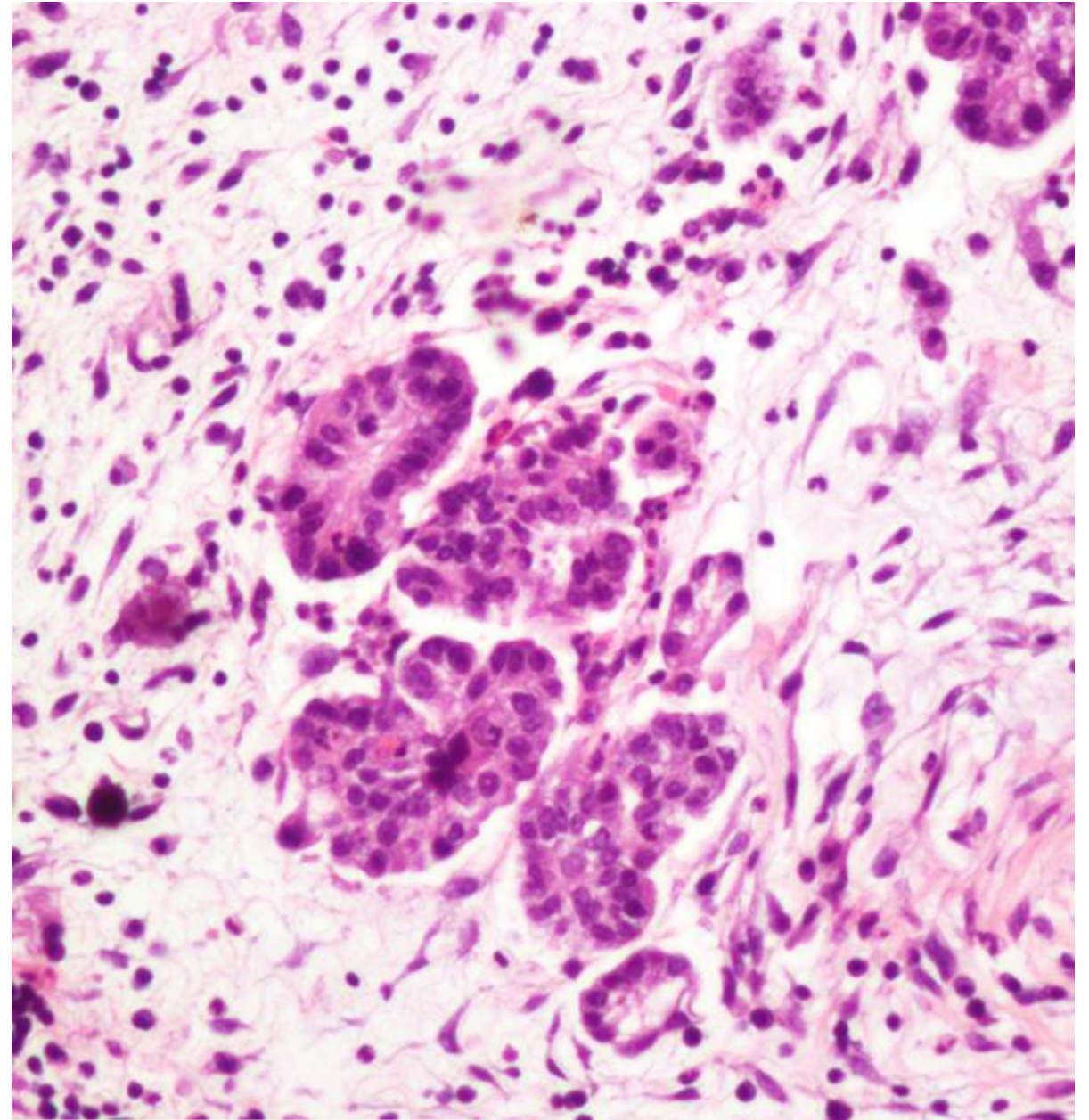
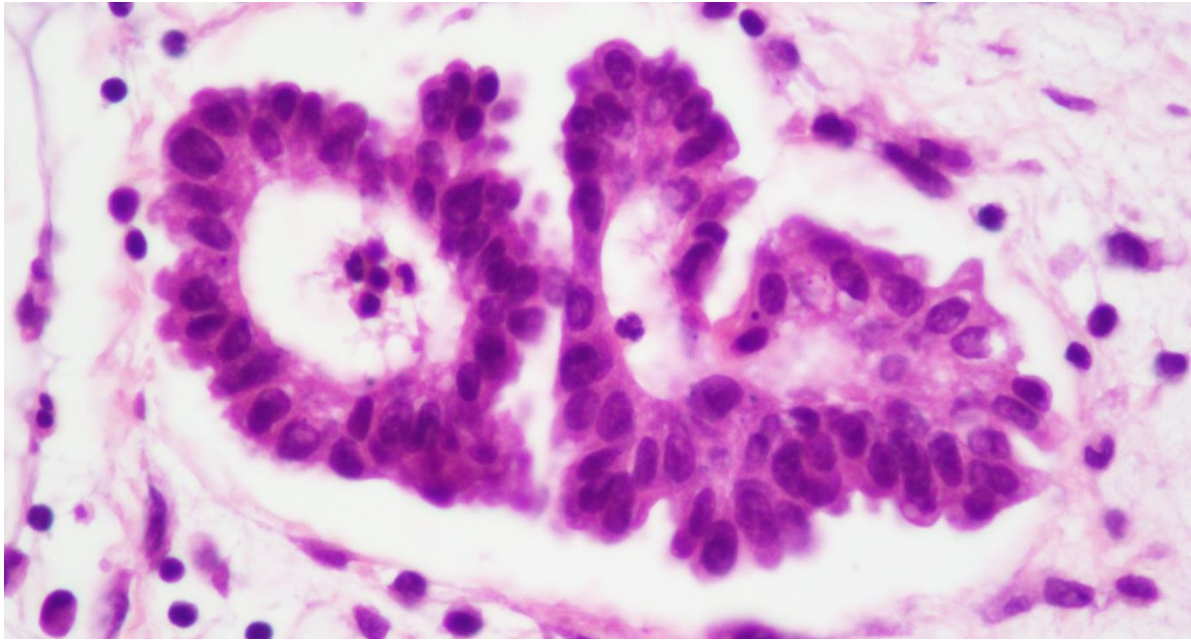
High Grade Serous Ca, post-treatment

High Grade Serous Ca, post-treatment

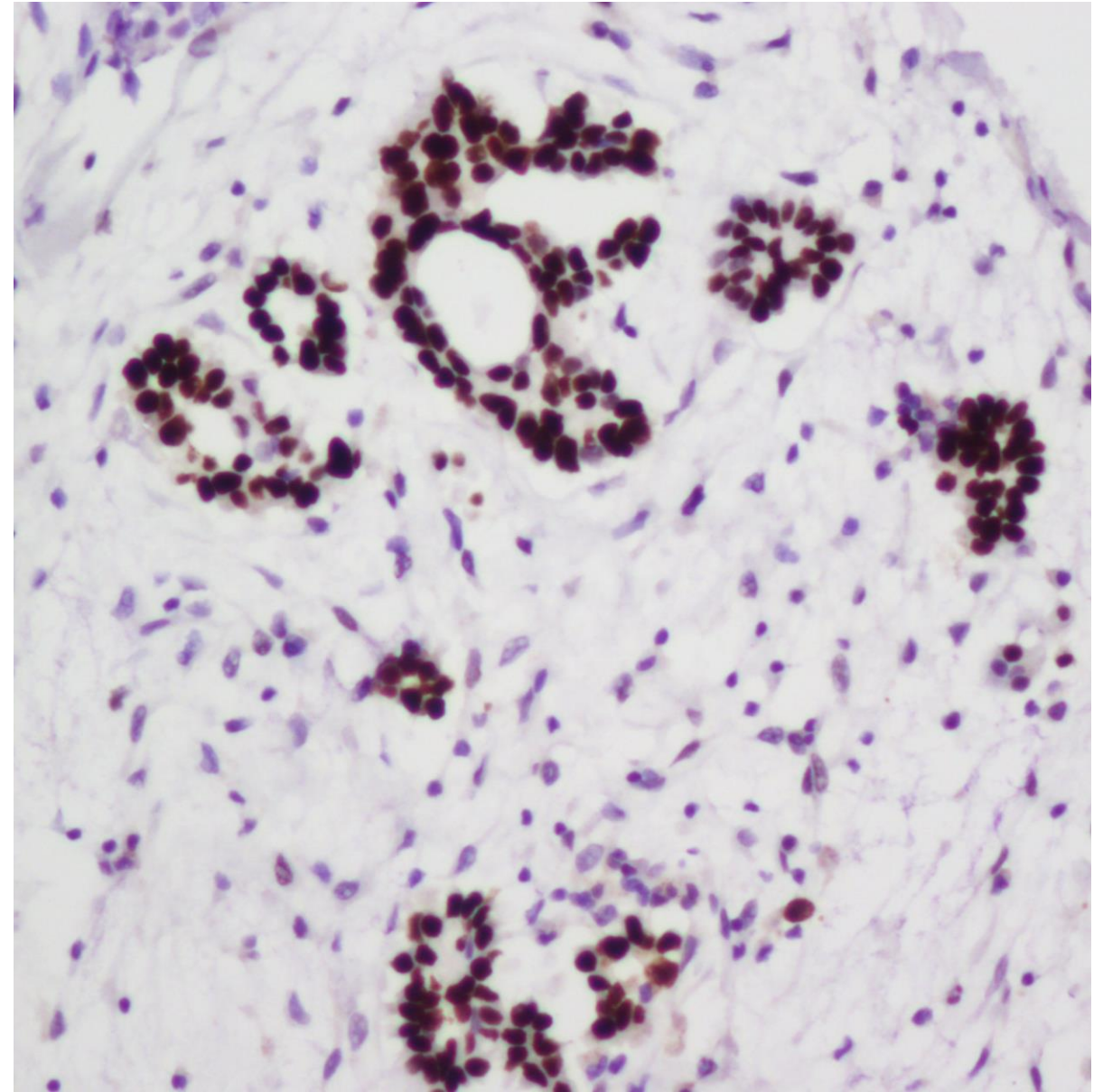
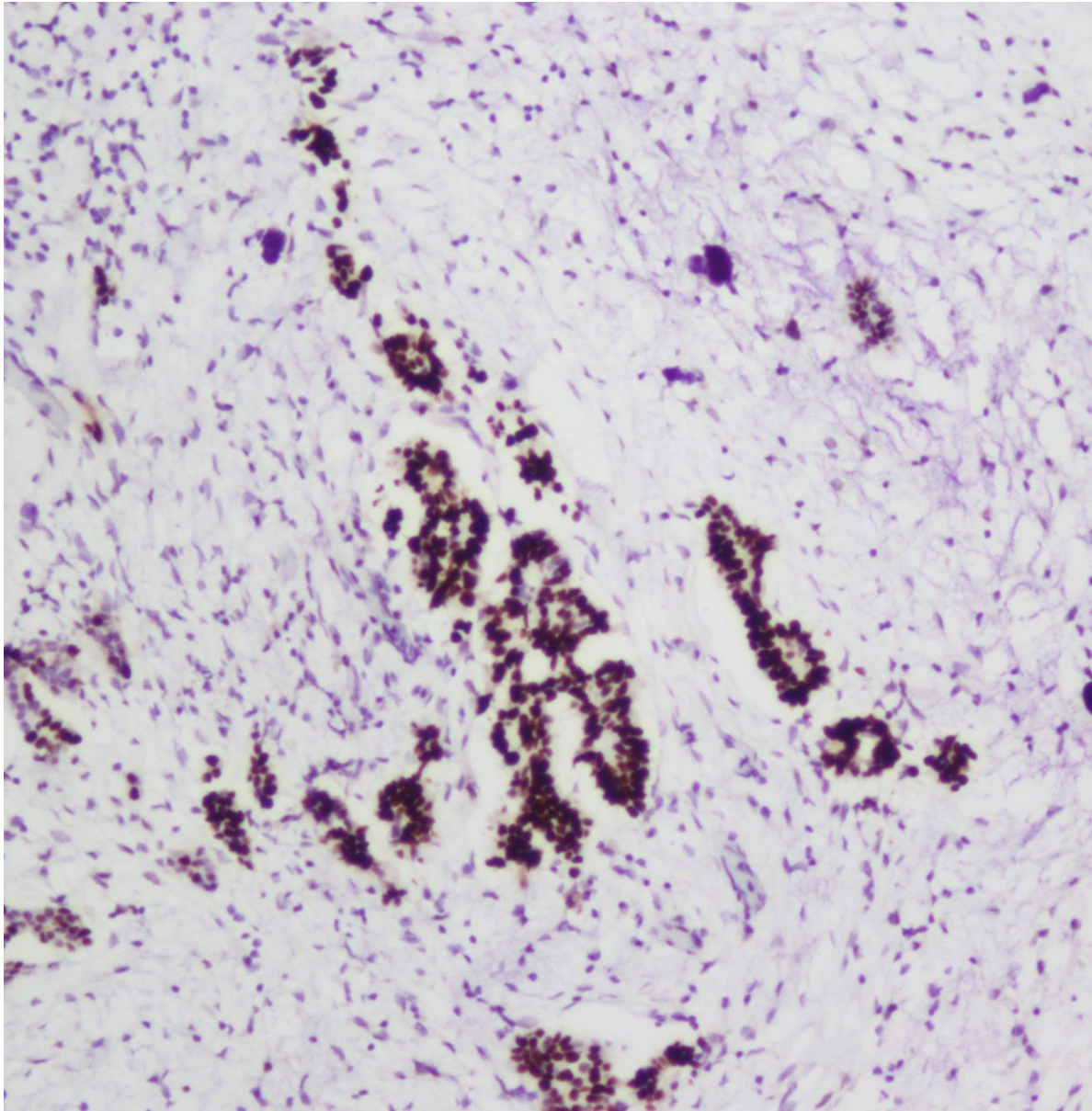


WT1 +

p53

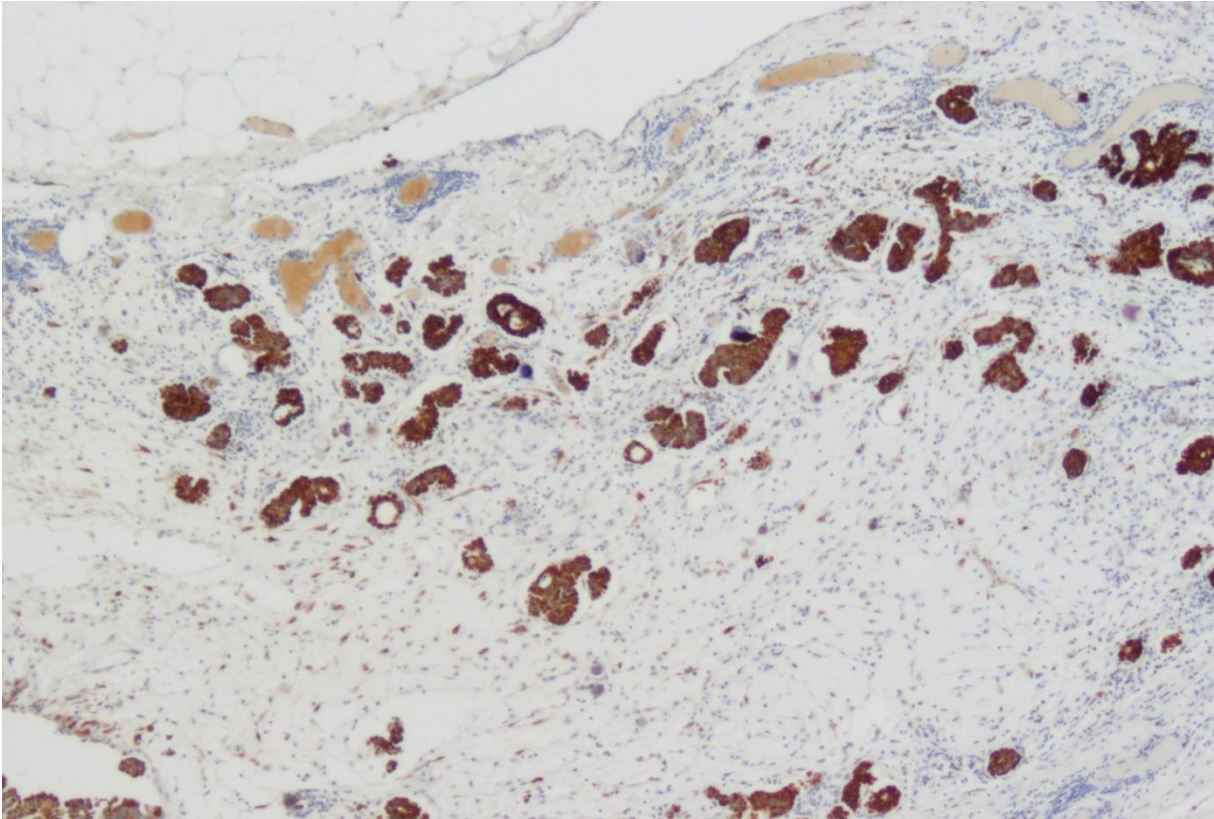


High Grade Serous Ca, post-treatment

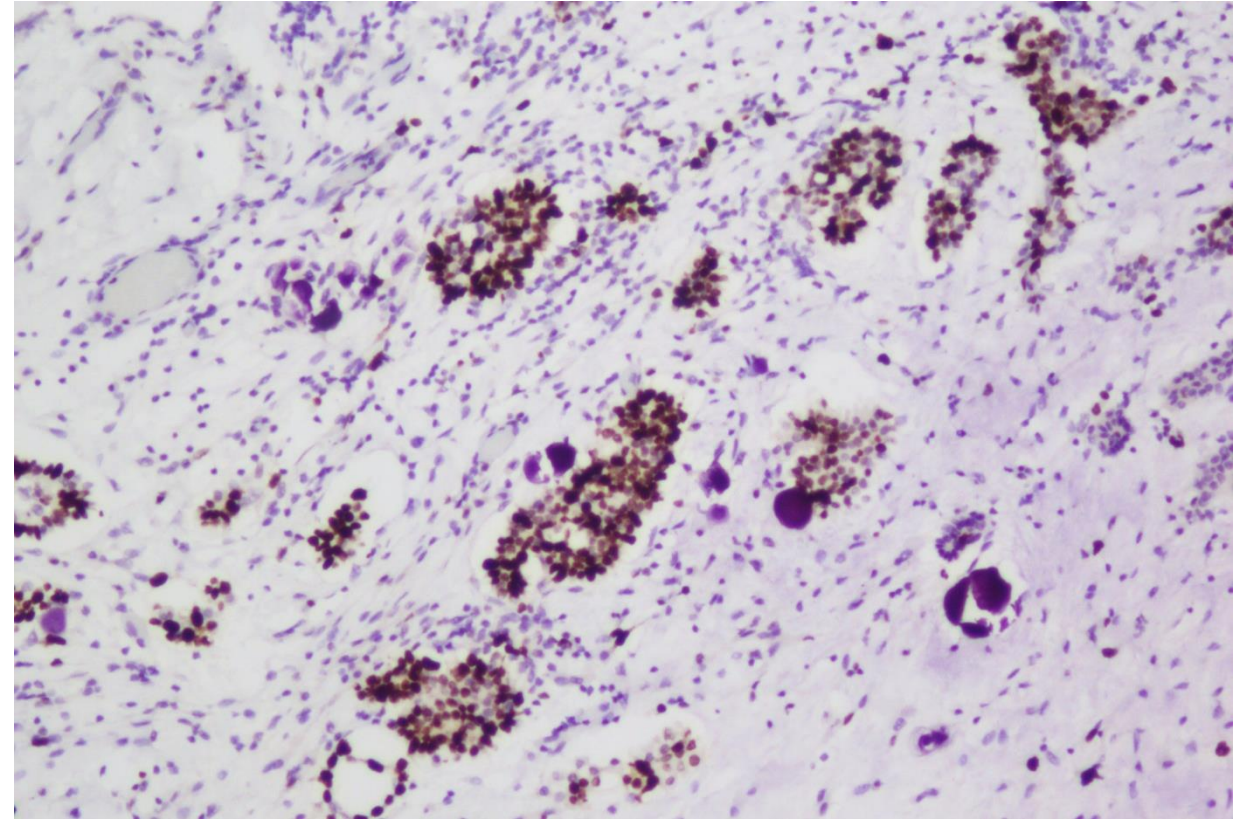


High Grade Serous Ca, post-treatment aberrant p53 (over expression)

High Grade Serous Ca, post-treatment aberrant p53 (over expression)

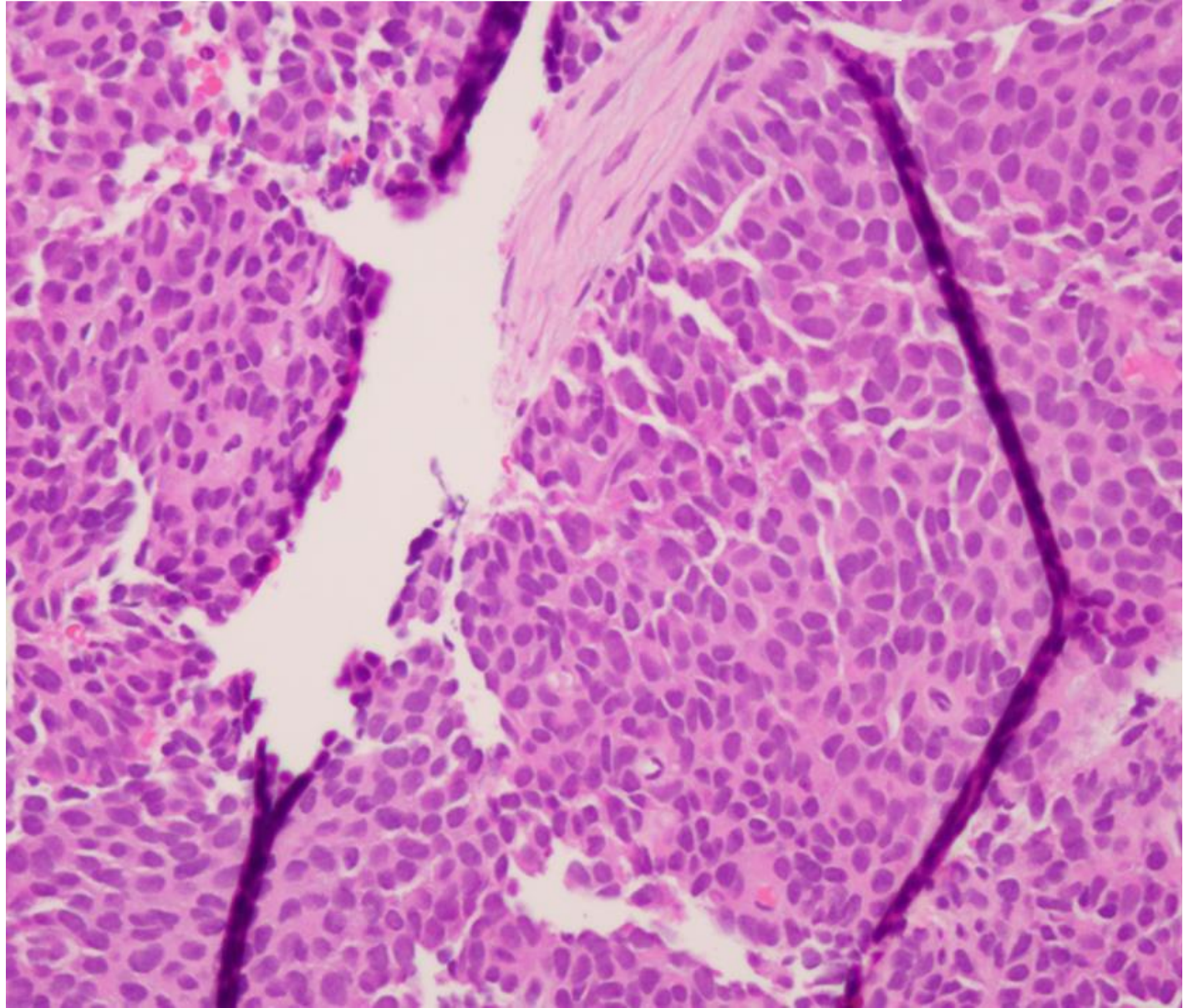
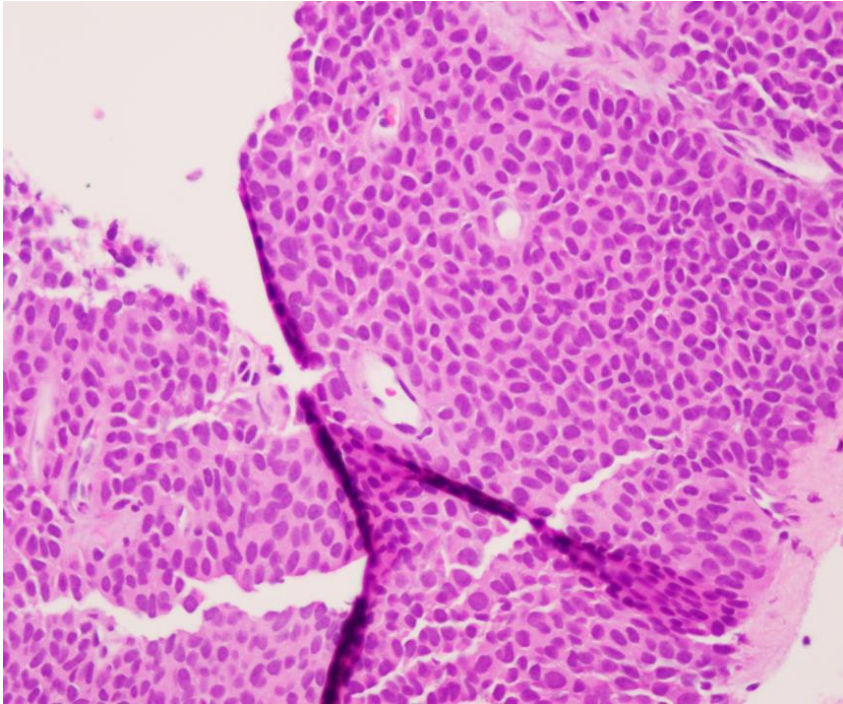
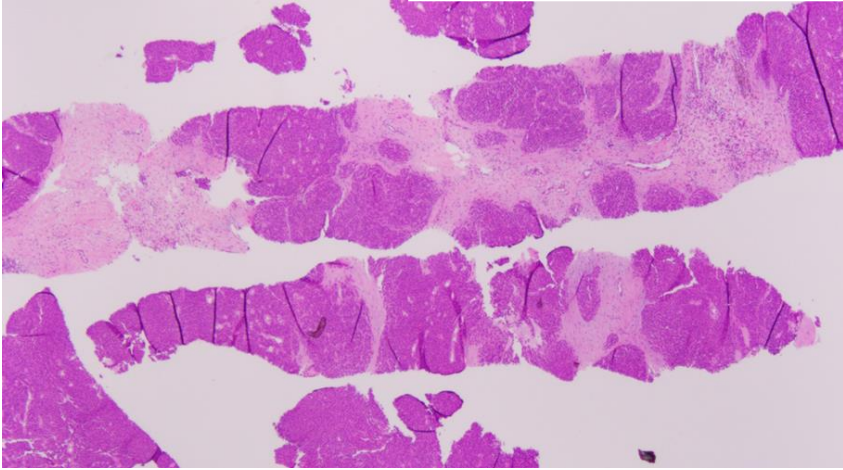


p16 block staining pattern

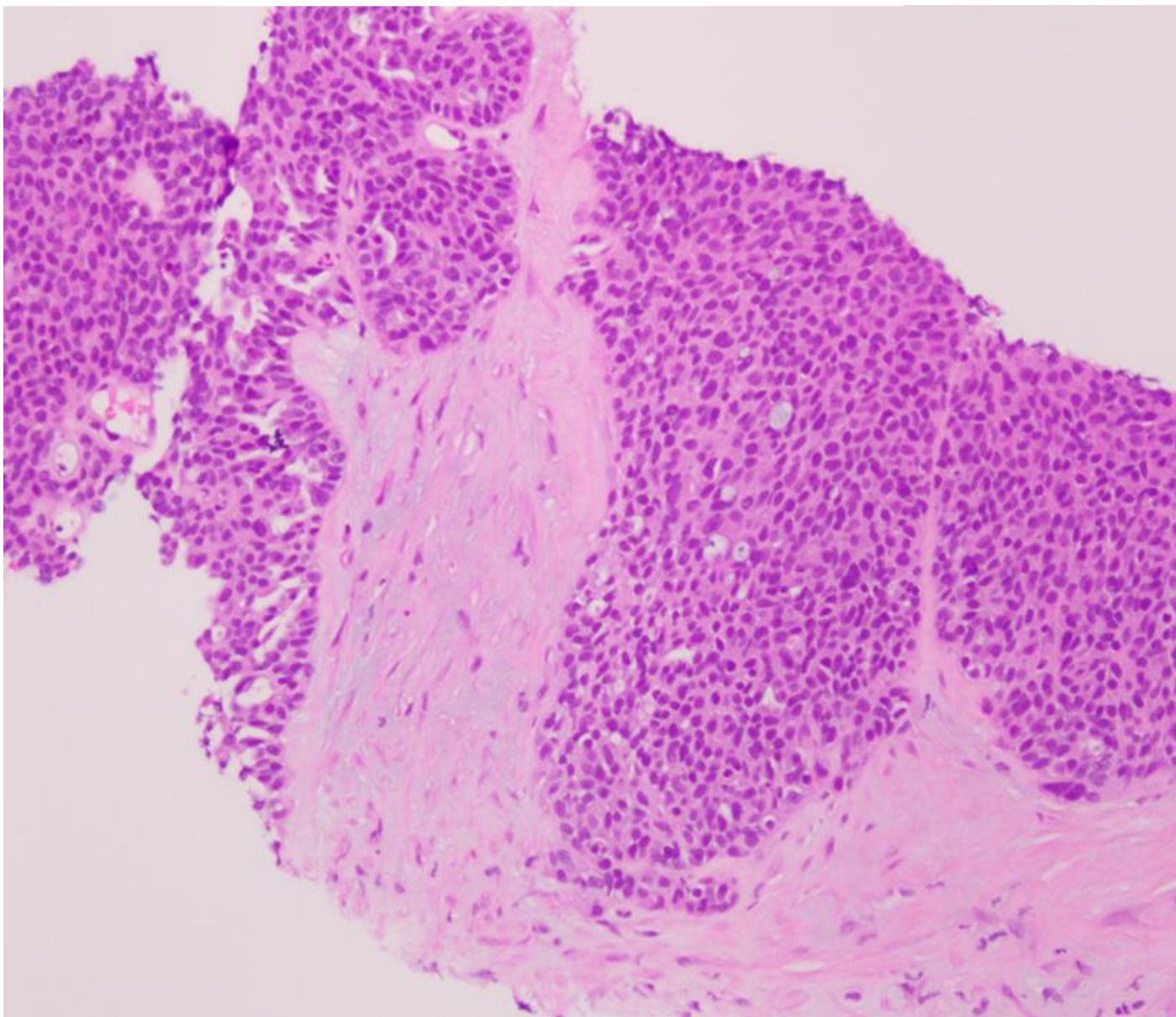
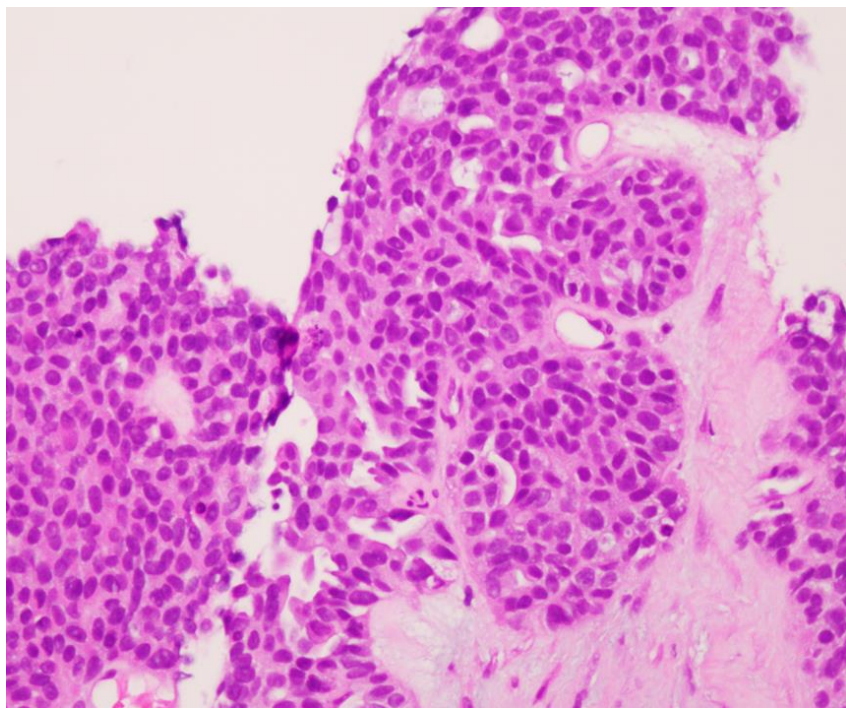
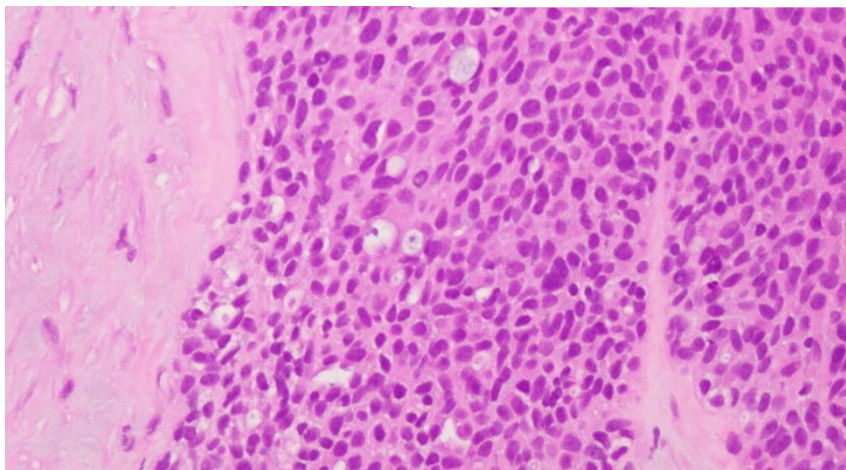


High Ki-67 proliferative index

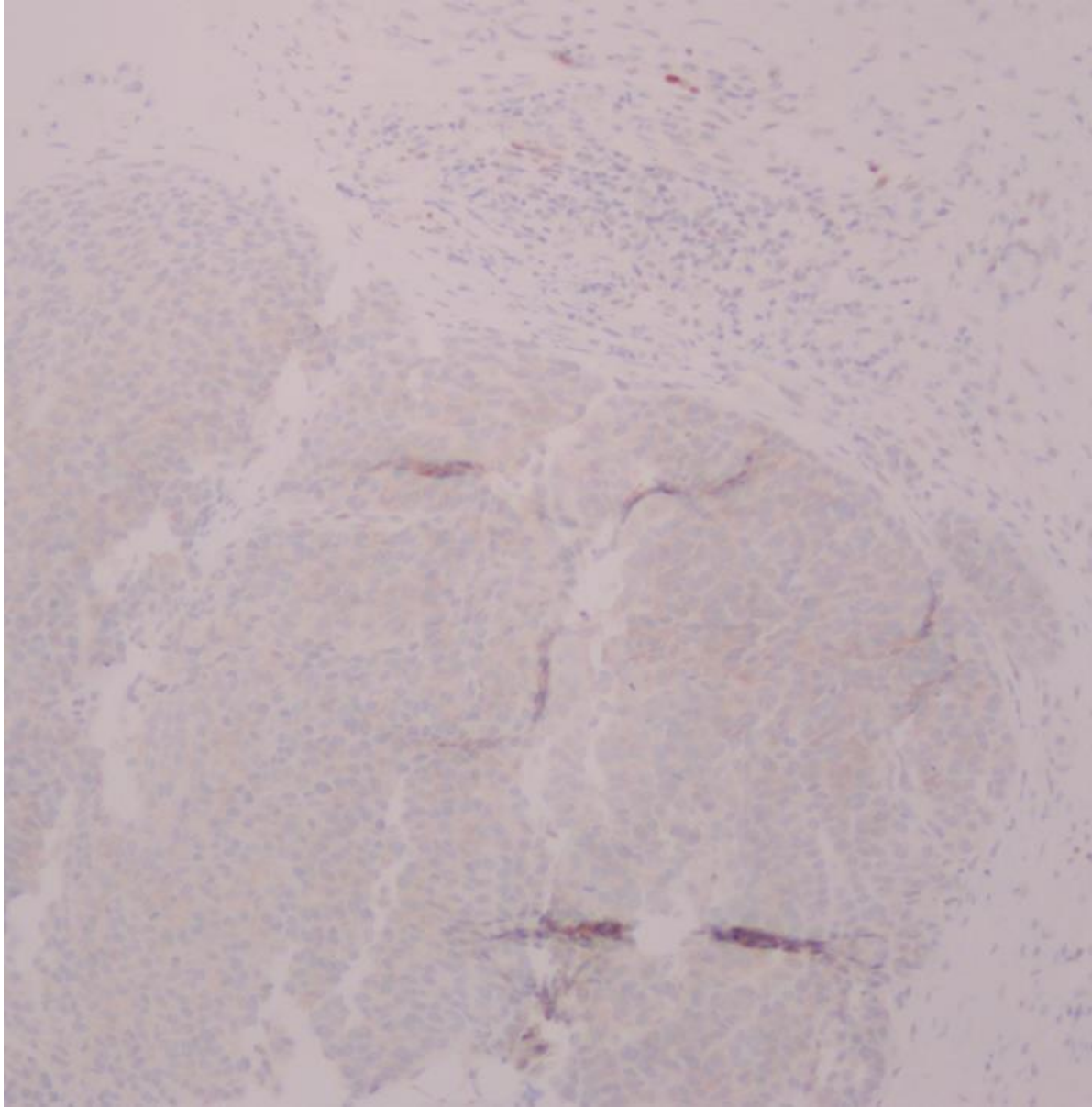
High Grade Serous Ca, core biopsy



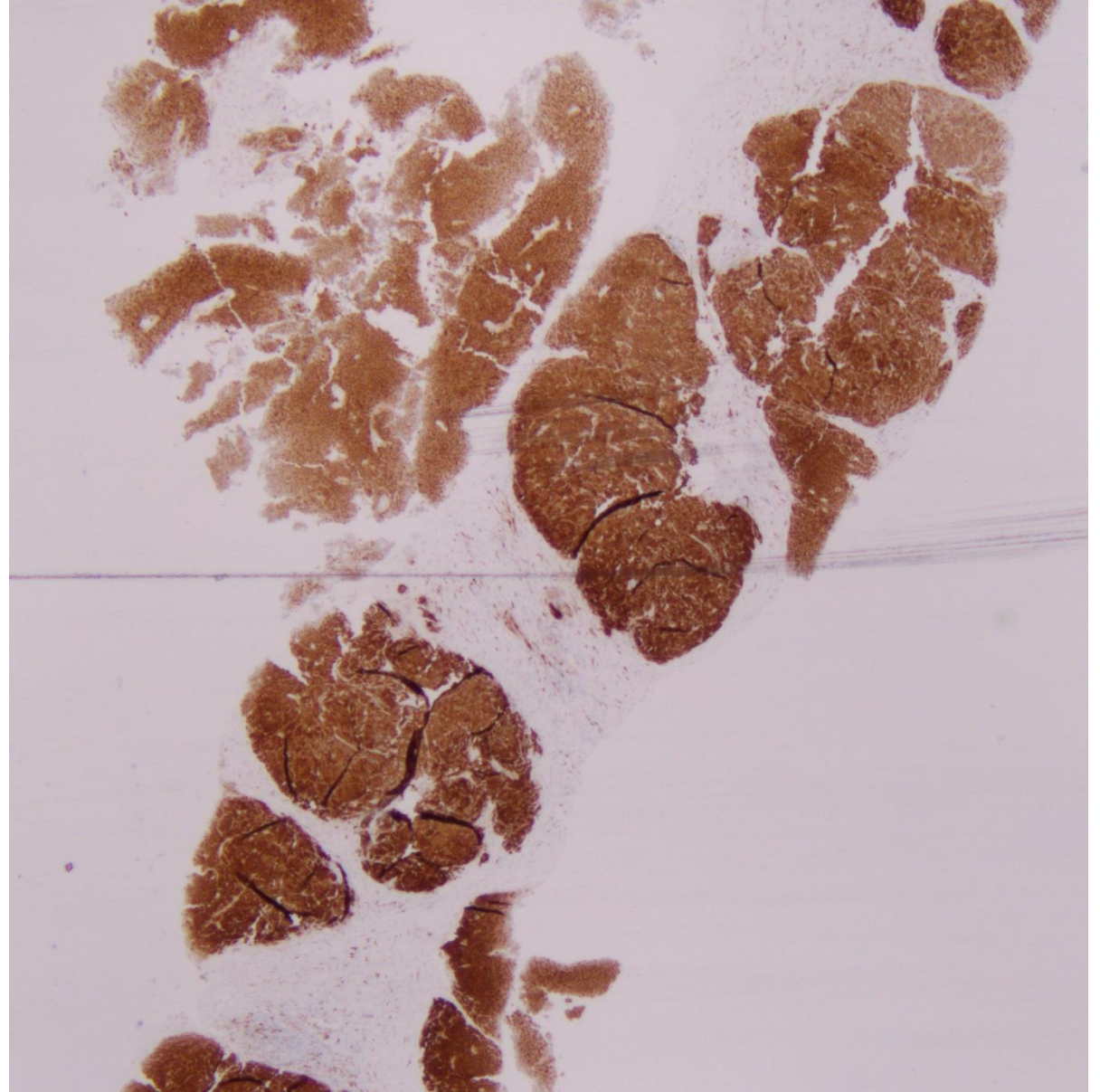
High Grade Serous Ca, core biopsy, deeper section



High Grade Serous Ca, core biopsy

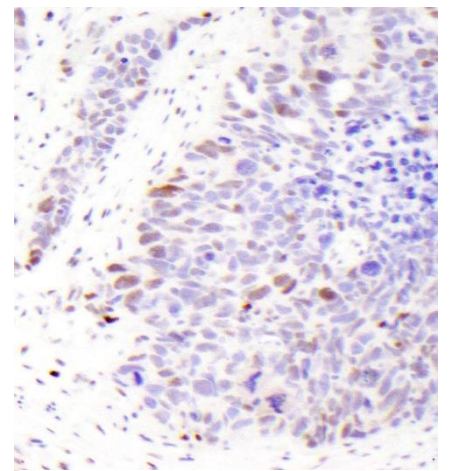


p53 null

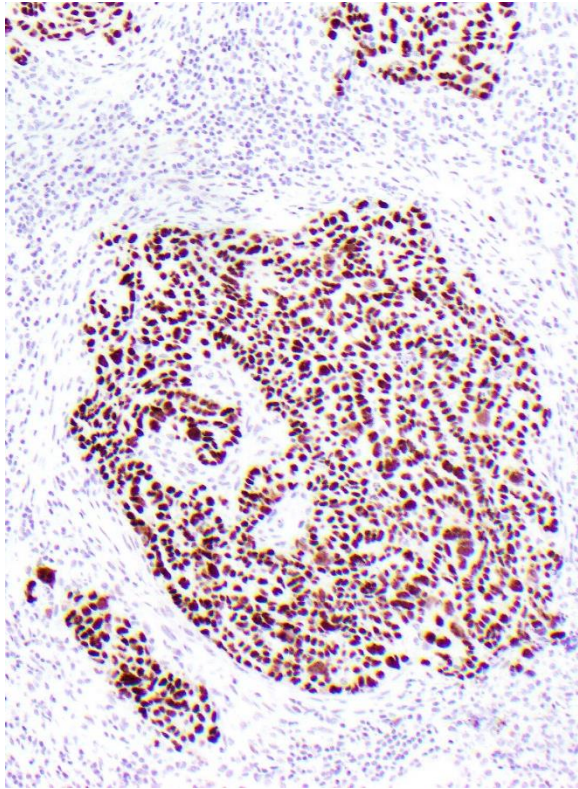


p16 +

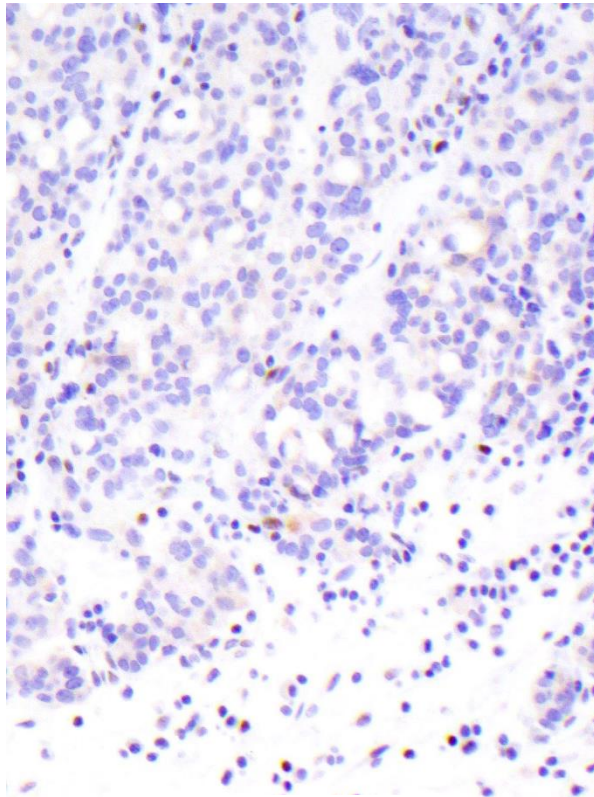
Extrauterine High Grade Serous Carcinoma: p53



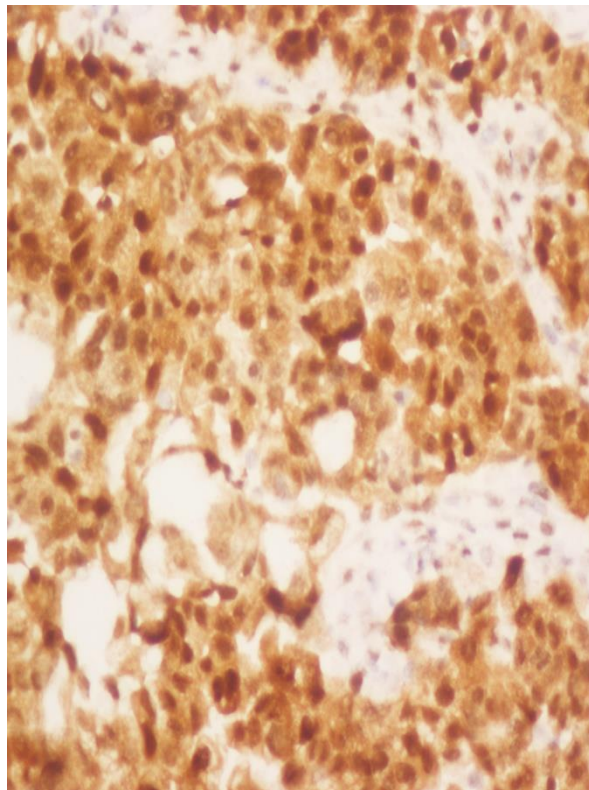
Wild-type, < 10% of cases



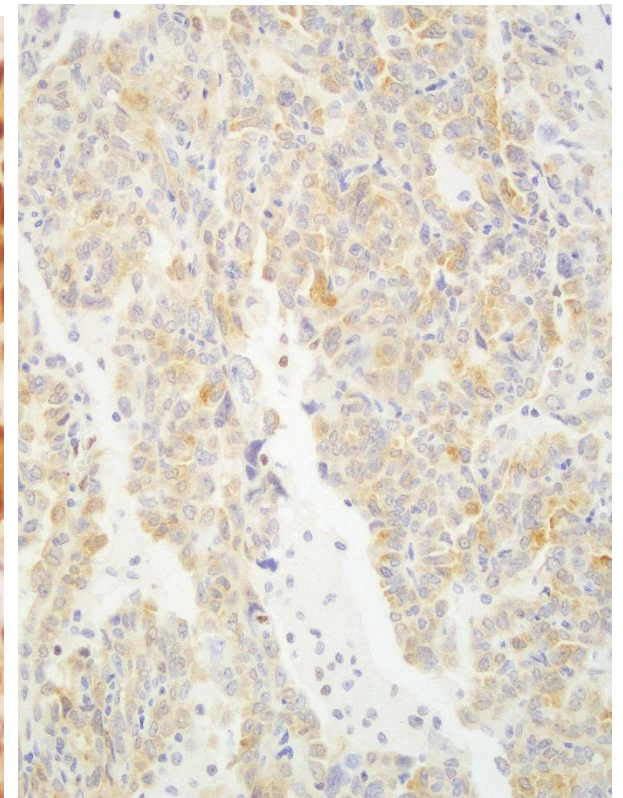
Nuclear overexpression



Null phenotype



Cytoplasmic overexpression



Attention to a Histotyping Pitfall

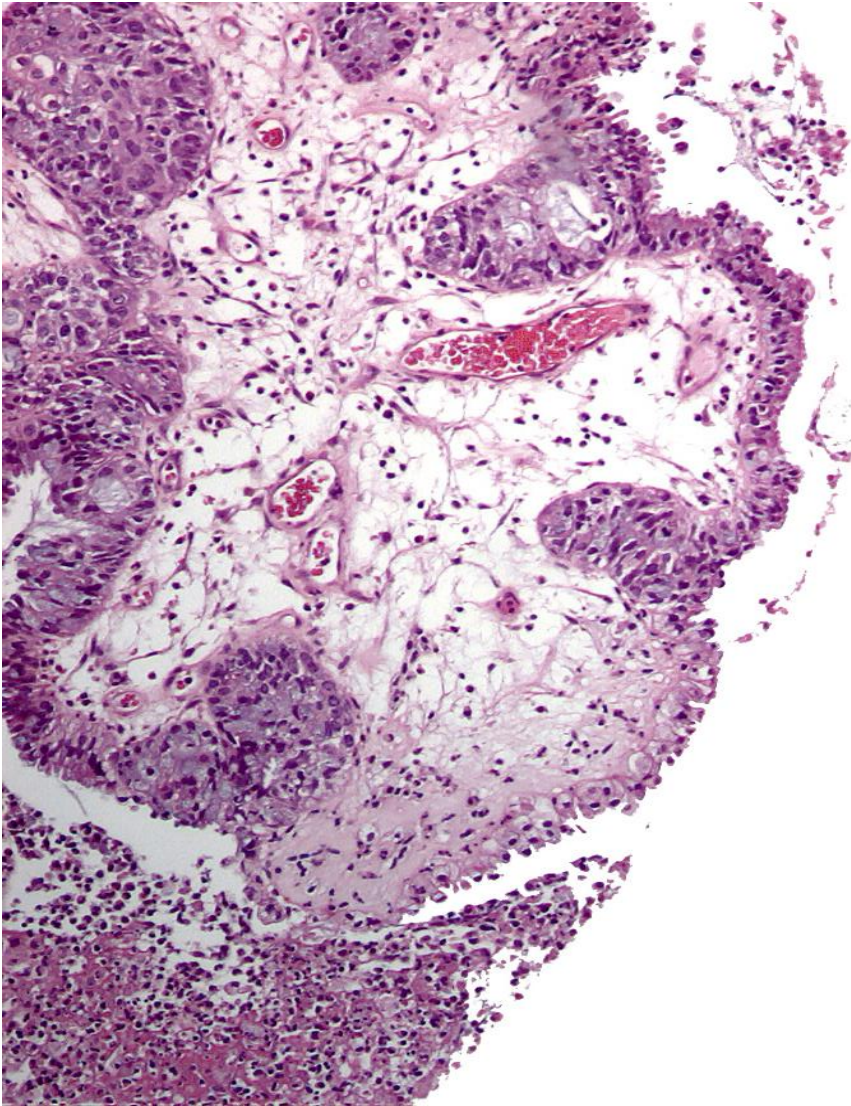
Endometrioid Ca with mucinous metaplasia

- Should not be designated as mucinous Ca
or seromucinous Ca

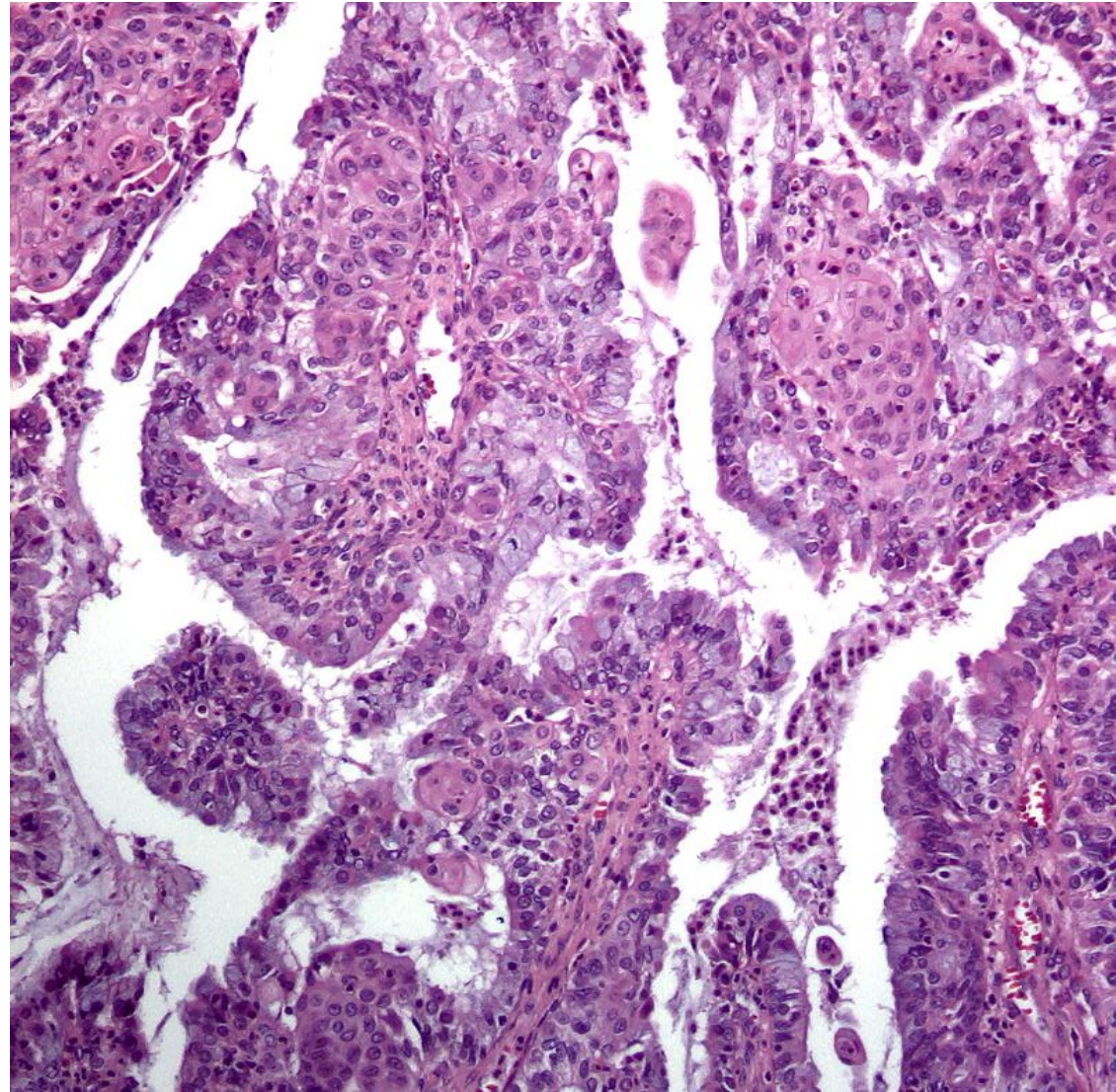
Seromucinous Ca arising in a seromucinous borderline tumor is a

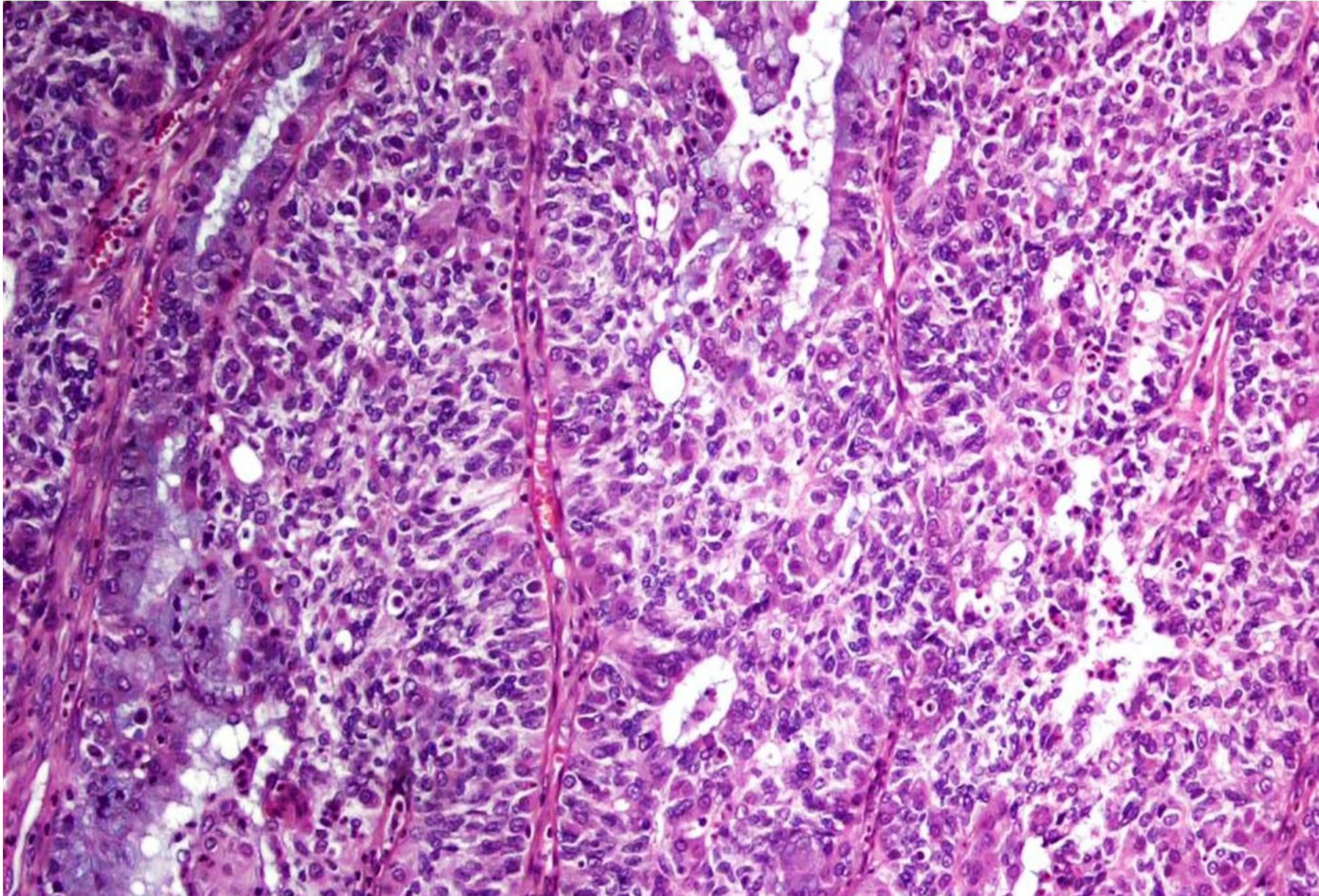
RARE TUMOR

Papillae Lined by Endocervical-Type Epithelium and Stromal Edema

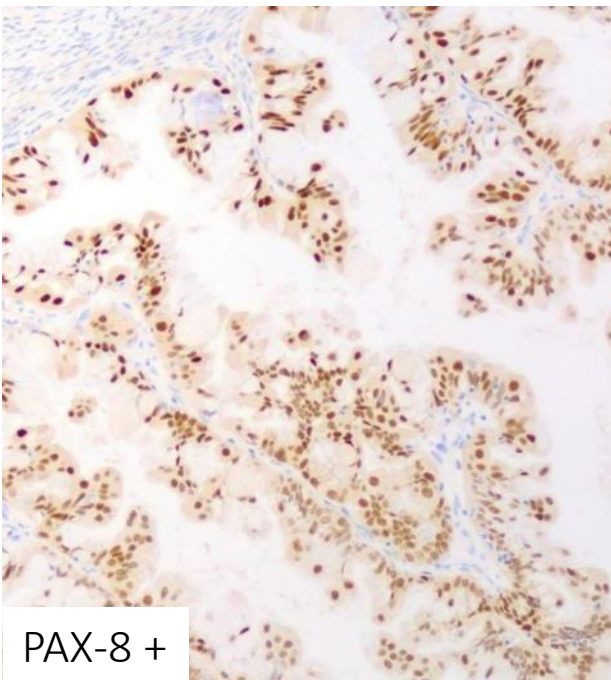
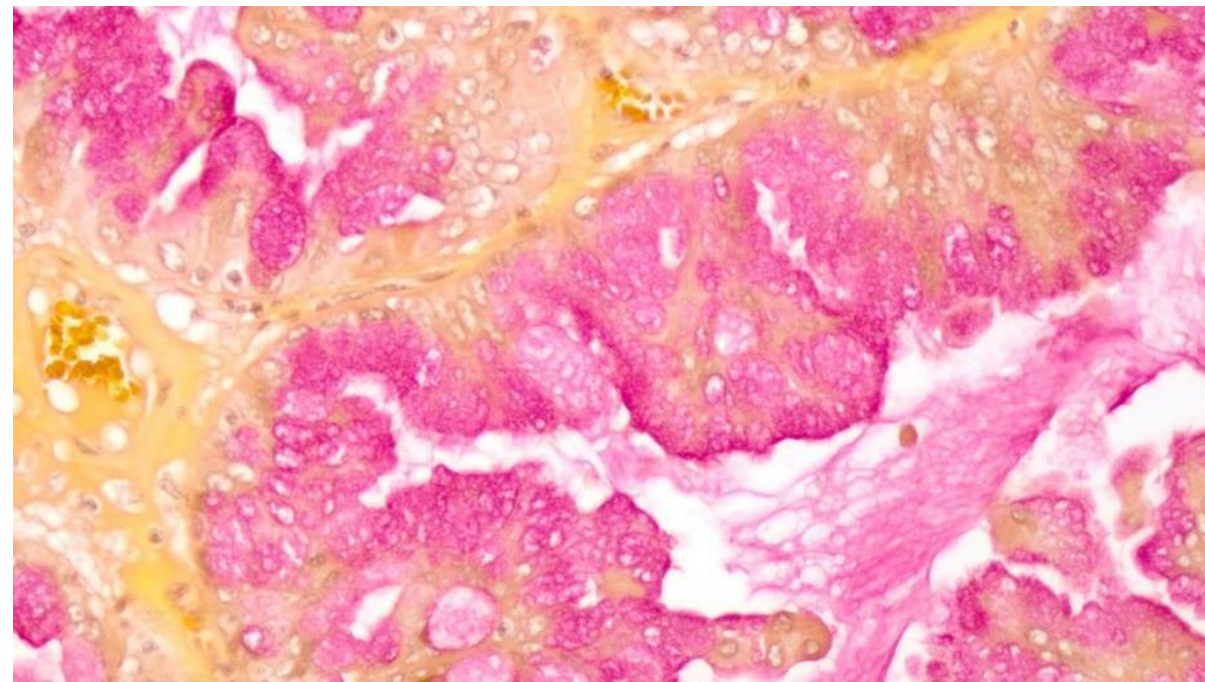
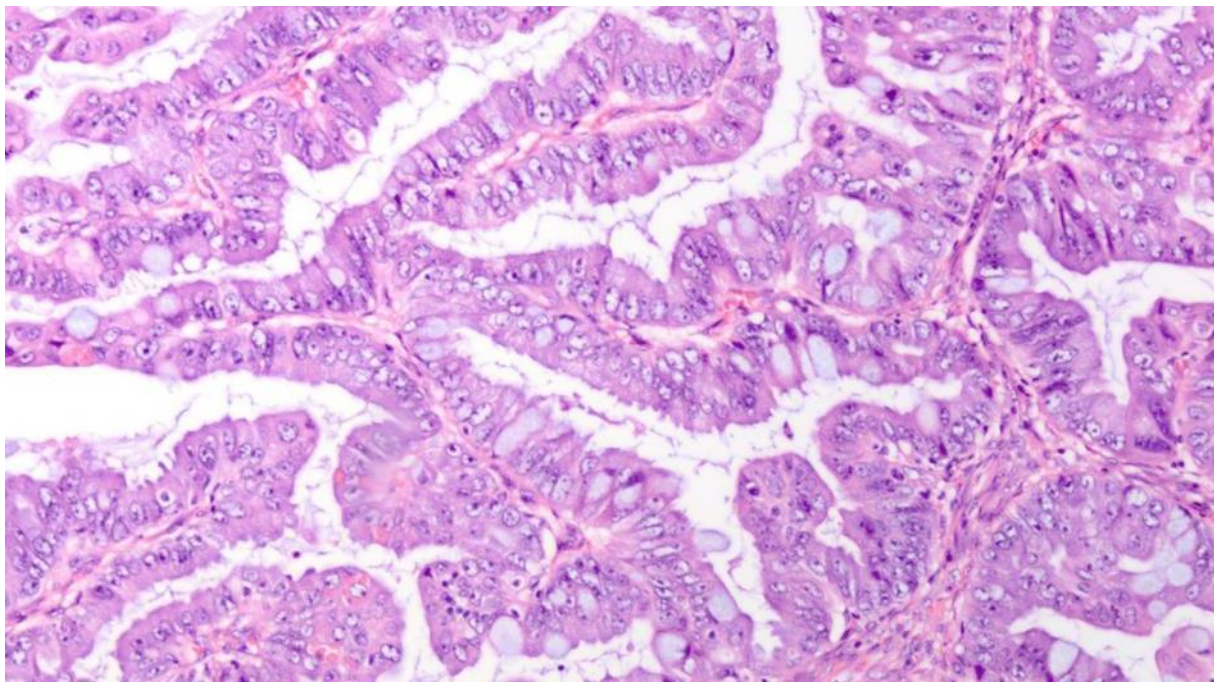


Papillae Lined by Endocervical-Type Epithelium with Squamoid Areas

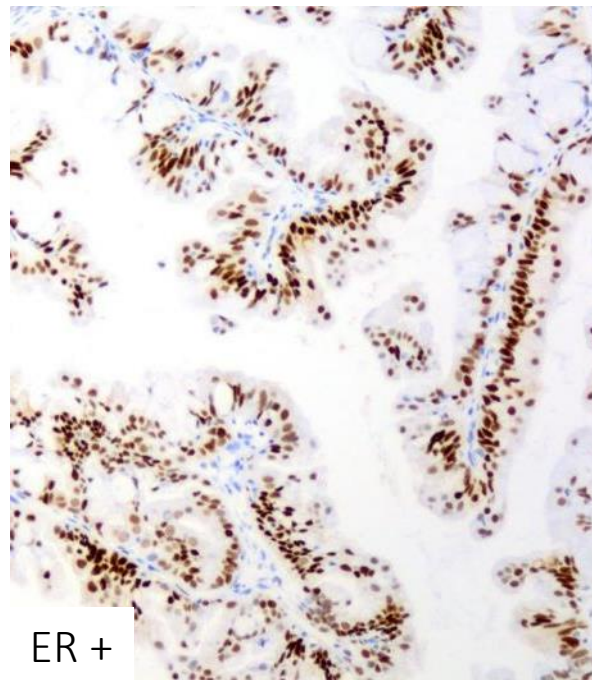




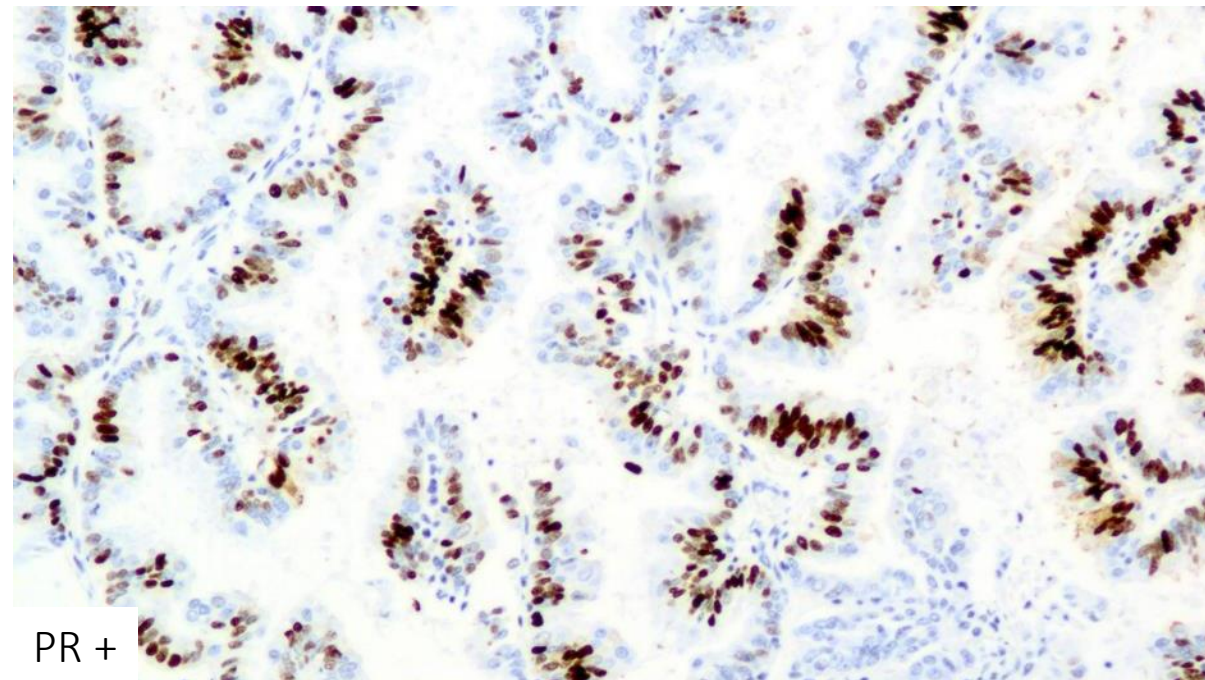
Endometrioid Carcinoma with Mucinous Metaplasia



PAX-8 +



ER +



PR +

1233 Primary Ovarian Endometrioid Adenocarcinoma With Mucinous Metaplasia (POEM): An Under Recognized Entity With Therapeutic Implications

Charanjeet Singh, Preetha Ramalingam, Elizabeth Euscher, Anais Malpica. University of Texas MD Anderson Cancer Center, Houston, TX.

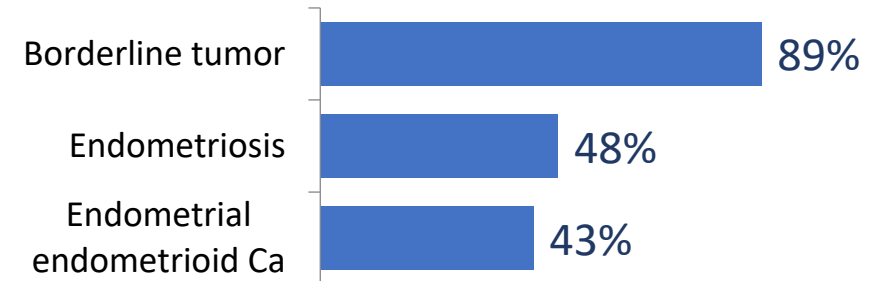
Background: Mucinous metaplasia is well-recognized in endometrial endometrioid adenocarcinoma (EEC), but not in ovarian endometrioid carcinoma. Misdiagnosis has therapeutic implications as ovarian mucinous carcinomas are increasingly being treated with chemotherapy regimens used for colonic tumors. In this study, we present our experience with cases of POEM and highlight the pathologic features that can lead to their correct identification.

Design: 37 cases of POEM with available slides and follow up (f/u) from 2000-2014 were reviewed. Pathologic parameters recorded included laterality, tumor size, initial diagnosis, presence of endometriosis, type of borderline component, amount of mucinous metaplasia, other endometrioid adenocarcinoma associated cytologic changes, tumor grade, presence and pattern of invasion, tumor stage and concurrent endometrial pathology. Clinical parameters including patient age, adjuvant chemotherapy and f/u were recorded.

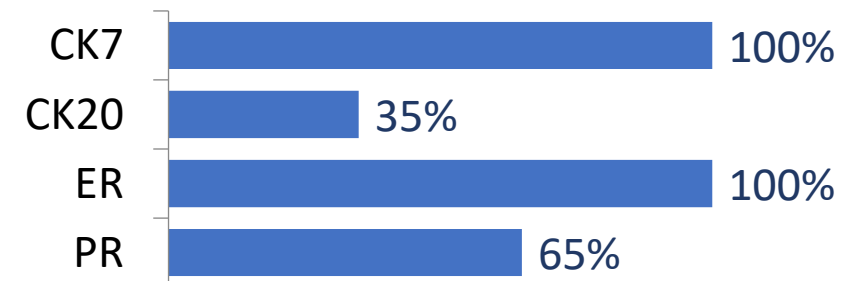
Results: Patients' (pts) age ranged from 26-71 yrs (mean, 51). Tumor laterality: 18 left, 10 right, 9 bilateral. Tumor size ranged from 2.5 to 48 cm (mean 12.7). All 32 consult cases, reclassified as POEM, were initially diagnosed as: 22 mucinous carcinoma/adenocarcinoma, NOS (59%), 10 mucinous borderline tumor with foci suspicious for carcinoma (27%). According to the tumor grade, cases were distributed as: grades 1 and 2 (32 cases), grade 3 (5 cases). The percentage of mucinous metaplasia in POEM ranged from 5-95% (mean 47%). Squamous metaplasia was seen in 17 cases, while 18 and 6 cases had secretory and clear changes, respectively. 26 cases showed only expansile invasion (EI), 9 EI and infiltrative invasion and 2 only infiltrative invasion. The histology of the borderline component was endocervical (12), endometrioid (3) or mixed (21). 18 cases had endometriosis. Tumor stage of POEMs: 23 Stage-I, 3 Stage-II, 3 Stage-III and 2 Stage-IV. 16 cases had concurrent grade 1 EEC (5), grade 2 EEC (9) or complex atypical hyperplasia (2). 20 pts. received adjuvant chemotherapy. F/u ranged from 1-96 mos (mean 11). At most recent f/u, 28 pts are alive without evidence of disease while 4 died of disease and 5 died of other causes.

Conclusions: POEMs are under recognized and due to mucinous metaplasia can be misdiagnosed as ovarian mucinous carcinomas, resulting in incorrect therapy. These tumors are frequently associated with a borderline tumor-either mixed or endocervical type (89%), endometriosis (48%) and EEC (43%). Presence of squamous metaplasia, secretory change or a nonintestinal type borderline tumor can facilitate the correct diagnosis of POEM.

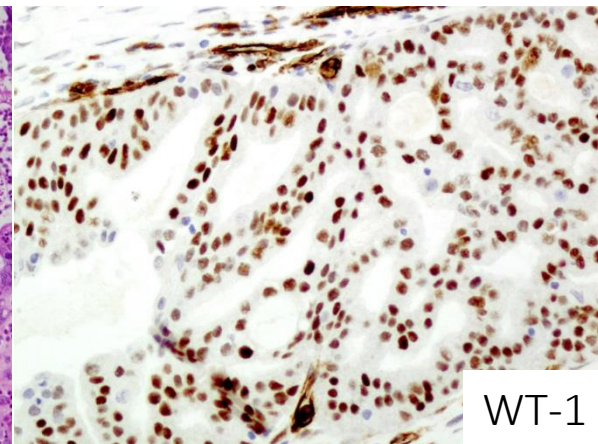
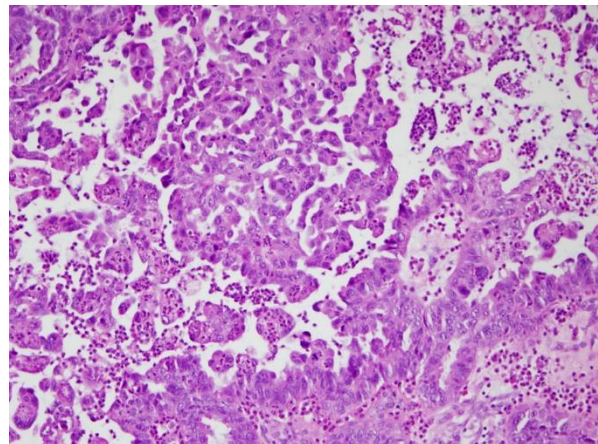
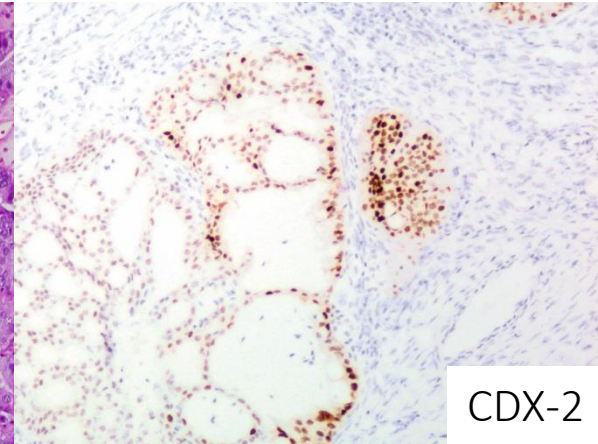
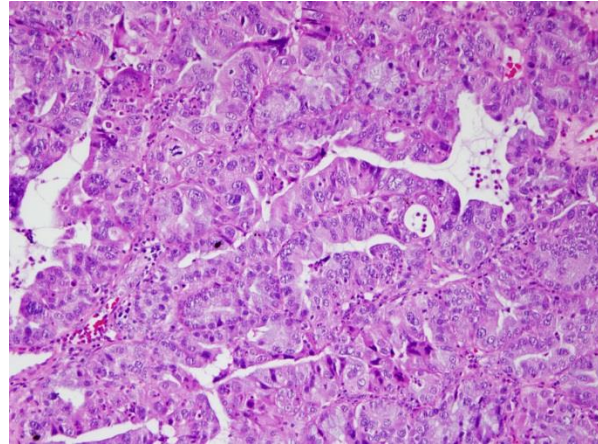
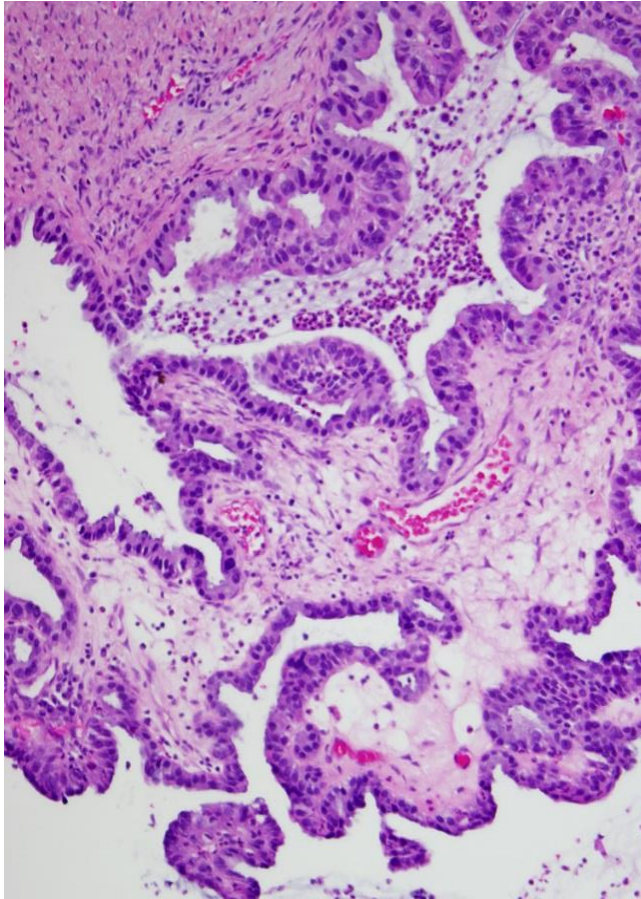
- 37 cases
- Association with:

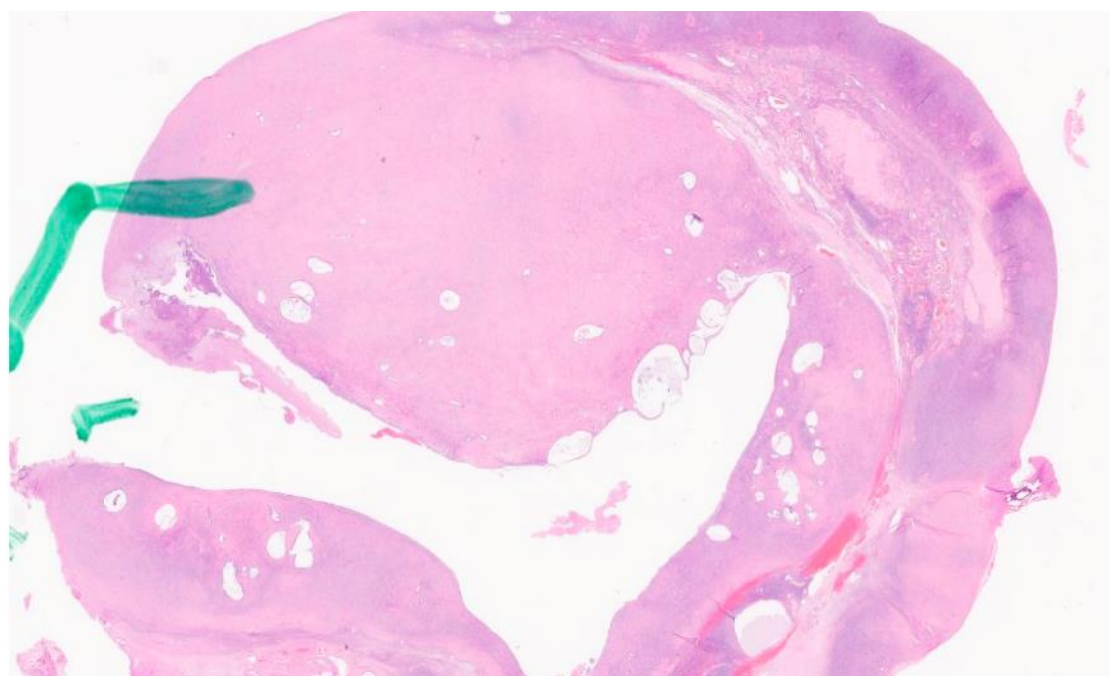
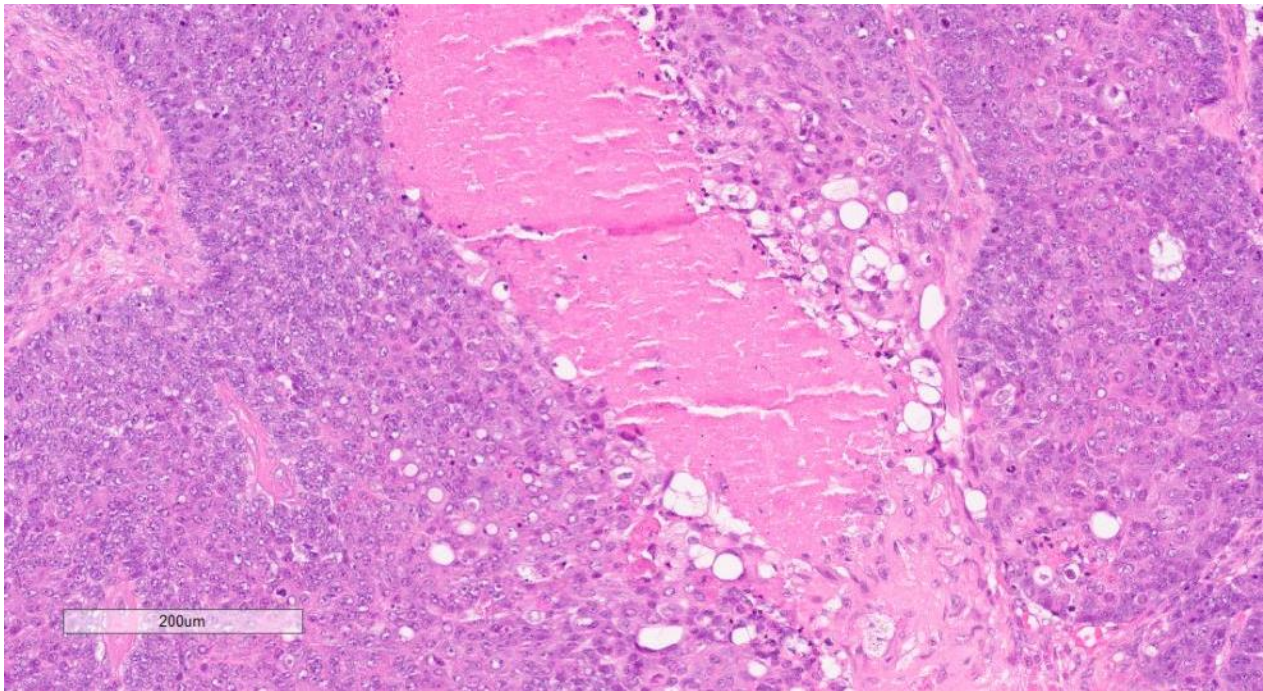
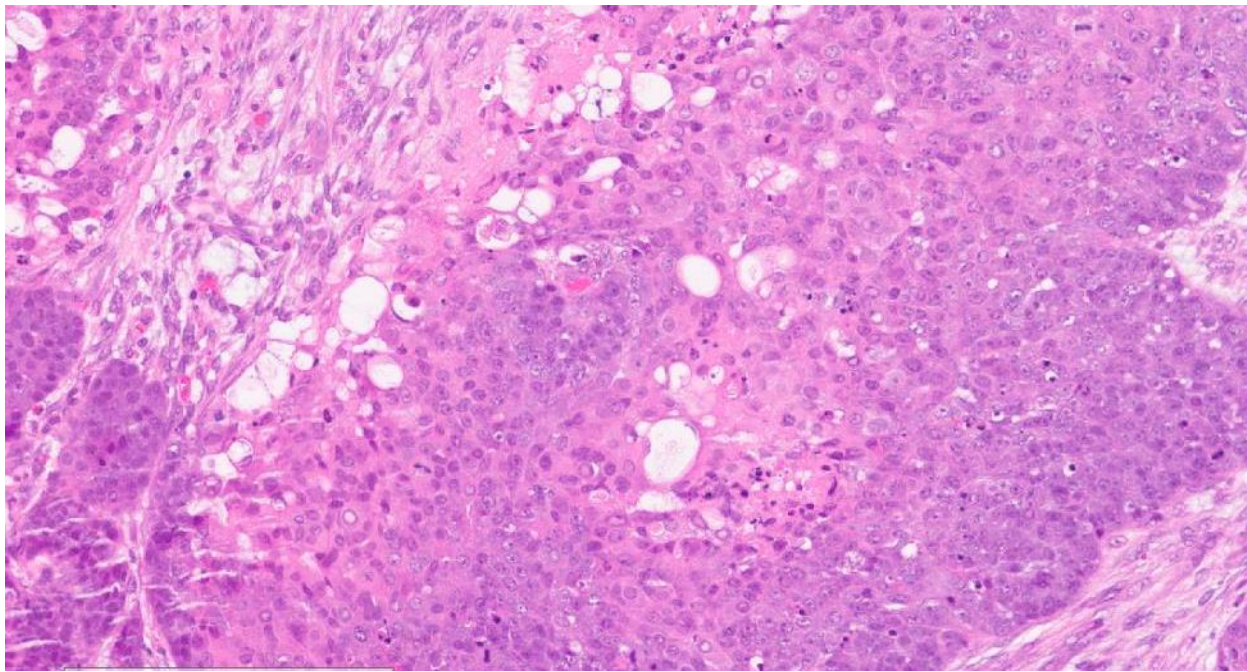
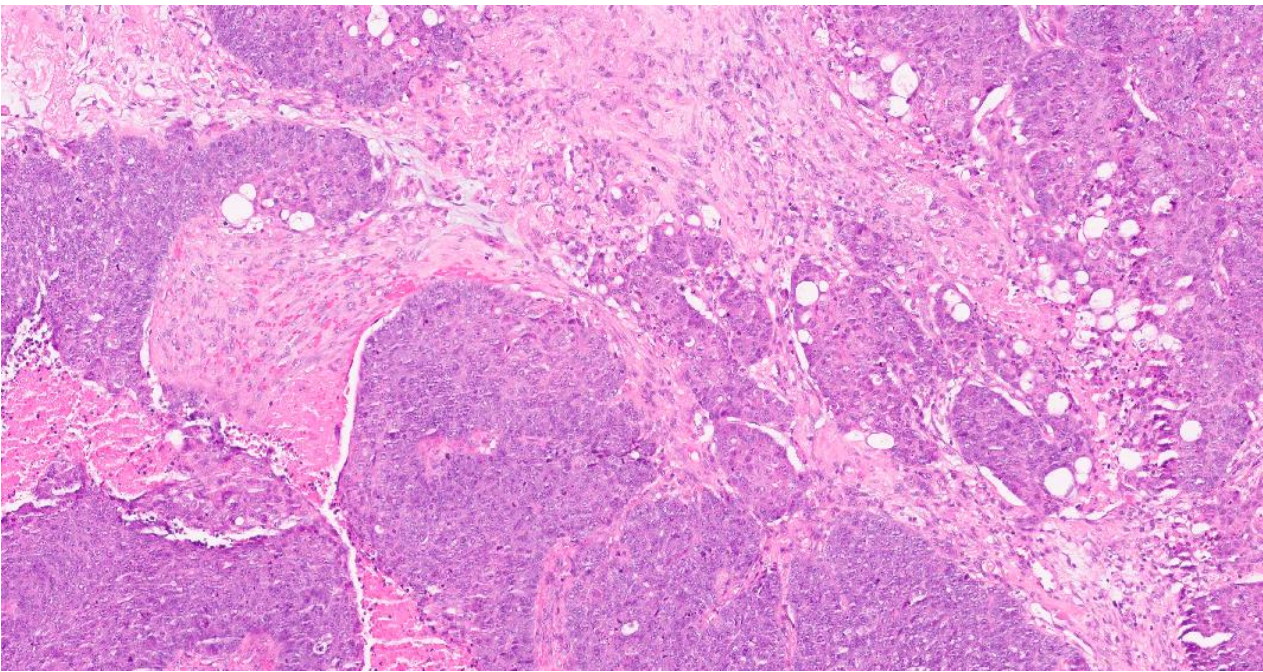


- 71% expansile pattern of invasion
- 59% initially diagnosed as mucinous carcinoma
- IHC



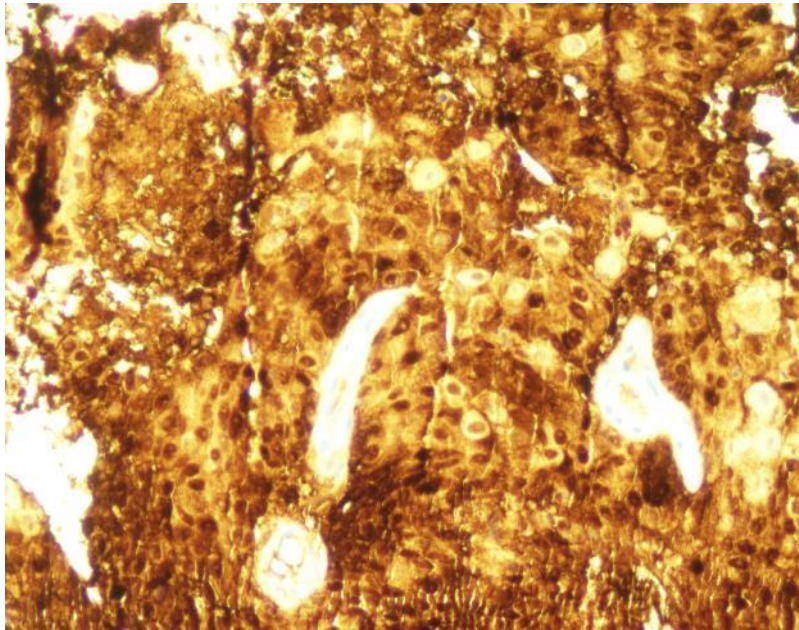
Seromucinous Carcinoma Arising in a Seromucinous Borderline is a Rare Tumor



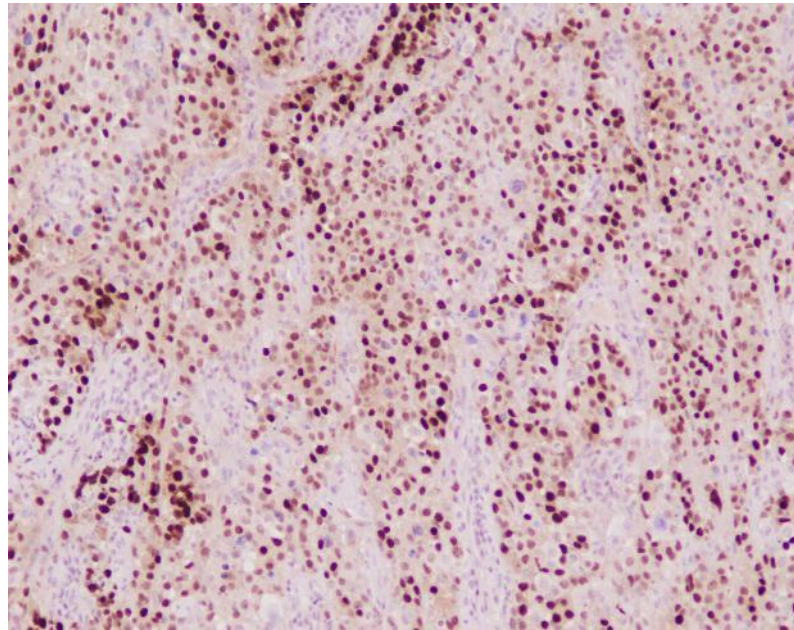


Endometrioid Ca, high grade, pilomatrix-like

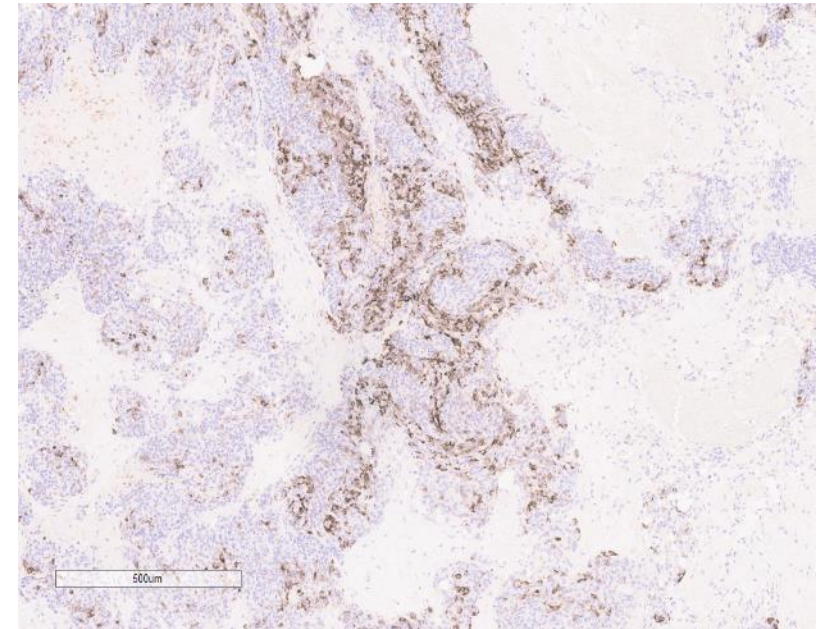
Endometrioid Ca, high grade, pilomatrix-like



Beta-catenin +

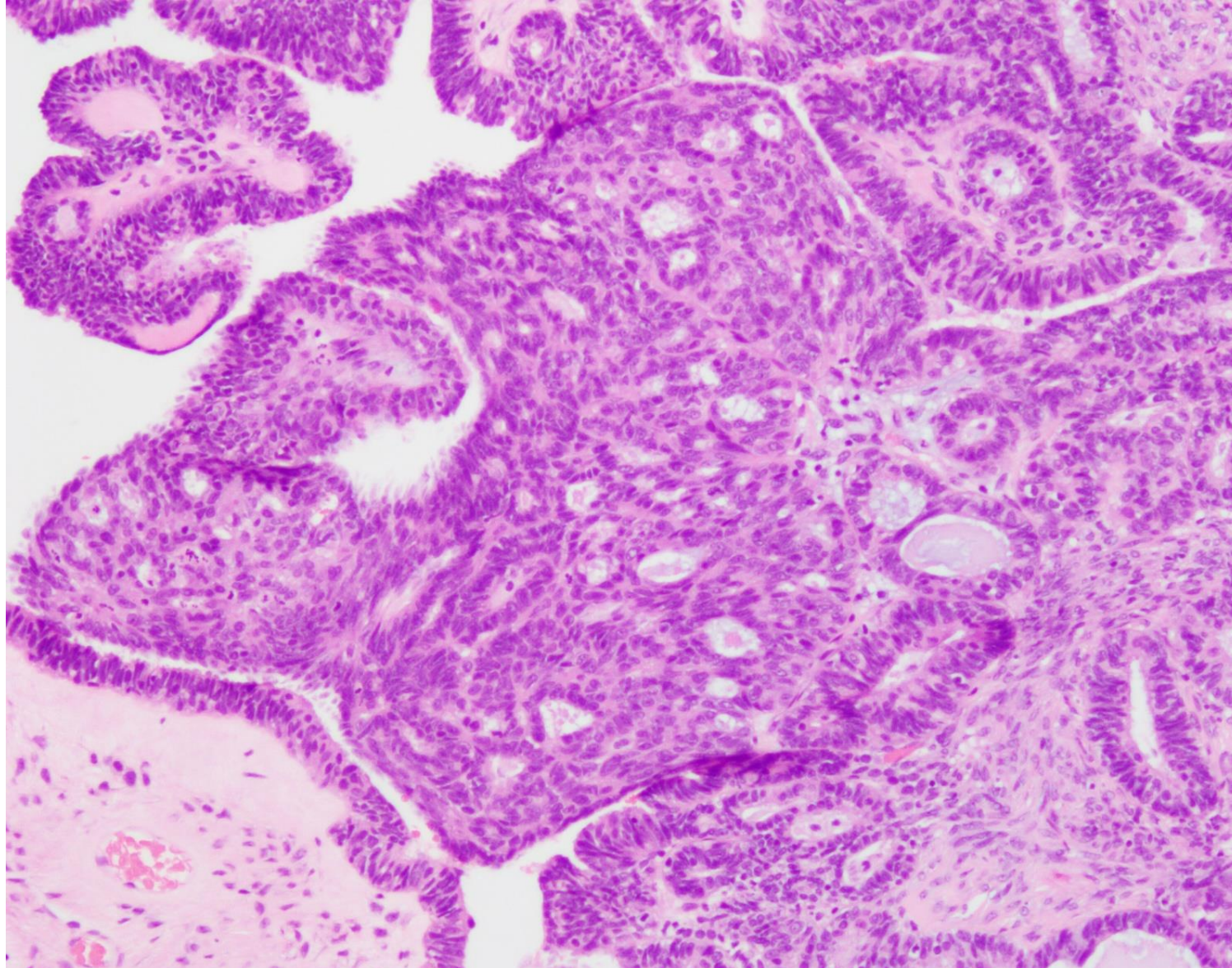


CDX2 +

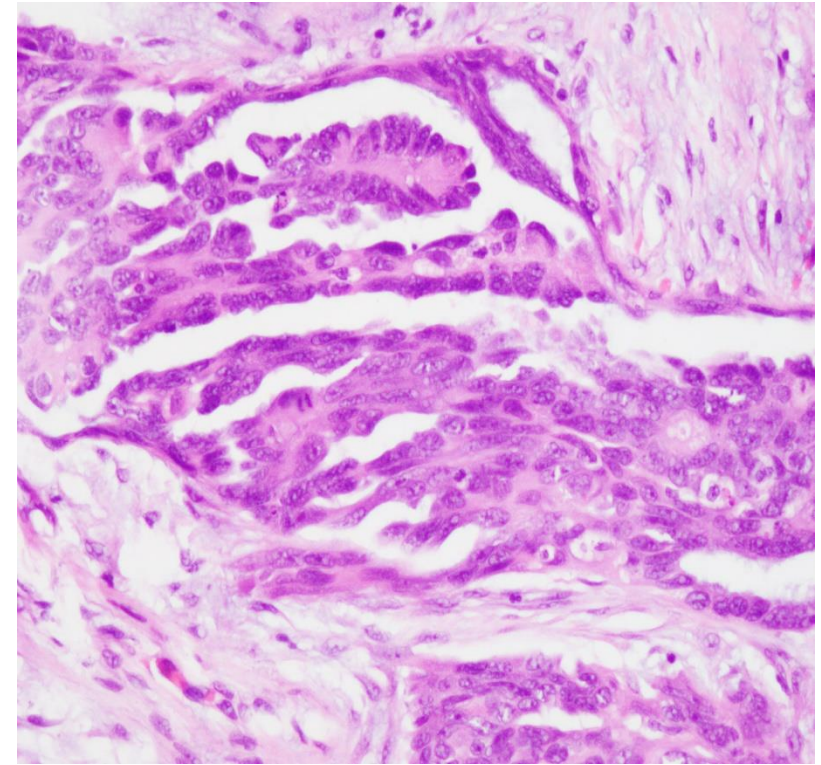
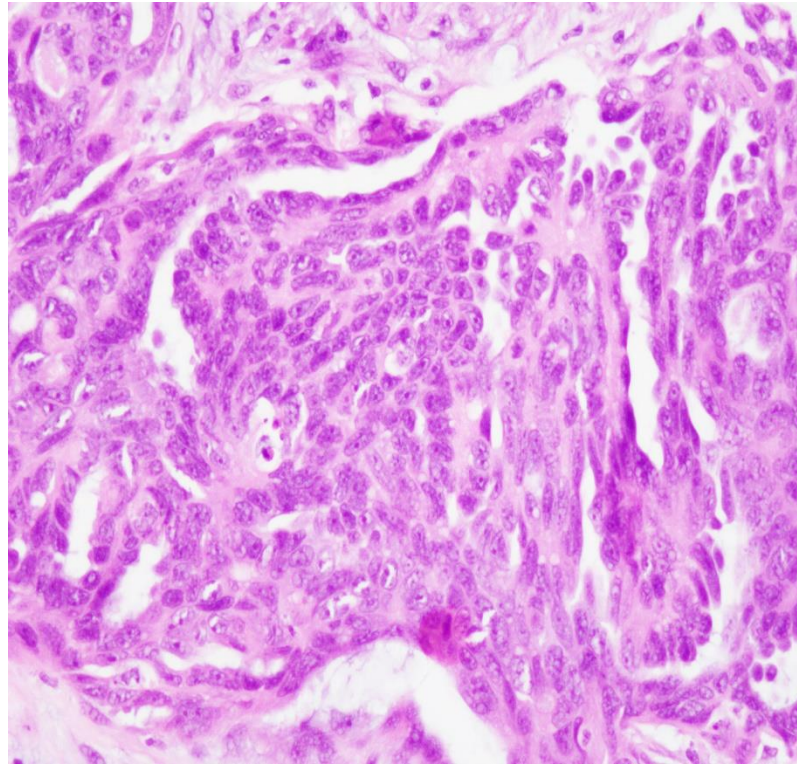
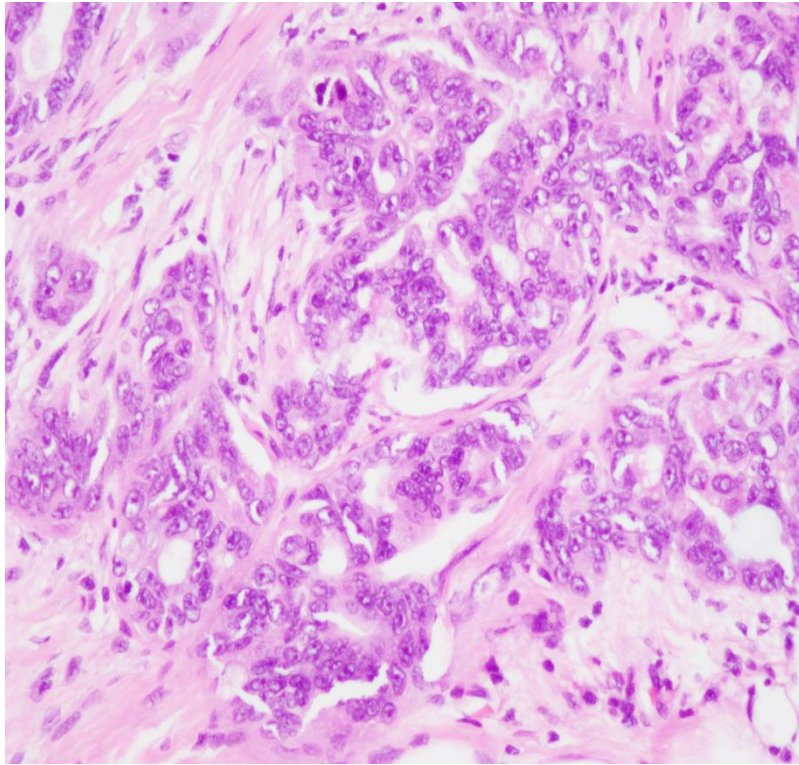


Synaptophysin +

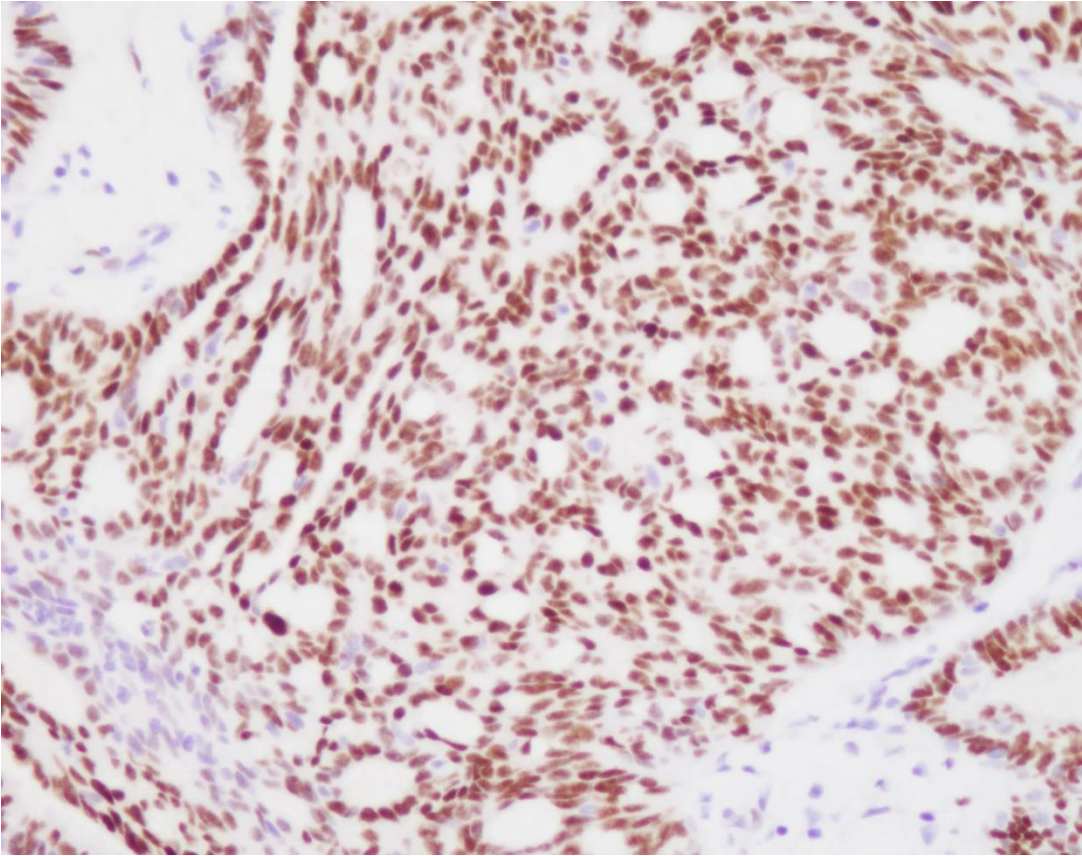
Endometrioid Ca Mimicking Serous Ca



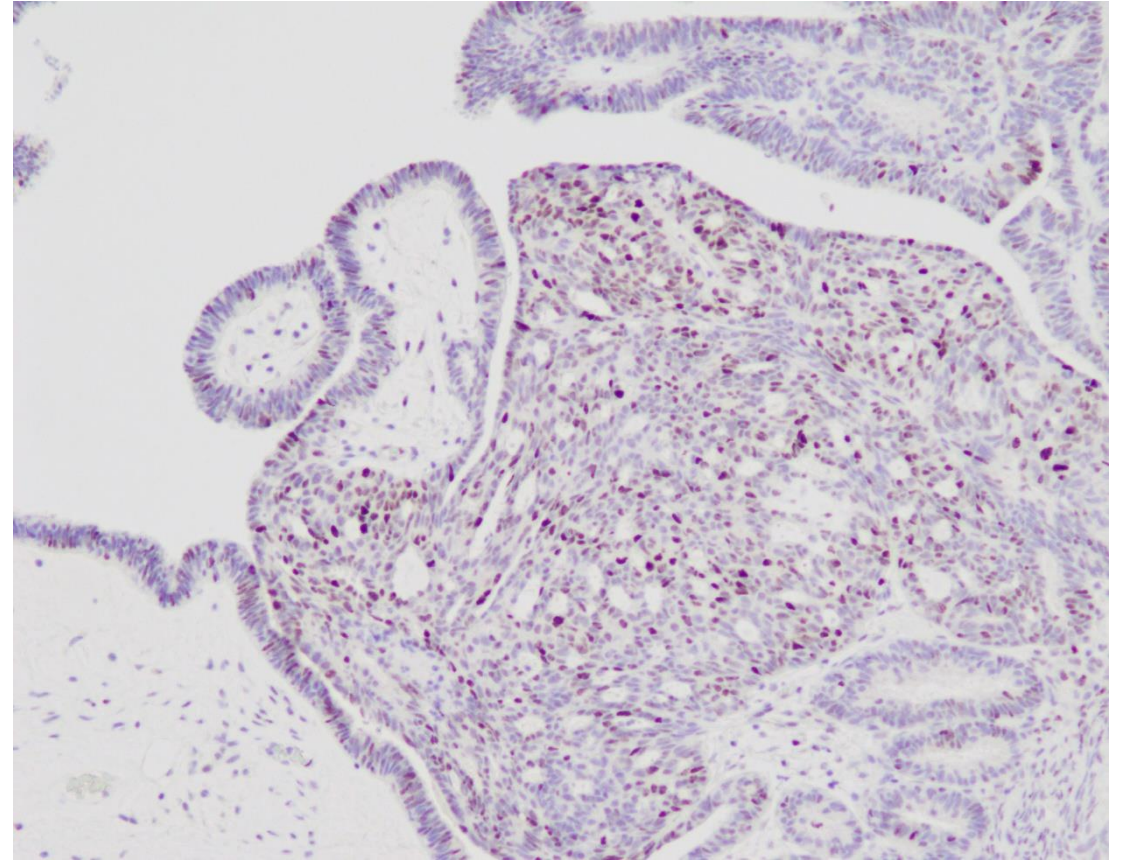
Endometrioid Ca Mimicking Serous Ca



Endometrioid Ca Mimicking Serous Ca

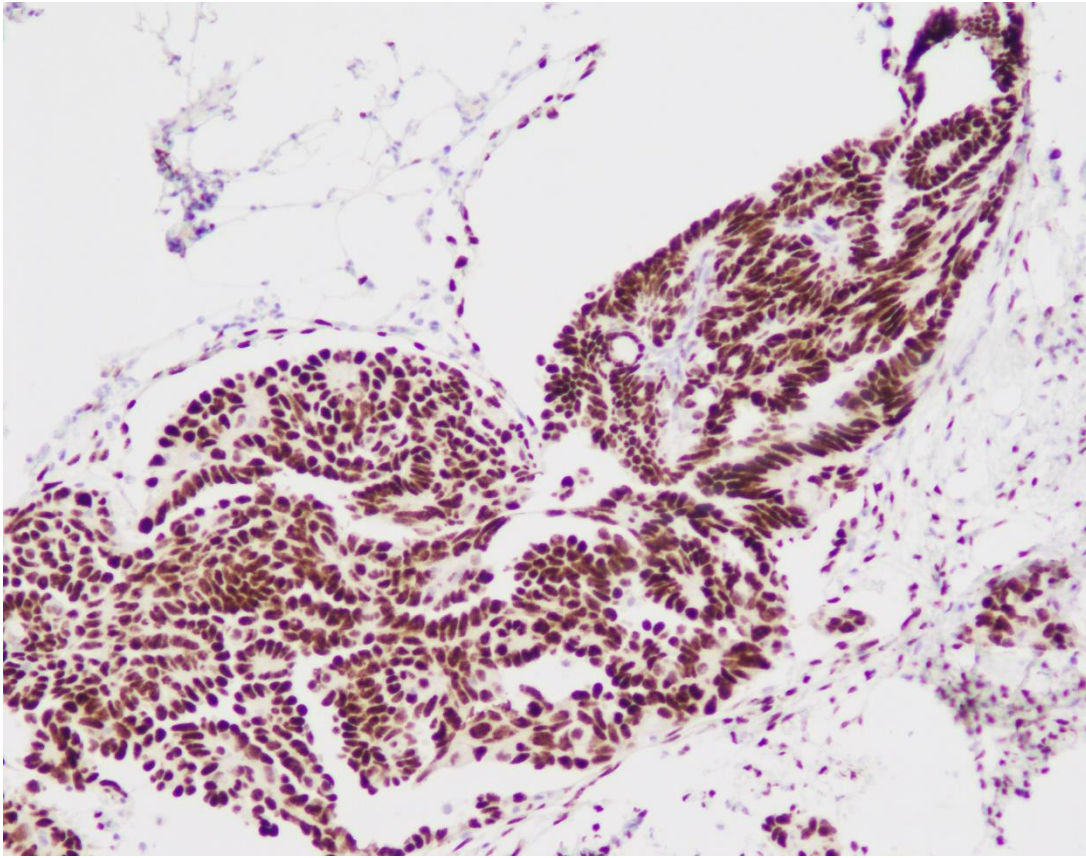


WT-1 +

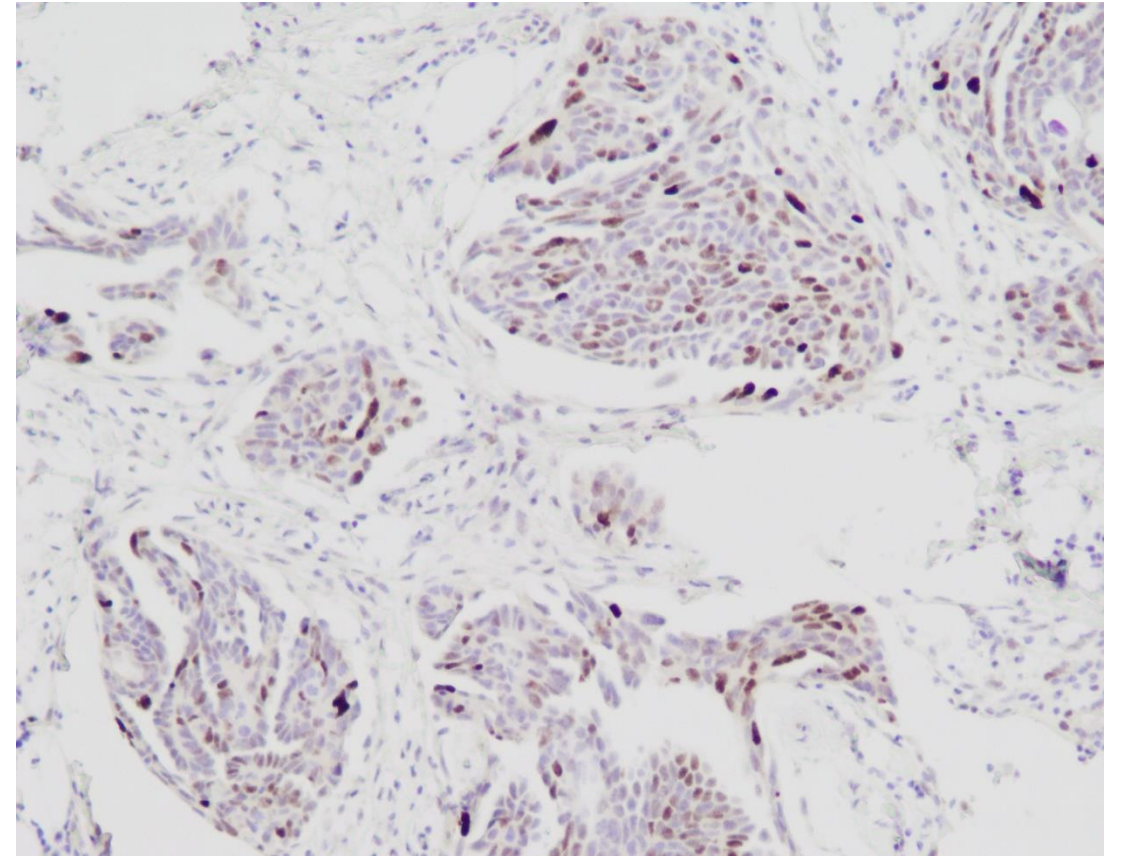


p53, wild type

Endometrioid Ca Mimicking Serous Ca

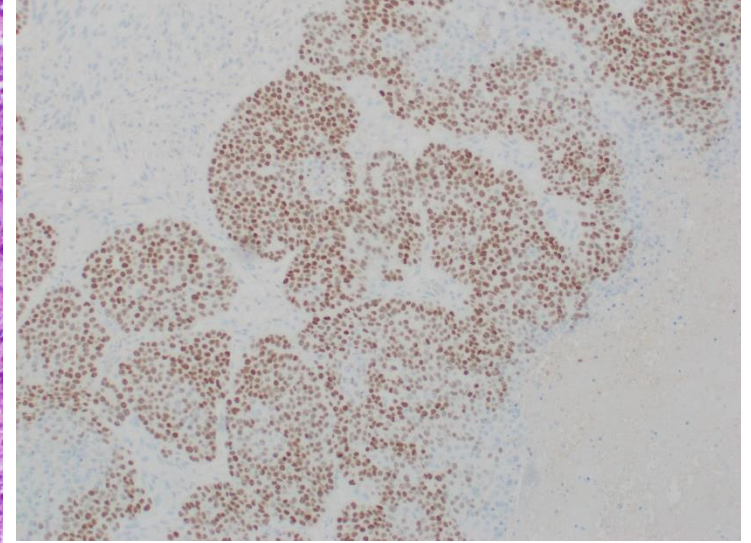
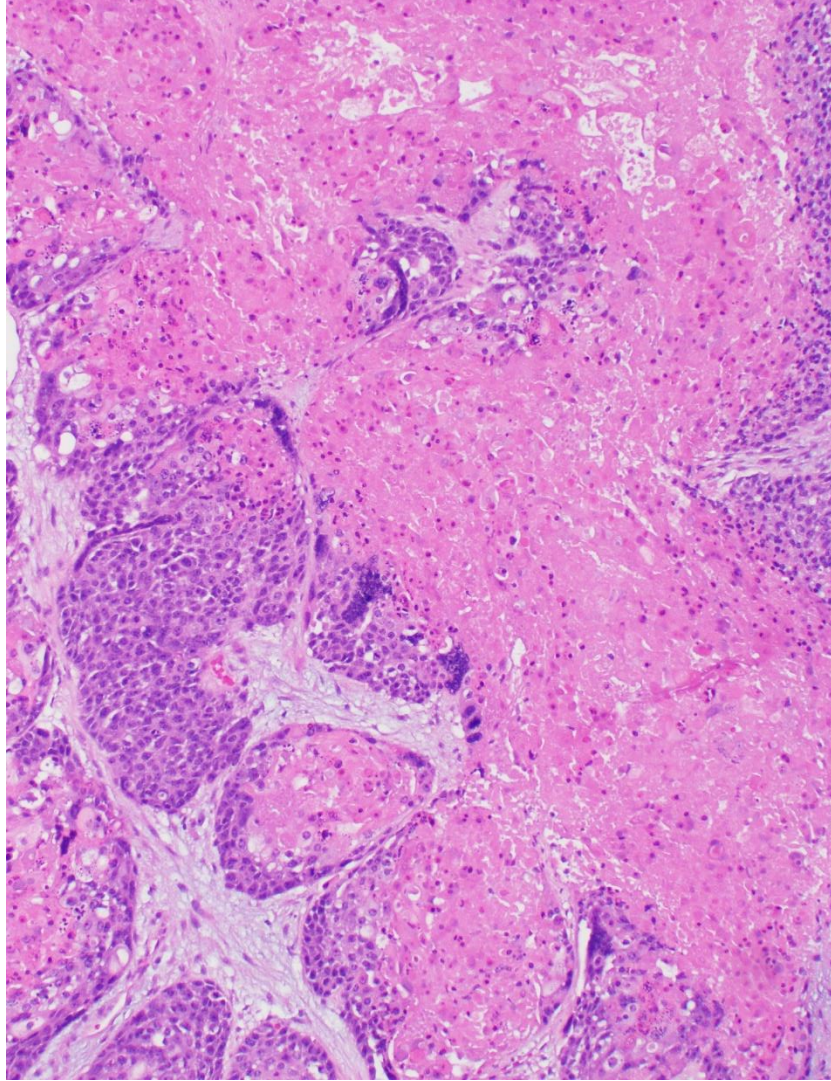
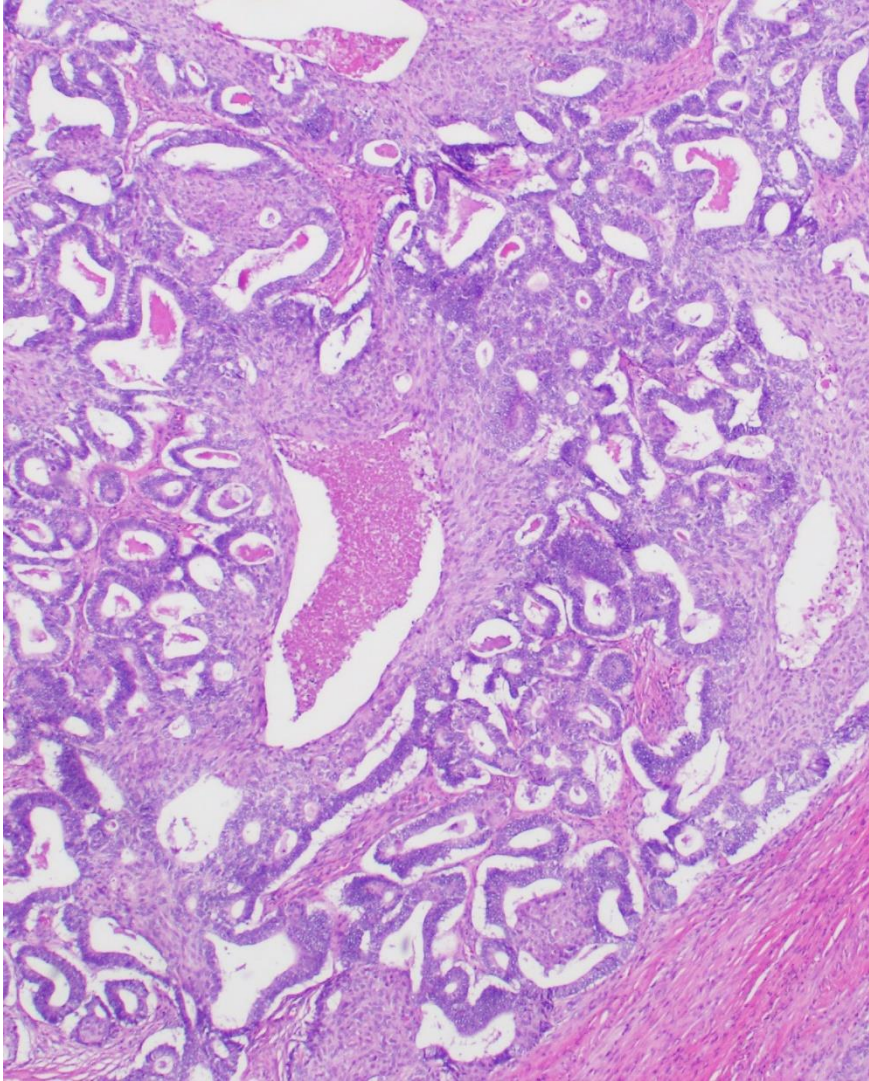


WT-1 +



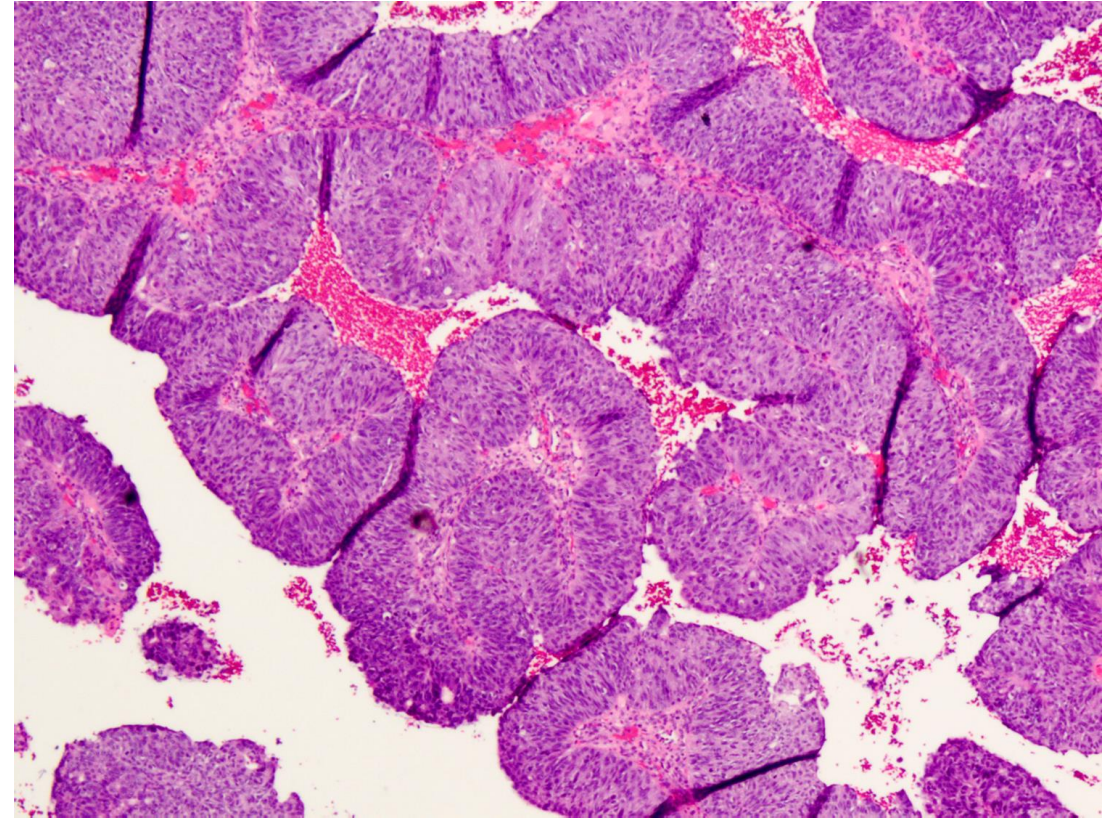
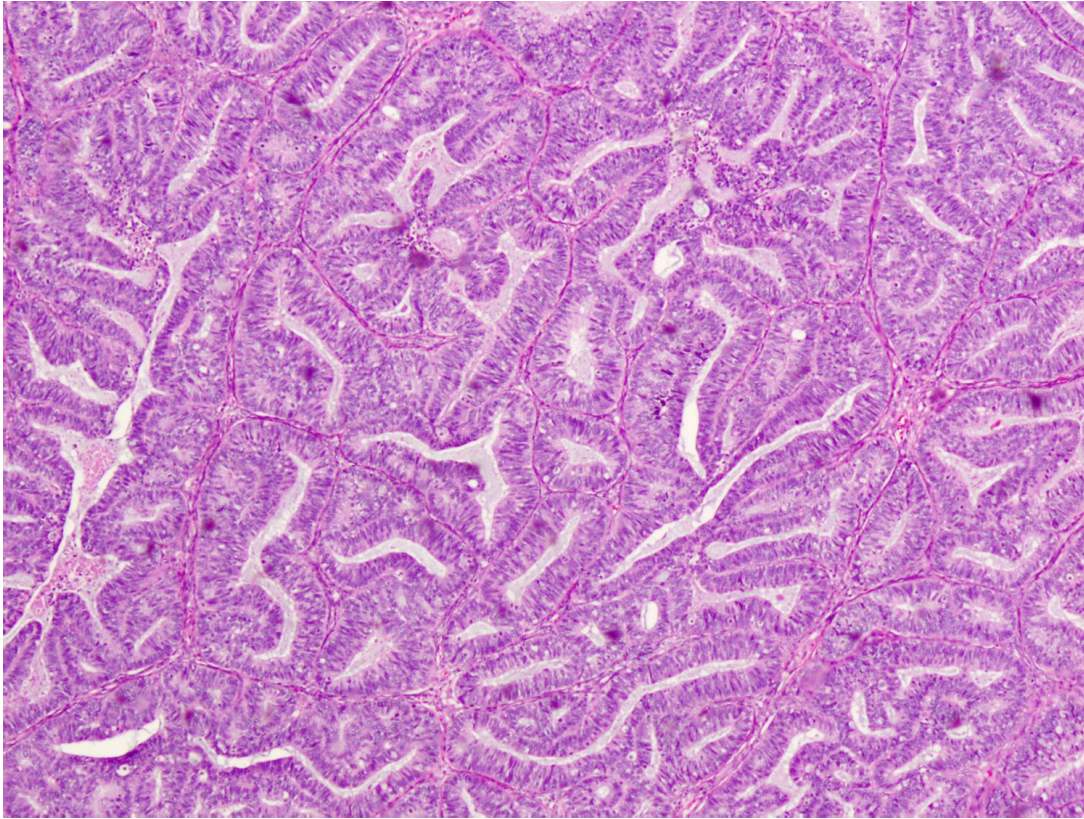
p53, wild type

Endometrioid Ca and Poorly Differentiated SCa

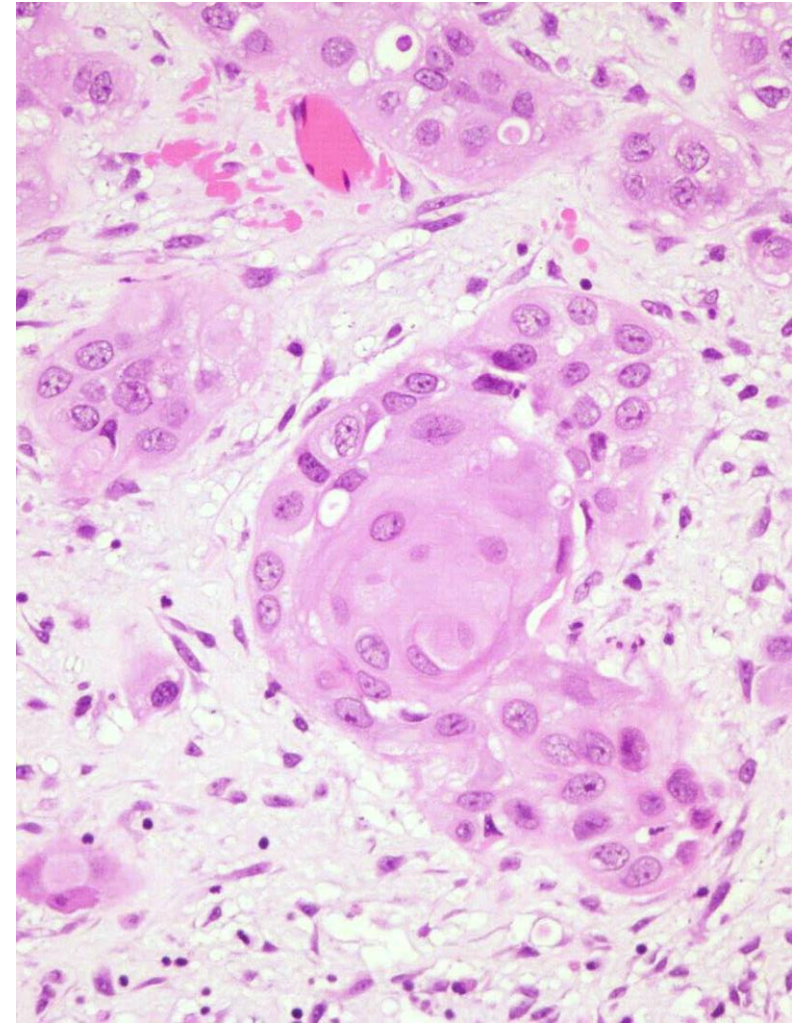
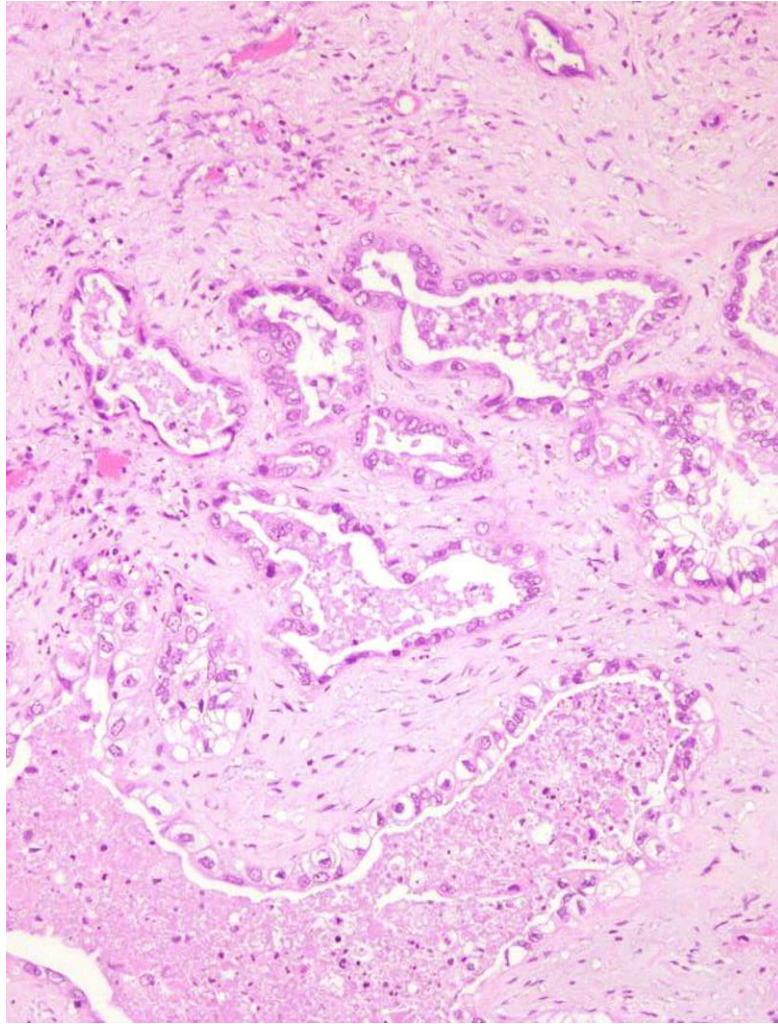
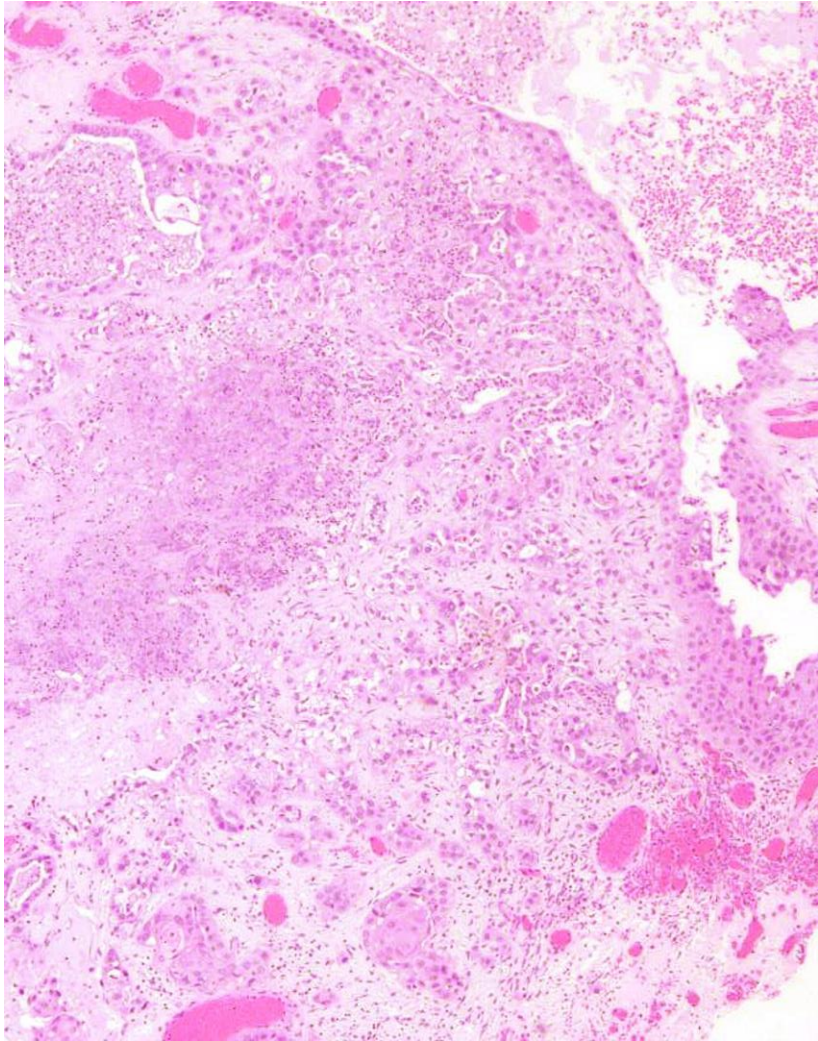


p40

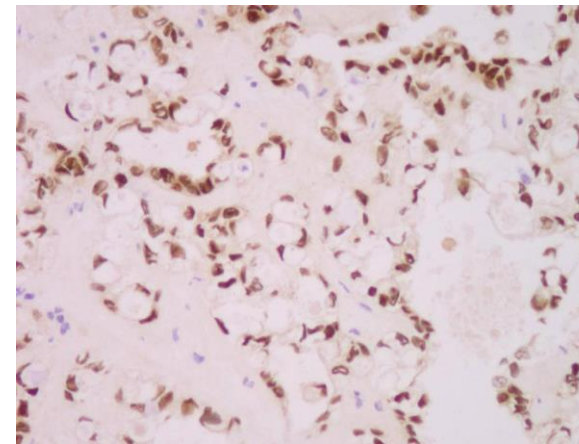
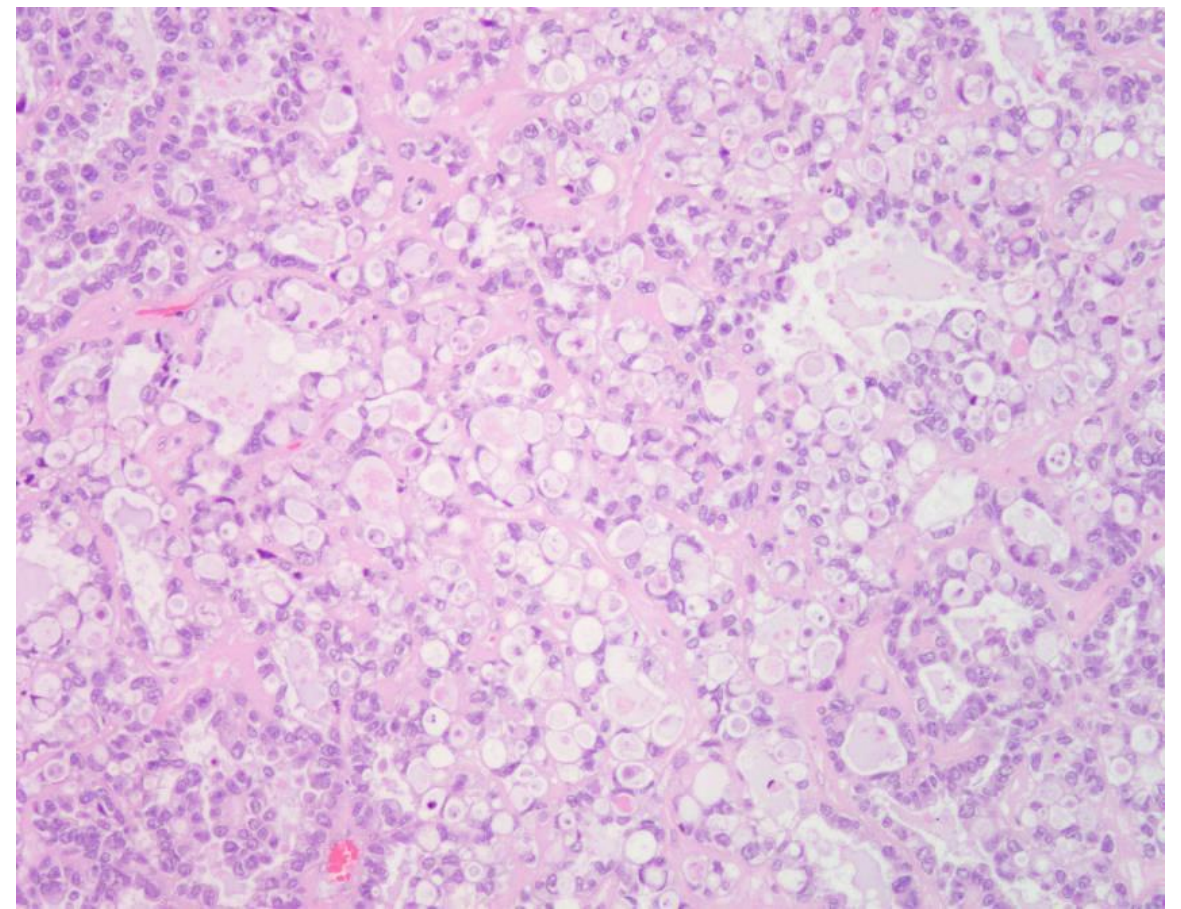
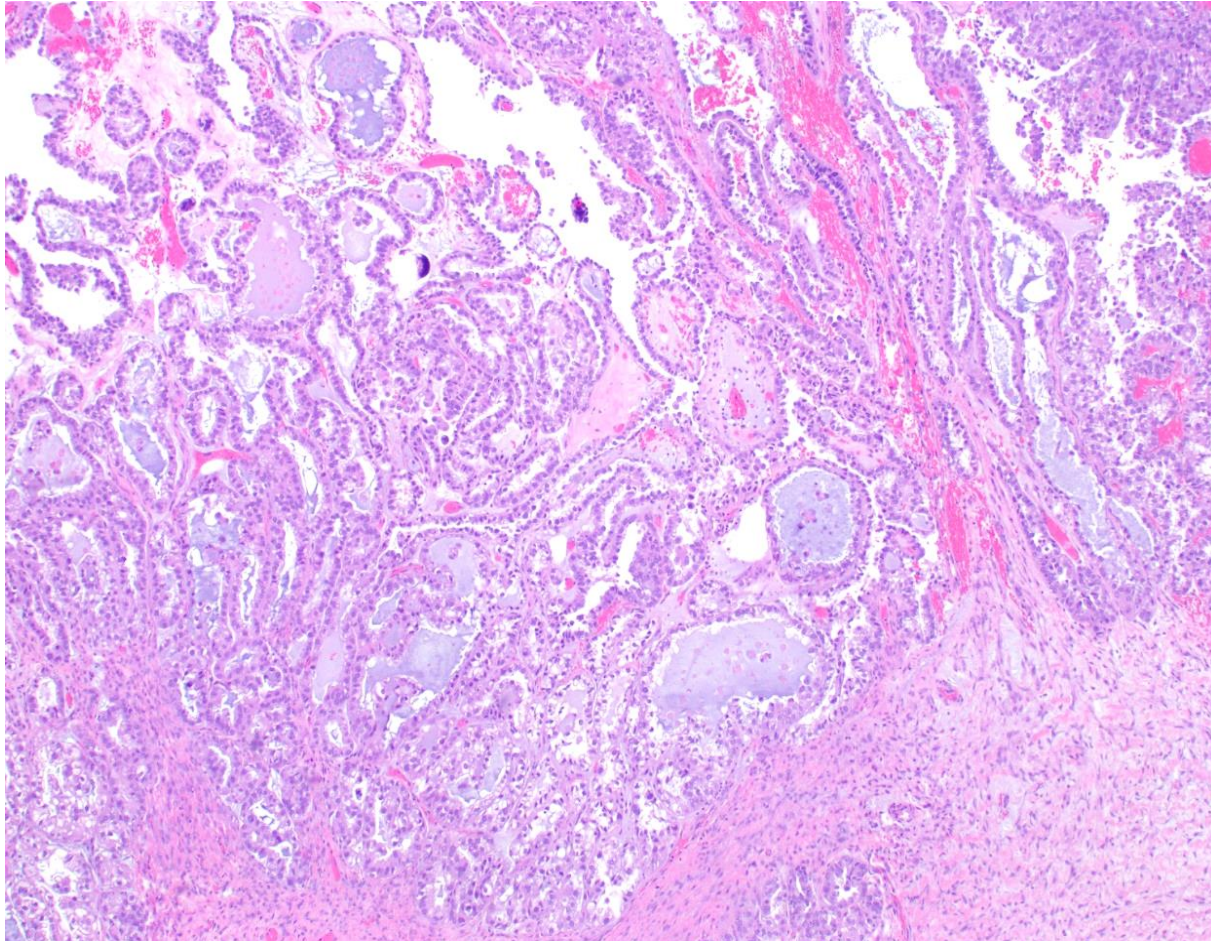
Endometrioid Ca with a Transitional Cell Pattern



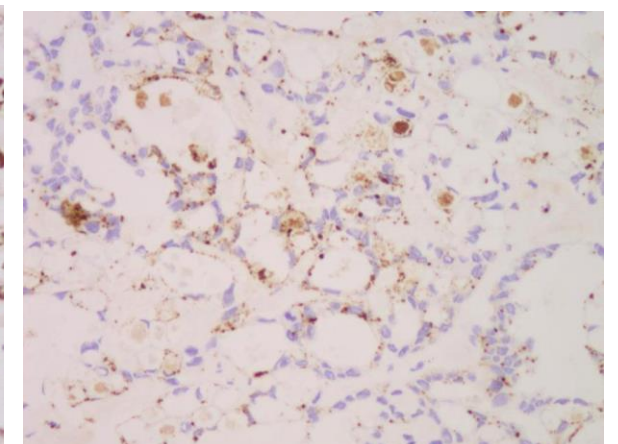
Clear Cell Carcinoma with Squamous Differentiation



Clear Cell Carcinoma with Abundant Mucin or Signet-Ring Cells

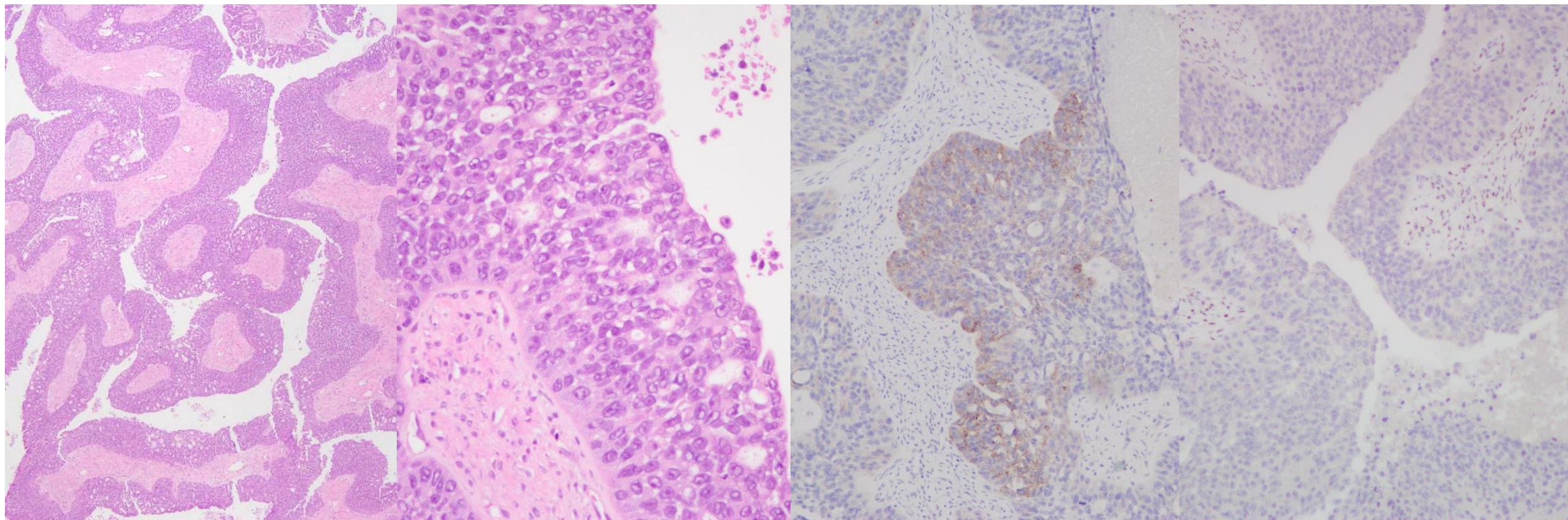


PAX-8 +



Napsin A +

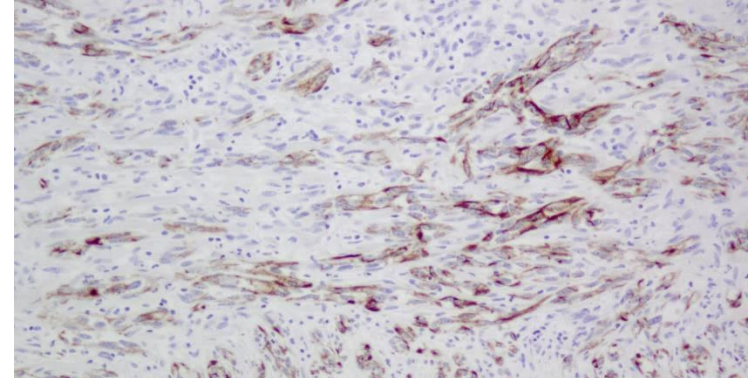
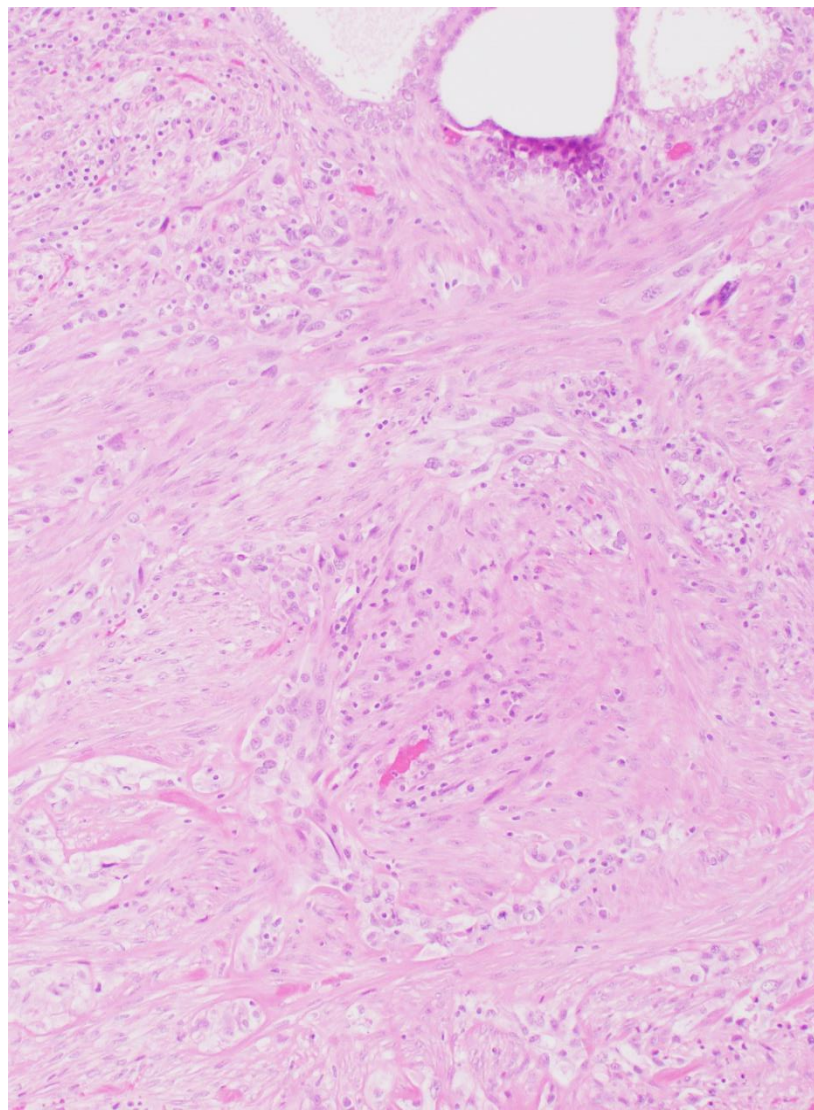
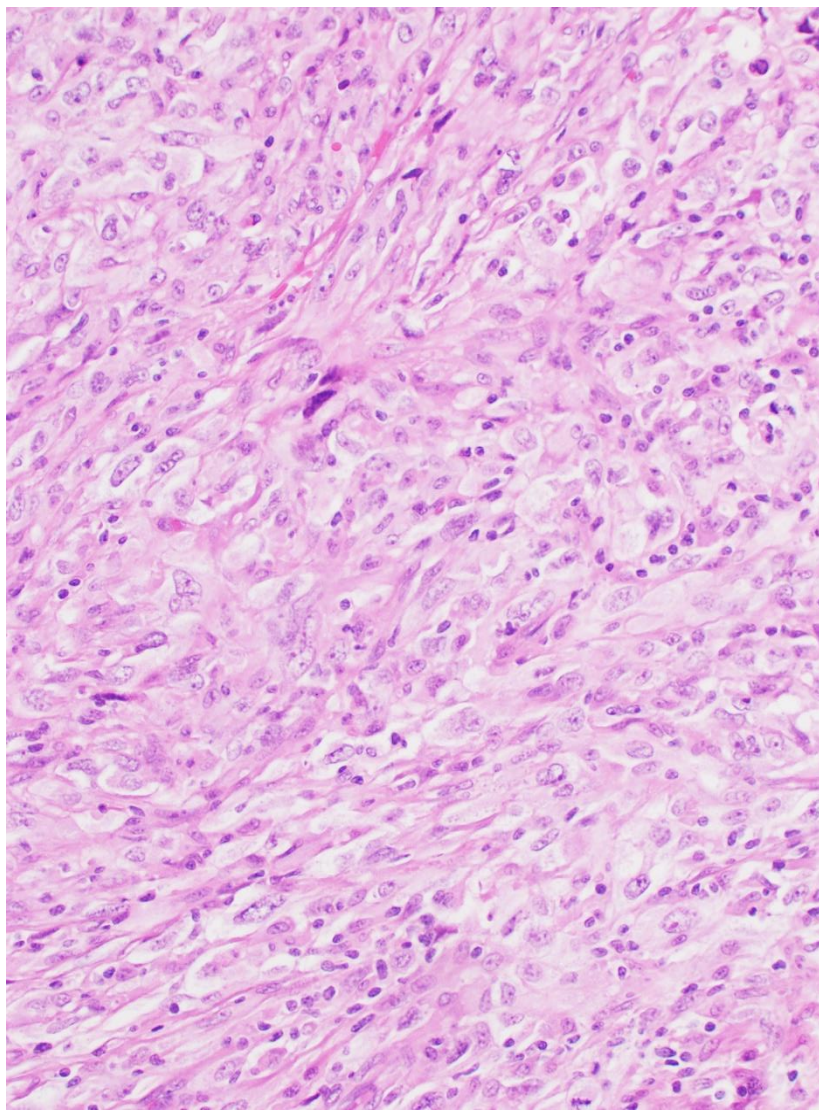
Clear Cell Carcinoma with Transitional Cell Pattern



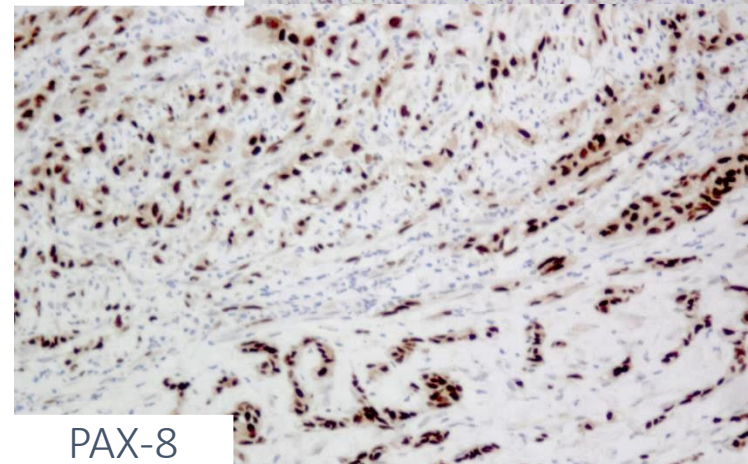
p504s

WT-1

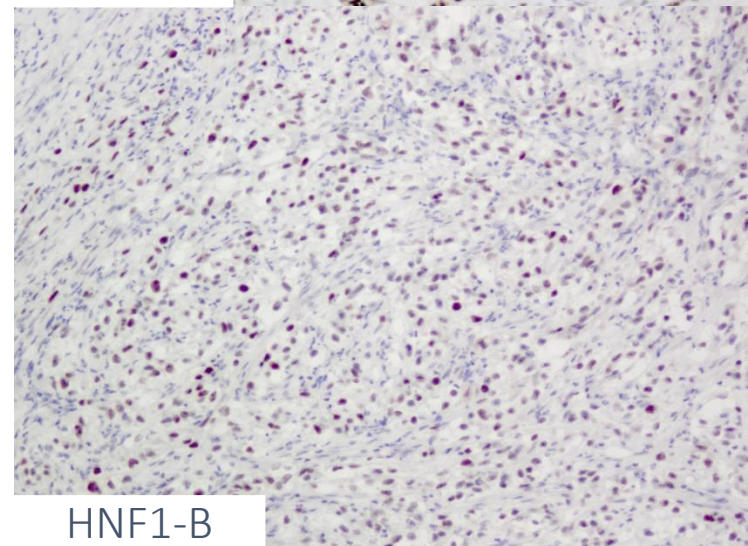
Clear Cell Carcinoma with Sarcomatoid Features



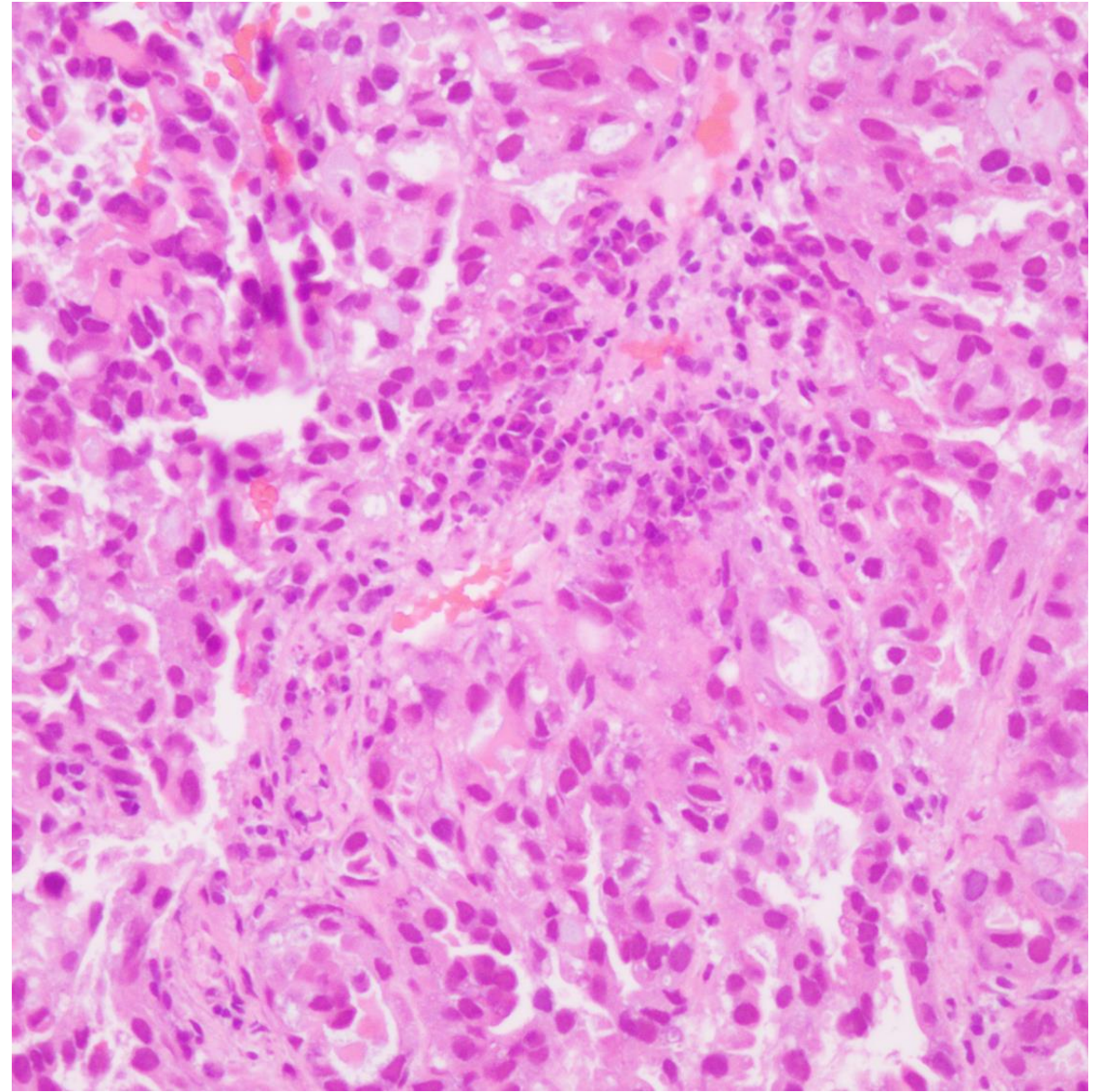
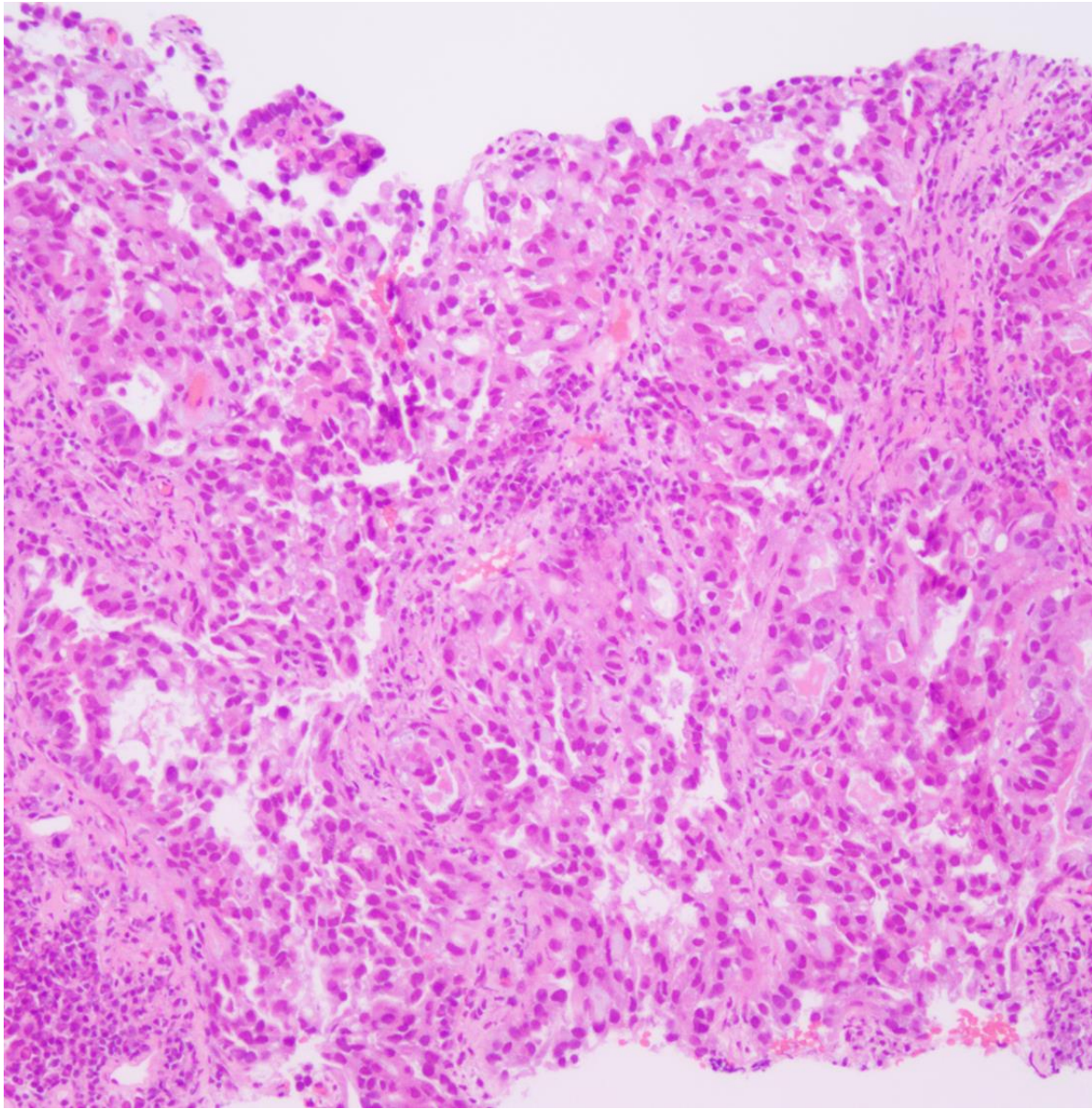
Keratin



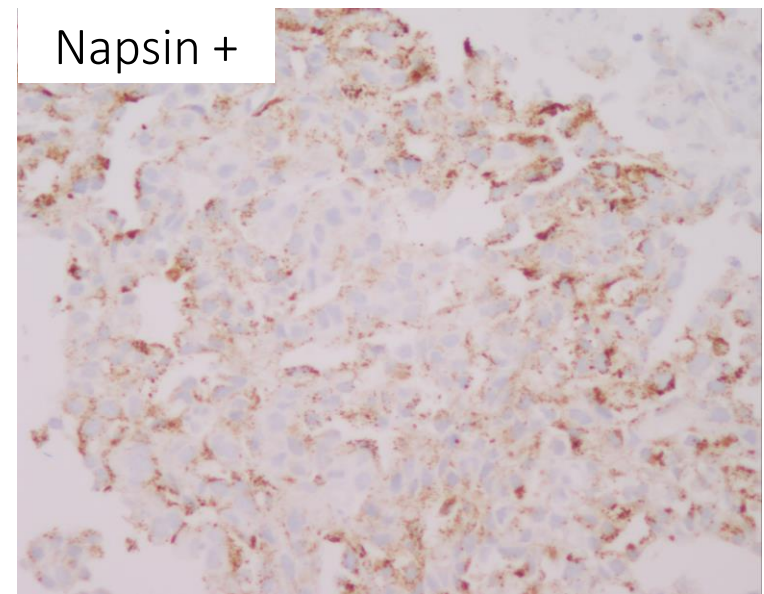
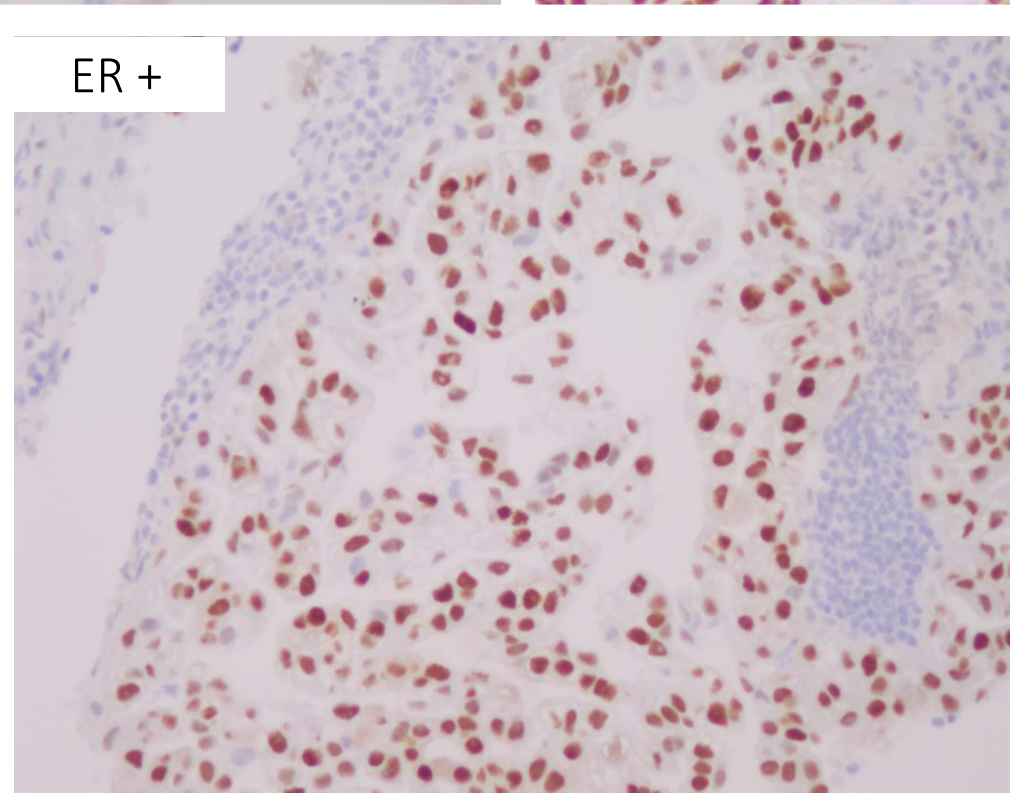
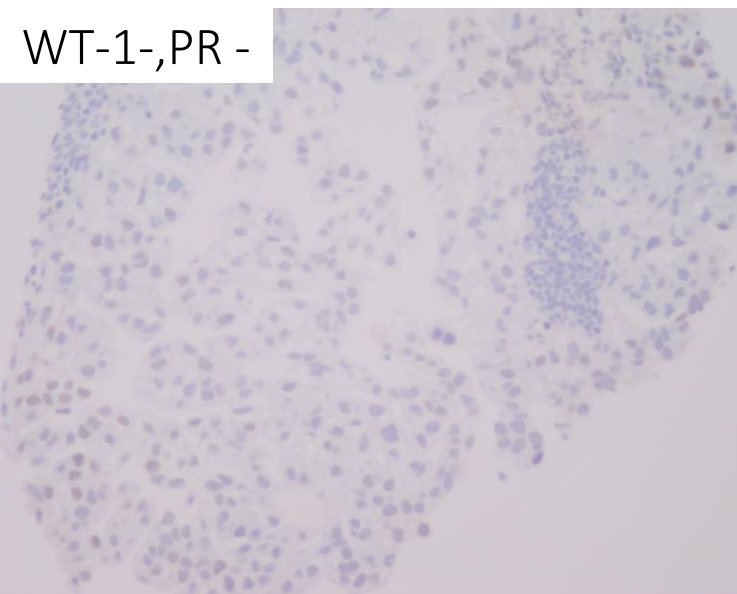
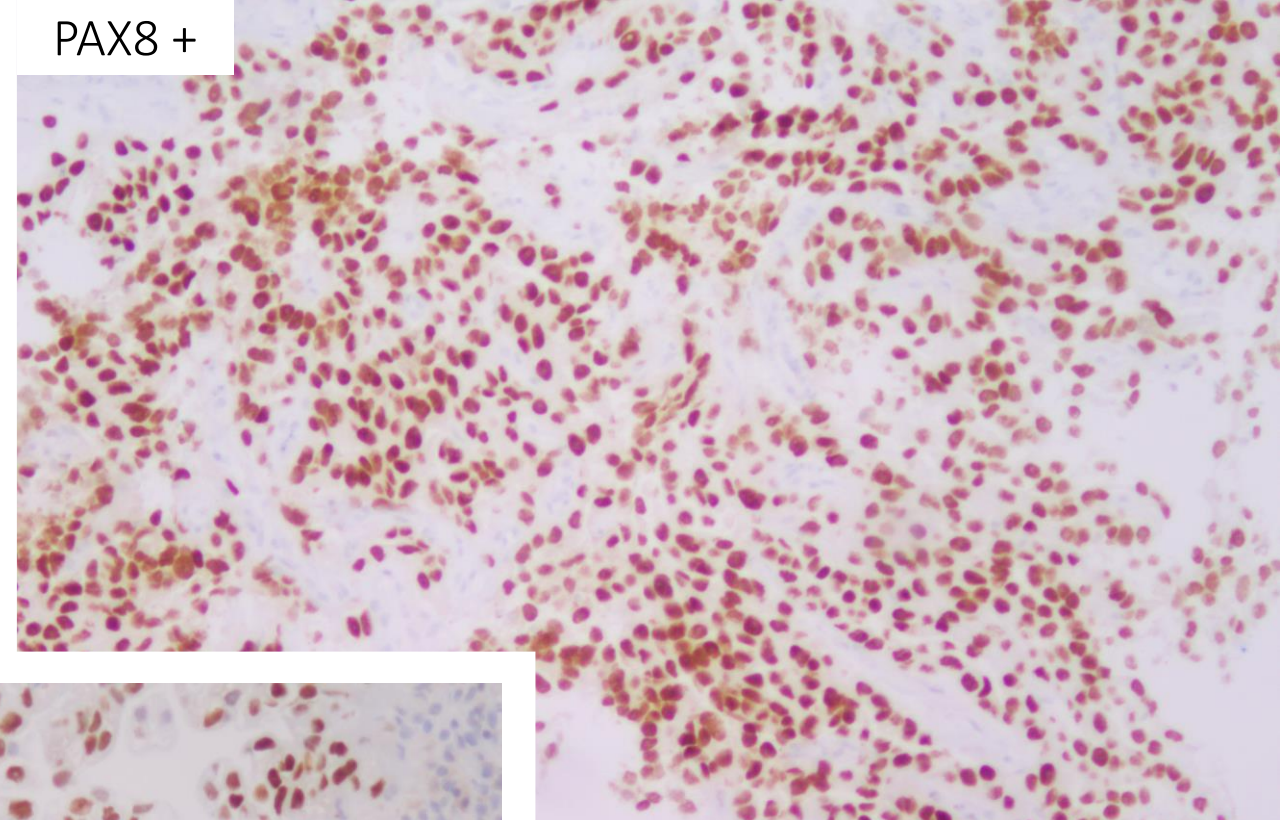
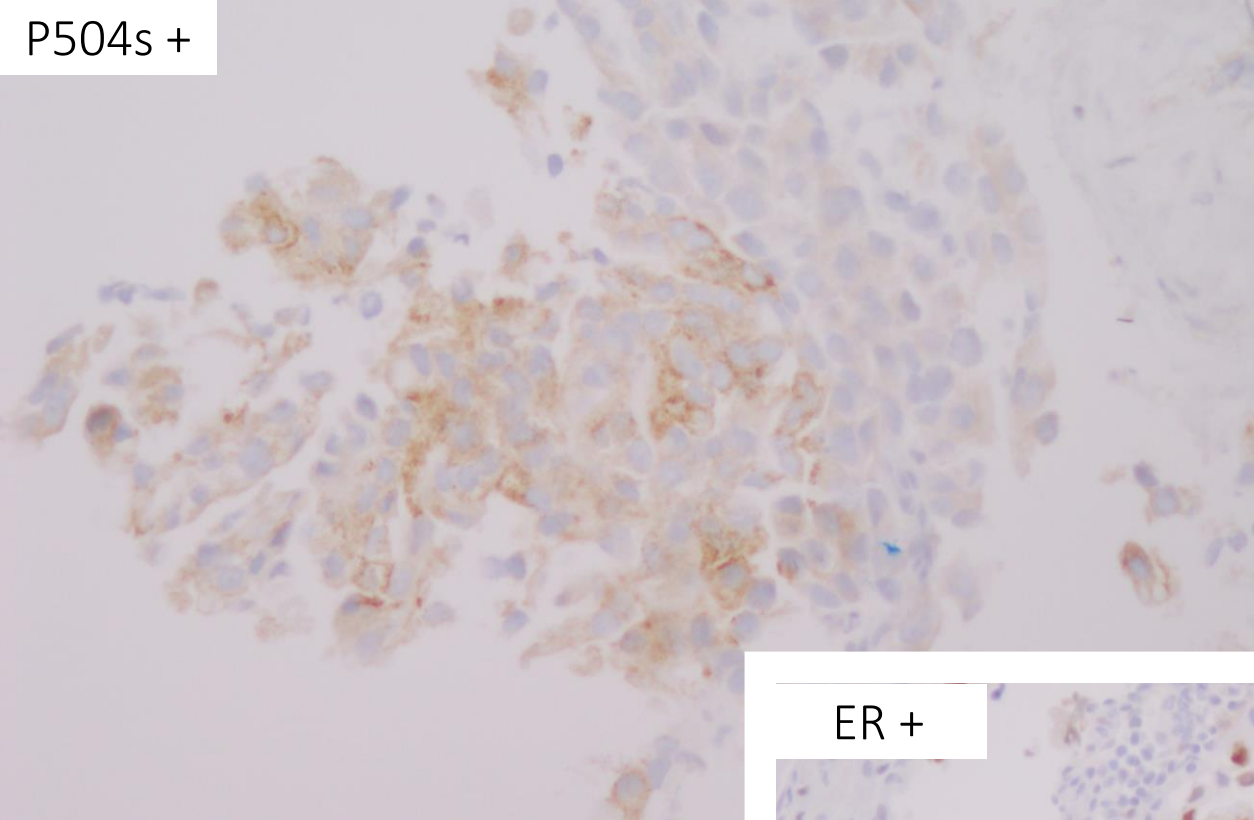
PAX-8



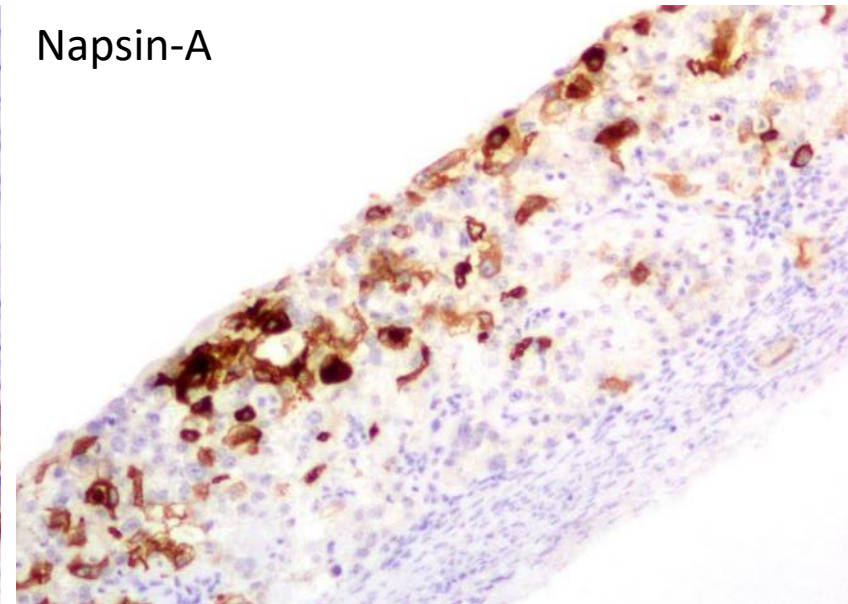
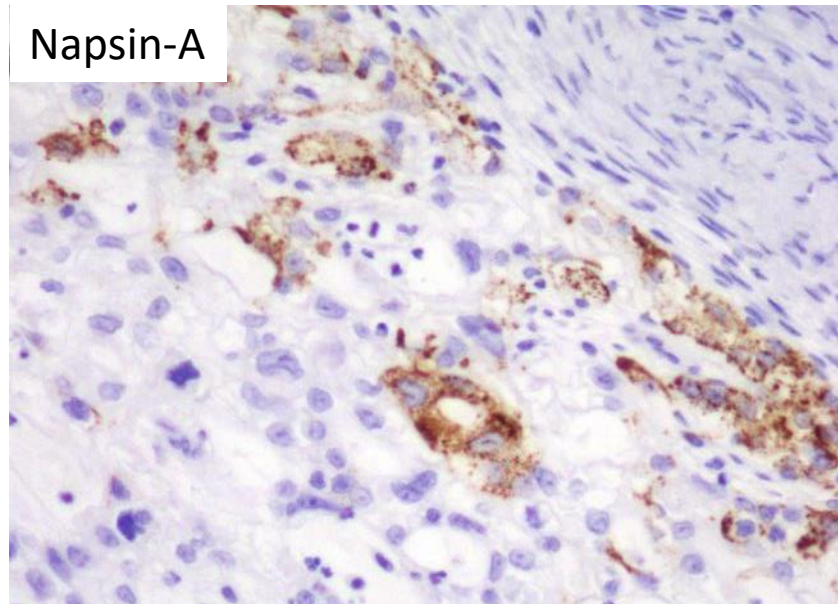
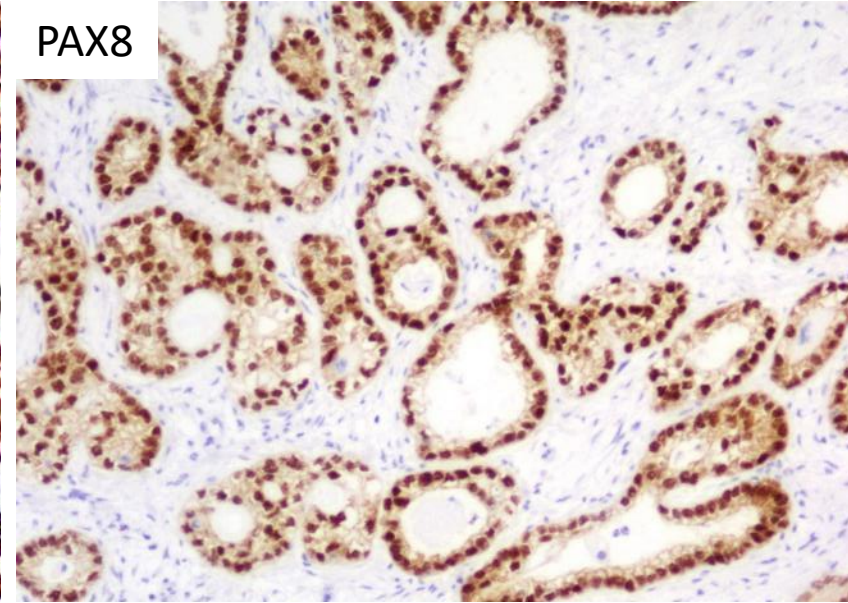
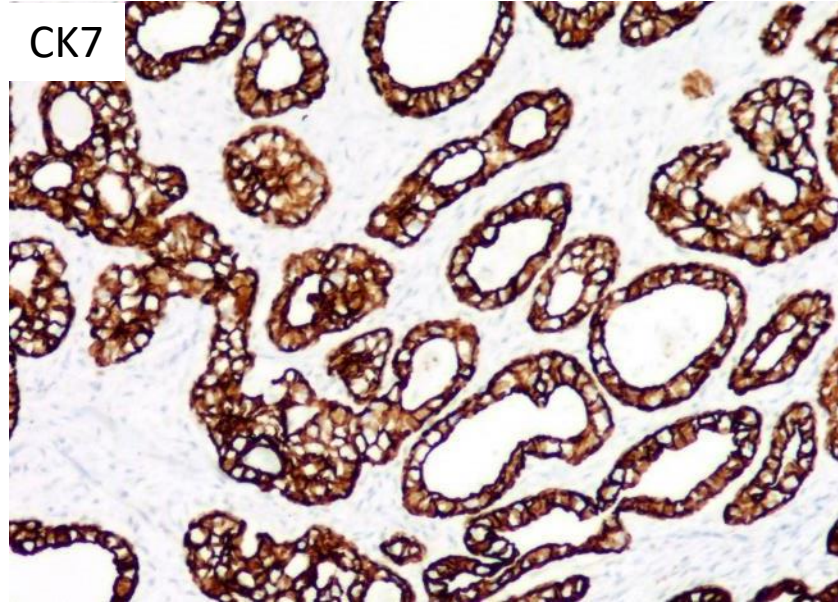
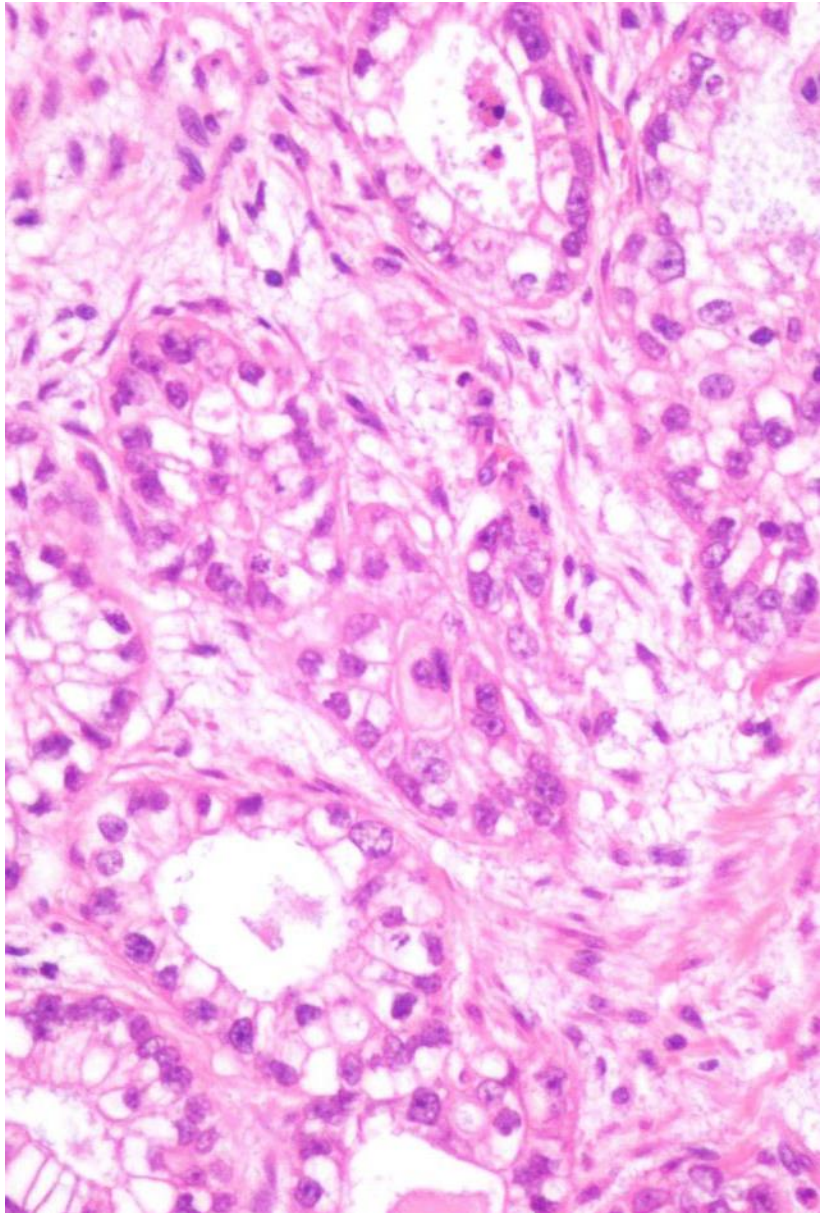
HNF1-B



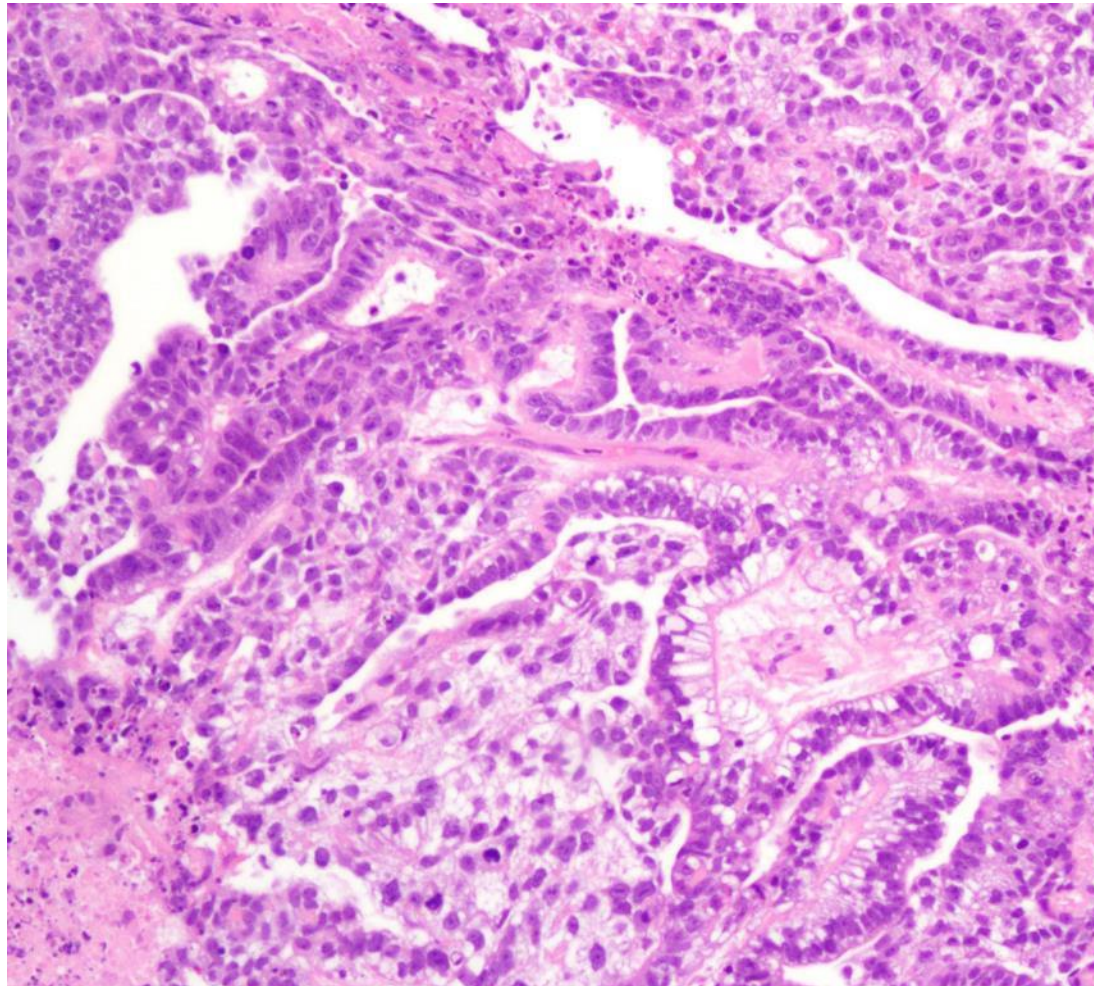
Clear Cell Ca, core bx



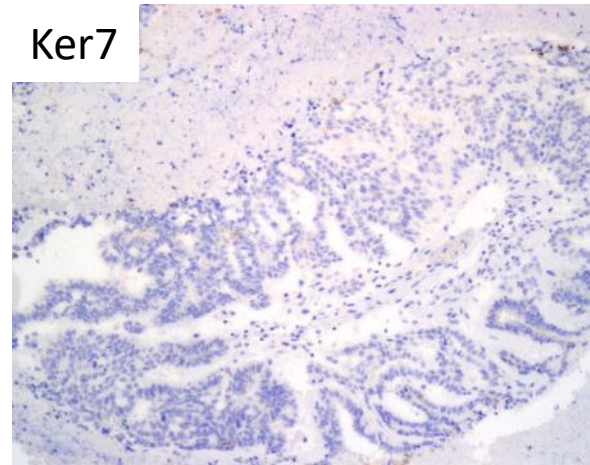
Clear Cell Carcinoma and Yolk Sac Tumor



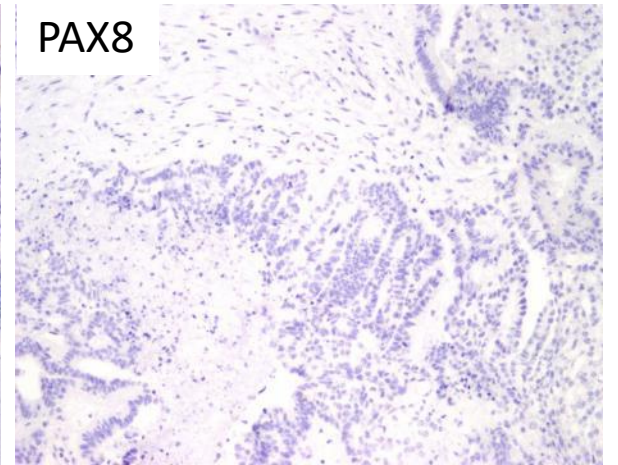
Clear Cell Carcinoma and Yolk Sac Tumor



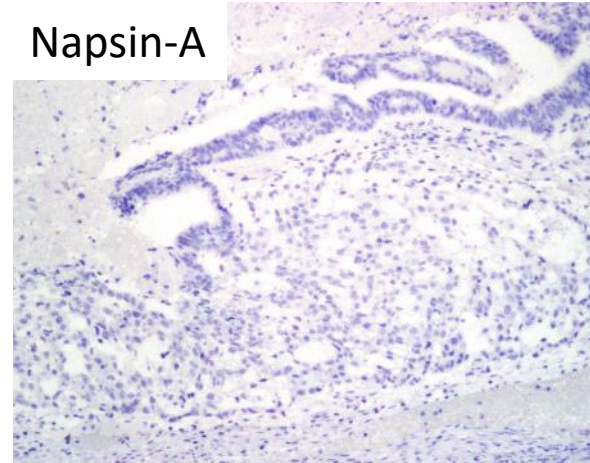
Ker7



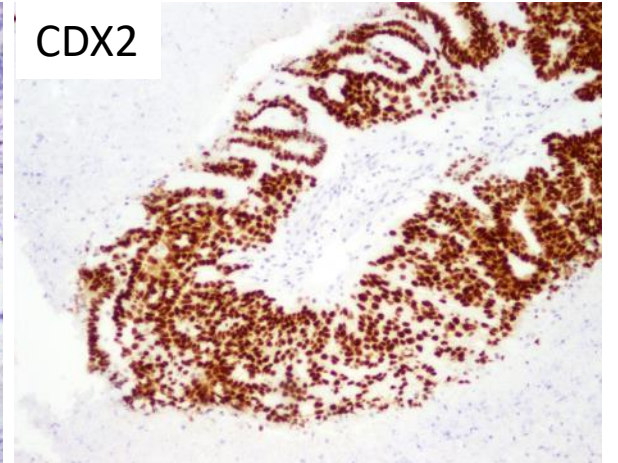
PAX8



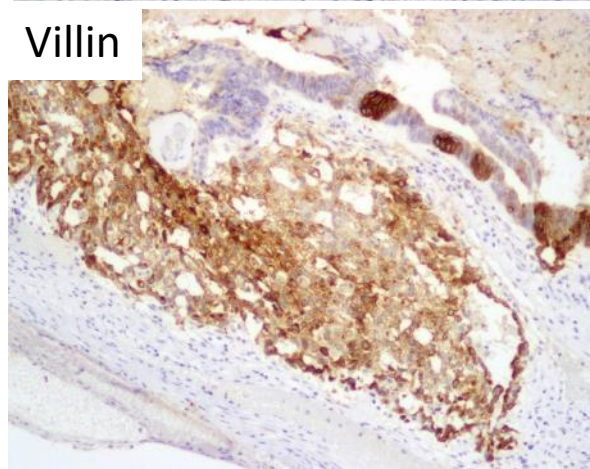
Napsin-A



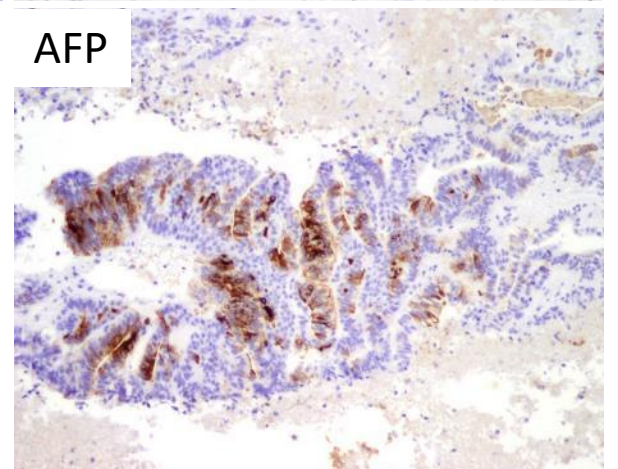
CDX2



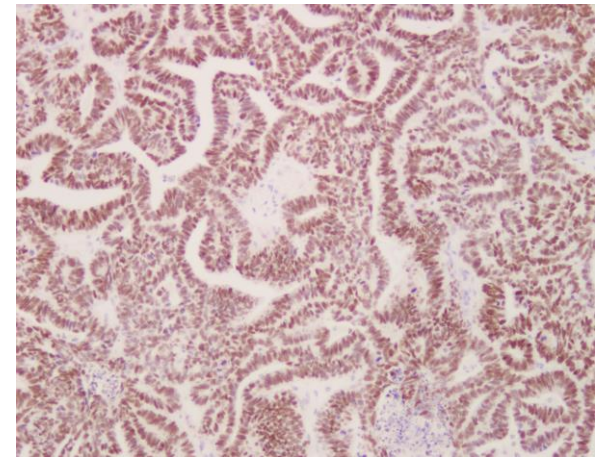
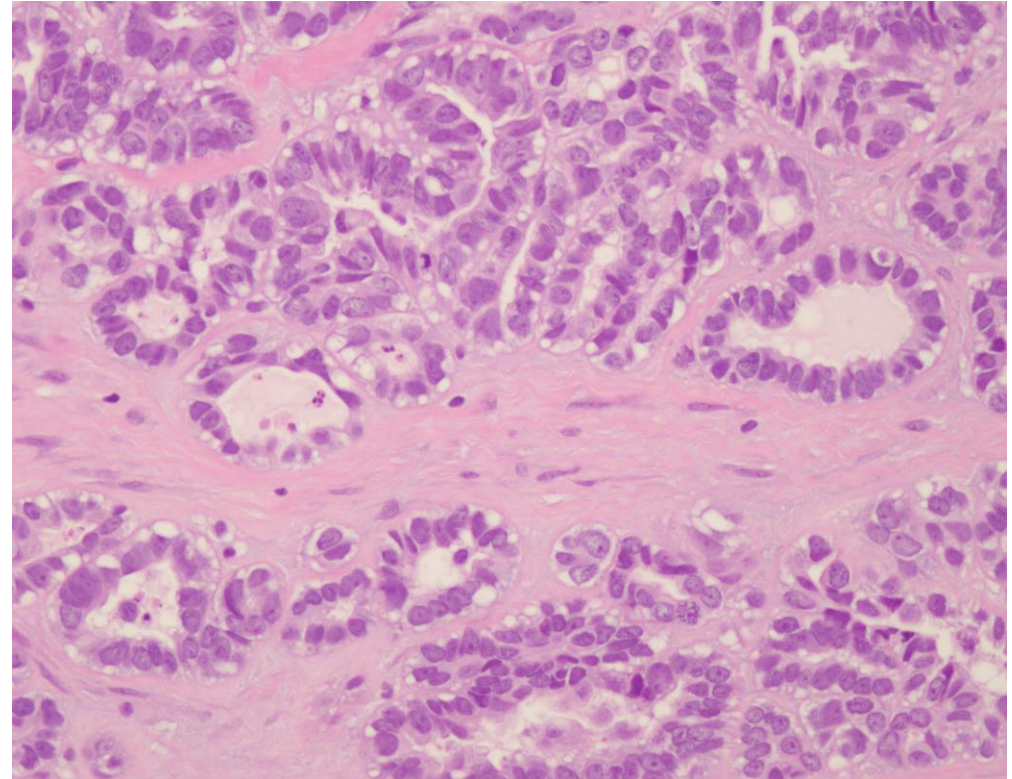
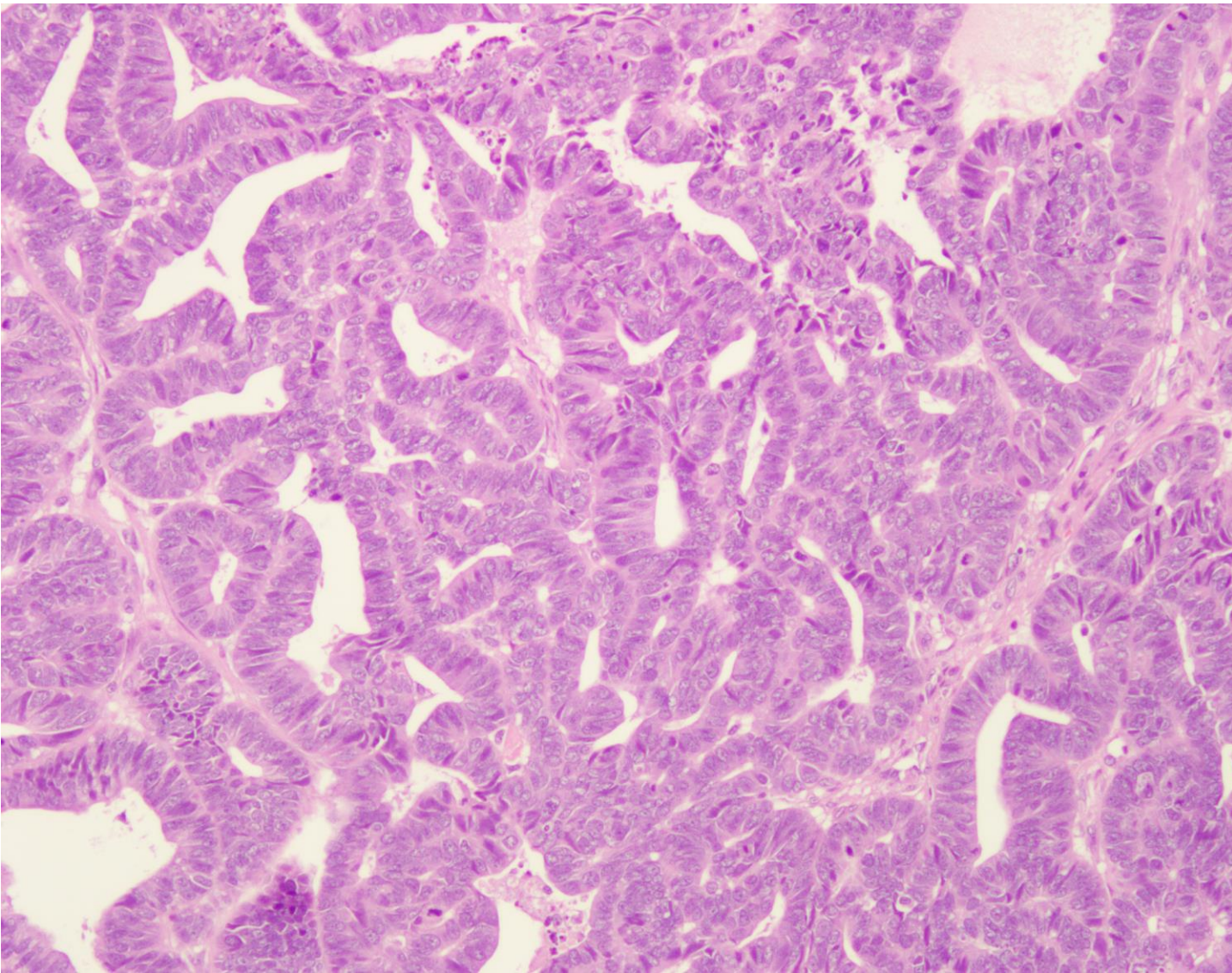
Villin



AFP

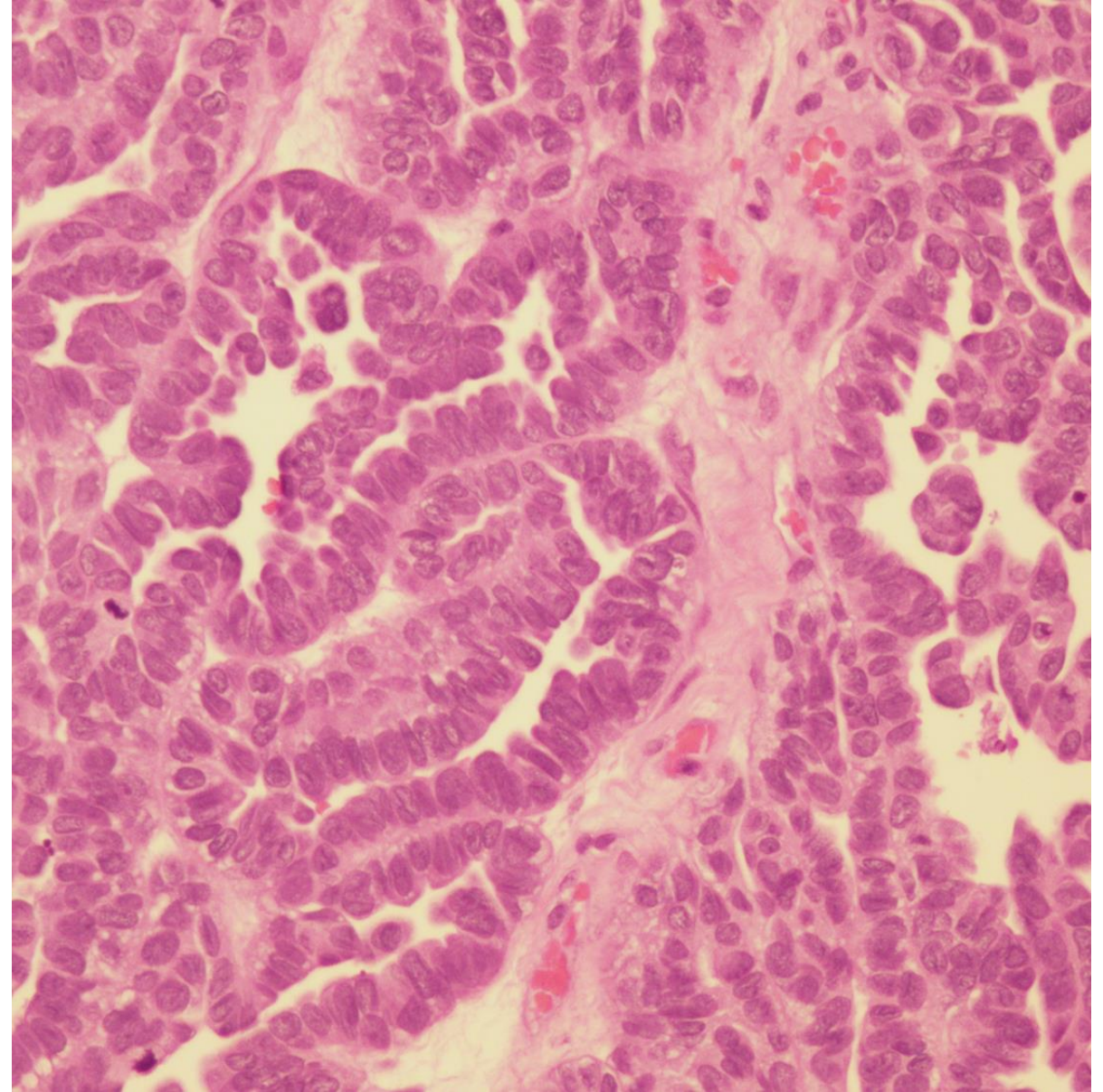
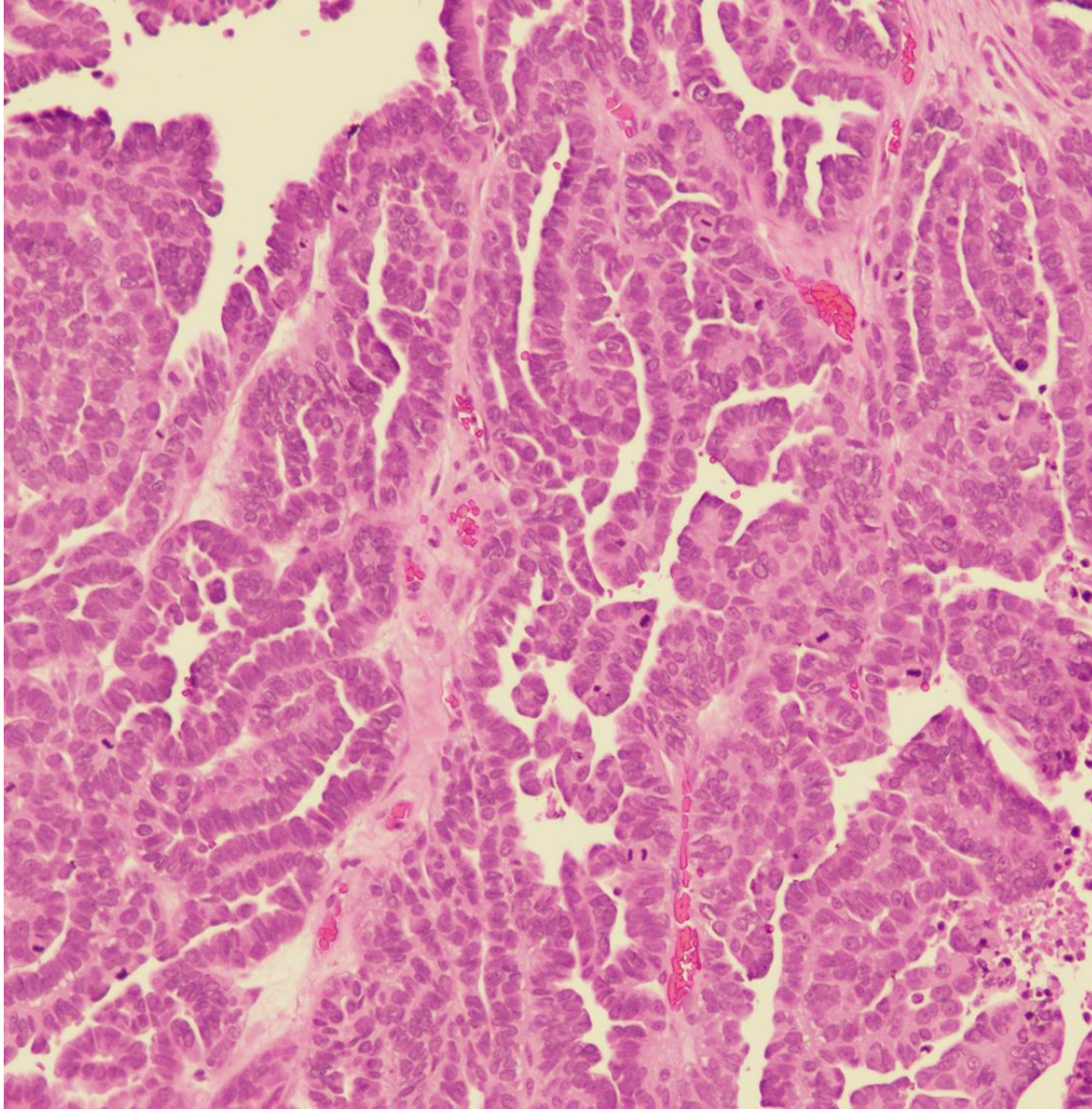


Mesonephric-like Ca

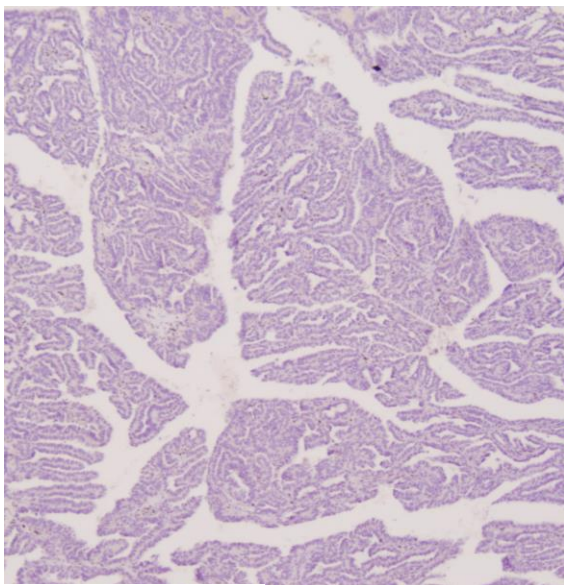
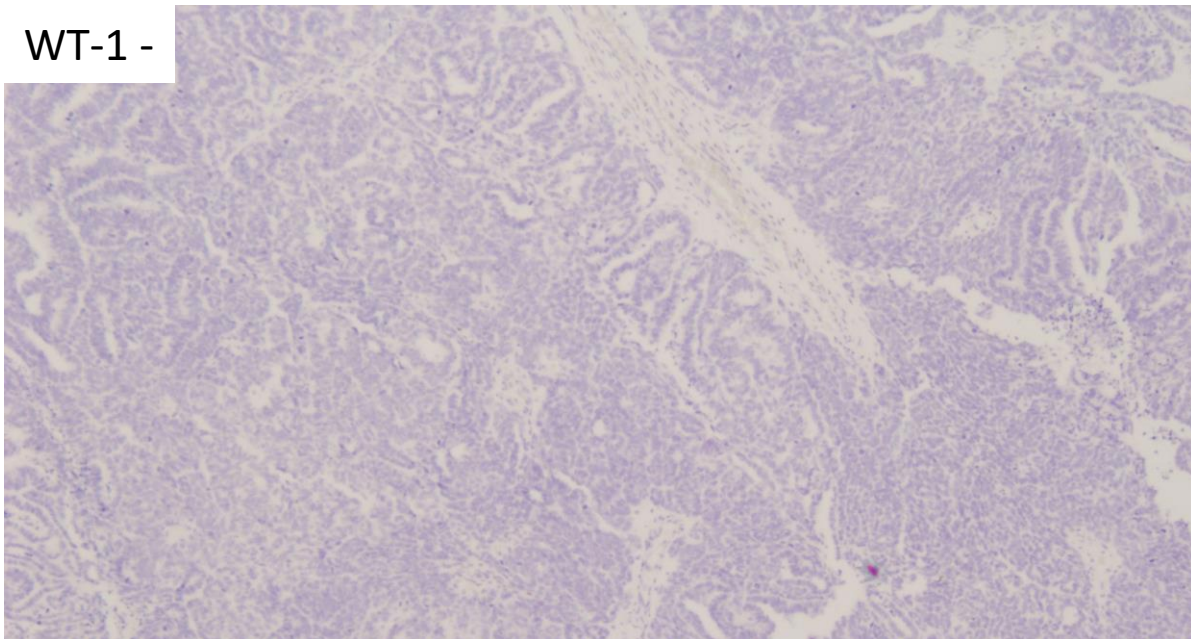


GATA-3 and/or TTF1 +

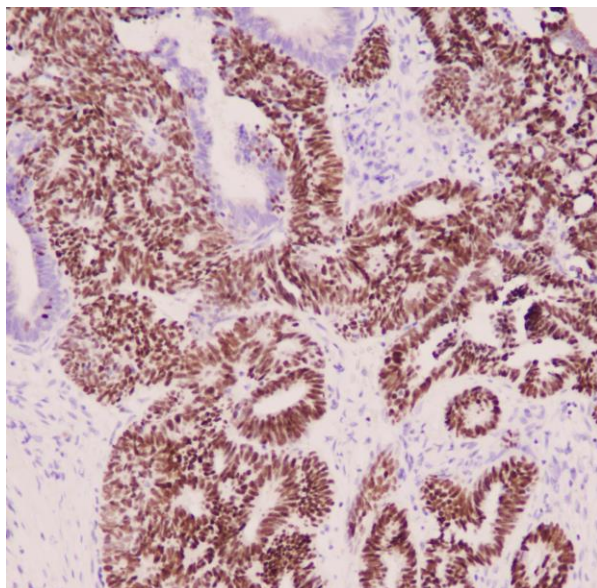
Mesonephric-like Ca



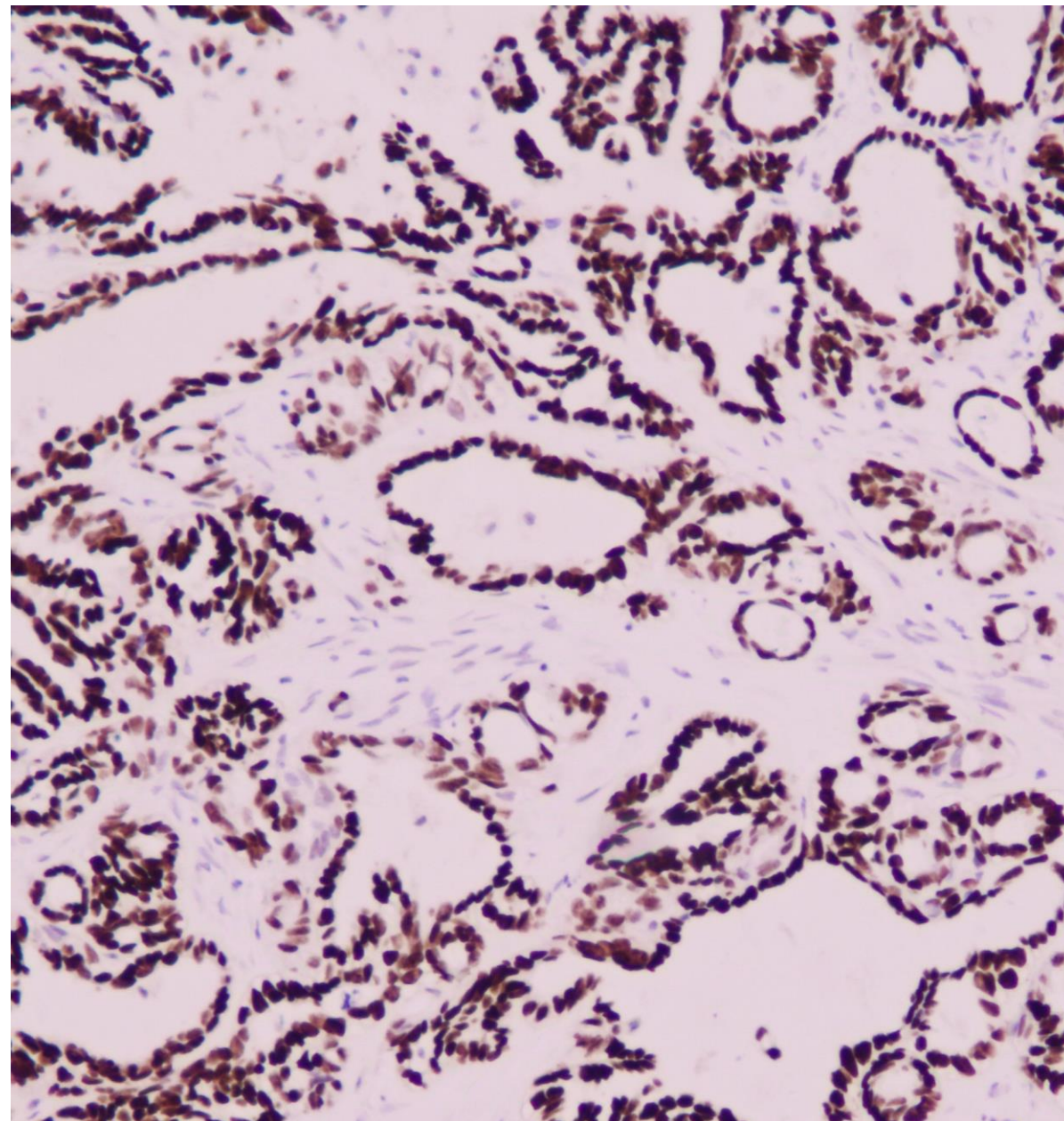
WT-1 -



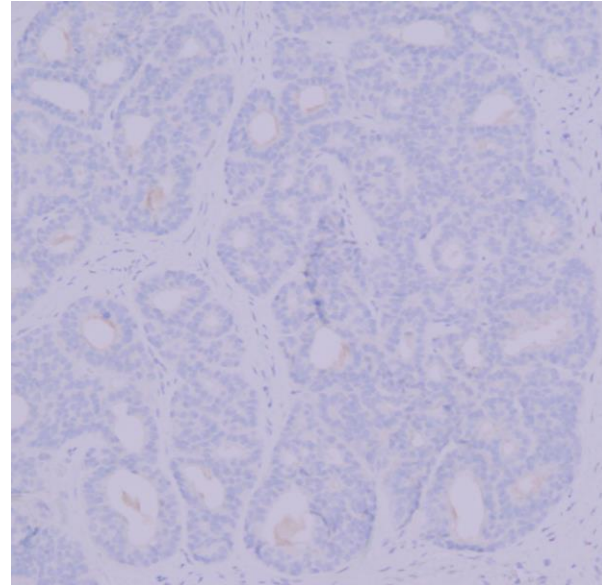
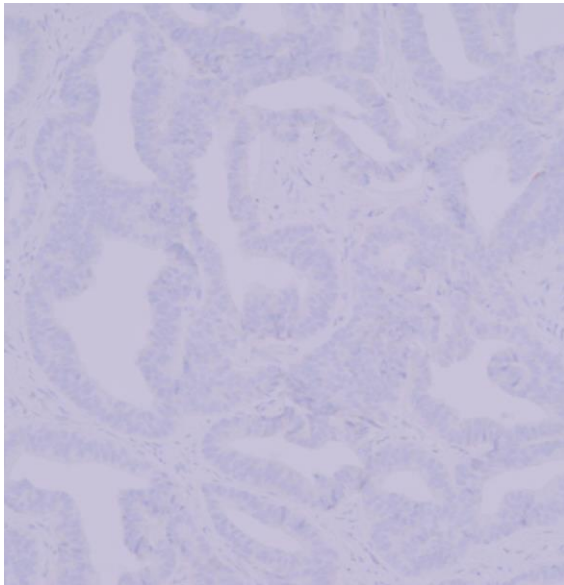
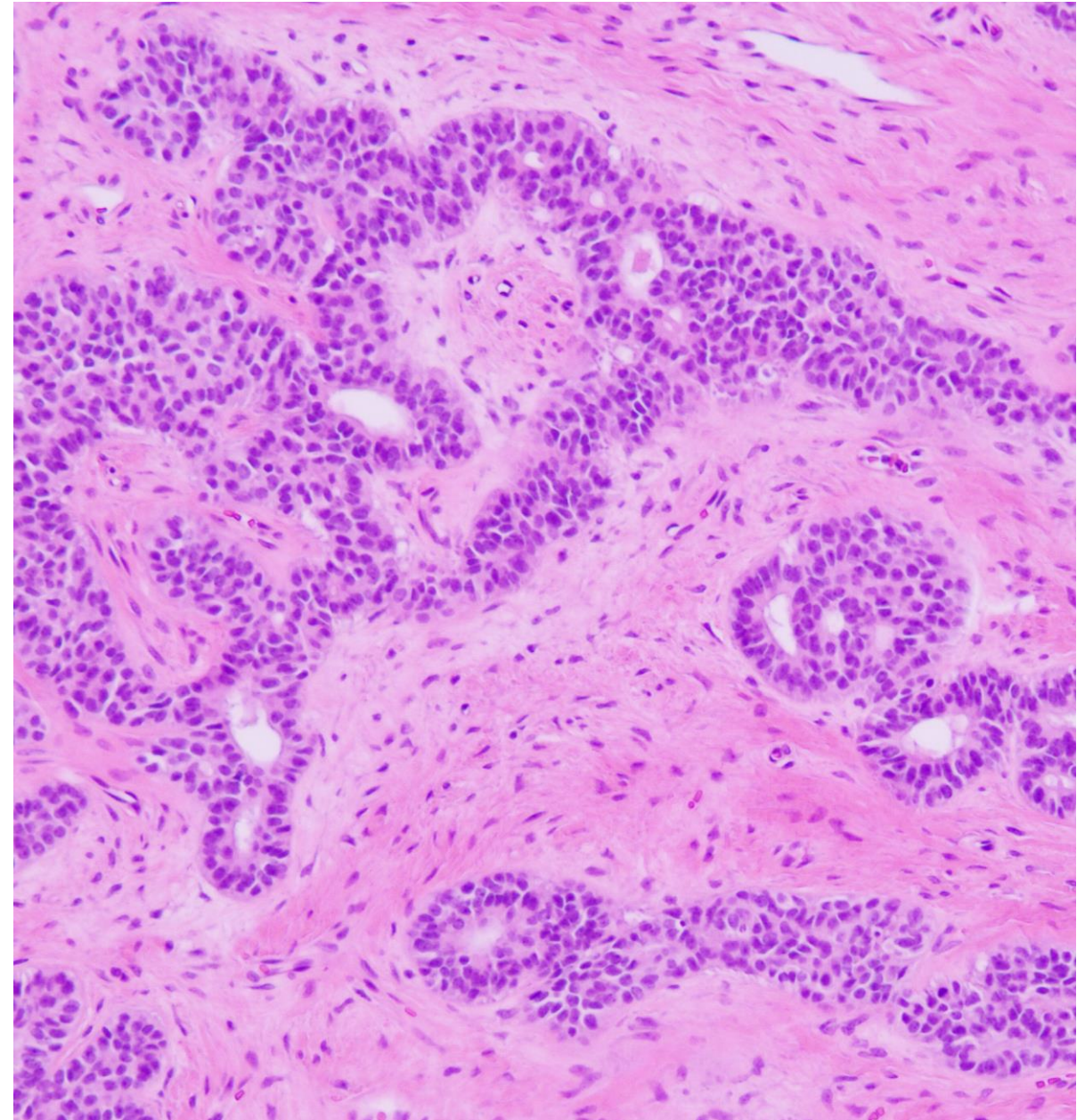
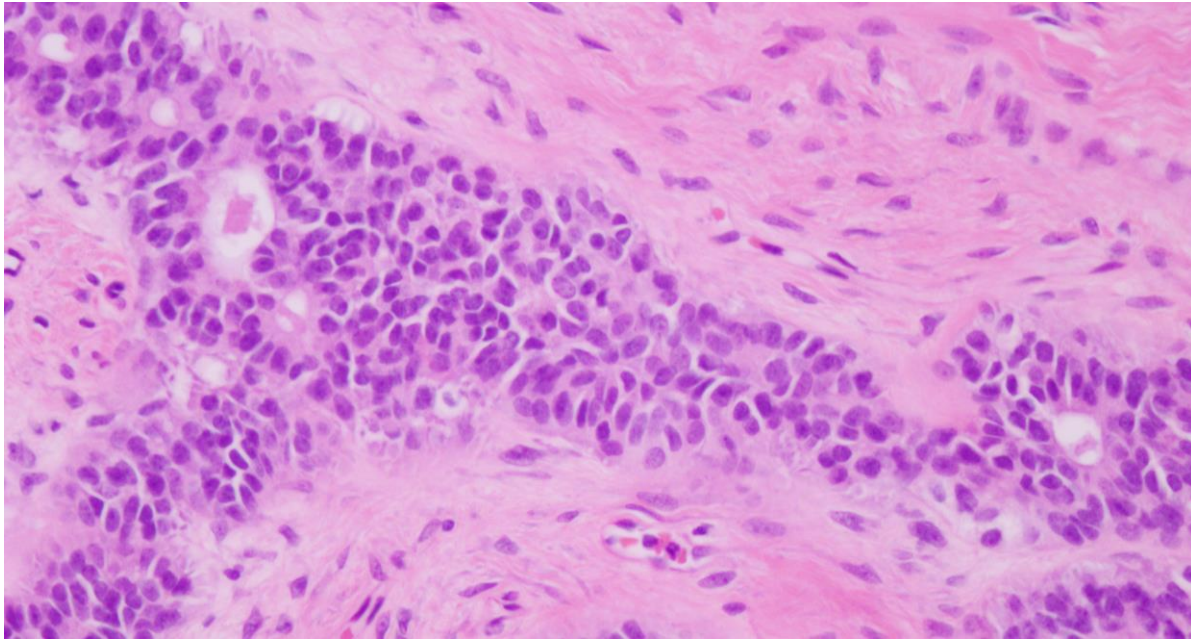
ER and PR -



GATA-3 +



TTF-1 +

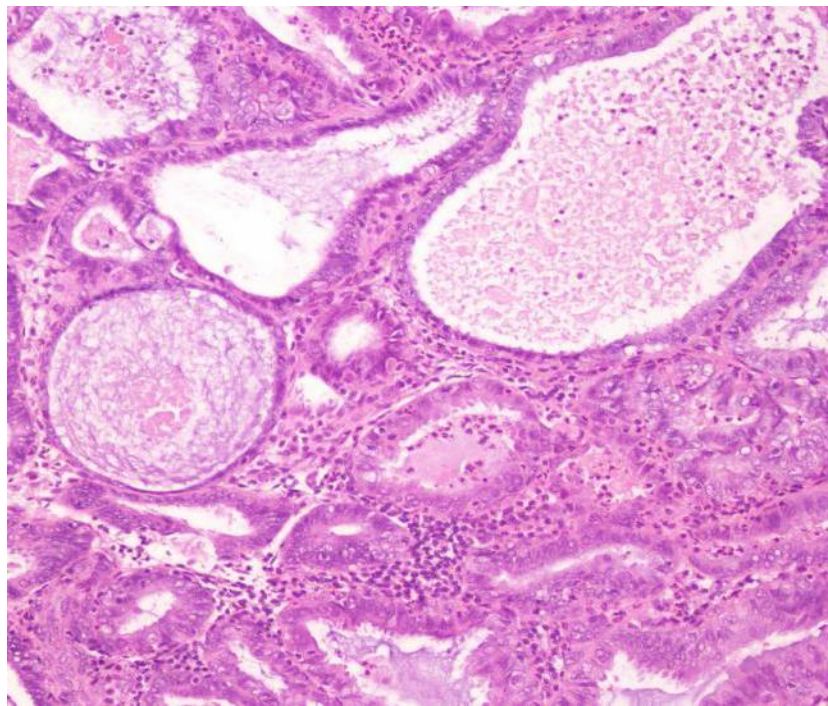
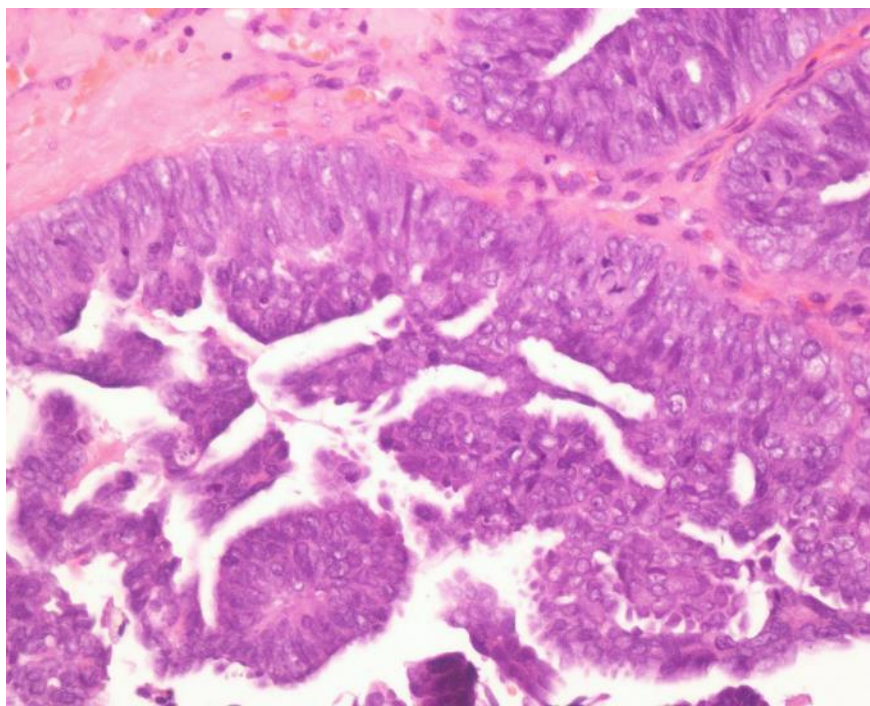
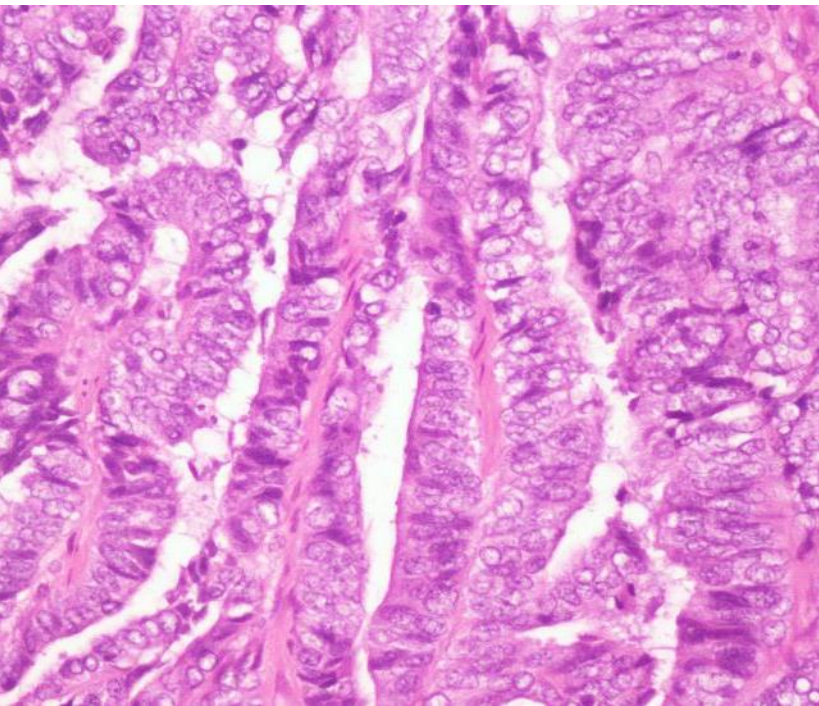
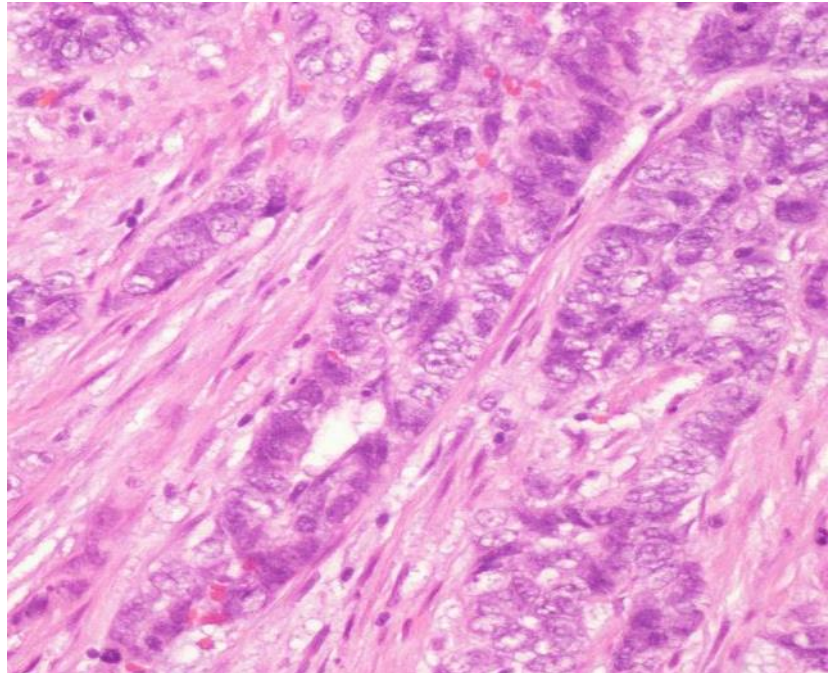
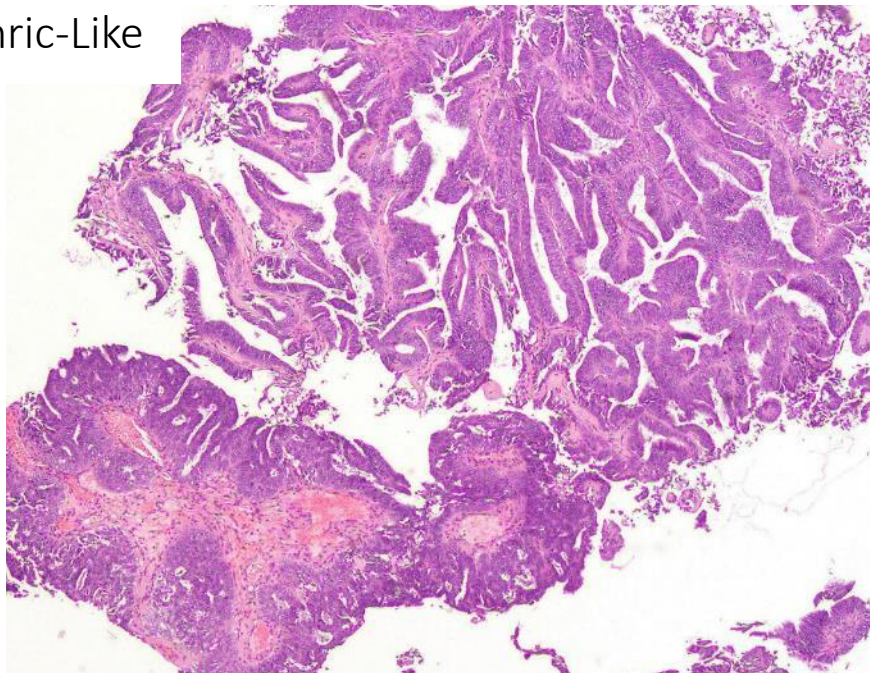
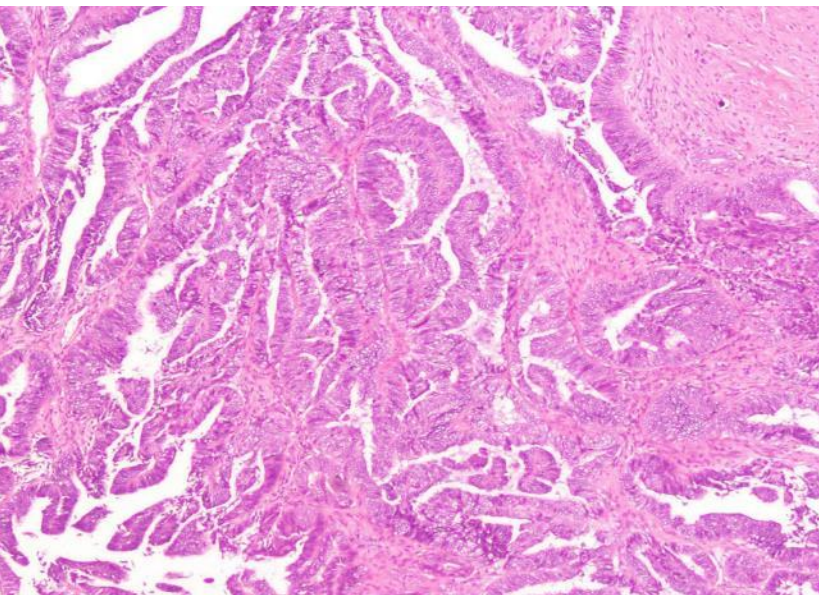


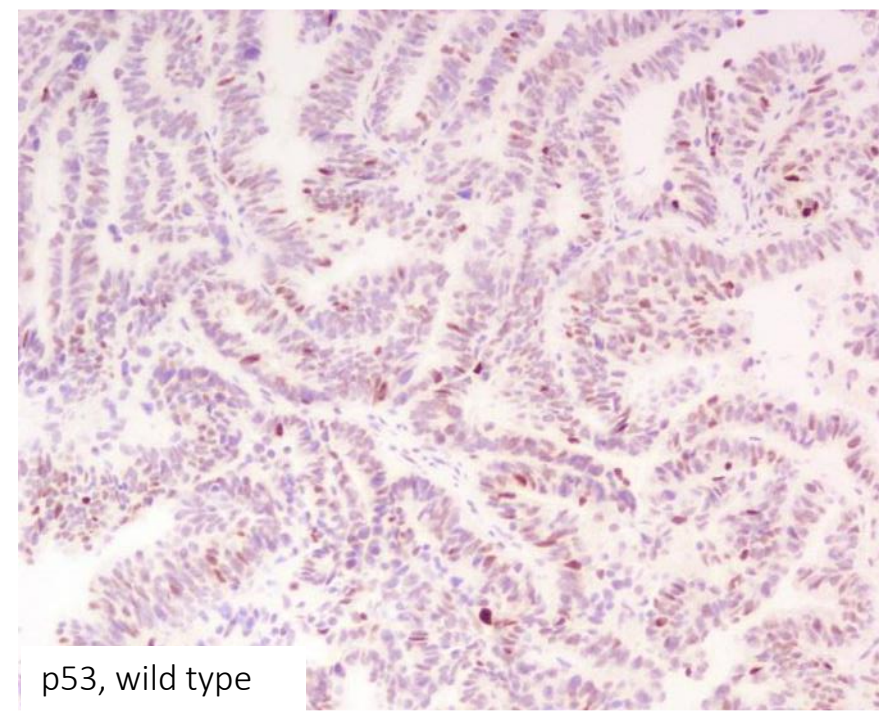
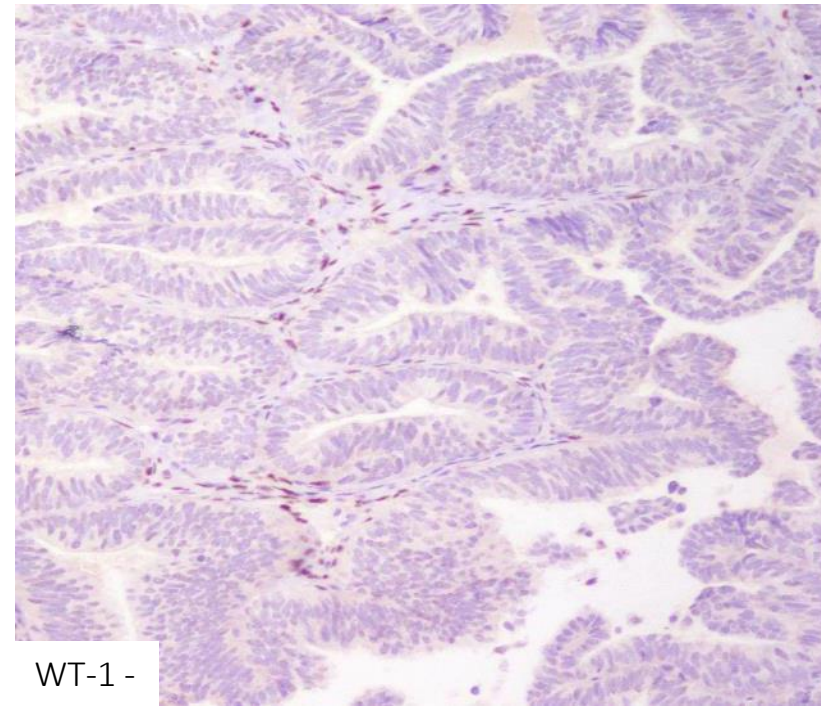
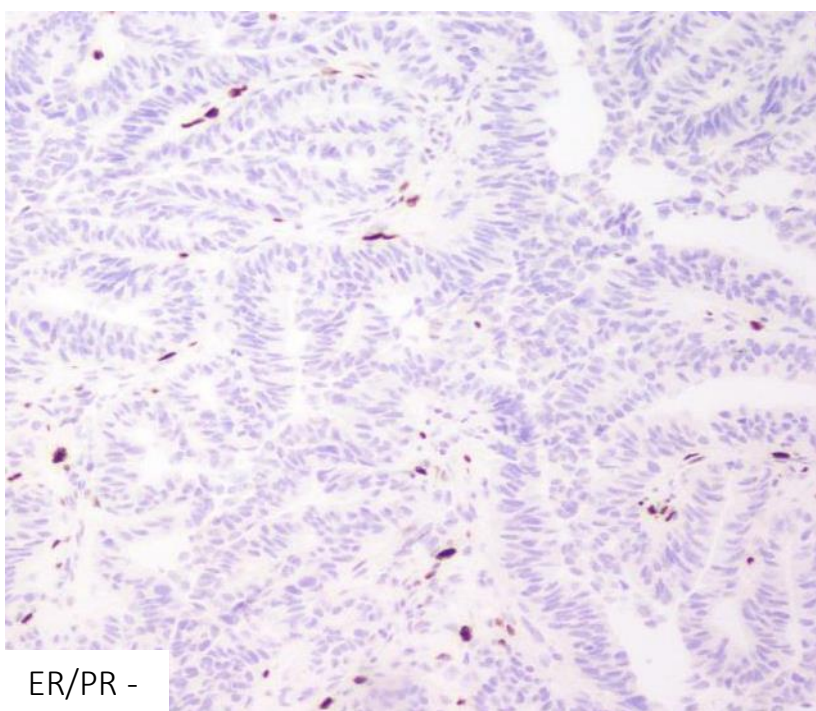
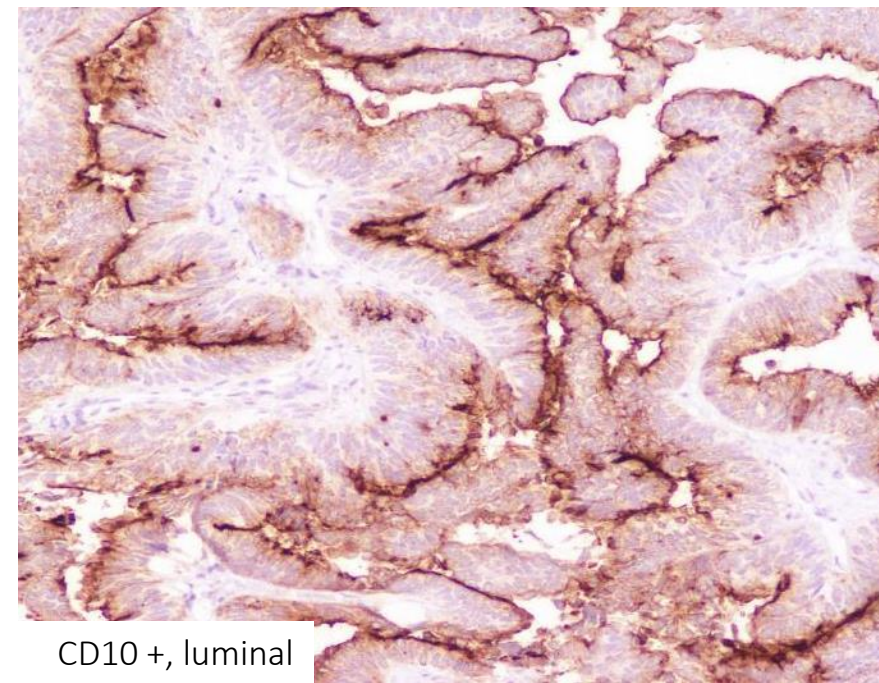
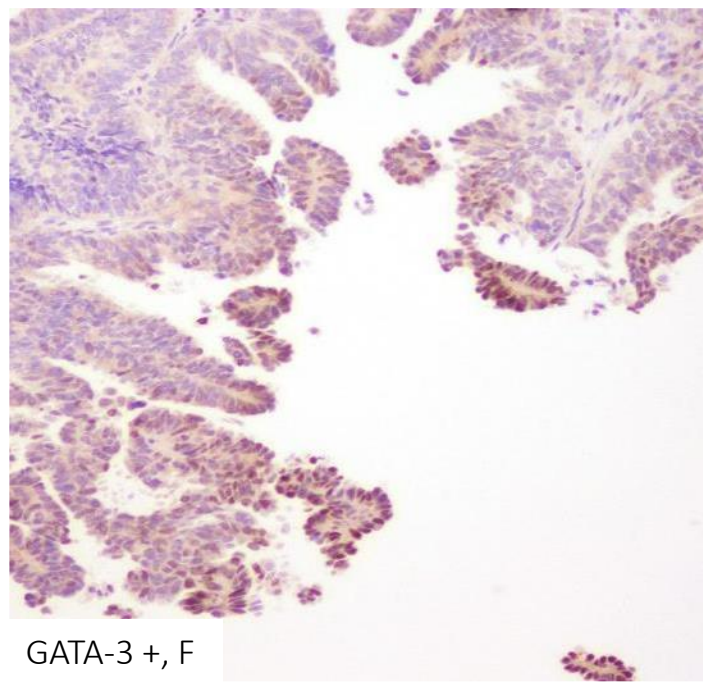
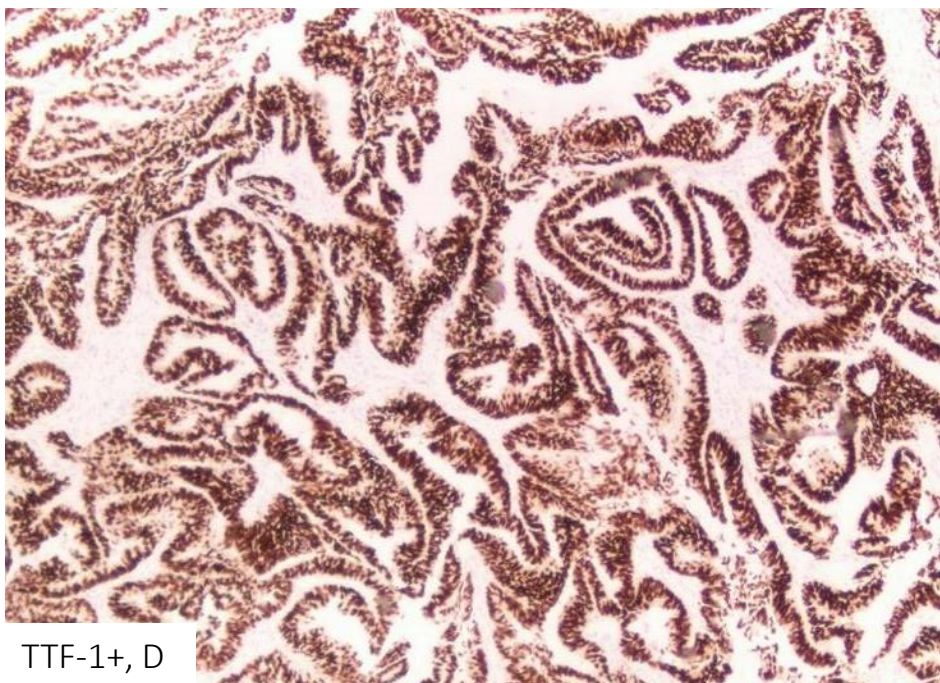
ER and PR -

SF-1, calretinin and inhibin -

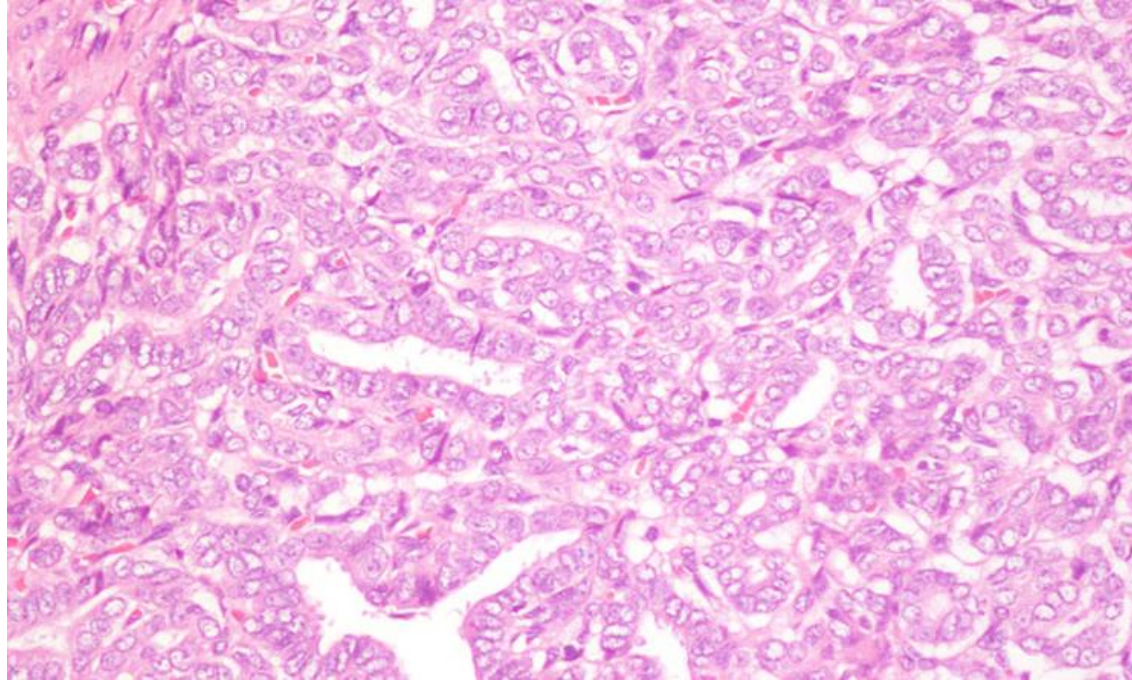
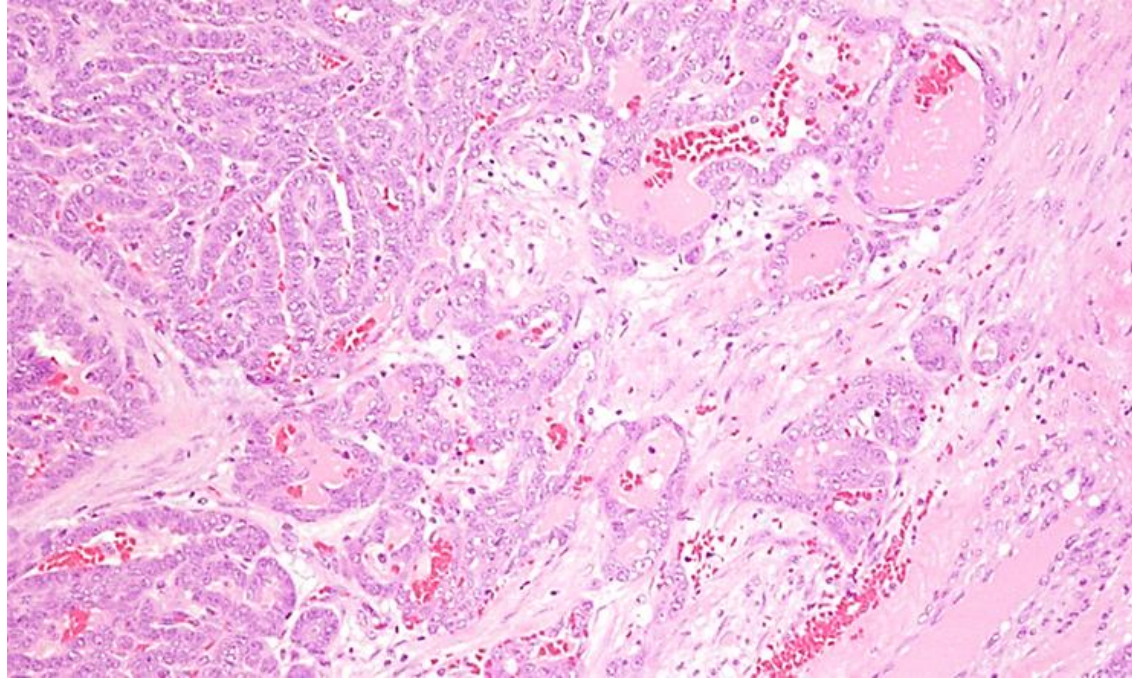
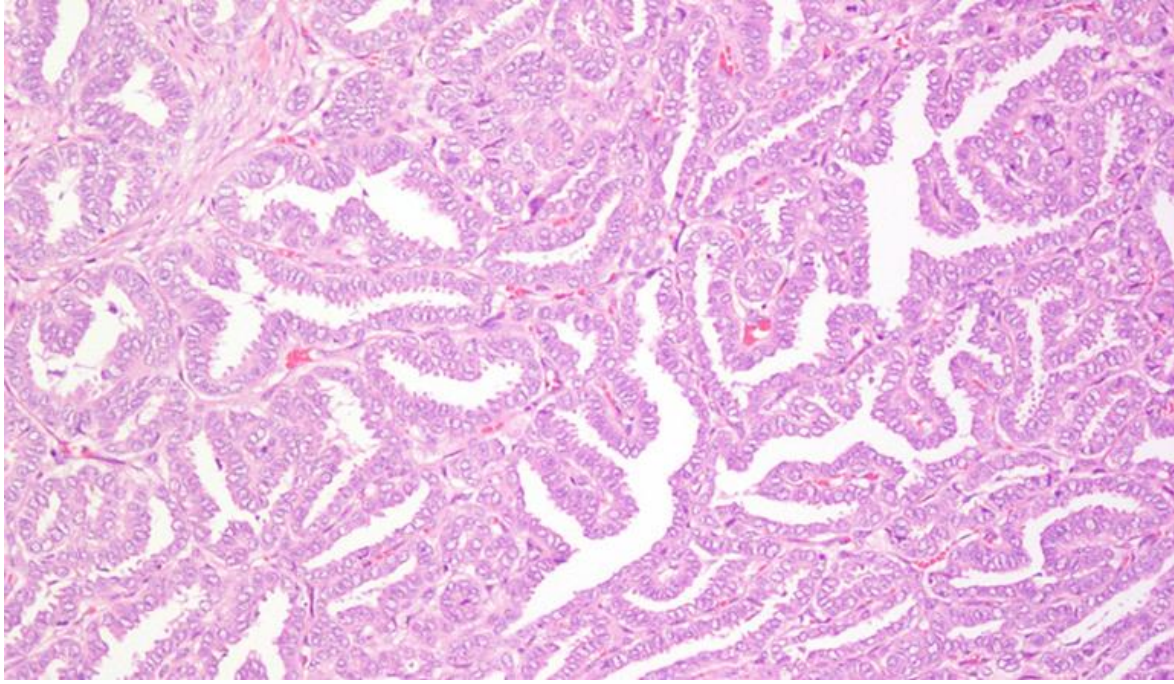
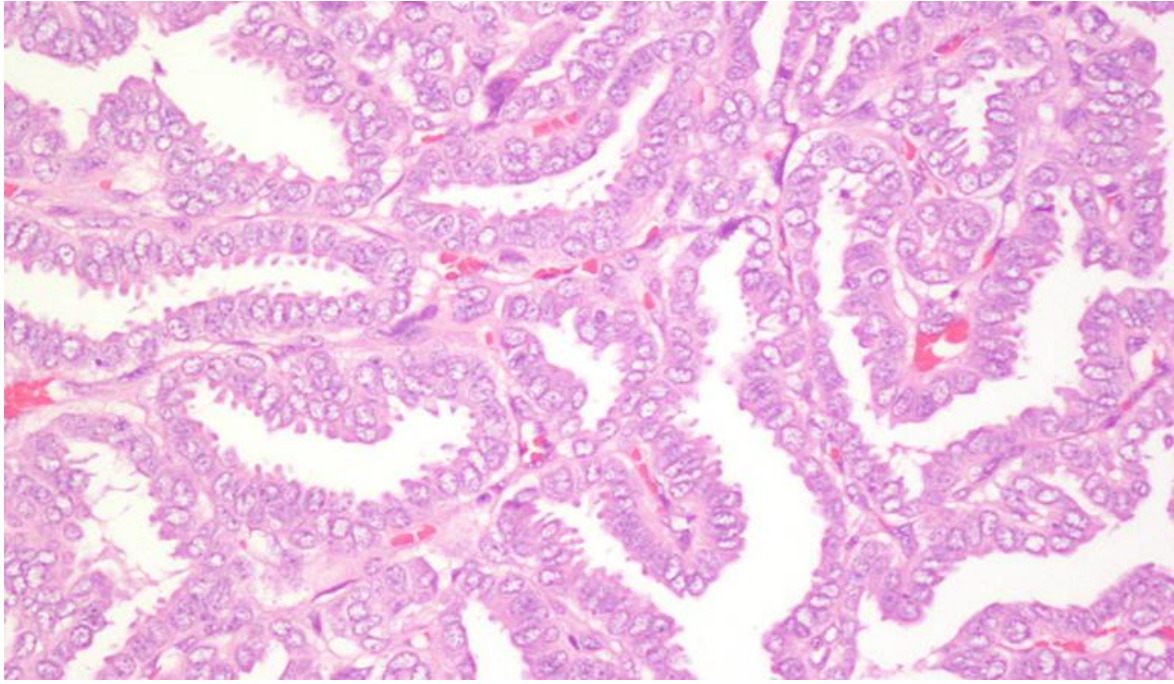
Mesonephric-like Ca

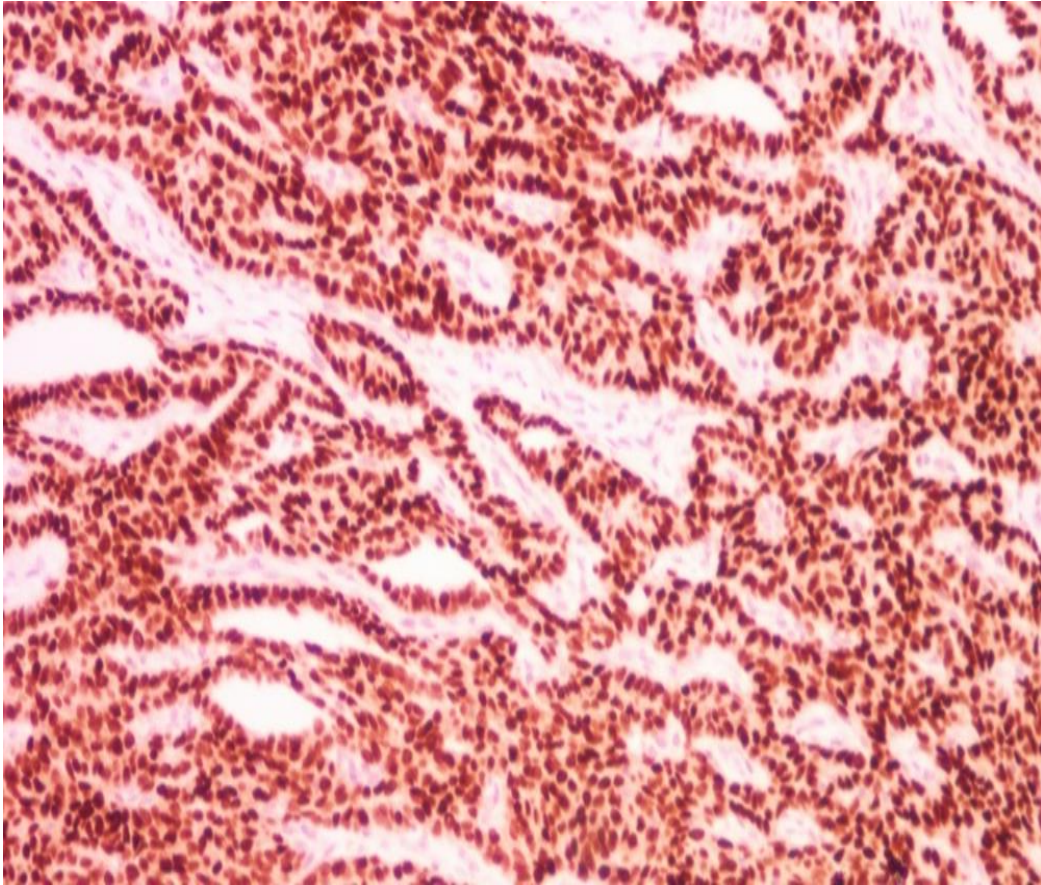
Endometrioid vs Serous... Think Mesonephric-Like



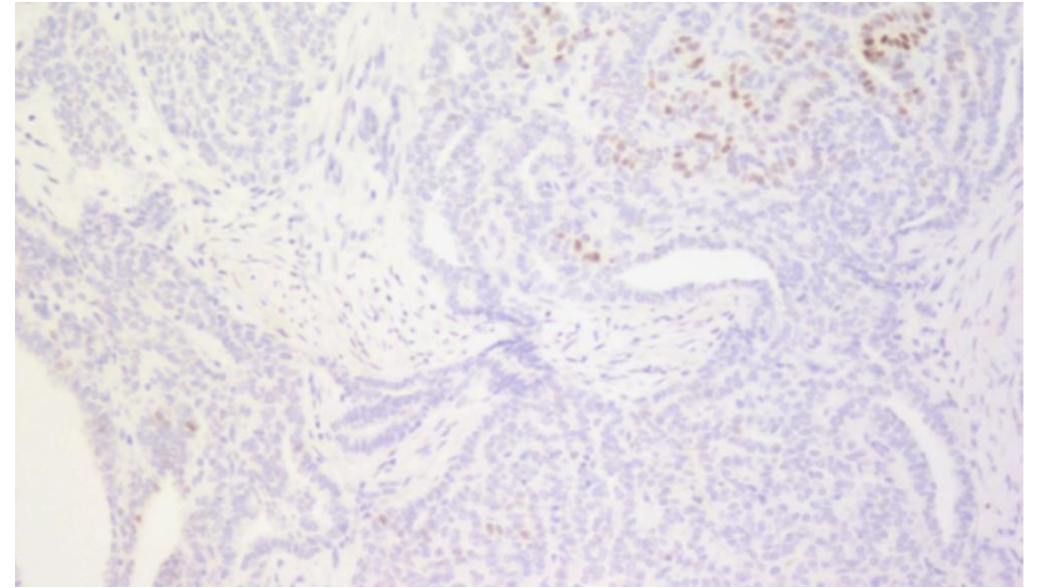


Mesonephric-like Ca after the Dx of LGSCa

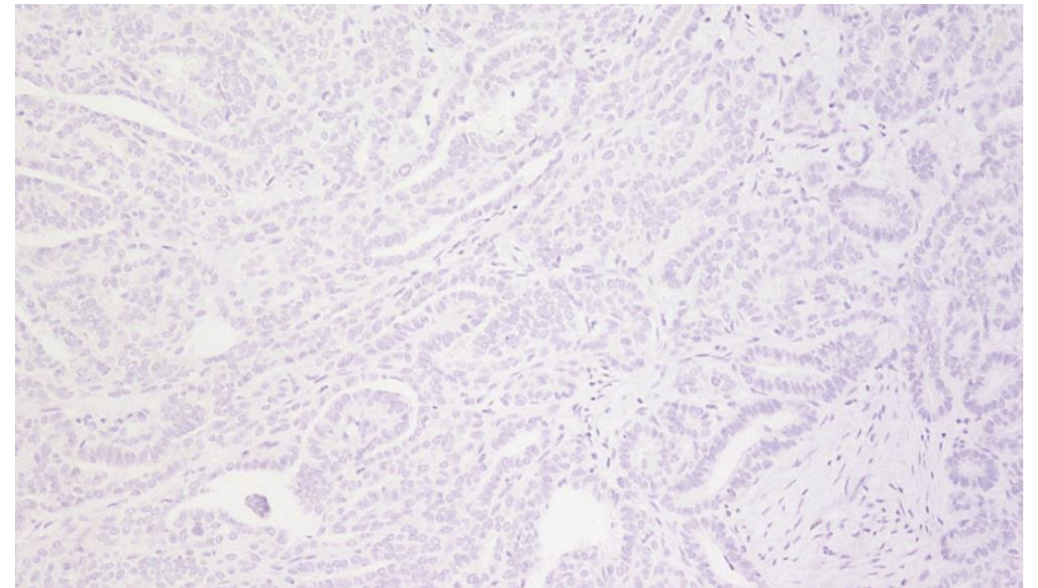




TTF-1+



ER/PR rare cells +



WT-1 -



Extrauterine Mesonephric-like Carcinoma *A Comprehensive Single Institution Study of 33 Cases*

Elizabeth D. Euscher, MD, Mario L. Marques-Piubelli, MD,* Preetha Ramalingam, MD,*
Ignacio Wistuba, MD,* Barrett C. Lawson, MD,* Michael Frumovitz, MD,†
and Anais Malpica, MD**

(Am J Surg Pathol 2023;00:000–000)

Pts' age: 37-74 yrs (median, 59 yrs)

Advanced stage disease (FIGO III/IV), 13

Sarcomatous differentiation, 2

Associations:

 endometriosis (63%)

 borderline tumor (21%)

 part of a mixed Ca (42%)

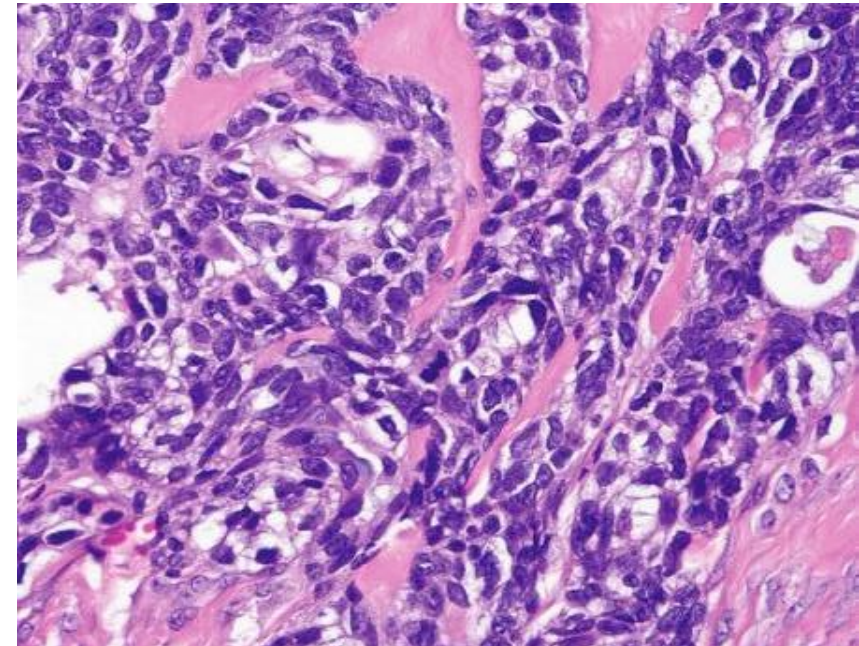
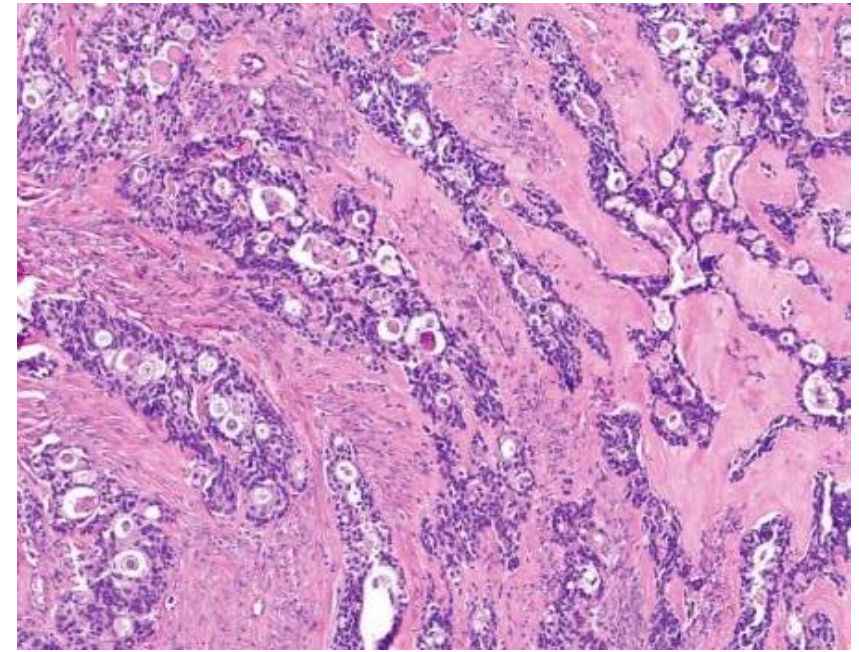
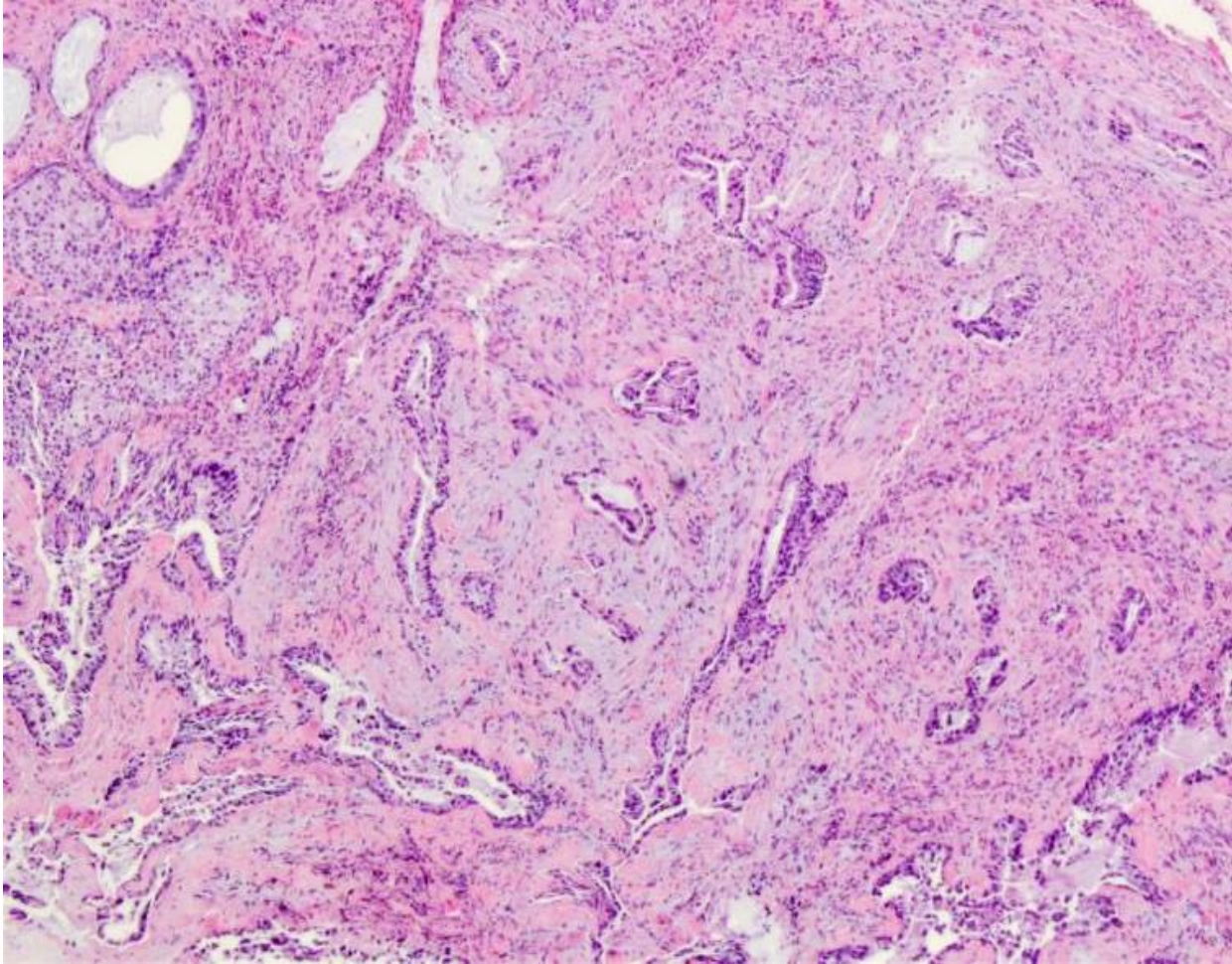
Misclassified, 42%

Molecular Findings: *Kras*>>>>*Tp53*, *SPOP*, *PIK3CA*

Metastasis: liver, lung, peritoneum

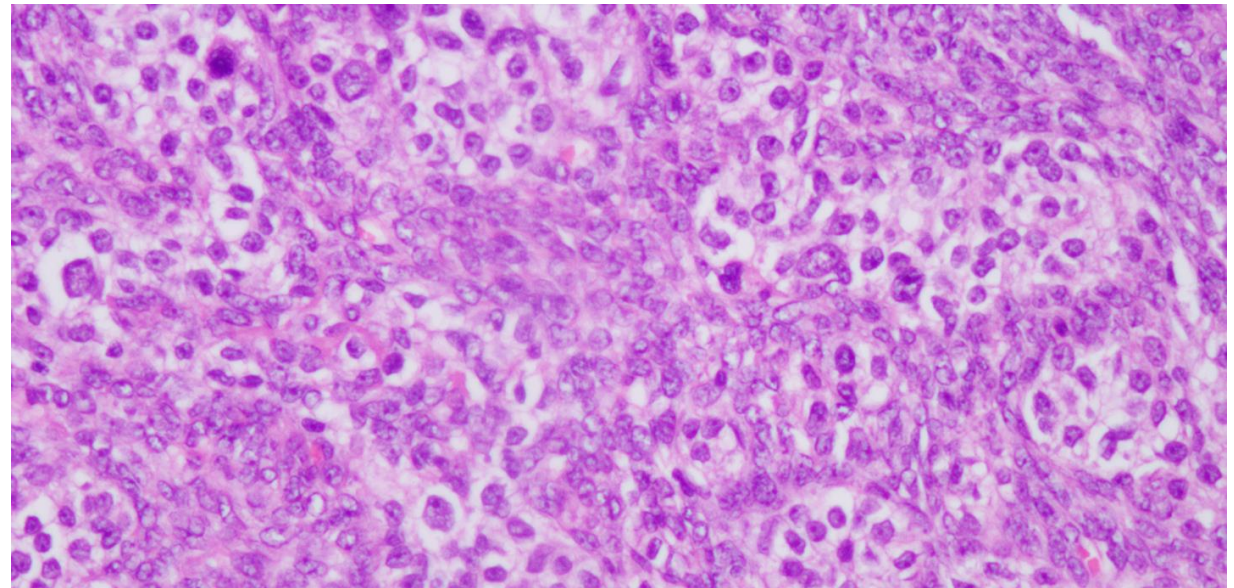
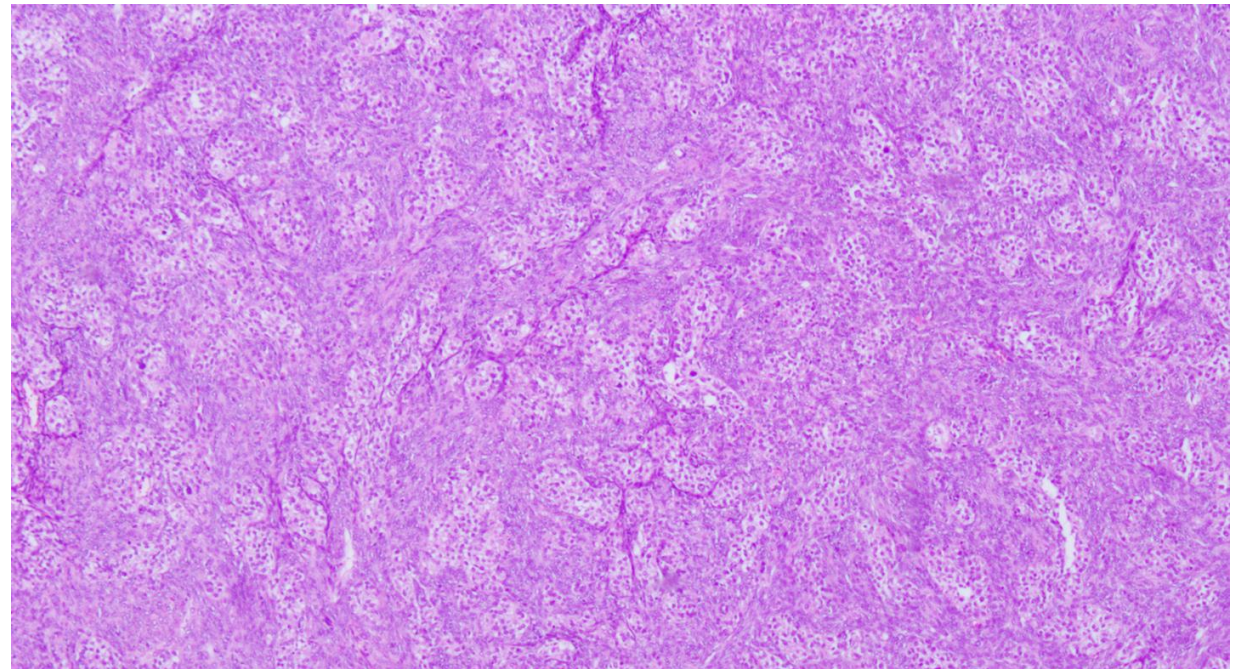
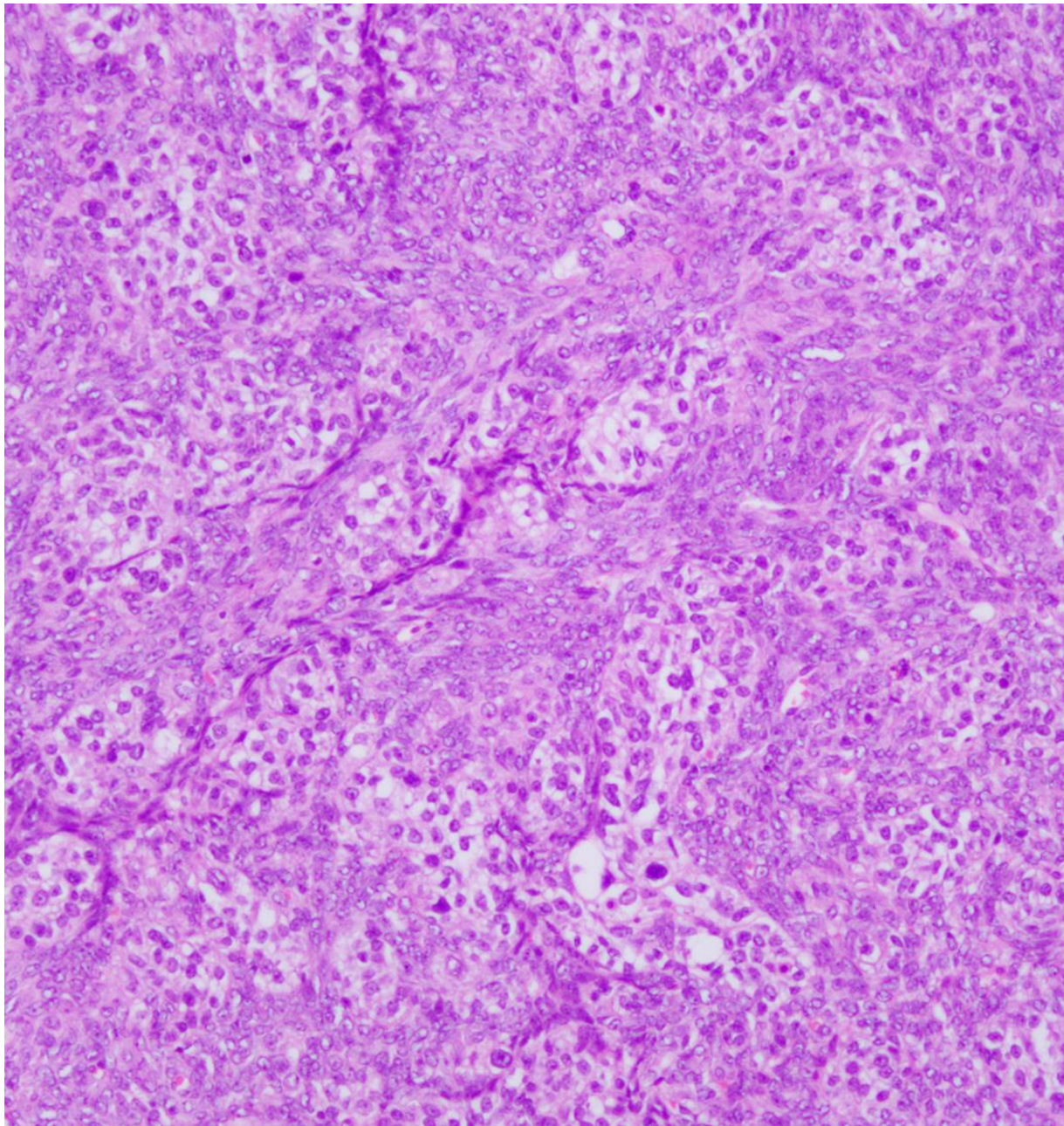
More aggressive than low grade endometrioid Ca

Malignant Brenner Tumor

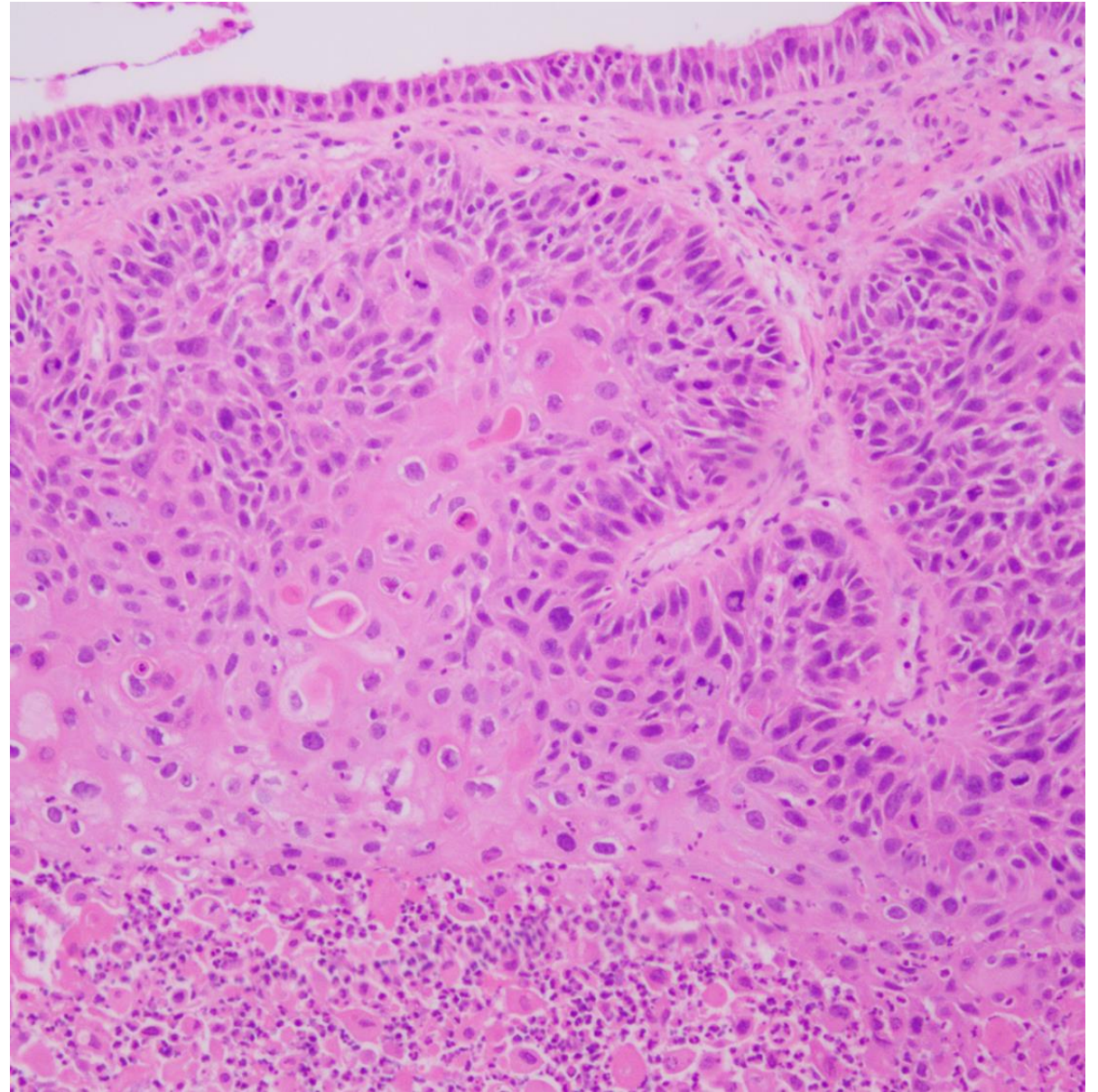
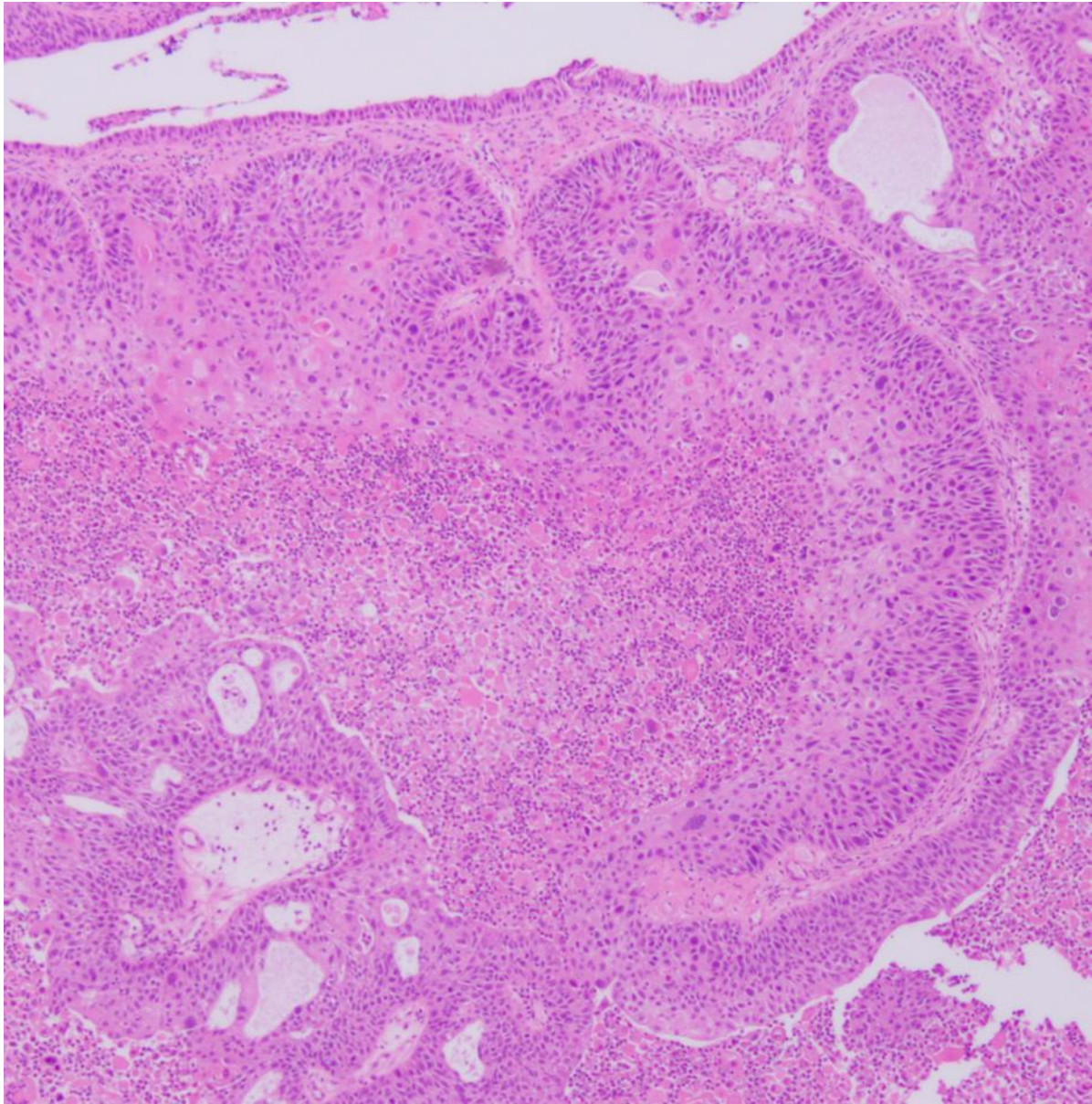


Molecular Findings

- *PIK3CA* mutations
- *MDM2* amplification

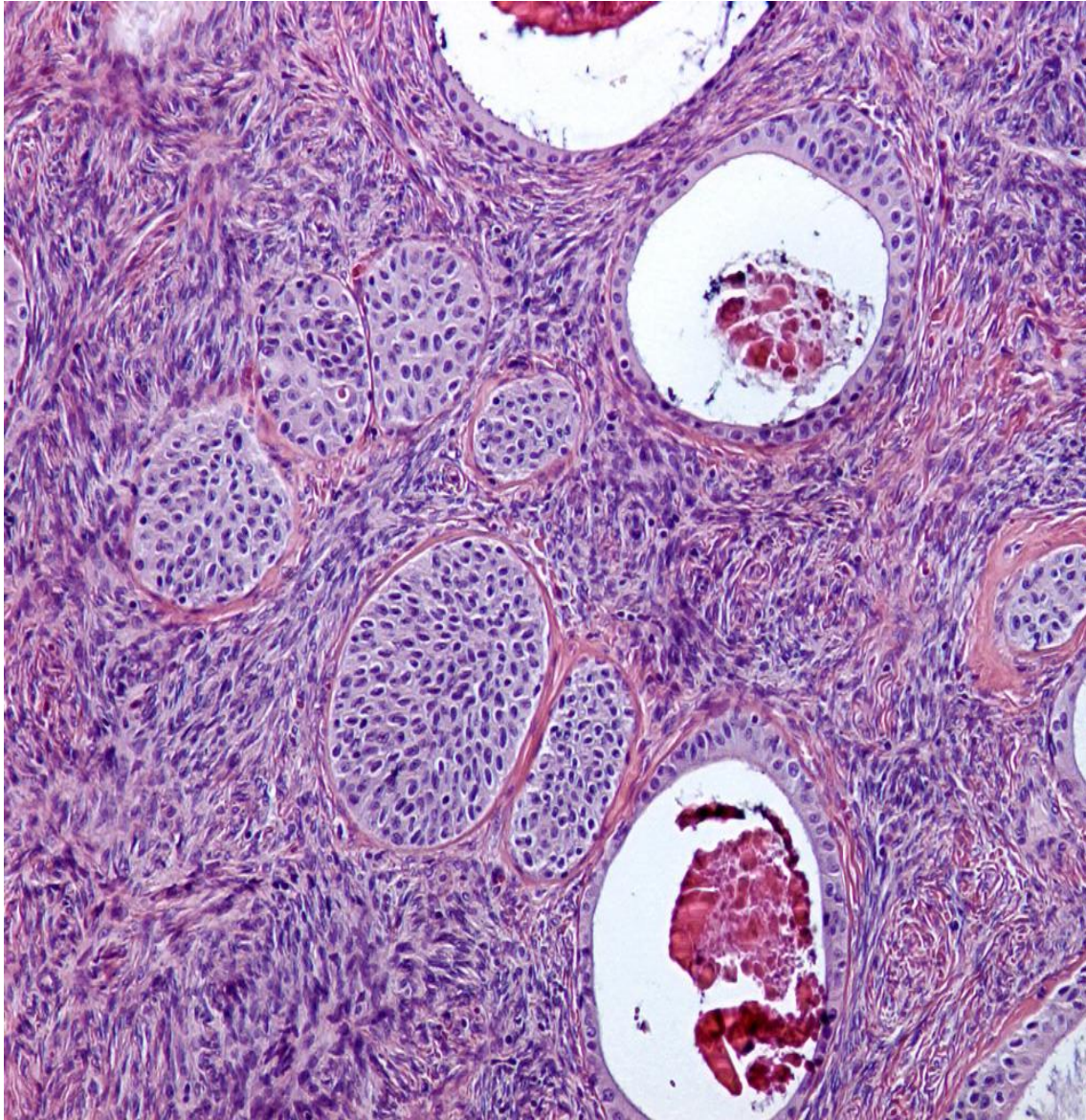


Malignant Brenner Tumor

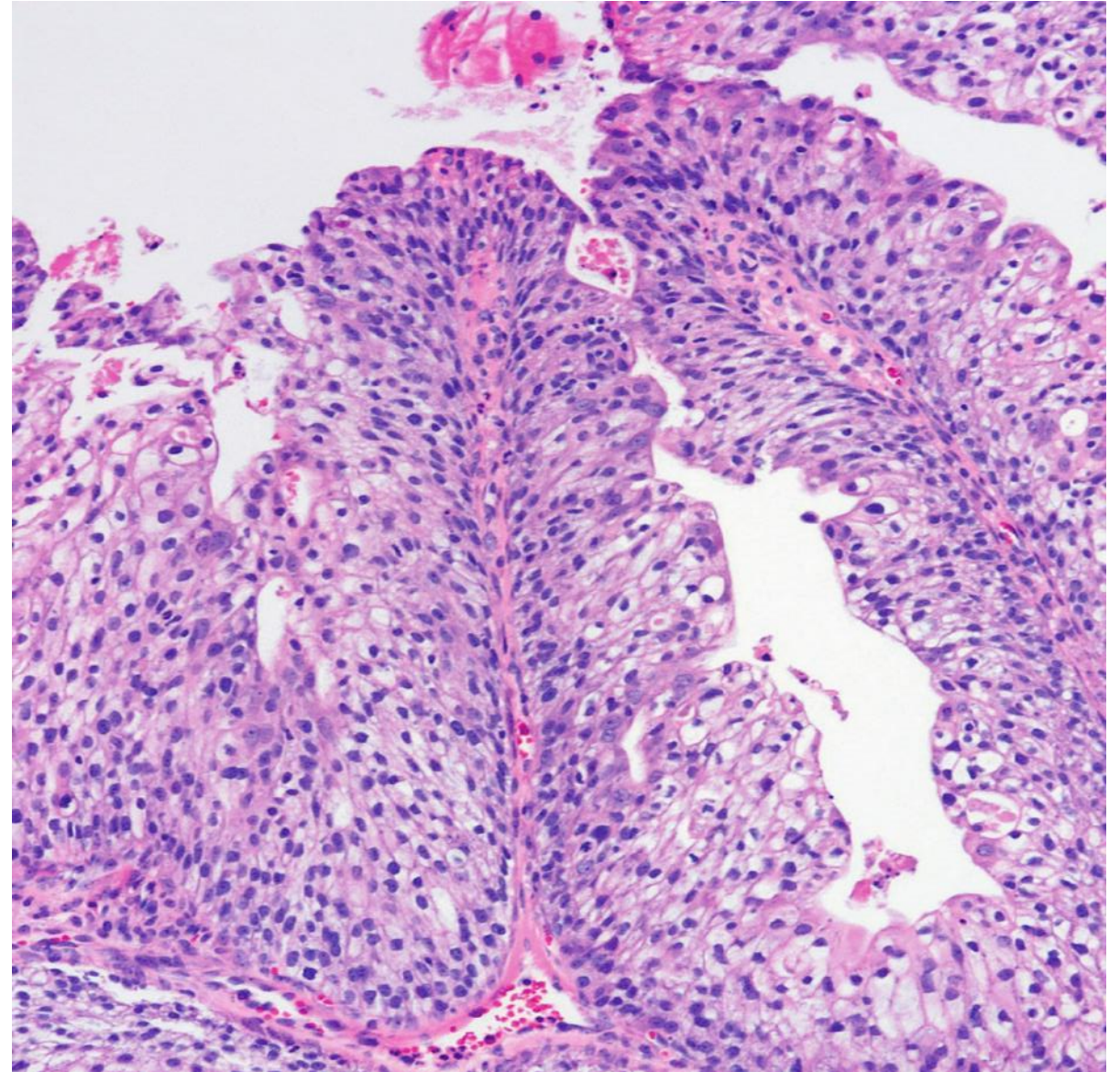


Malignant Brenner Tumor

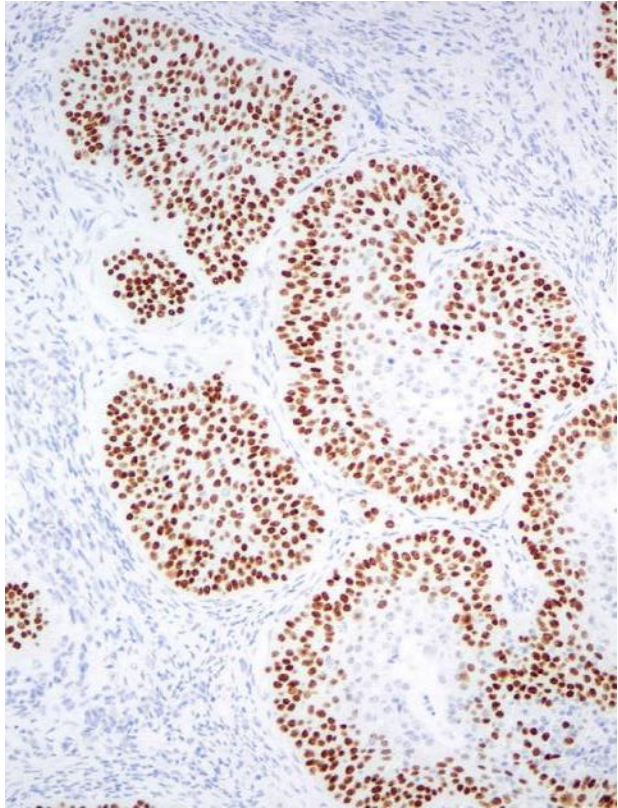
Brenner Tumor



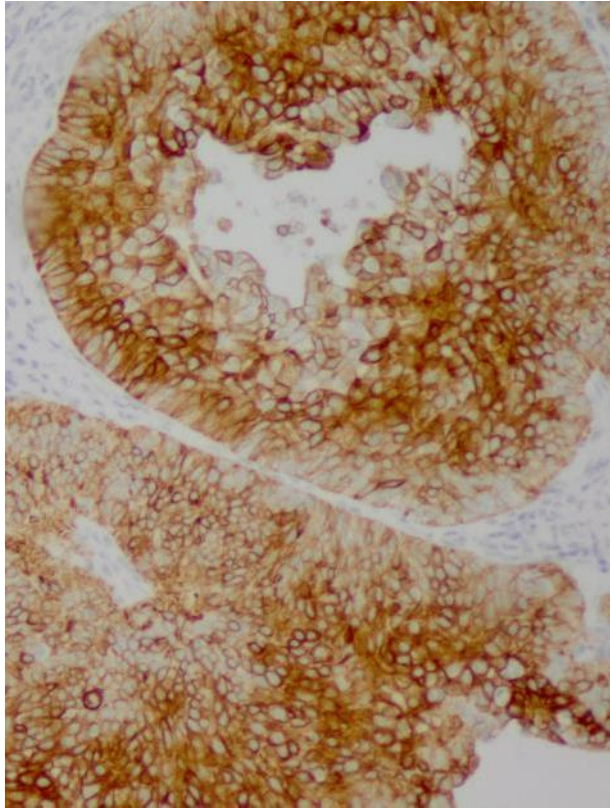
Borderline Brenner Tumor



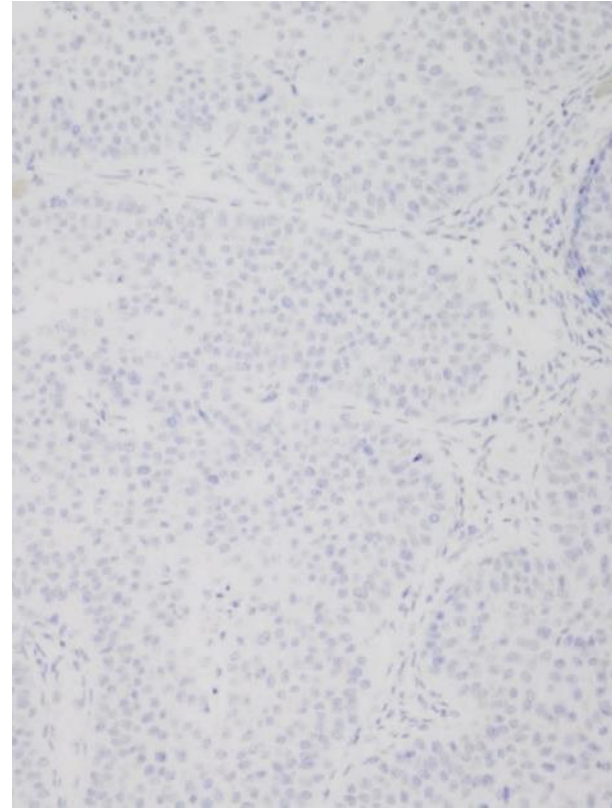
Malignant Brenner Tumor



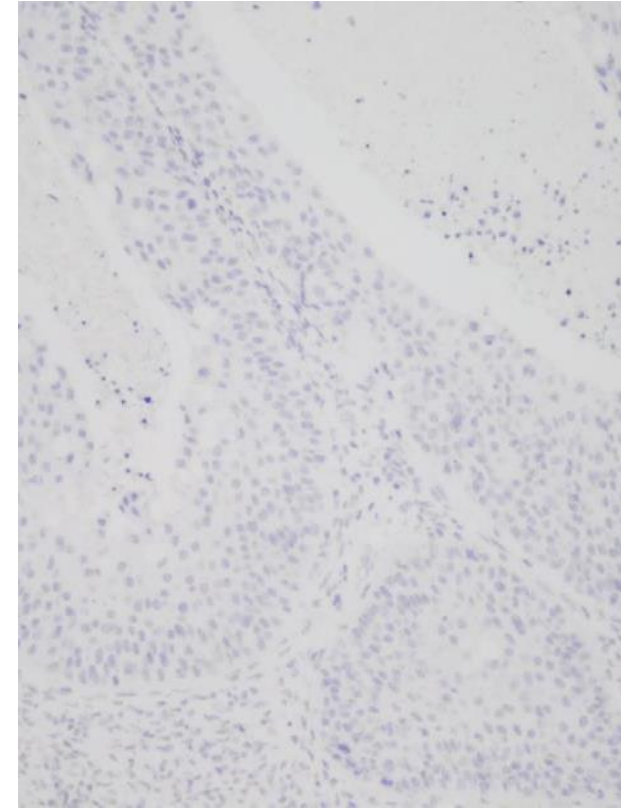
p63 +
GATA3 +



Ker 7 +



Ker 20 -



WT-1 -



Twilight Epiphany



Live Oak Friends Meeting House

James Turrell, Houston, Texas