

# PATOLOGÍA DEL CÁNCER DE CÉRVIX Y VULVA

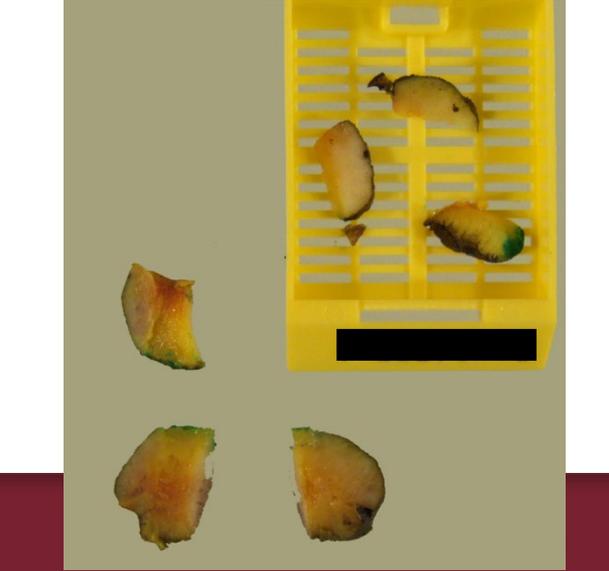
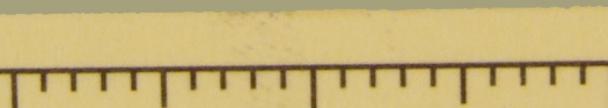
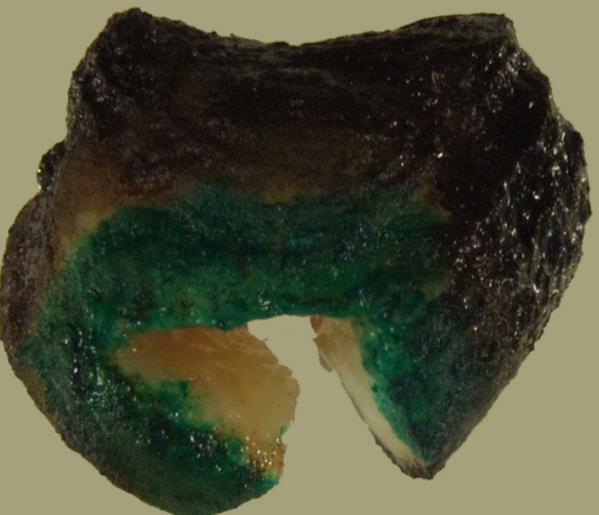
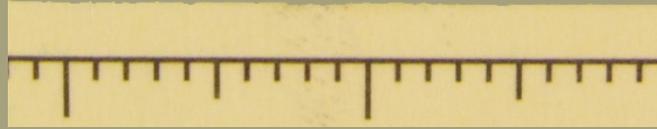
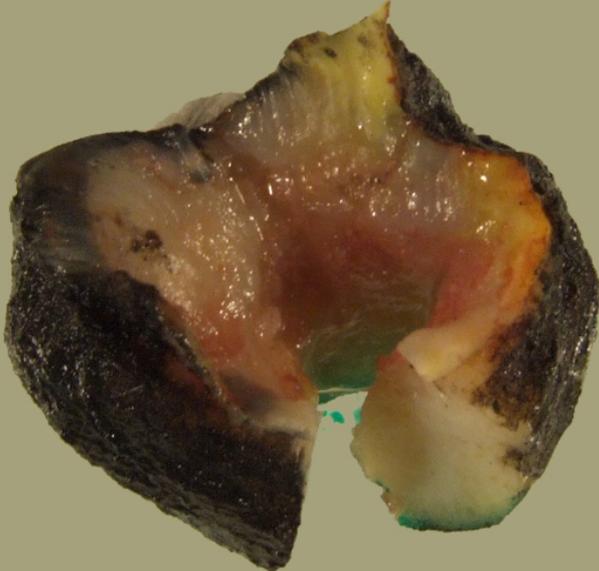
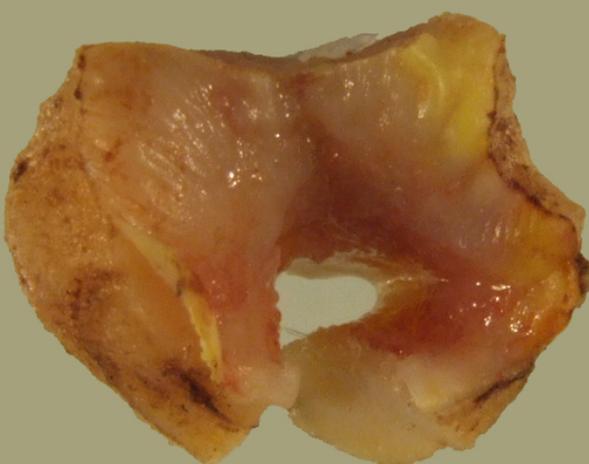
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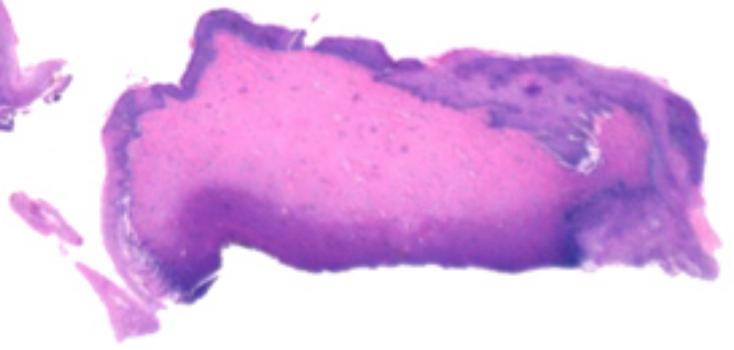
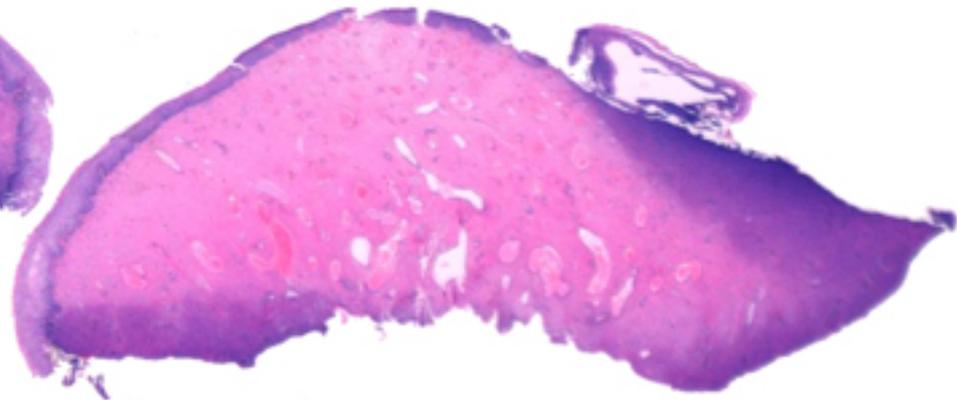
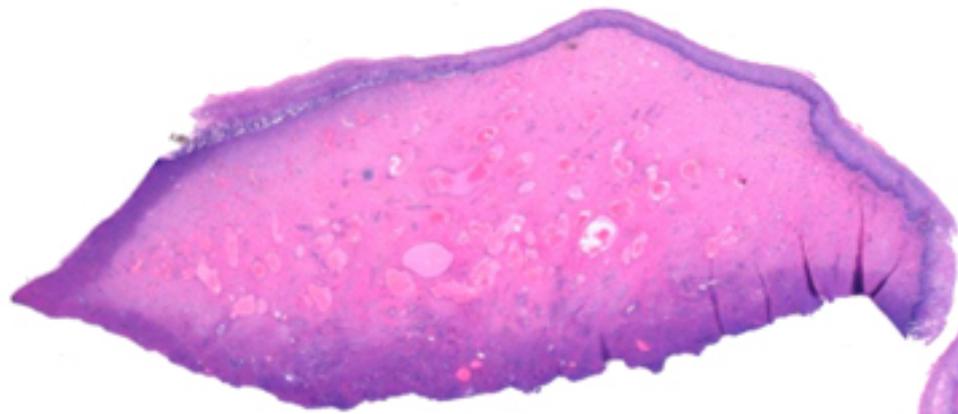
# CARCINOMA DE CÈRVIX

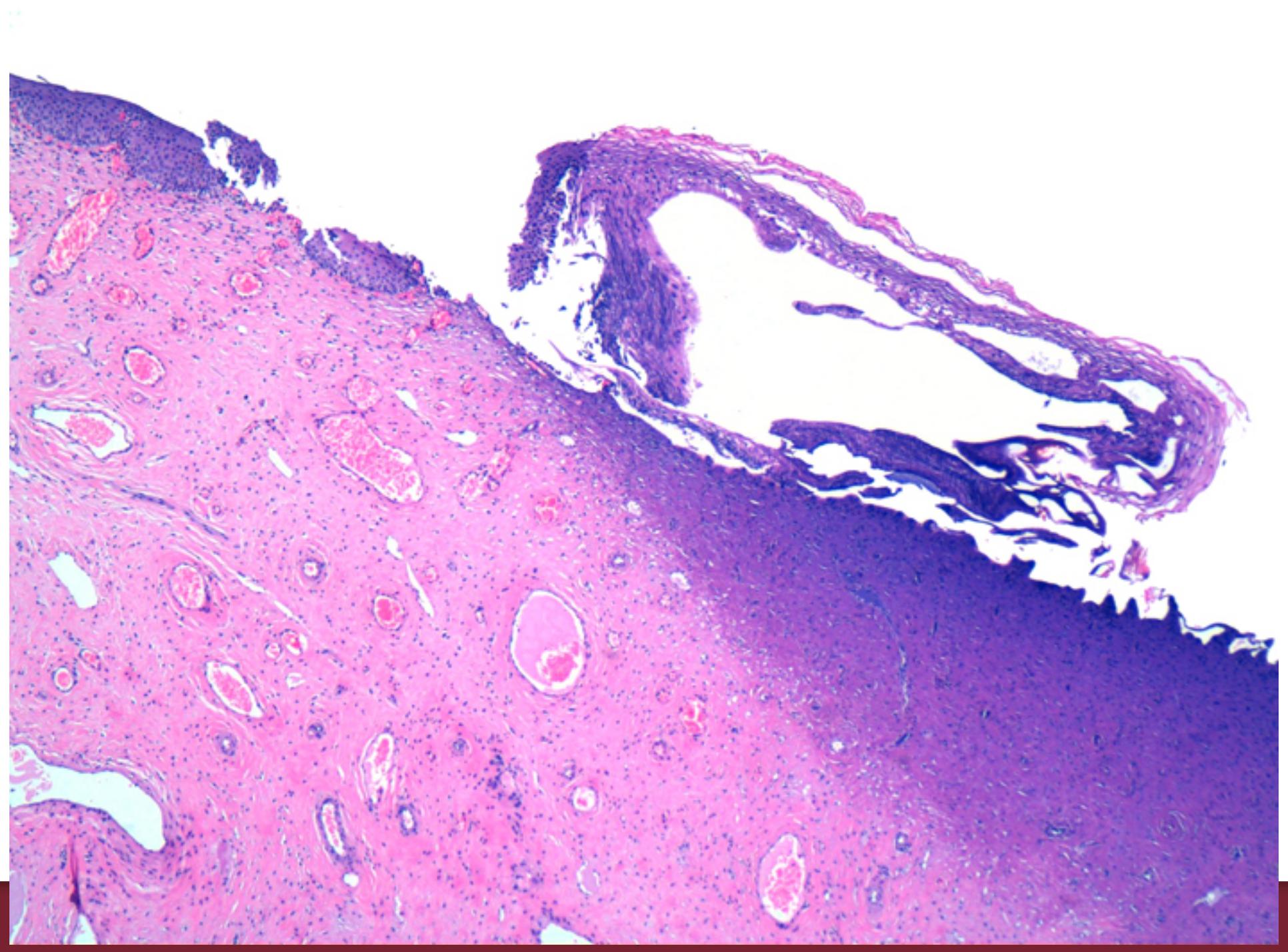
- 2º CÁNCER MÁS FRECUENTE EN MUJERES.
- 3er CÁNCER GINECOLÓGICO MÁS FRECUENTE EN PAISES DESARROLLADOS.
- DISMINUCIÓN DE LA INCIDENCIA Y MORTALIDAD POR SCREENING CITOLÓGICO.

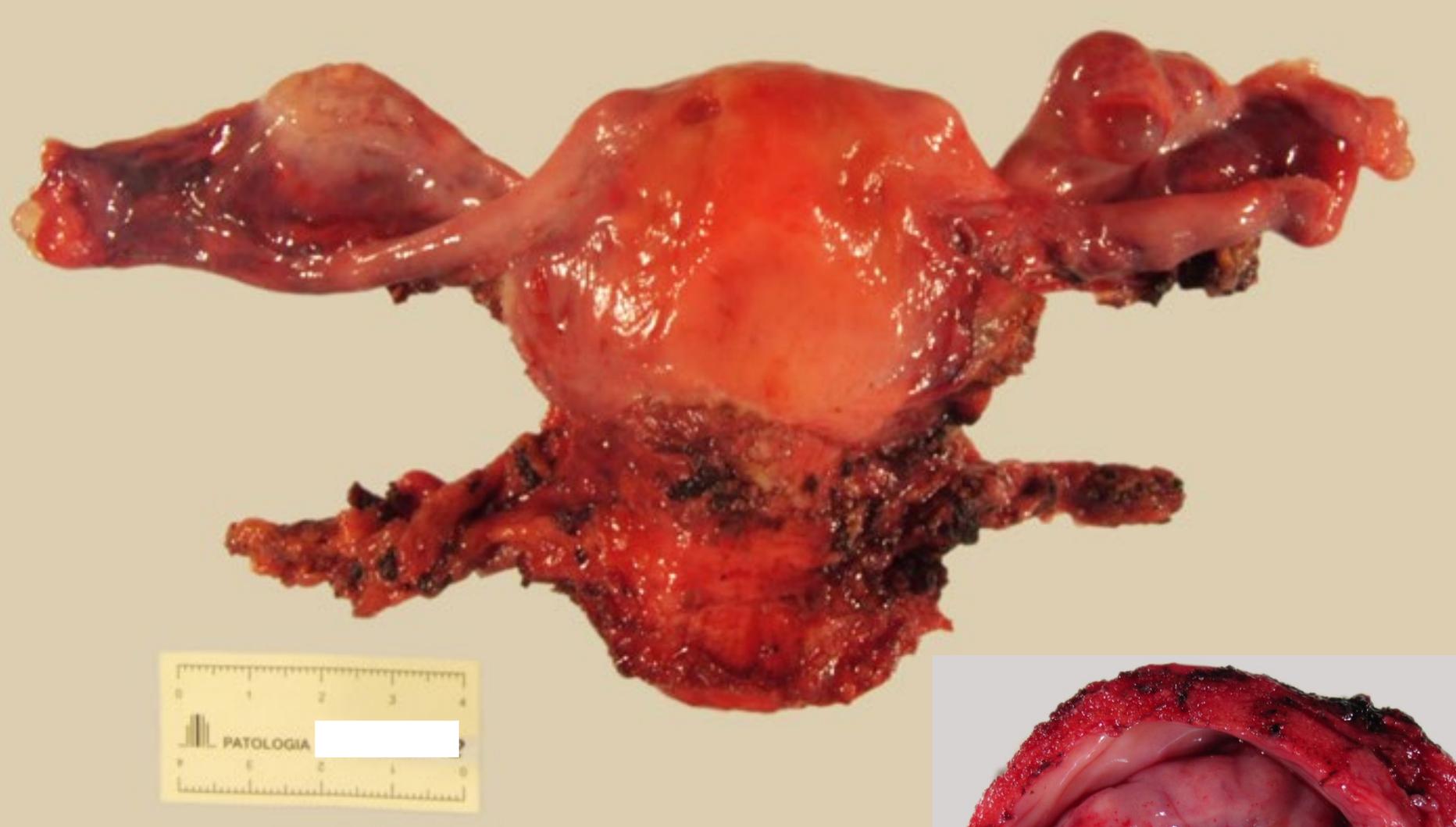
# TIPOS DE MUESTRAS

- CITOLOGIA
- BIOPSIA / LEGRADO
- CONIZACIÓN CON ASA
- CONIZACIÓN FRIA
- TRAQUELECTOMIA
- HISTERECTOMIA SIMPLE
- HISTERECTOMIA RADICAL

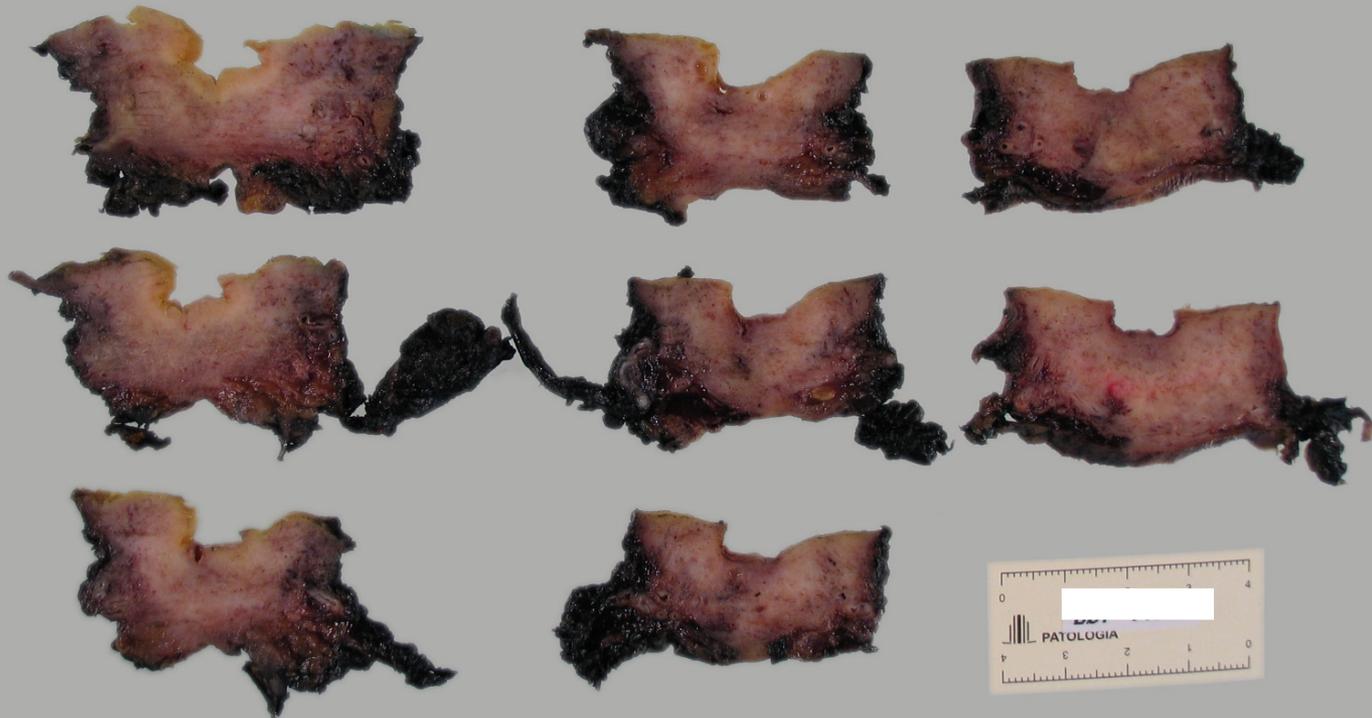


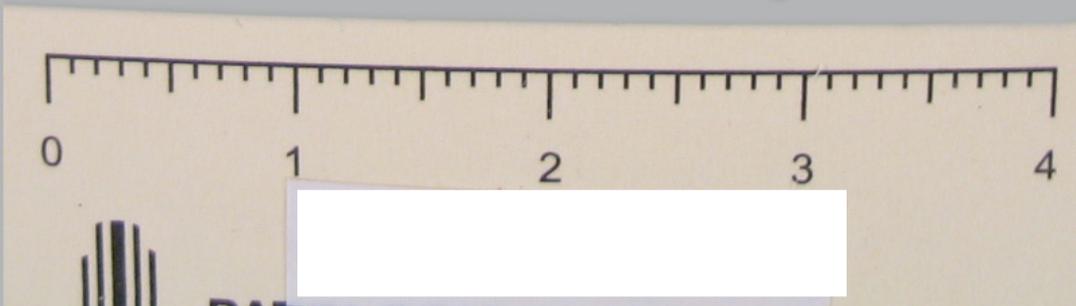
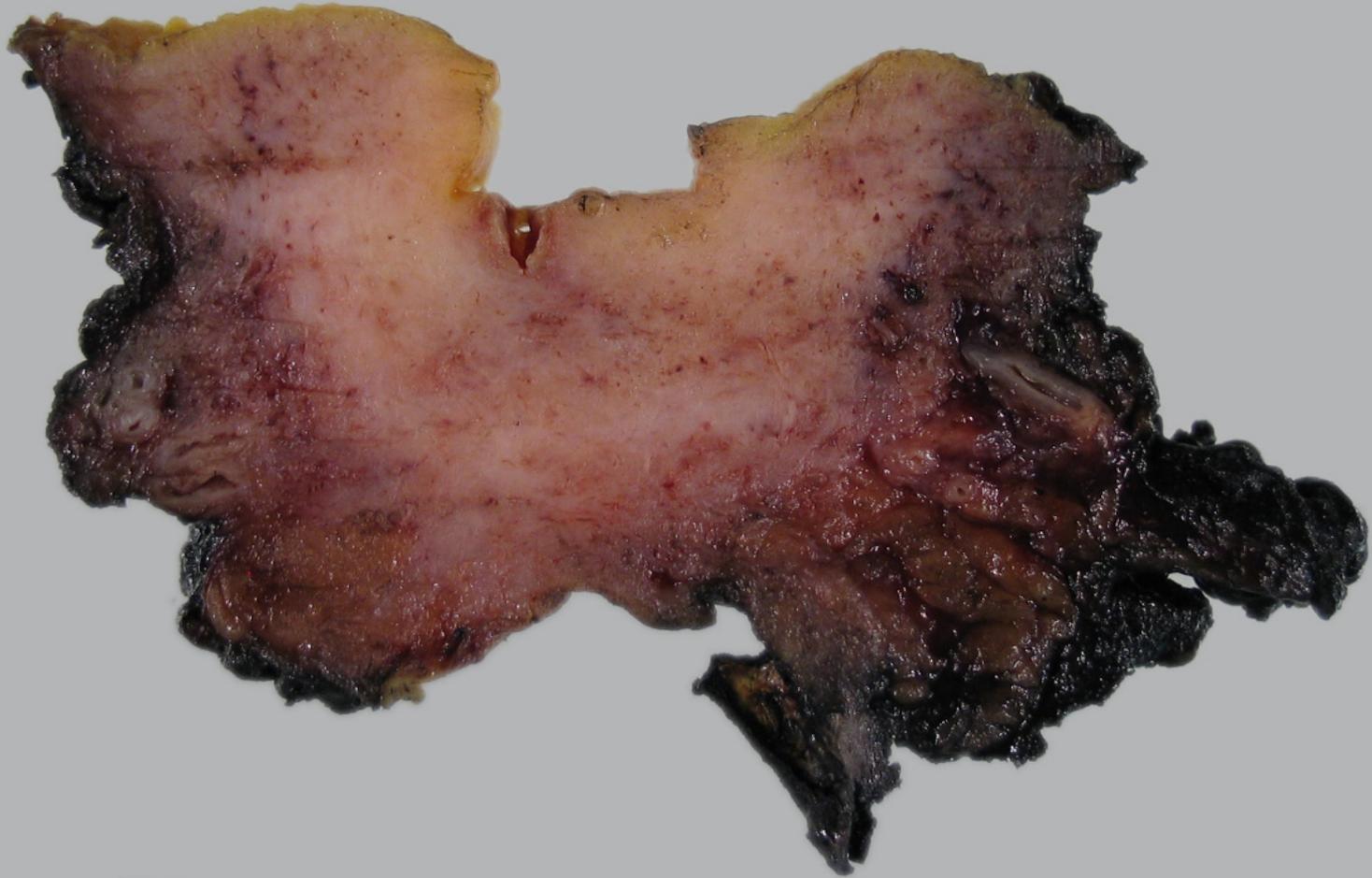












# TUMORES EPITELIALES DEL CÉRVIX

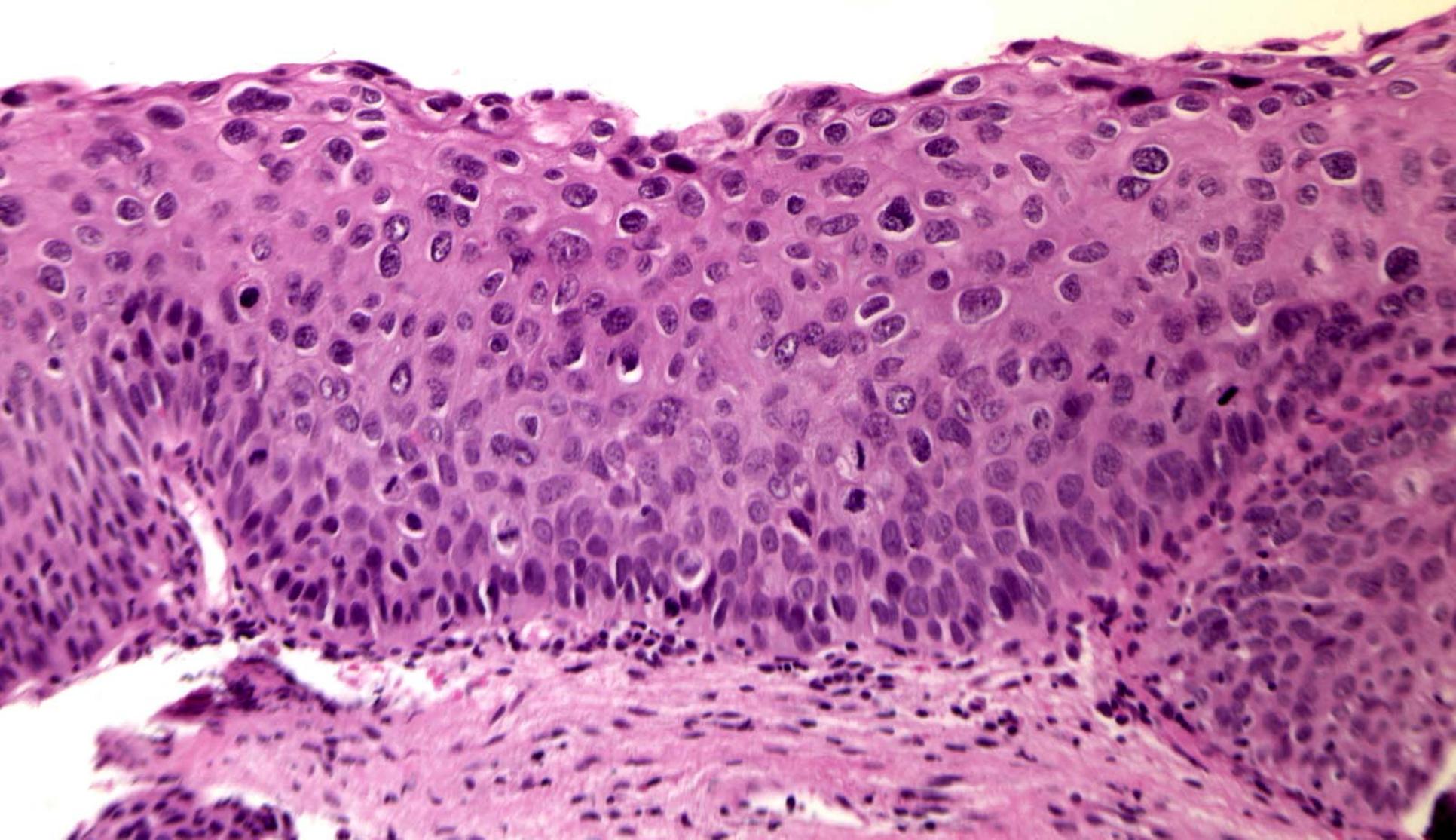
- TUMORES ESCAMOSOS
- TUMORES GLANDULARES
- OTROS TUMORES EPITELIALES

# Lesiones precursoras escamosas

Bethesda Classification	Normal	Low-grade squamous intraepithelial lesion (LSIL)		High-grade squamous intraepithelial lesion (HSIL)		Invasive cancer	
Cervical Intraepithelial Neoplasia (CIN)	Normal	Flat condyloma	CIN 1	CIN 2	CIN 3		Invasive cancer
Dysplasia	Normal	Flat condyloma	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Carcinoma in situ	Invasive cancer
Histology of the Squamous Cervical Epithelium							

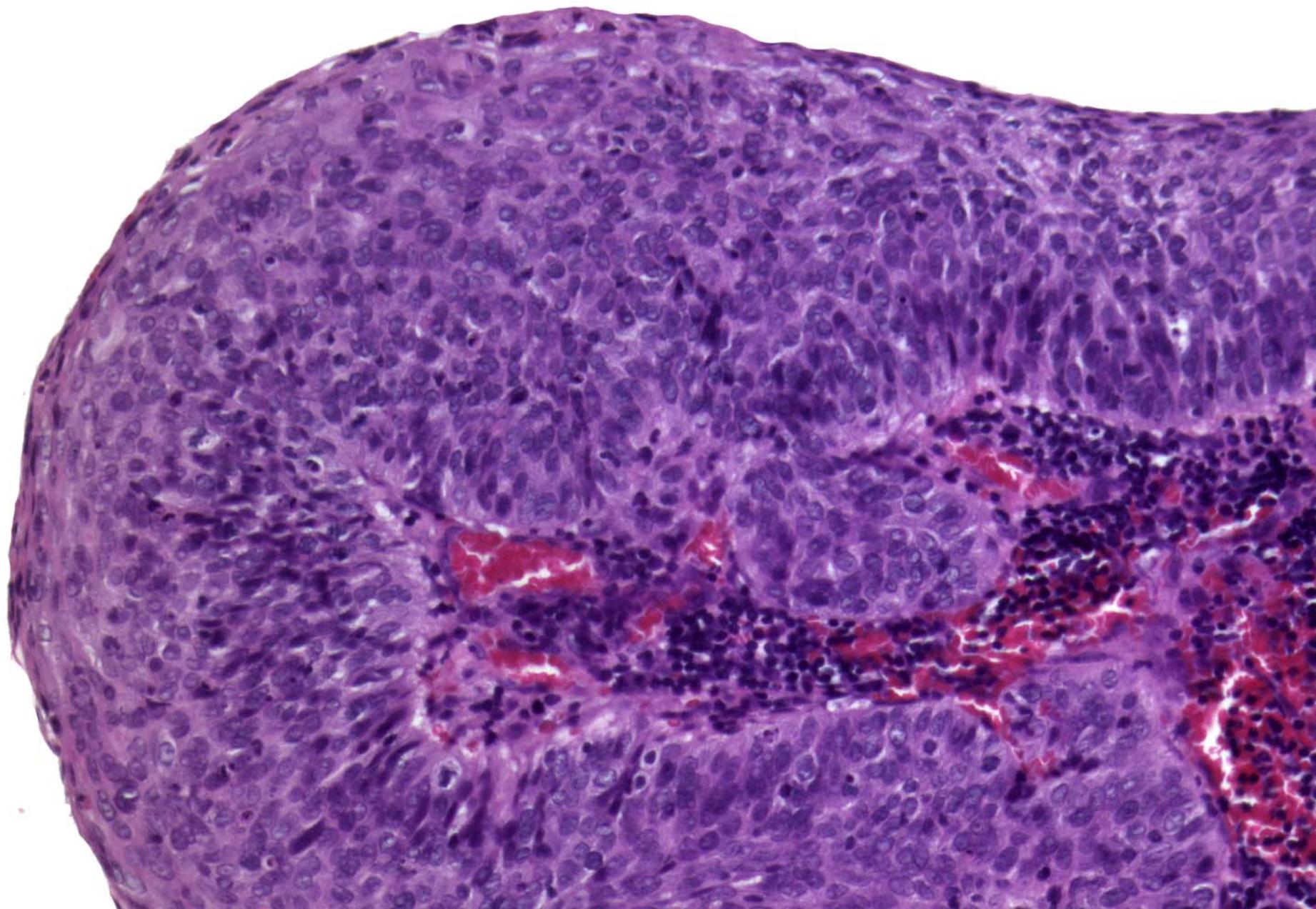
# LSIL

- HPV
- 80% de mujeres a los 20a
- 5% de mujeres a los 50a
- La mayoría regresan en 1 año
- 1/3 p16+
- No hay biomarcadores que predigan si LSIL persistirá, progresará o regresará



# HSIL

- HPV
- 20 años antes que carcinoma
- p16+
- 1/3 progresará a carcinoma si no se trata
- 30-50% pueden regresar a LSIL
- 1/3 p16+
- No hay biomarcadores que predigan si HSIL progresará o regresará



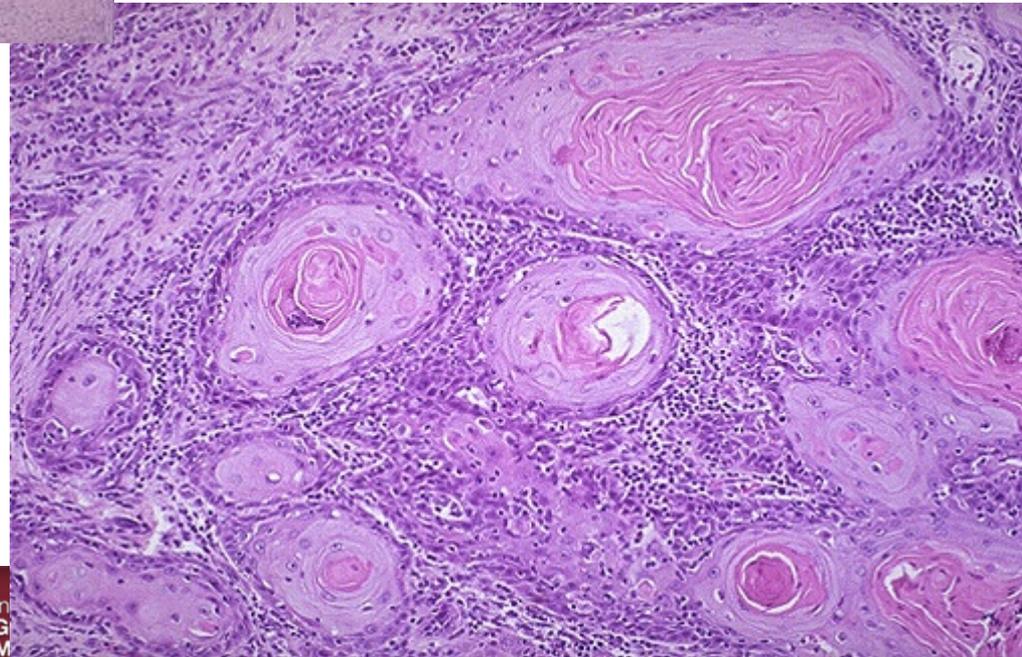
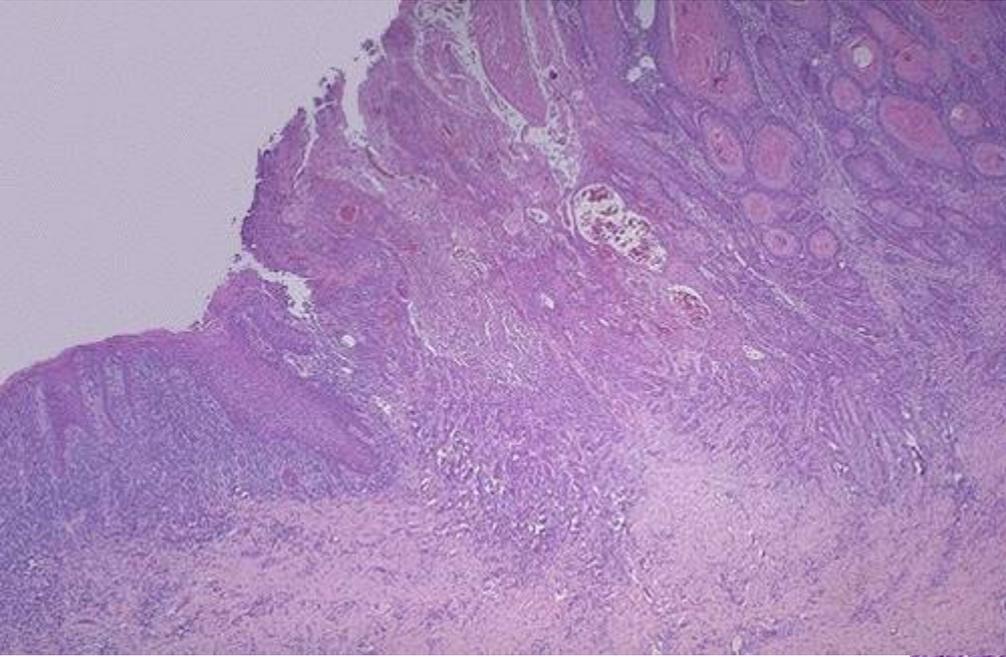
# Carcinoma escamoso

- 80% de cànceres de cèrvix
- Edat media 55a (20 a > que HSIL)
- 30% abans dels 35 a
- Síntomas – sangrado / dolor / flujo
- Pràcticament todos relacionados con HPV
- No hay diferencias pronósticas entre las diferentes variantes

# Carcinoma escamoso. Clasificación

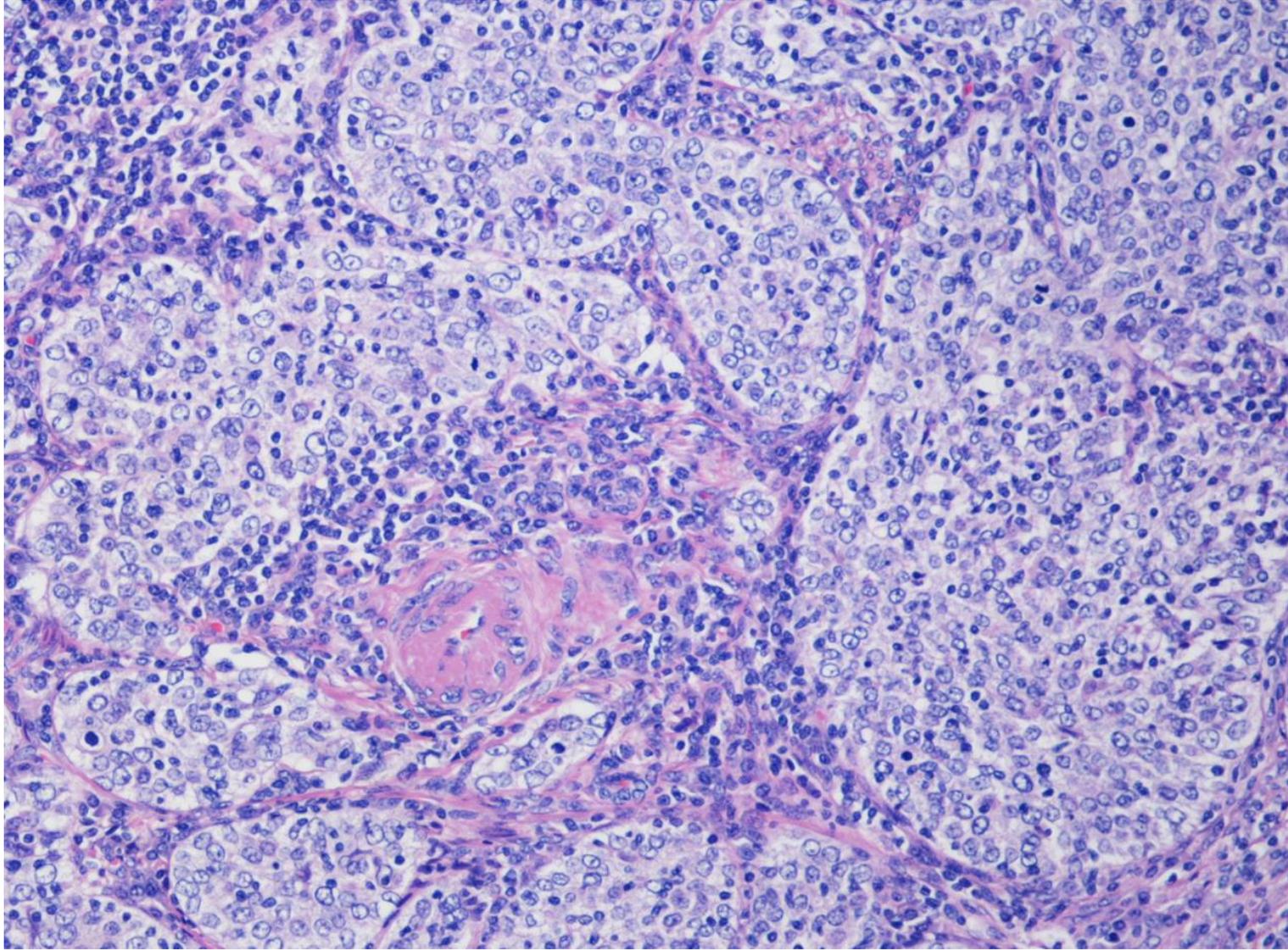
- Queratinizante
- No queratinizante
- Papilar
- Basaloide
- Condilomatoso (warty)
- Verrucoso
- Escamotransicional
- Linfopitelioma-like

# Carcinoma escamoso queratinizante

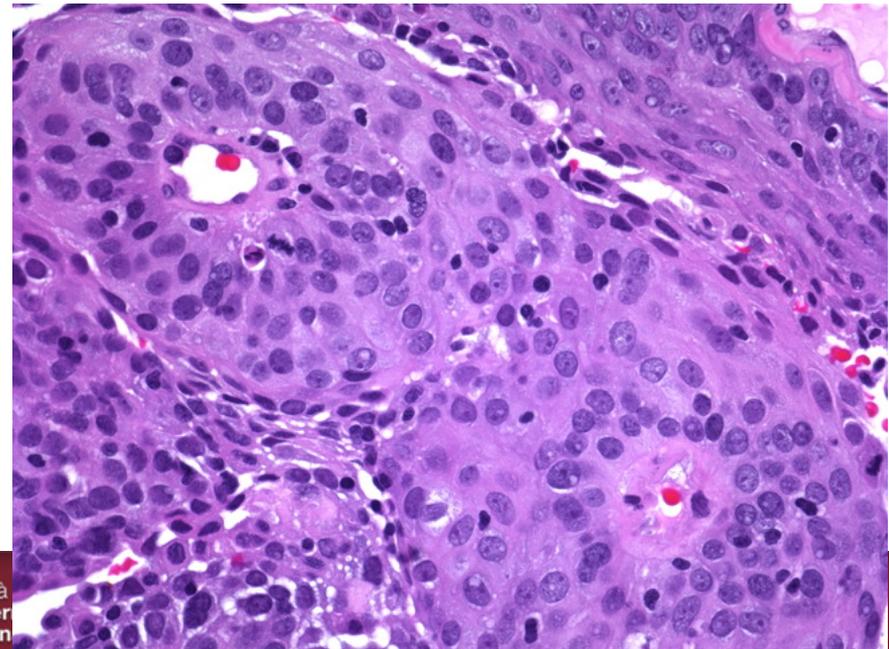
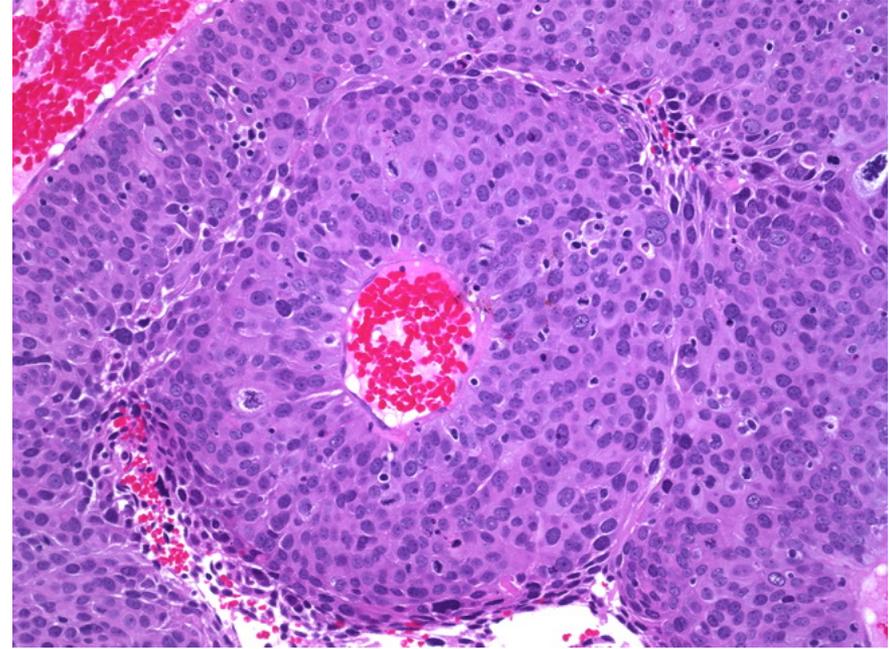


# Carcinoma escamoso no queratinizante

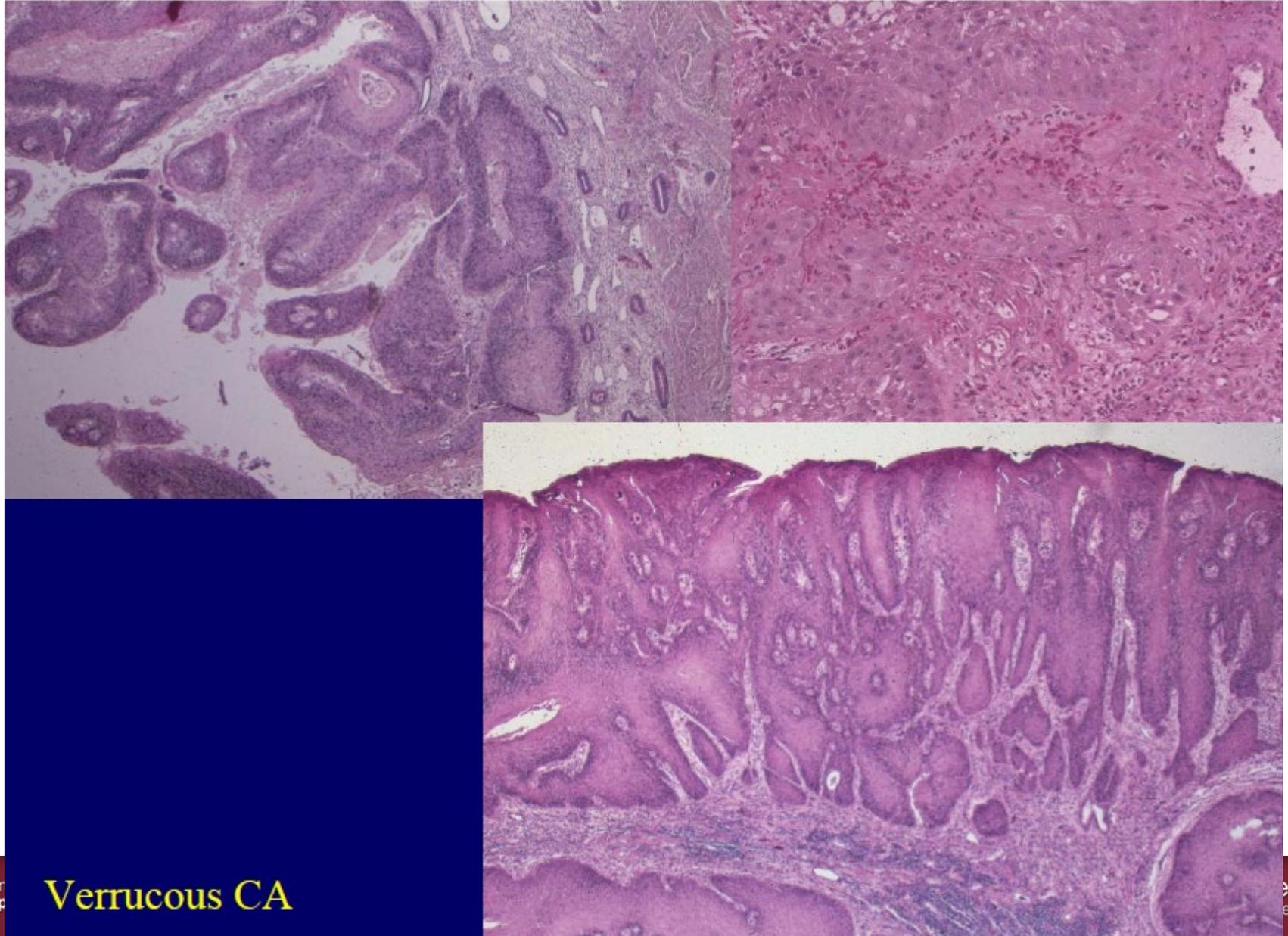
El tipo  
más  
frecuente



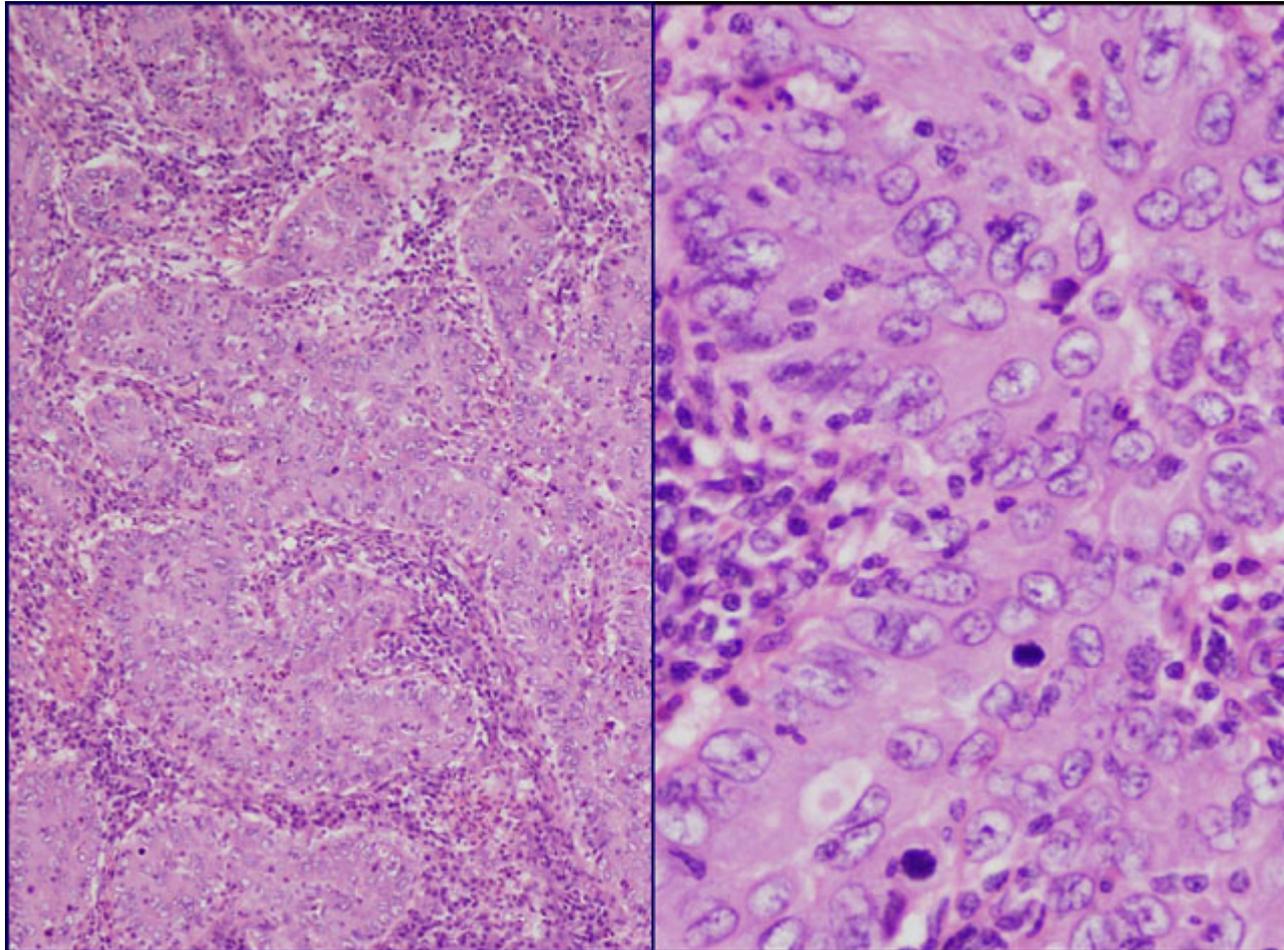
# Carcinoma escamoso papilar



# Carcinoma verrucoso



# Carcinoma escamoso tipo linfoepitelioma



# ADENOCARCINOMA

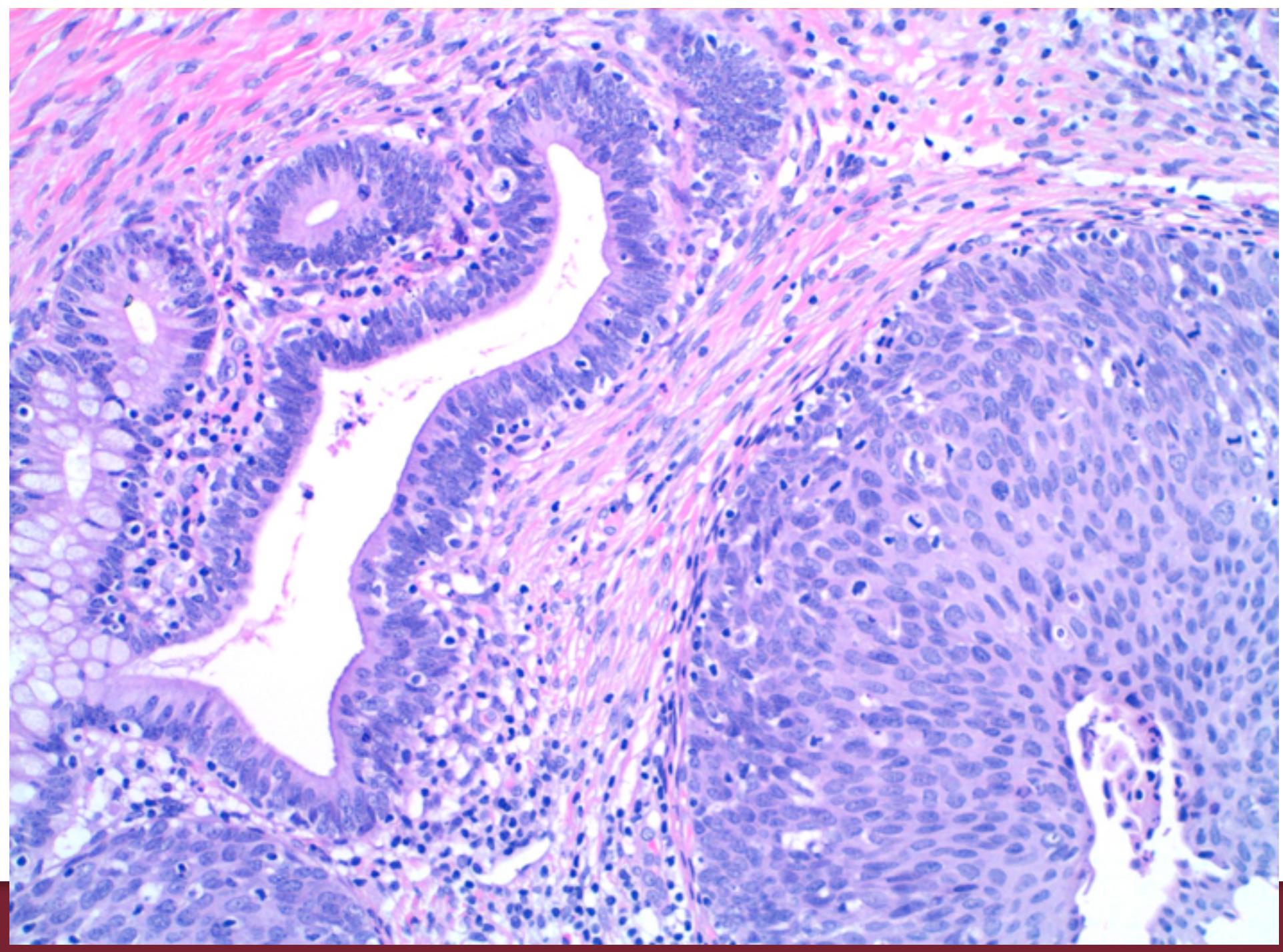
- 15-20% DE LAS NEOPLASIAS DE CÉRVIX.
- 50 AÑOS
- LESIÓN PRECURSORA ADENOCARCINOMA IN SITU.
- LA MAYORÍA SON DE TIPO ENDOCERVICAL.
- 50% EXOFÍTICO (POLIPOIDE O PAPILAR).
- CLÍNICA DE SANGRADO O MASA
- RELACIÓN CON HPV 18, 16, 45.

# ADENOCARCINOMA IN SITU

- ÉS LA LESIÓ PRECURSORA DEL ADENOCARCINOMA CERVICAL
  - EDAD MEDIA DE DIAGNÓSTICO (38) 10 AÑOS ANTES QUE ADC INFILTRANTE
  - CITOLOGÍA SIMILAR A ADC INFILTRANTE
  - LAS DOS LESIONES COEXISTEN A MENUDO
  - ESTÁN IMPLICADOS LOS MISMOS TIPOS DE HPV
  - ADC IS PRECEDE CRONOLÓGICAMENTE AL ADC INFILTRANTE

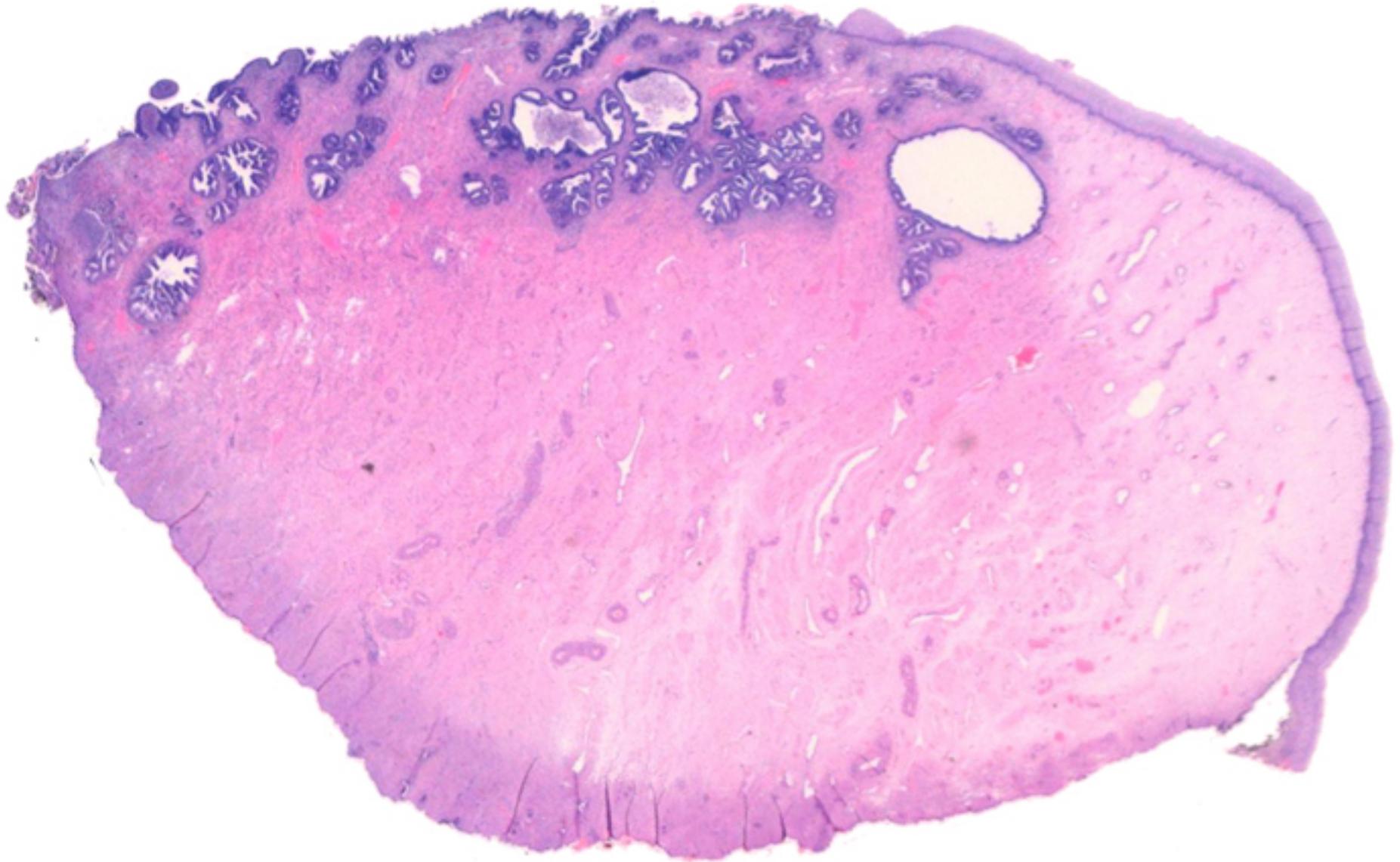
# ADENOCARCINOMA IN SITU. CARACTERÍSTICAS GENERALES

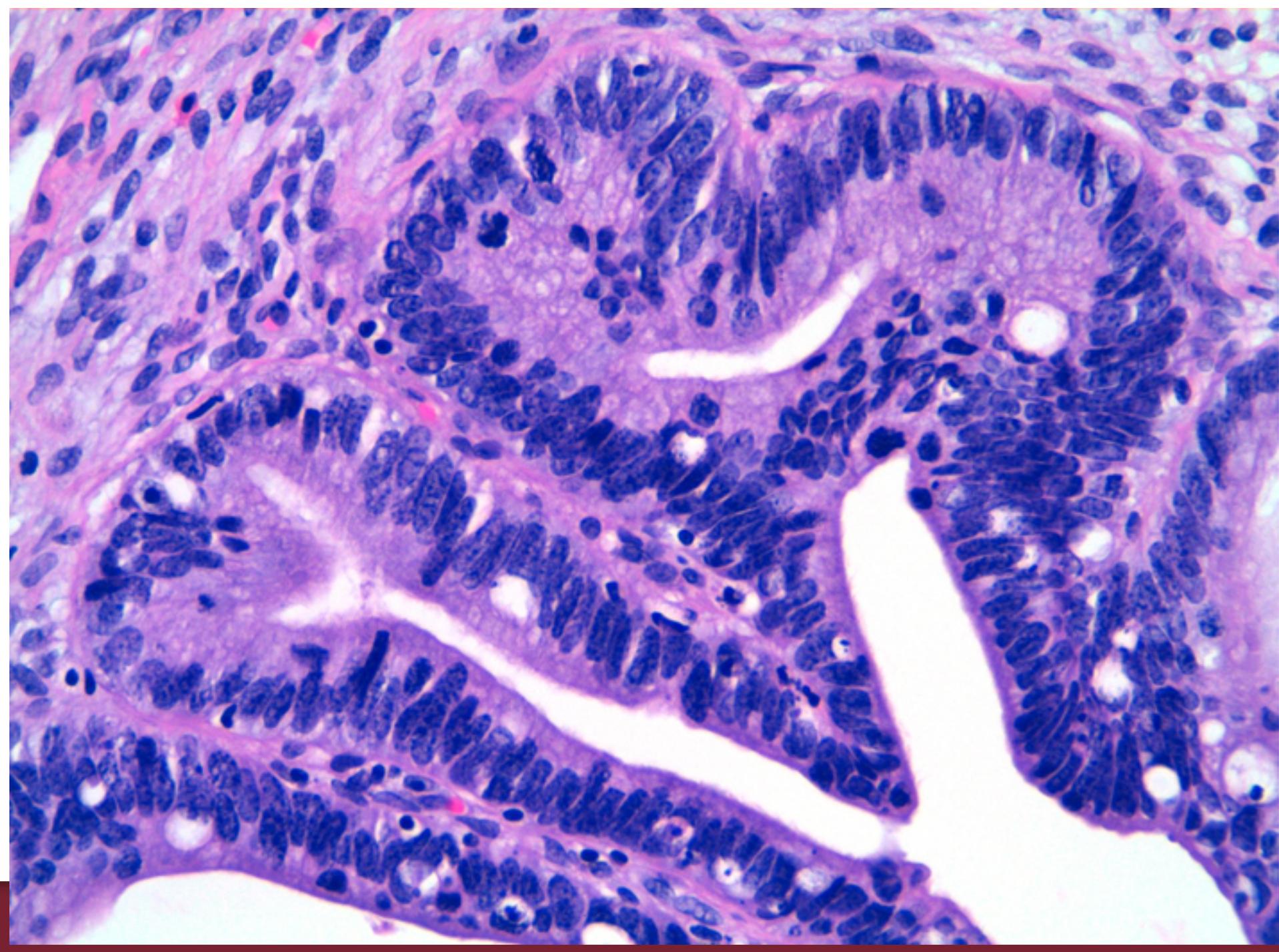
- AFECTACIÓN DEL EPITELIO SUPERFICIAL I GLANDULAR DE LA ZONA DE TRANSFORMACIÓN ESCAMO-COLUMNAR
- LESIÓN CONTÍNUA O LESIÓ MULTIFOCAL
- ASOCIACIÓN CON SIL (30-60%)
- LA MAYORÍA DE CASOS SON ASINTOMÁTICOS (HALLAZGO CASUAL EN SCREENING, BIOPSIAS, CONIZACIONES,...)

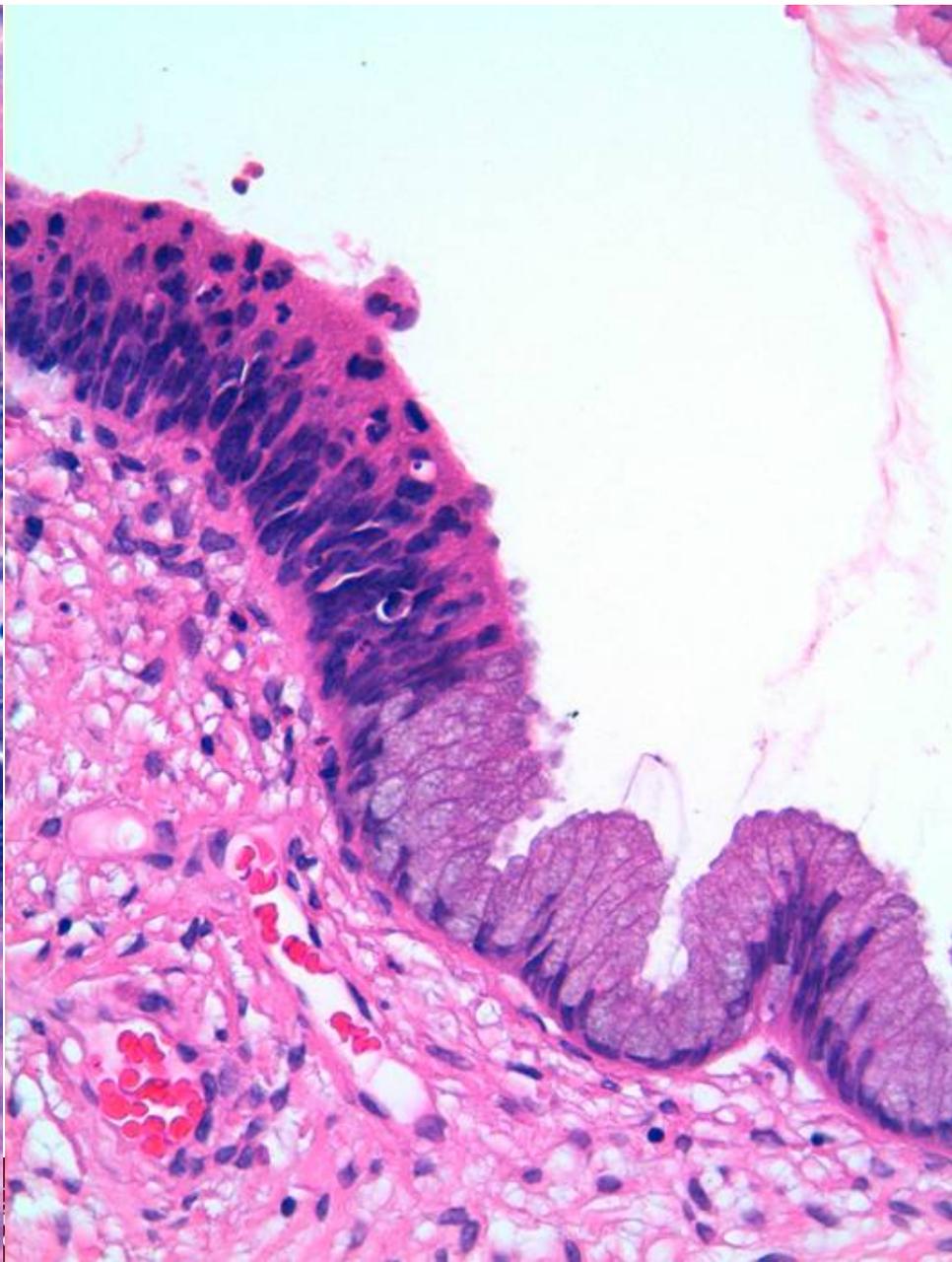
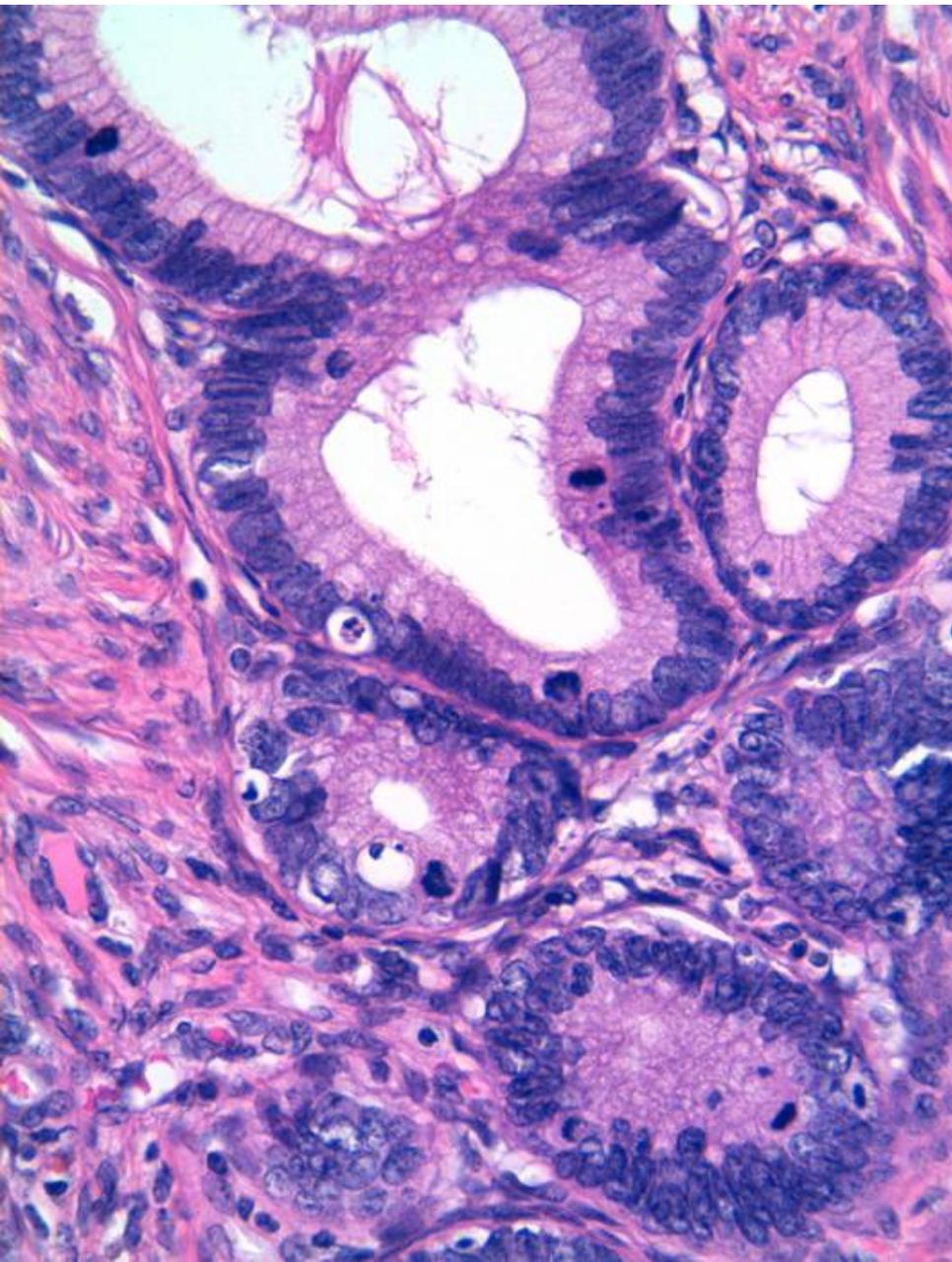


# ADENOCARCINOMA IN SITU. CRITERIOS DIAGNÒSTICS

- PRESERVACIÓN DE LA ARQUITECTURA GLANDULAR NORMAL
- NÚCLEOS GRANDES, HIPERCROMÁTICOS, CON ESTRATIFICACIÓN
- FIGURAS DE MITOSIS
- IMÁGENES DE APOPTOSIS
- TRANSICIÓN ABRUPTA CON EL EPITELIO ENDOCERVICAL NORMAL







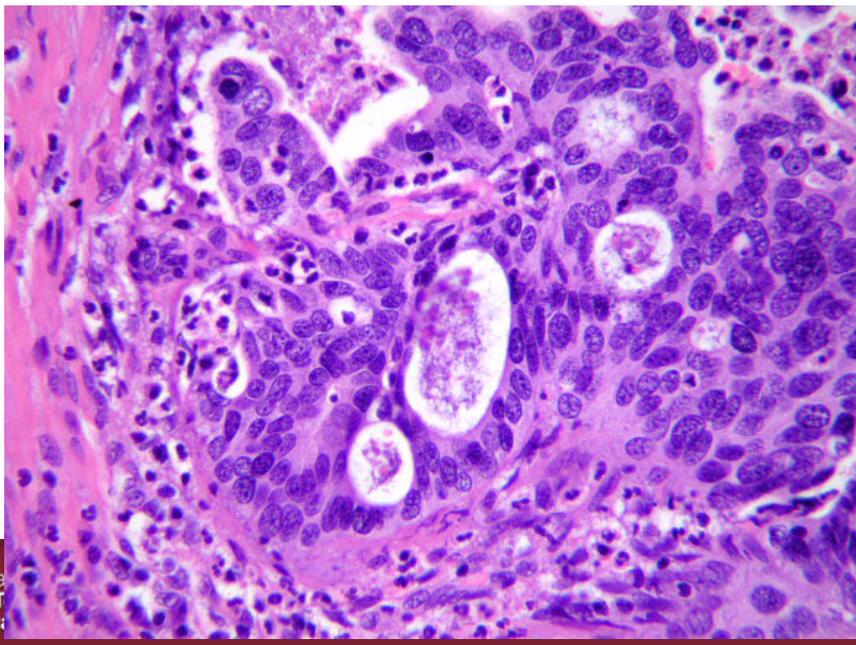
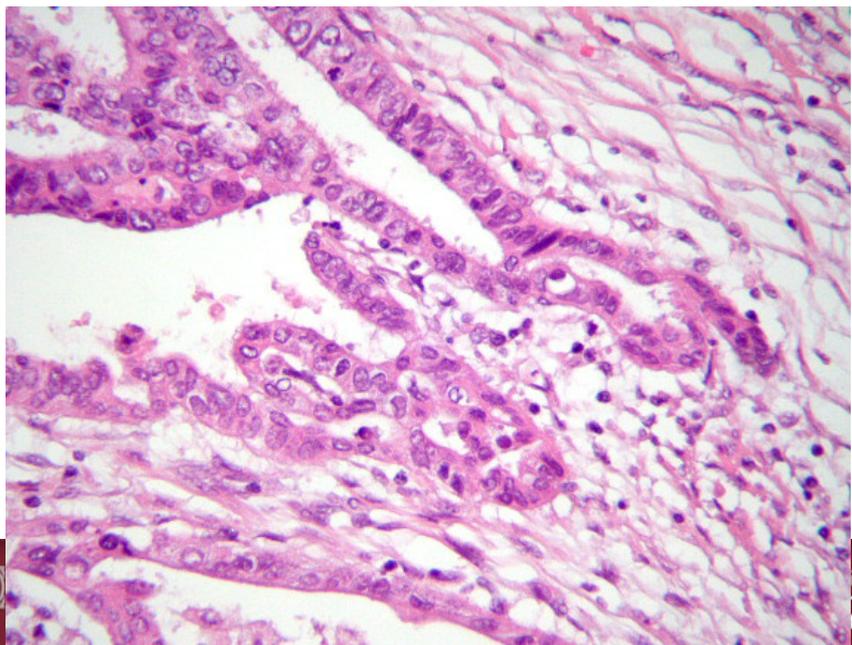
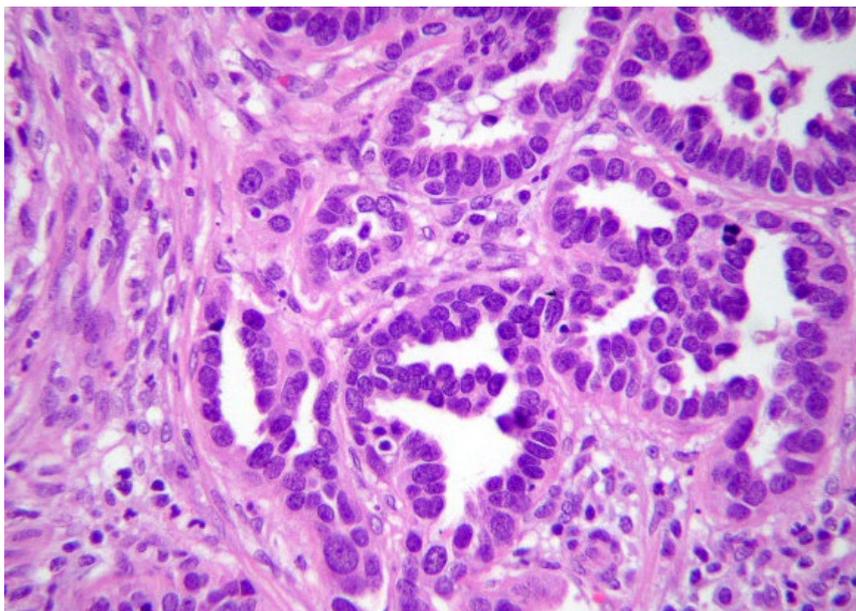
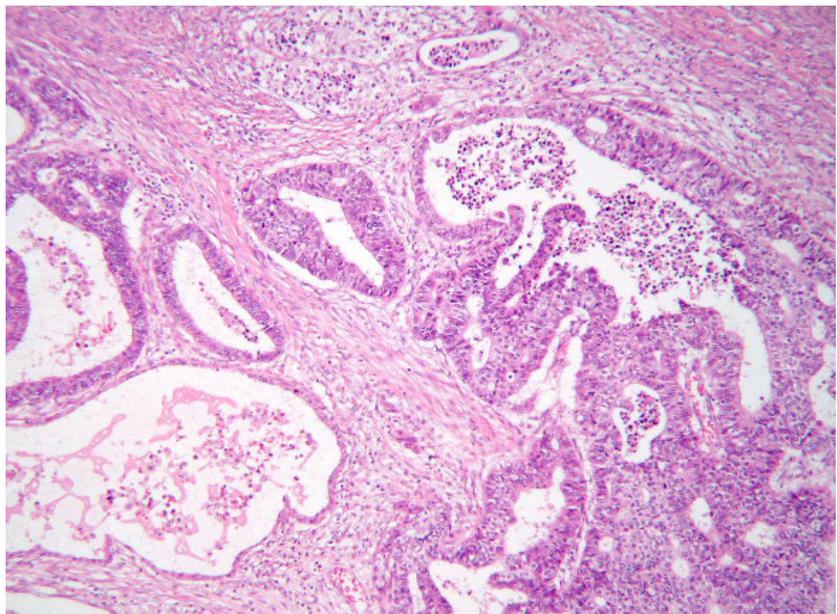
# ADENOCARCINOMA. CLASIFICACIÓN

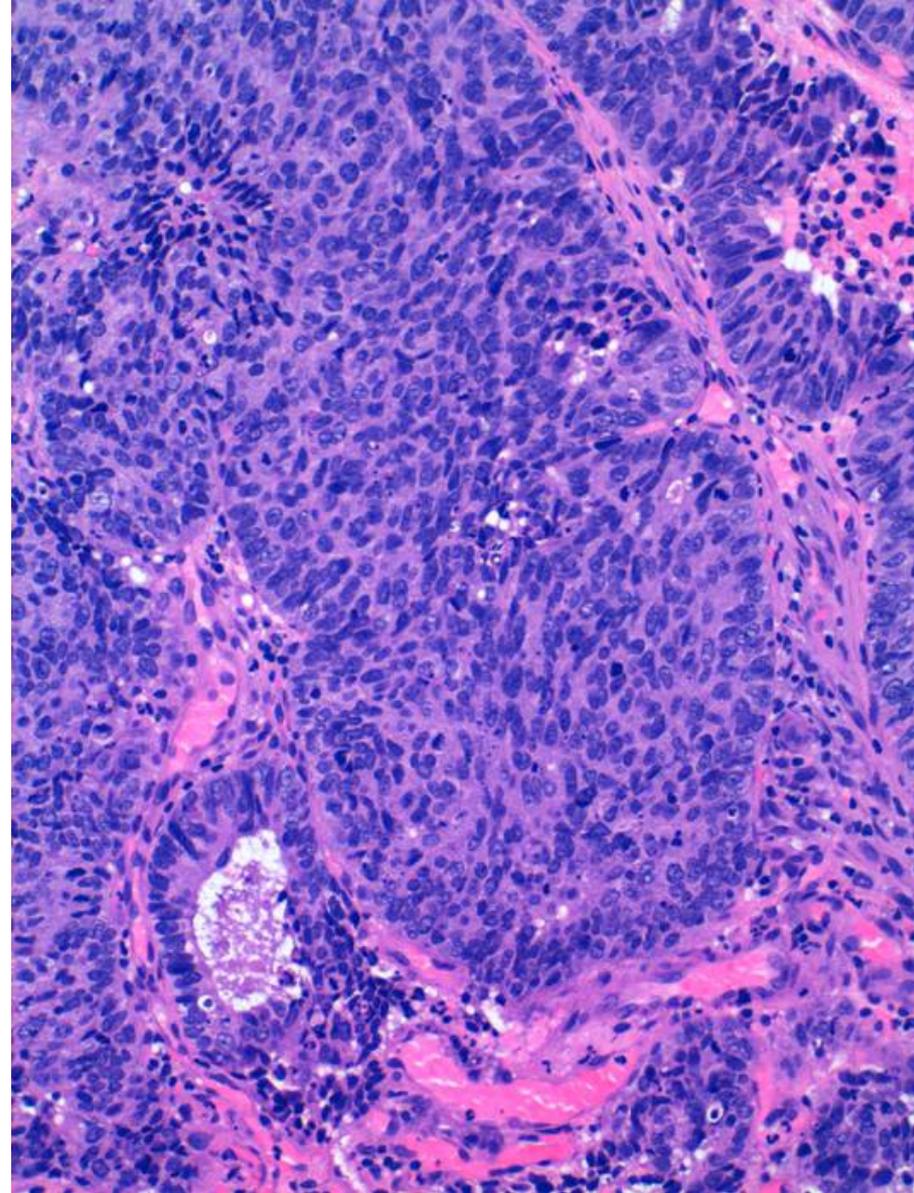
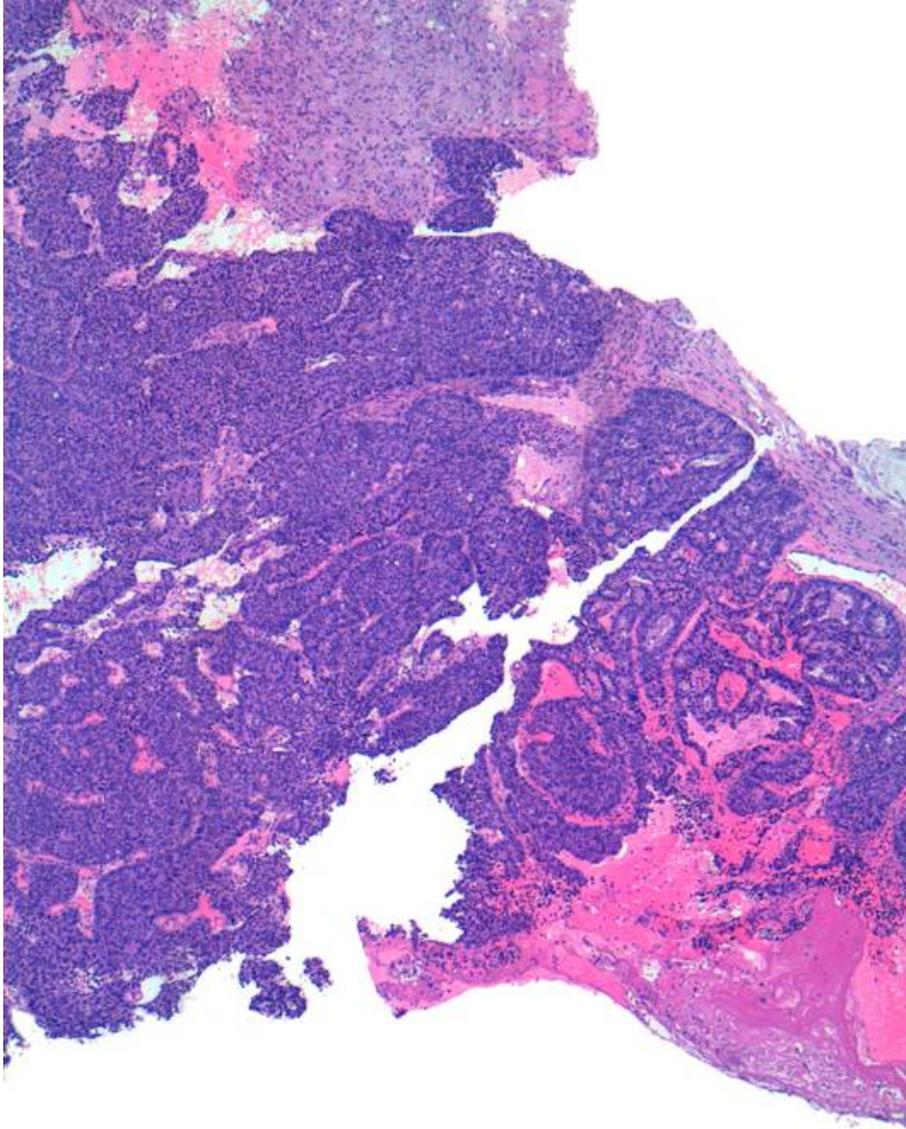
- ADENOCARCINOMA ENDOCERVICAL, TIPO USUAL.
- MUCINOSO
  - DE TIPO GÁSTRICO (MÍNIMA DESVIACIÓN)
  - INTESTINAL
  - DE CÉLULAS EN ANILLO DE SELLO
- VILLOGLANDULAR
- ENDOMETRIOIDE
- DE CÉLULAS CLARAS
- SEROSO
- MESONÉFRICO
- ADENOCARCINOMA CON CARCINOMA NEUROENDOCRINO

# ADENOCARCINOMA ENDOCERVICAL, TIPO USUAL

- 90% DELS ADENOCARCINOMES
- GRAN VARIABILITAT DE PATRONS HISTOLÒGICS
- MITOSIS APICALES
- HPV

# ADENOCARCINOMA





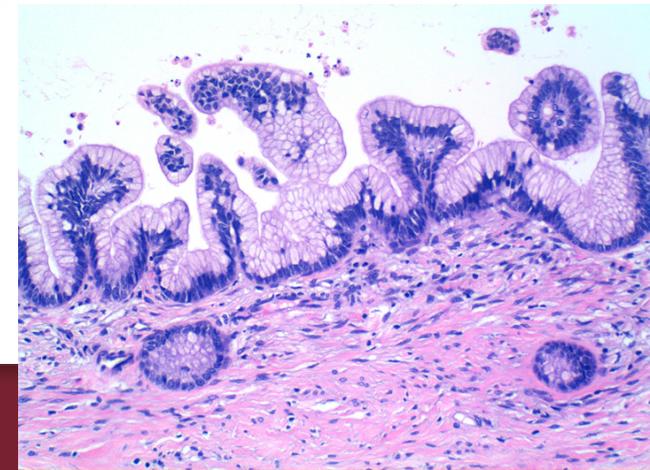
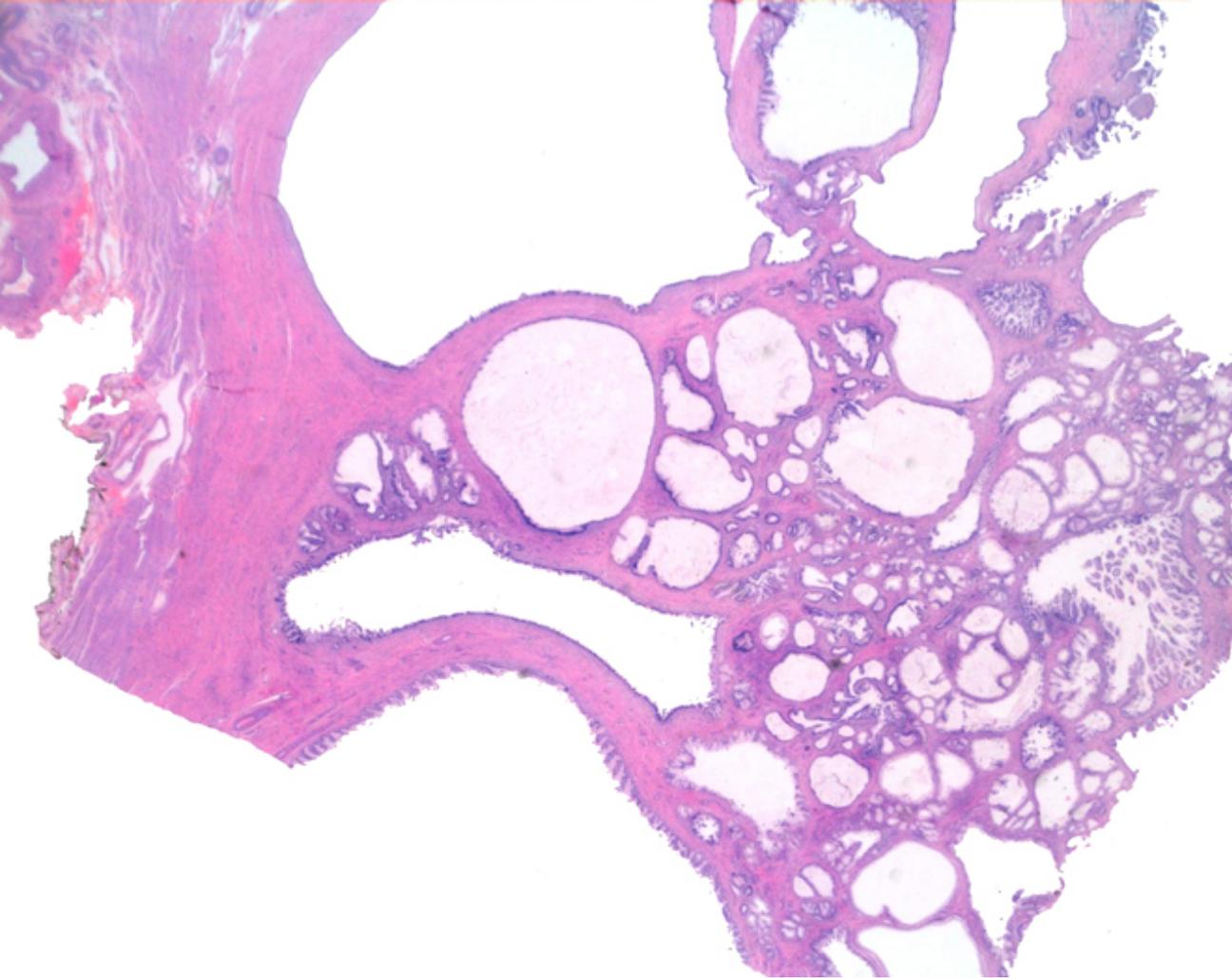
ADENOCARCINOMA POCO DIFERENCIADO

DIAGNÓSTICO DIFERENCIAL CON CARCINOMA ADENOESCAMOSO

# ADENOCARCINOMA MUCINOSO DE TIPO GÁSTRICO

- ADENOMA MALIGNUM / ADC DE MÍNIMA DESVIACIÓN
- 1% DELS ADENOCARCINOMES
- 40 ANYS
- SÍNDROME DE PEUTZ-JEGHERS
- ASSOCIACIÓ AMB ADENOCARCINOMA MUCINÓS OVÀRIC
- NO RELACIÓ CON HPV (p16-)
- MUCINAS DE GLÁNDULAS PILÓRICAS (MUC6 Y HIK1083)
- MUTACIONES p53 Y STK11 (50% ADC MD)
- PEOR PRONÓSTICO QUE ADC TIPO USUAL (30% vs 74% SUPERVIVENCIA A 5 A)

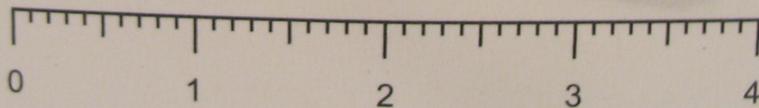
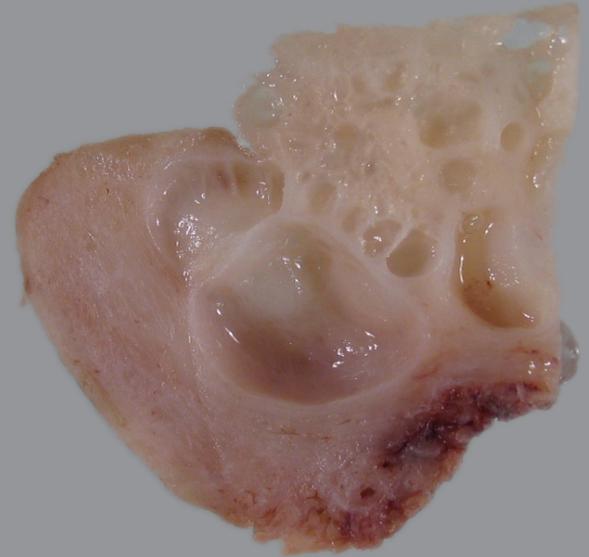
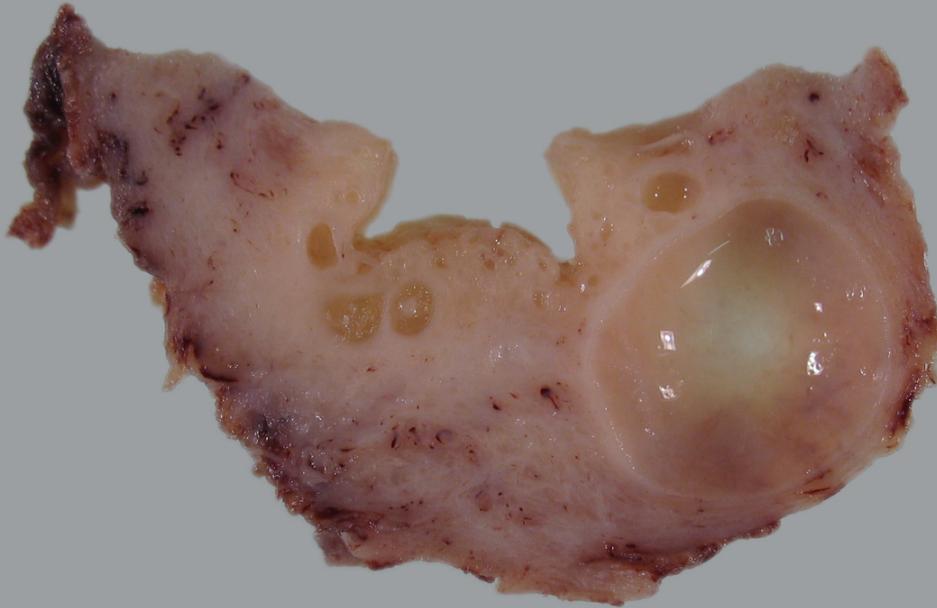
# ADENOCARCINOMA MUCINOSO DE TIPO GÁSTRICO



# ADENOCARCINOMA DE MÍNIMA DESVIACIÓN

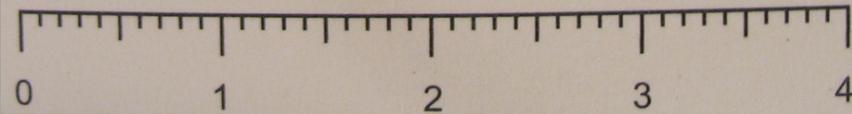
- GLÀNDULAS PEQUEÑAS
- MÁS RARAMENTE GLÀNDULAS QUÍSTICAS CON PROYECCIONES PAPILARES
- ESCASA RESPUESTA DESMOPLÁSICA
- ATIPIA CITOLÓGICA LEVE
- INVASIÓN PERINEURAL
- AFECTACIÓN PROFUNDA - PARAMETRIOS

# ADENOCARCINOMA DE MÍNIMA DESVIACIÓN



PATOLOGIA

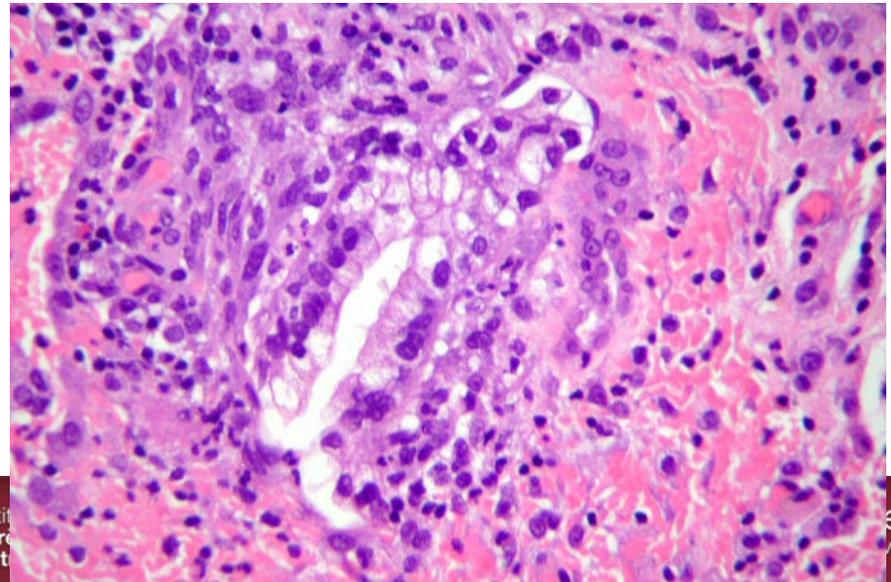
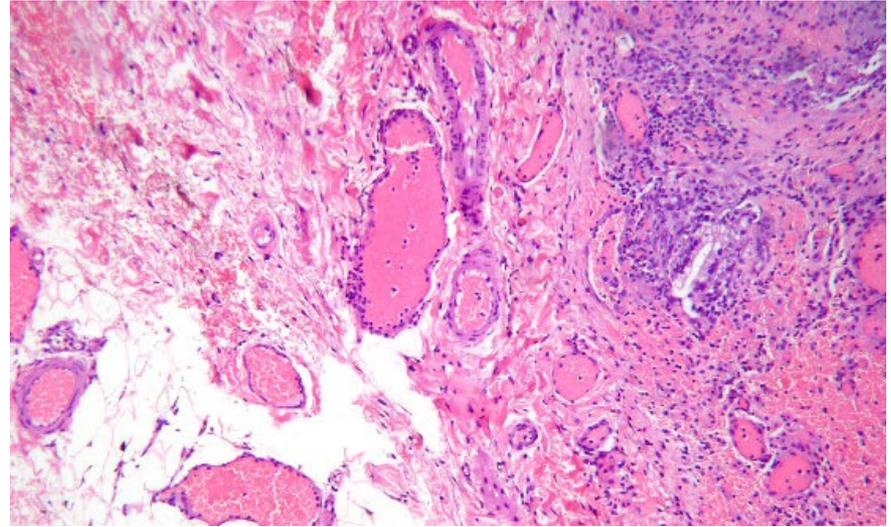
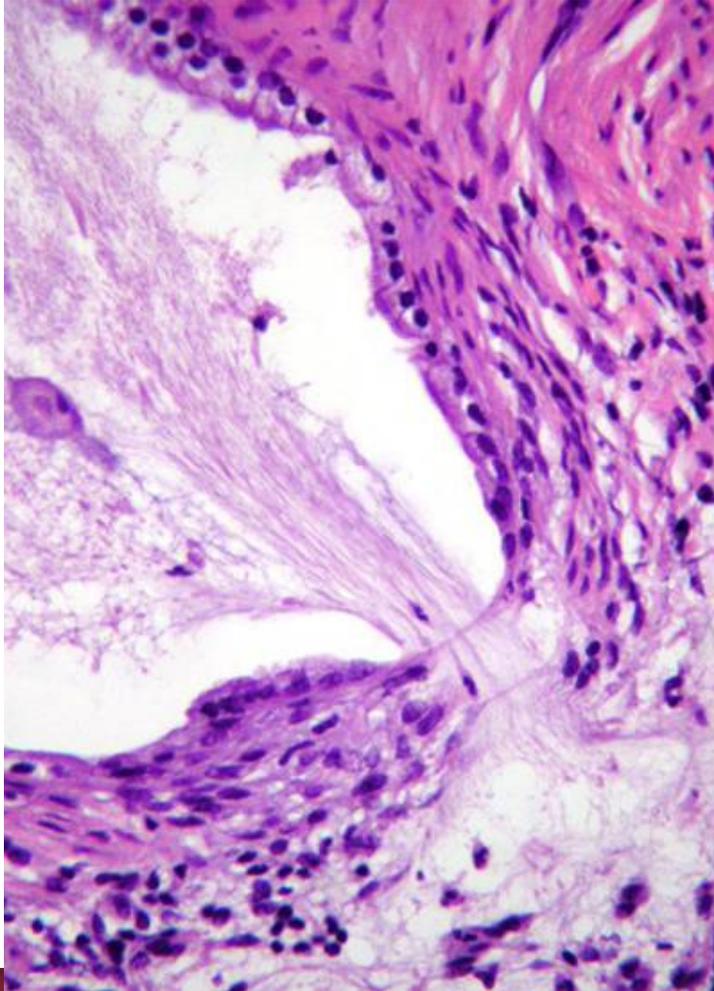
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PATOLOGIA

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# ADENOCARCINOMA DE MÍNIMA DESVIACIÓ



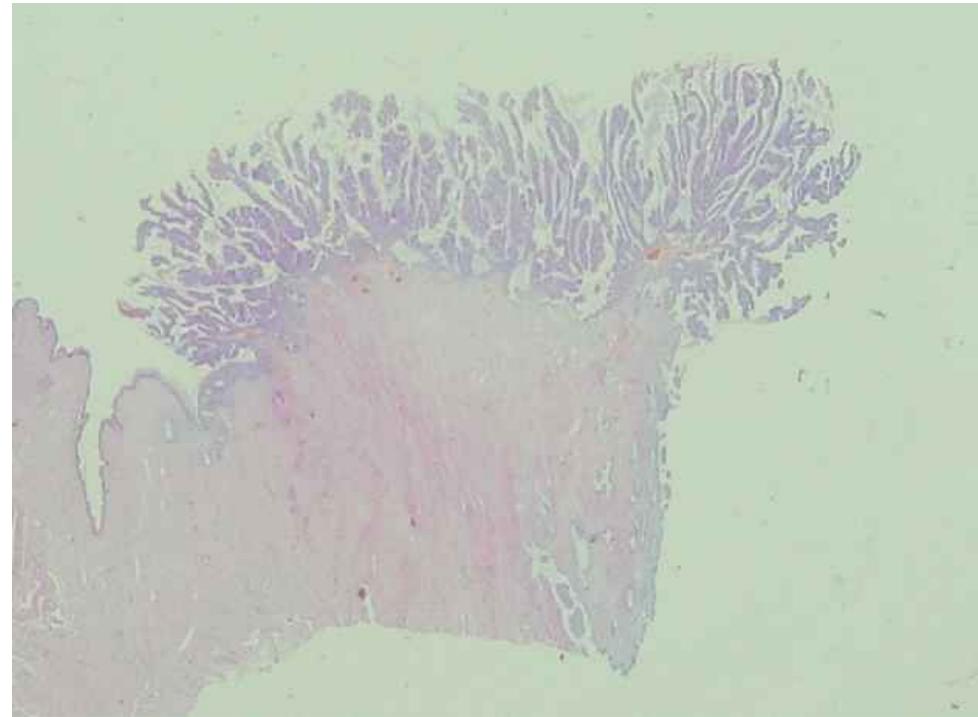
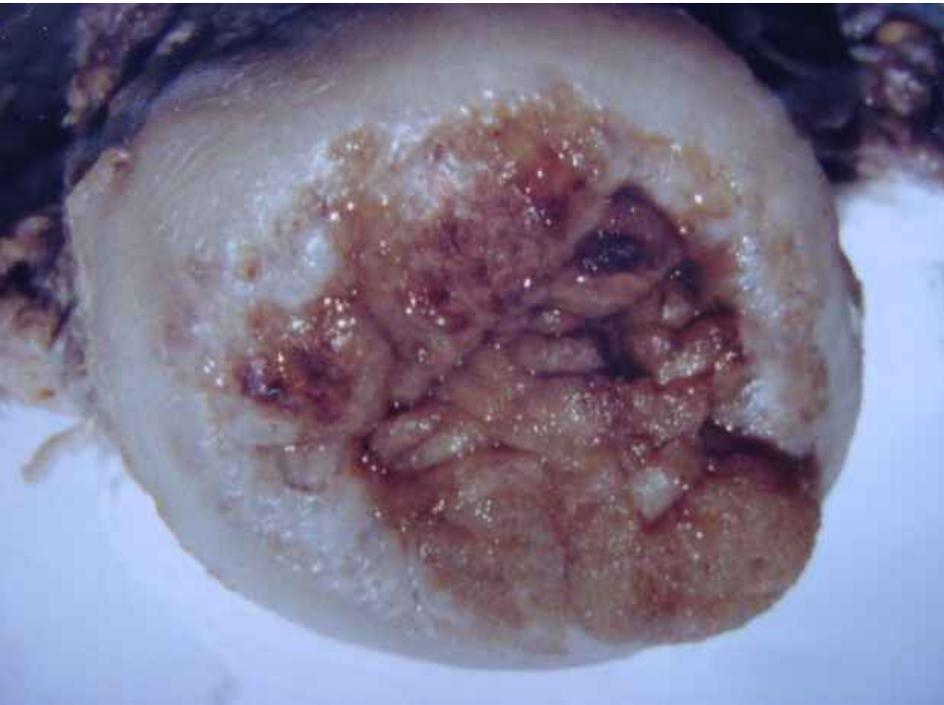
# ADENOCARCINOMA VILLOGLANDULAR

- 35 AÑOS
- HPV
- BUEN PRONÓSTICO
- NO DIAGNOSTICAR SI HAY COMPONENTE INFILTRATIVO PROMINENTE O ATIPIA CITOLÓGICA SEVERA
- NO DIAGNOSTICAR EN BIÓPSIAS, SI NO SE ESTUDIA TODA LA LESIÓN

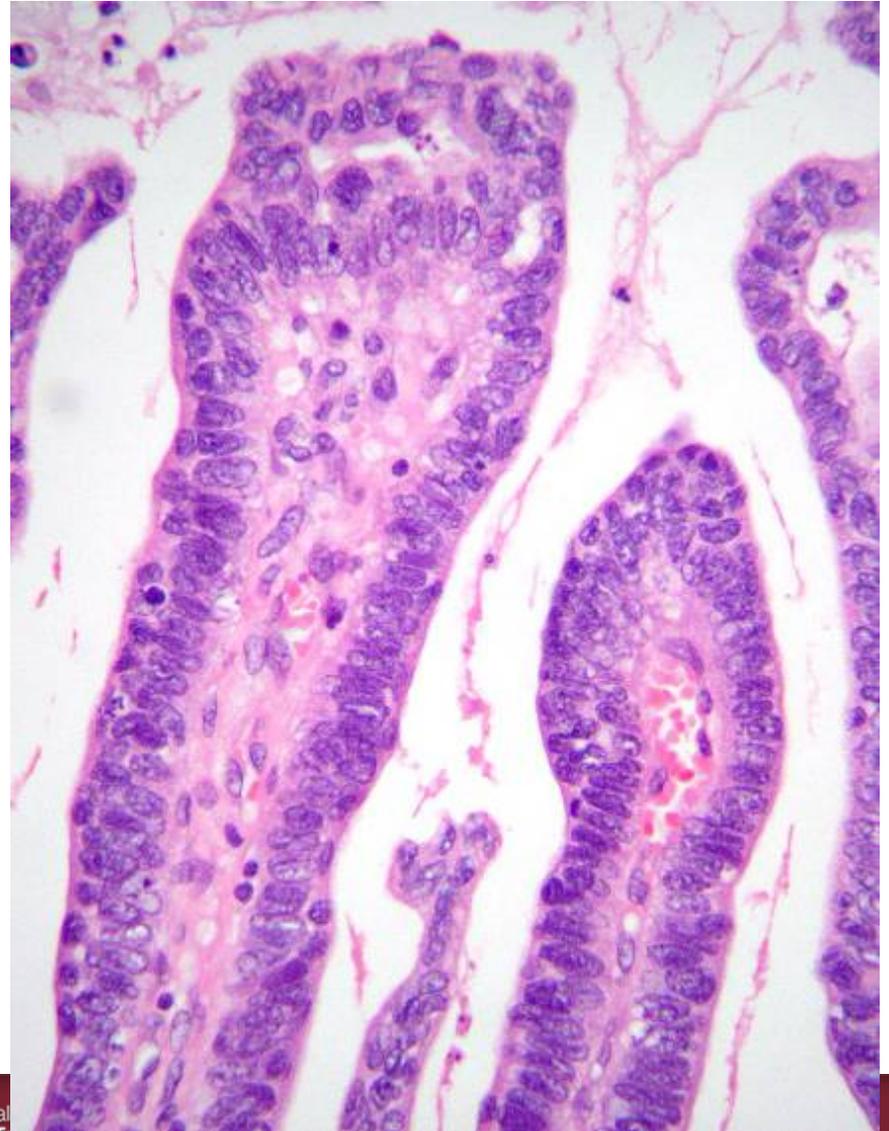
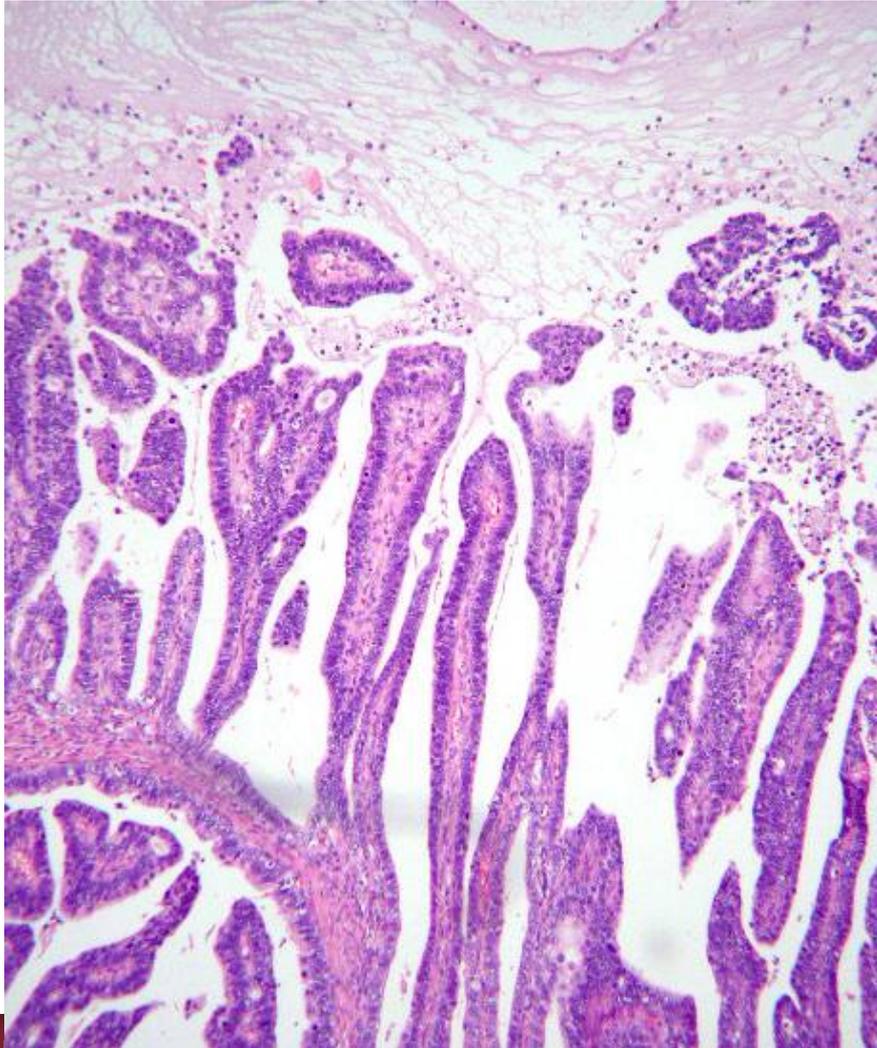
# ADENOCARCINOMA VILLOGLANDULAR

- COMPONENTE PAPILAR SUPERFICIAL
- PAPILAS ALTAS Y DELGADAS
- EPITELIO PARECIDO AL DEL ADC CONVENCIONAL
- PSEUDOESTRATIFICACIÓN
- ATIPIA LEVE-MODERADA
- POCA ACTIVIDAD MITÓTICA

# ADENOCARCINOMA VILLOGLANDULAR

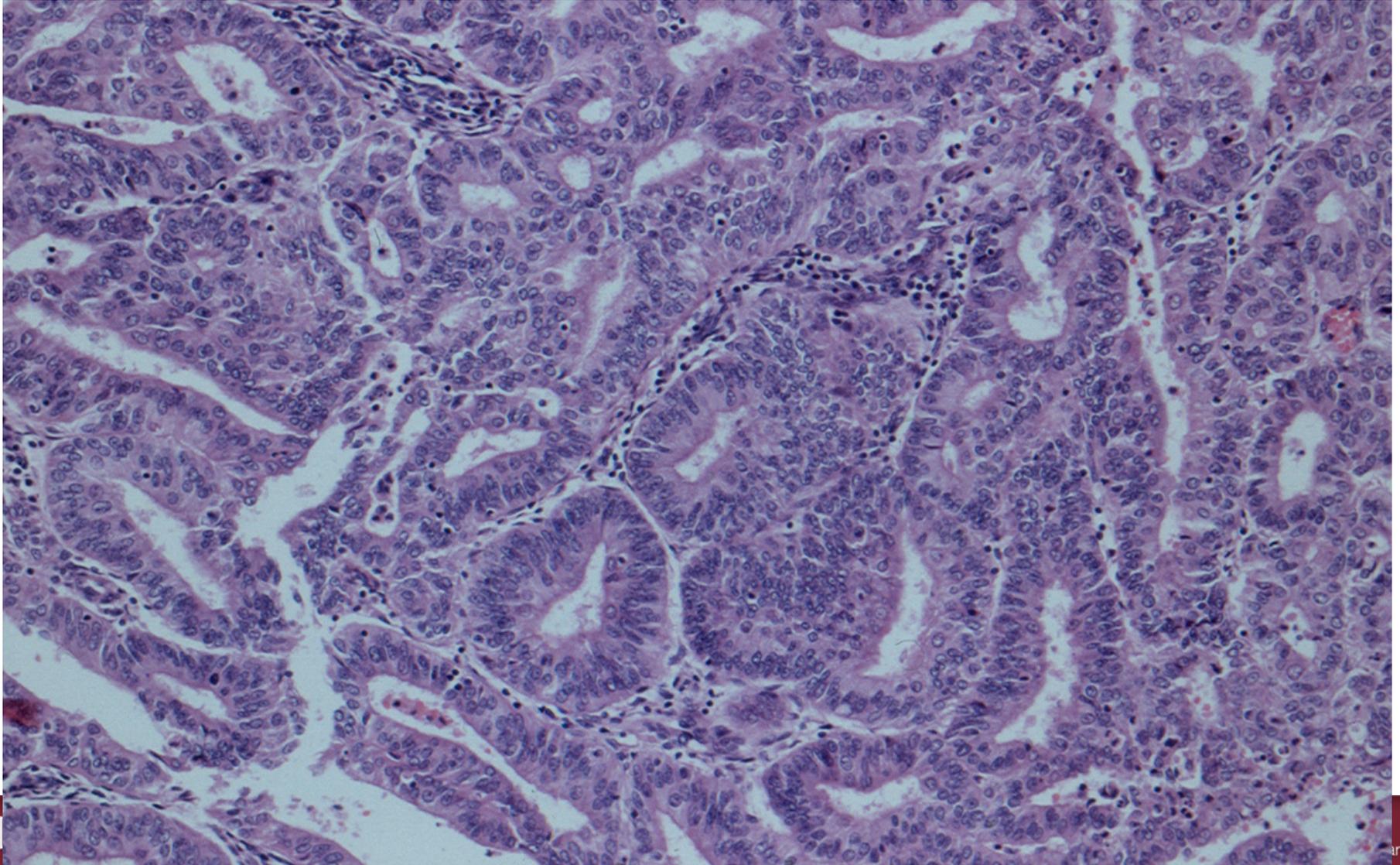


# ADENOCARCINOMA VILLOGLANDULAR

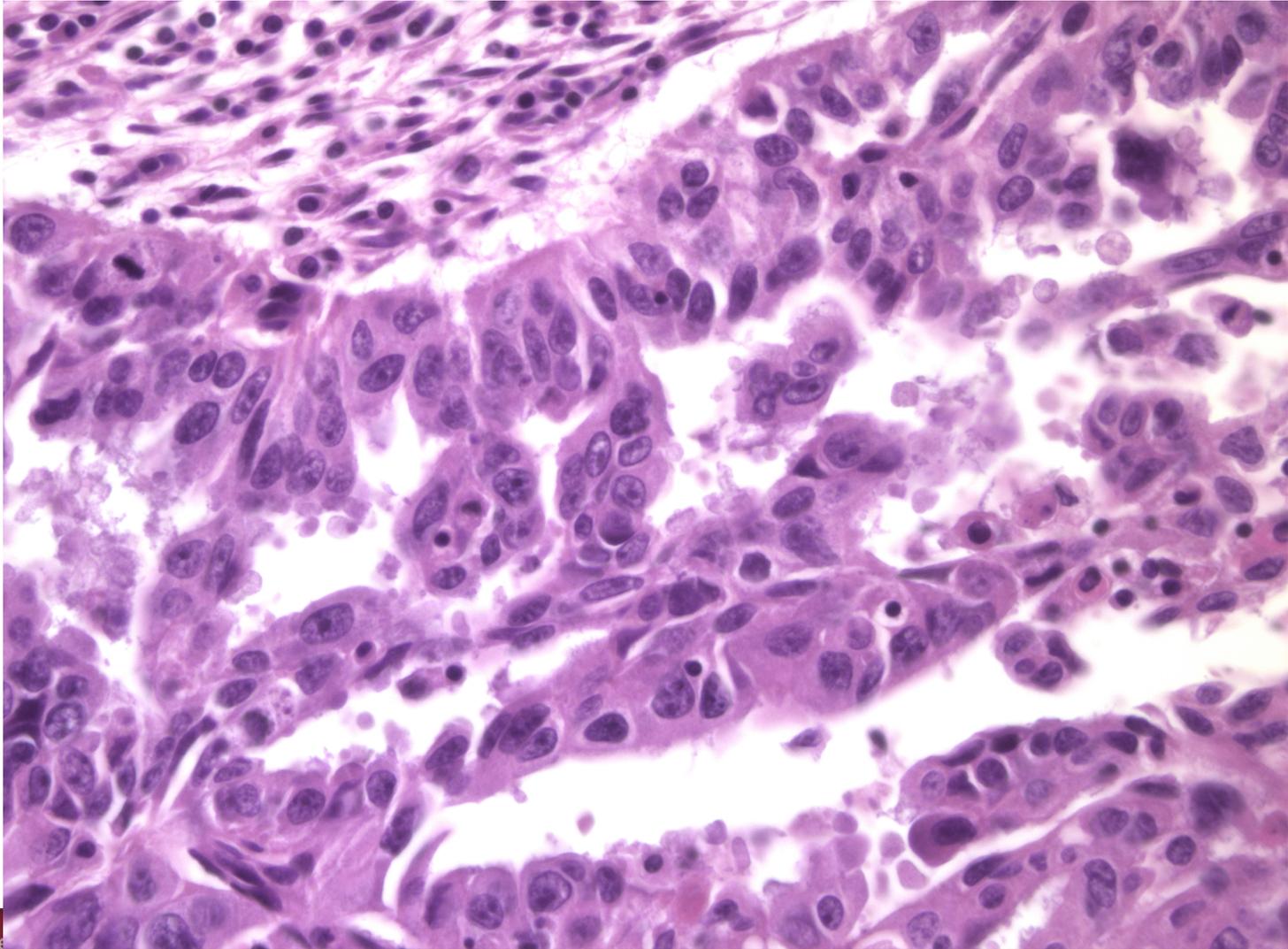


LOS ADENOCARCINOMAS  
ENDOMETRIOIDES , SEROSOS Y DE  
CÉLULAS CLARAS SON POCO  
FRECUENTES Y SIEMPRE SE HA DE  
DESCARTAR EXTENSIÓN DE TUMOR  
PRIMARIO ENDOMETRIAL /OVÁRICO

# CARCINOMA ENDOMETRIOIDE

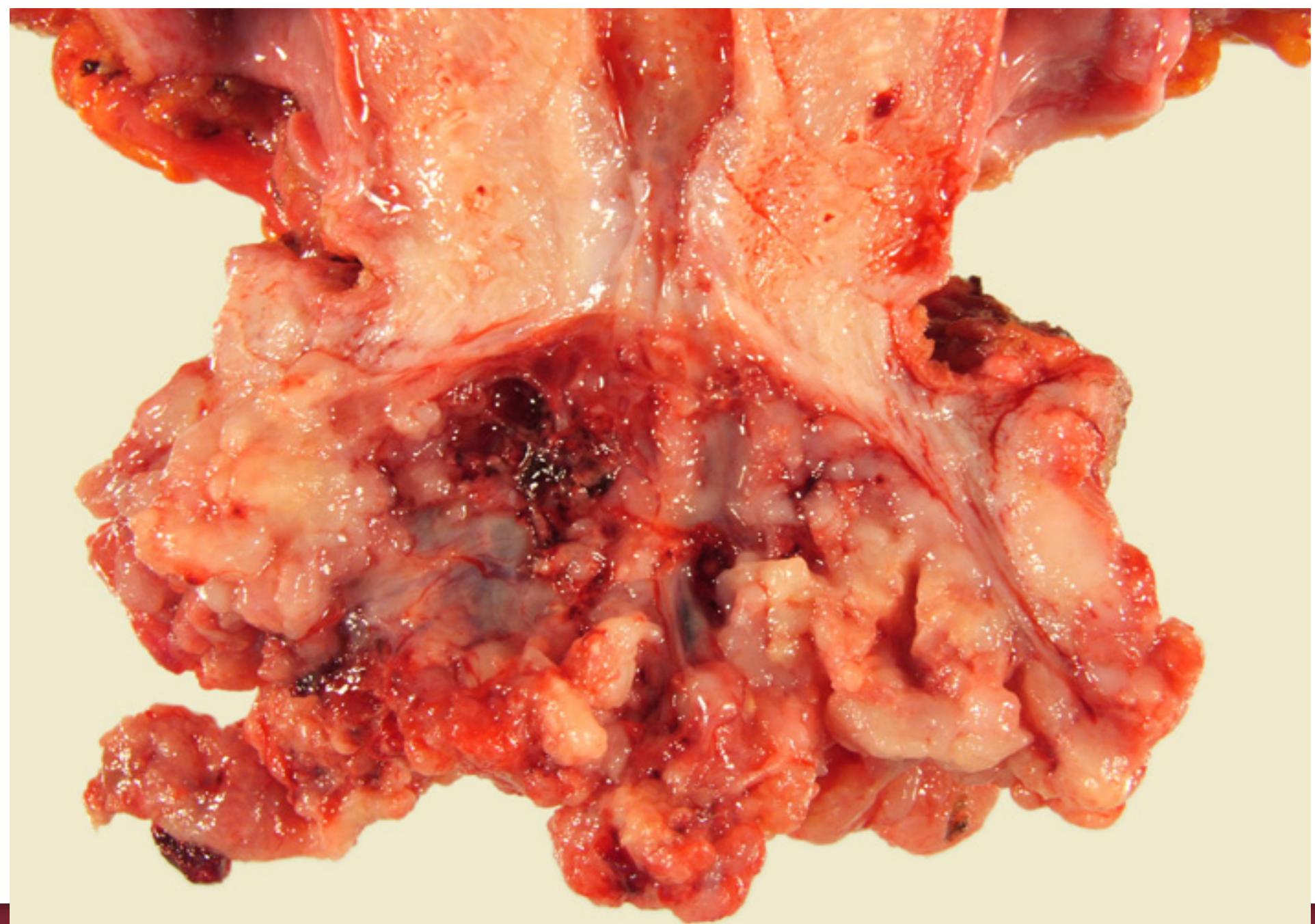


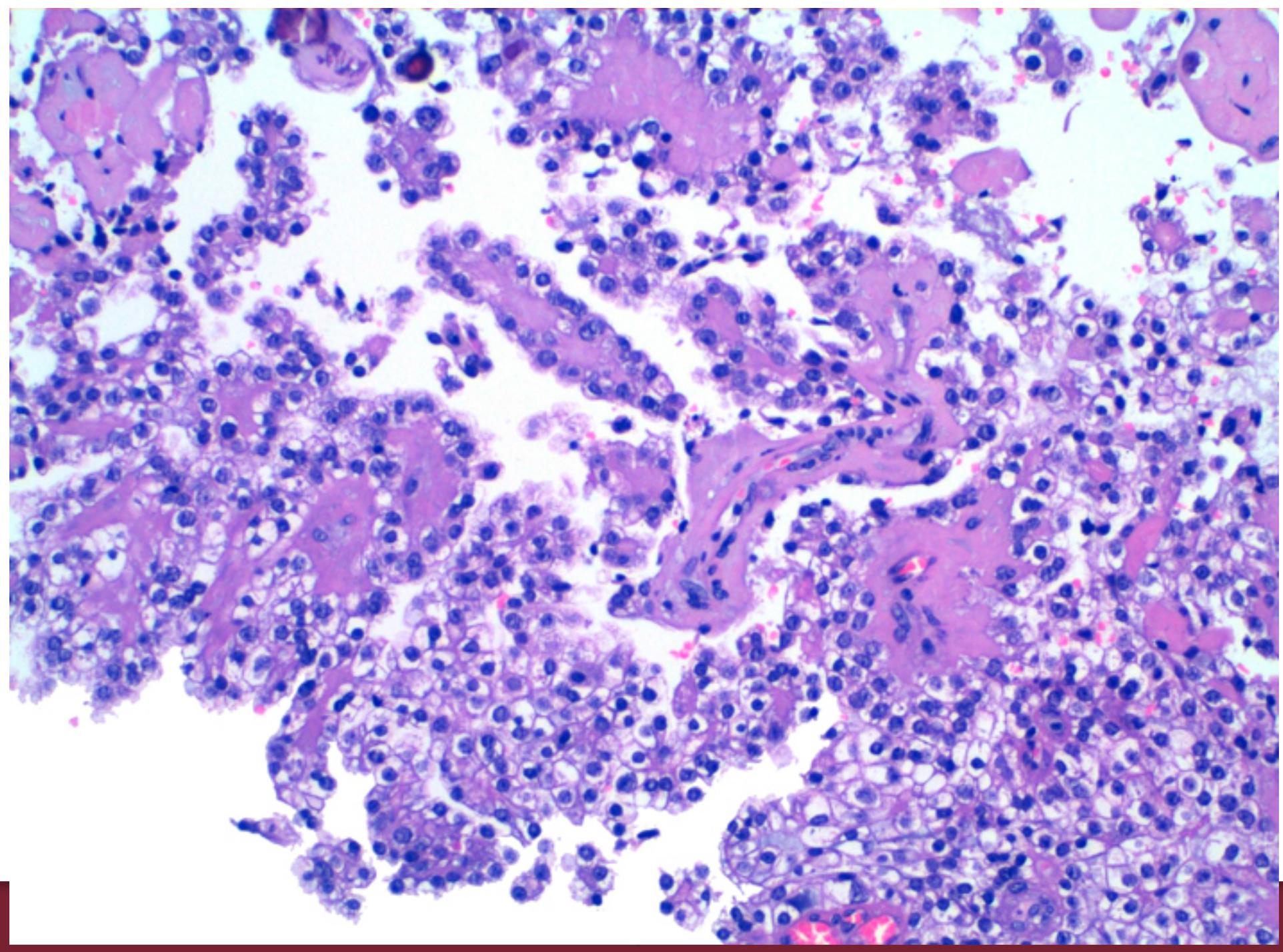
# CARCINOMA SEROSO



# CARCINOMA CÉLULAS CLARAS

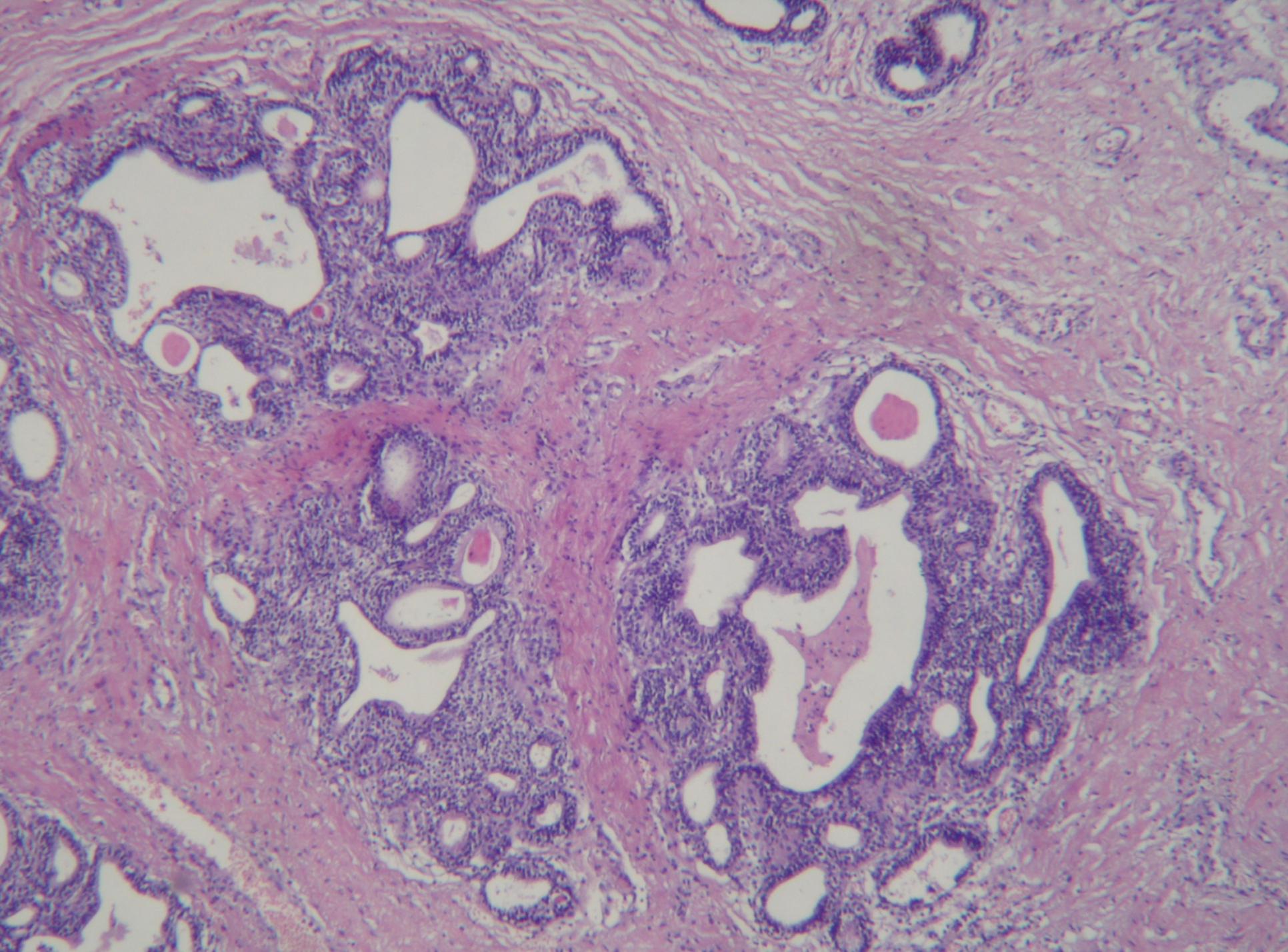


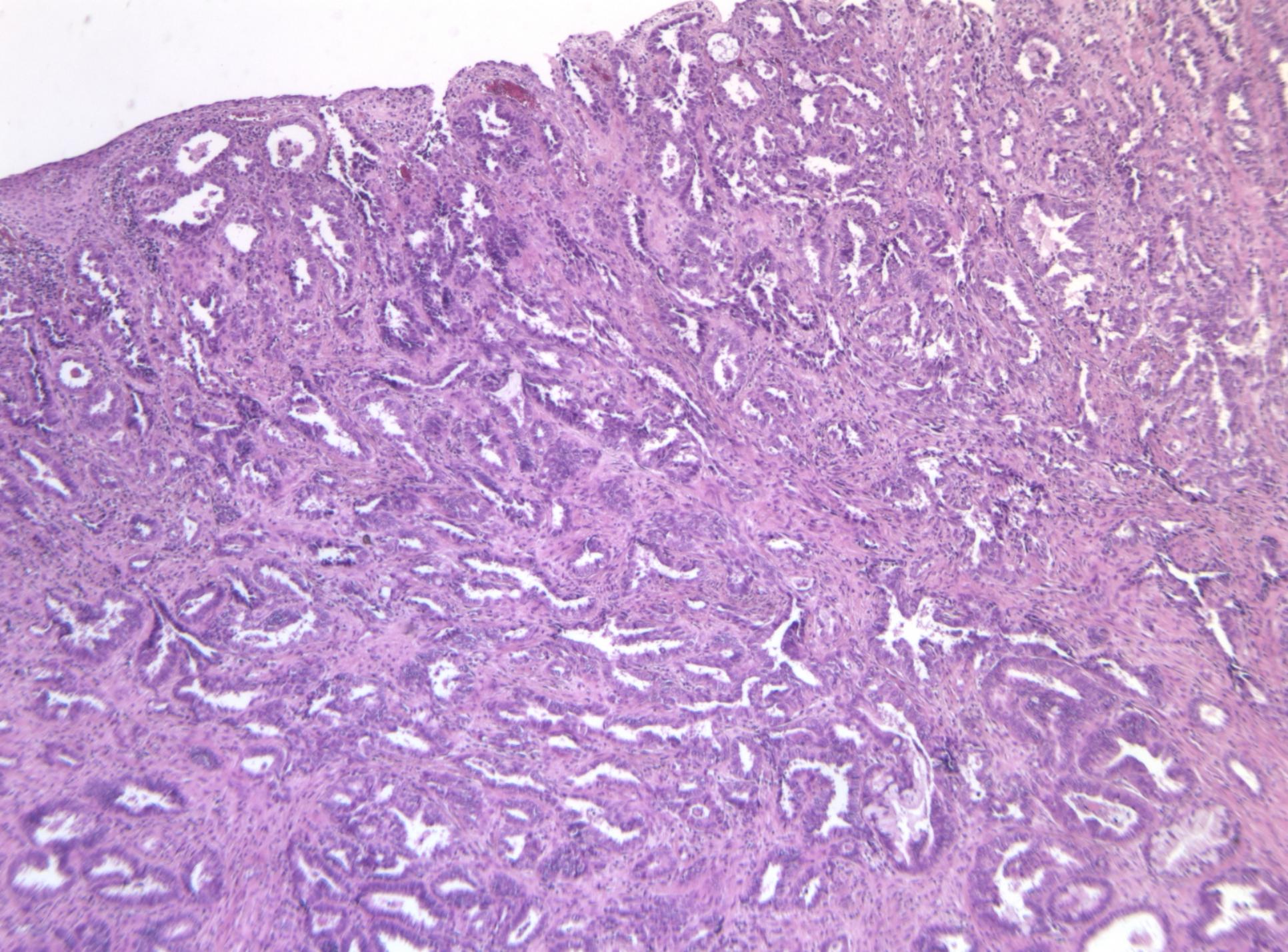


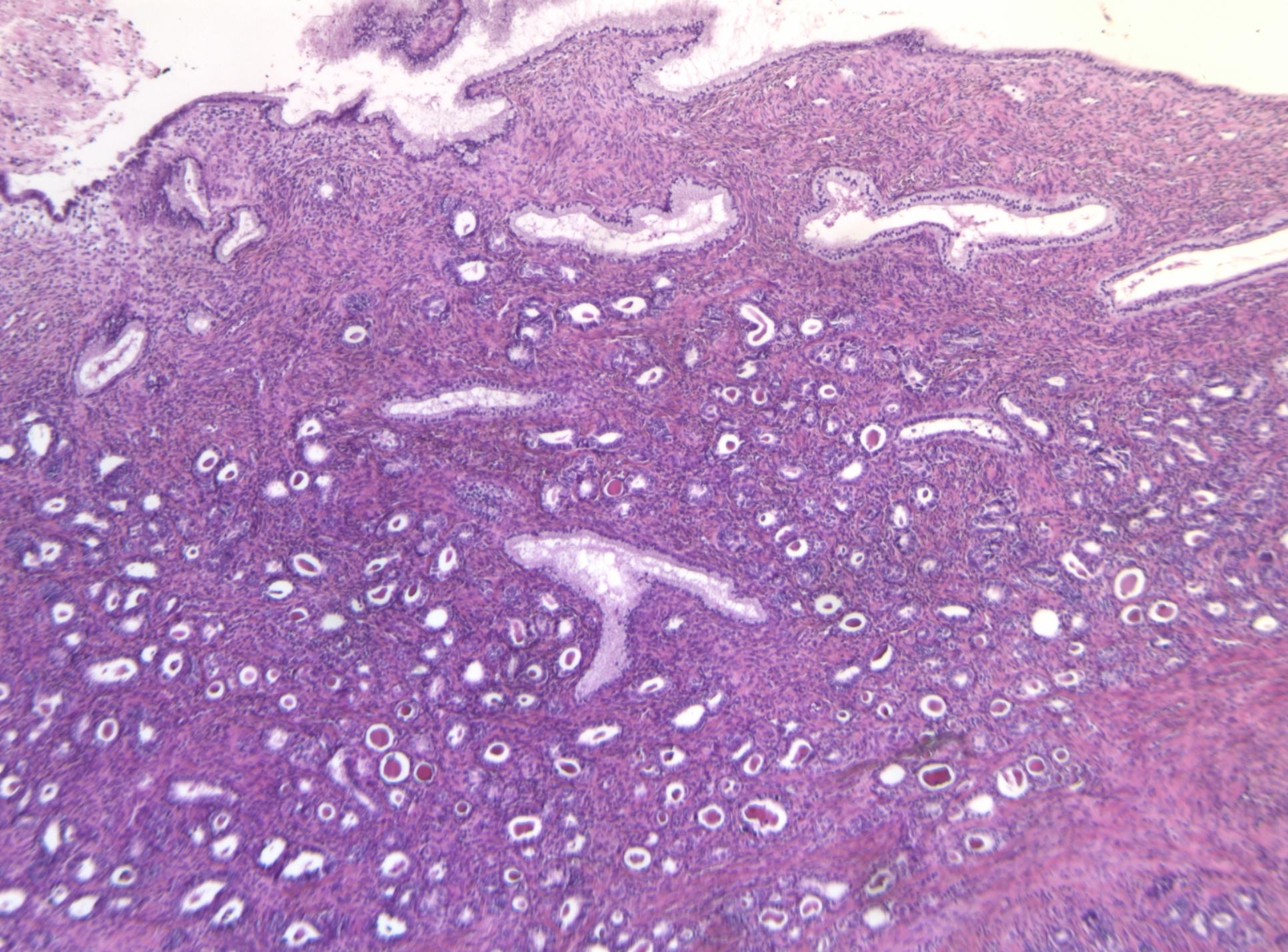


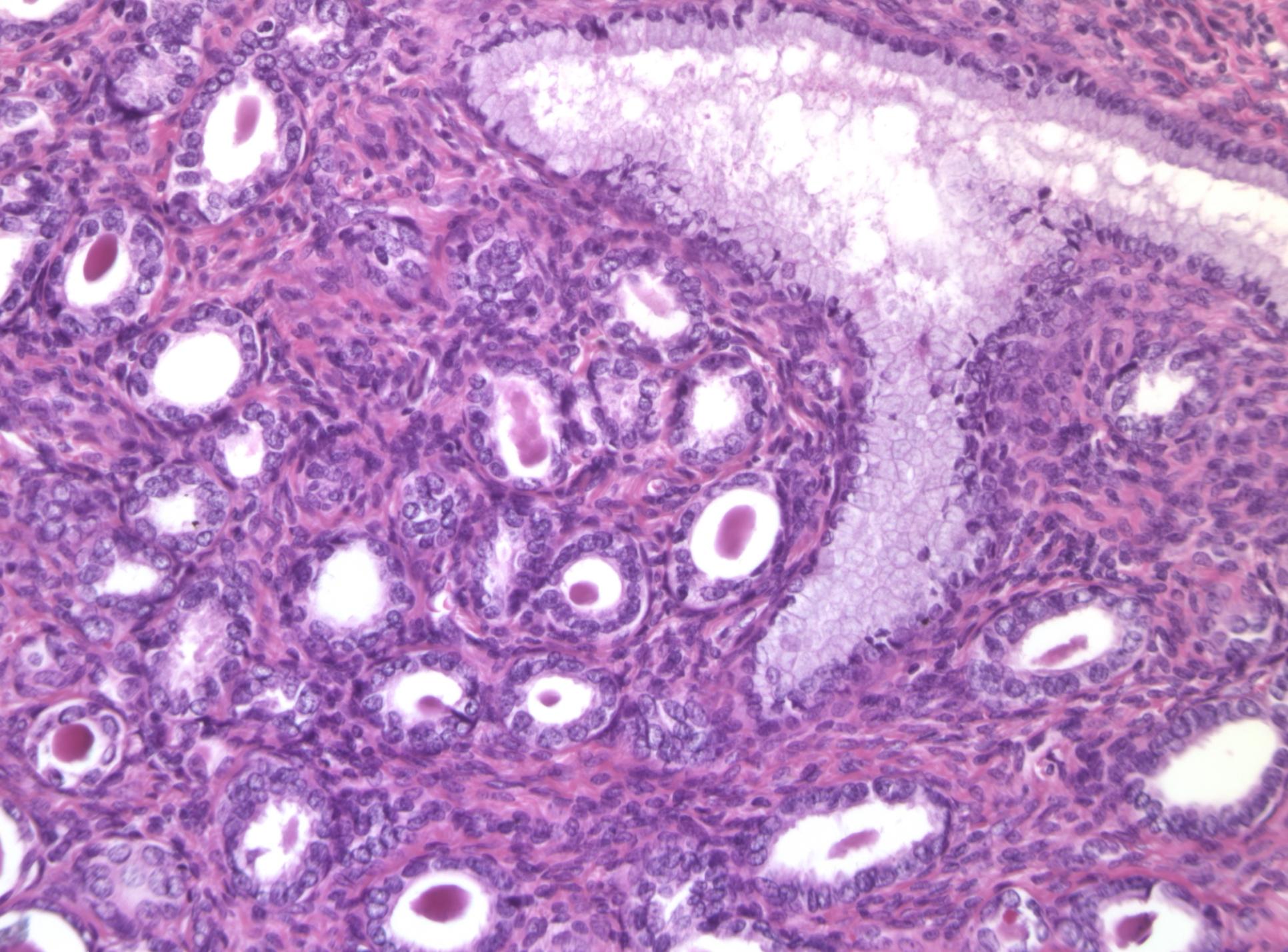
# ADENOCARCINOMA MESONÉFRICO

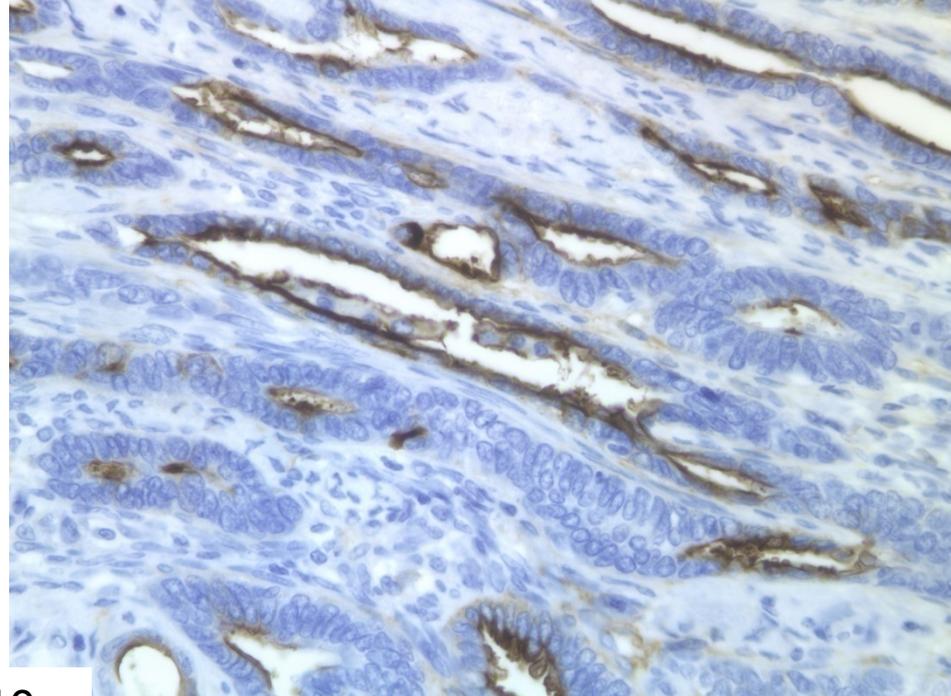
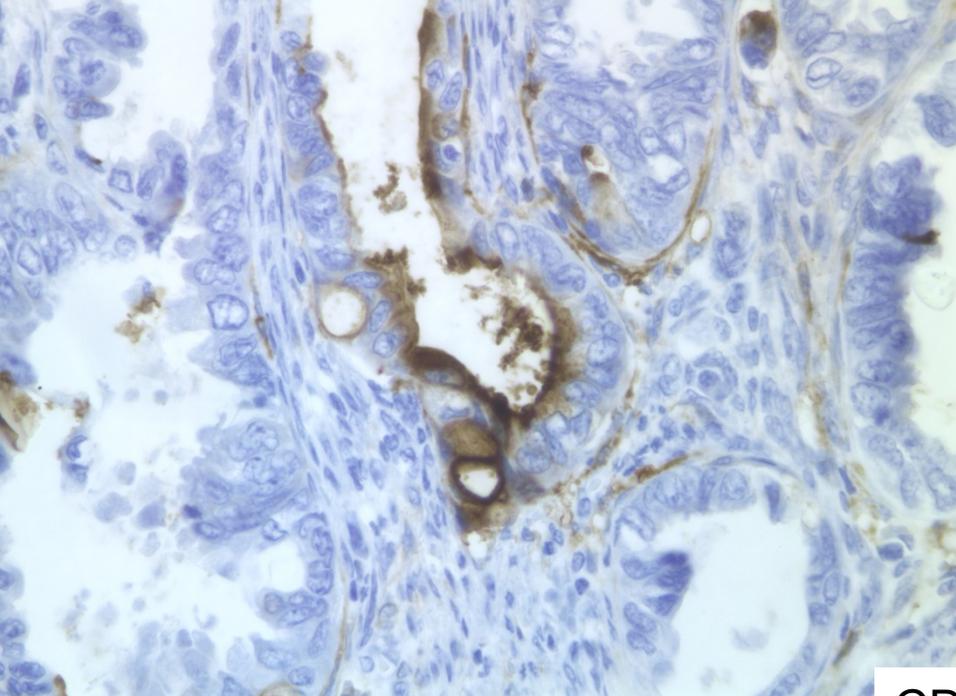
- 50 AÑOS
- NO HPV
- DERIVADOS DE RESTOS MESONÉFRICOS EN PARED LATERAL DE CÉRVIX.
- MUY POCO FRECUENTE.
- VARIEDAD DE PATRONES HISTOLÓGICOS
- EXPRESIÓN DE CD10



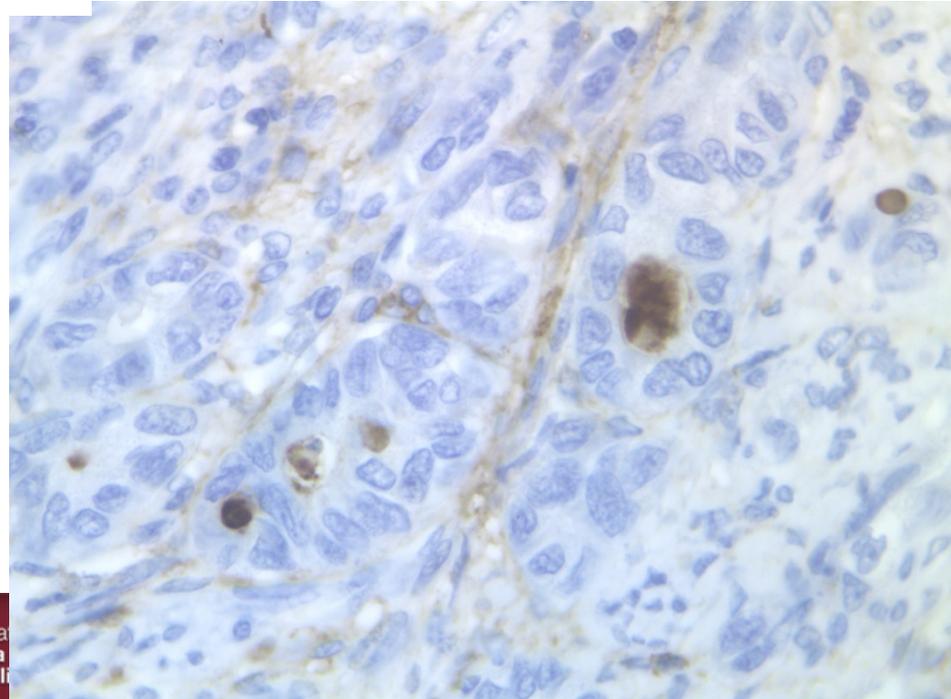
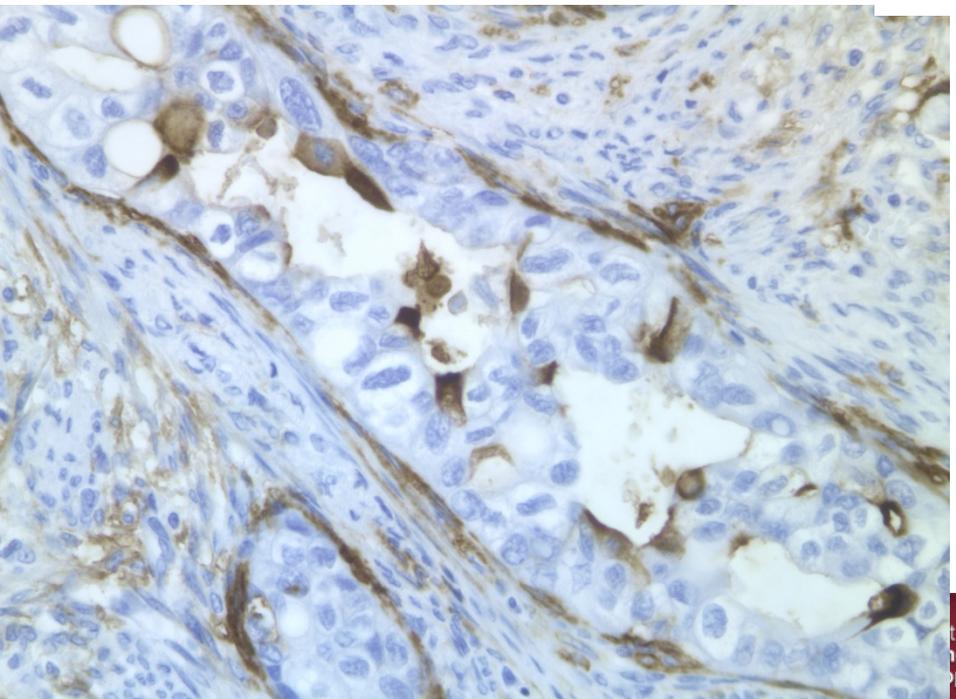






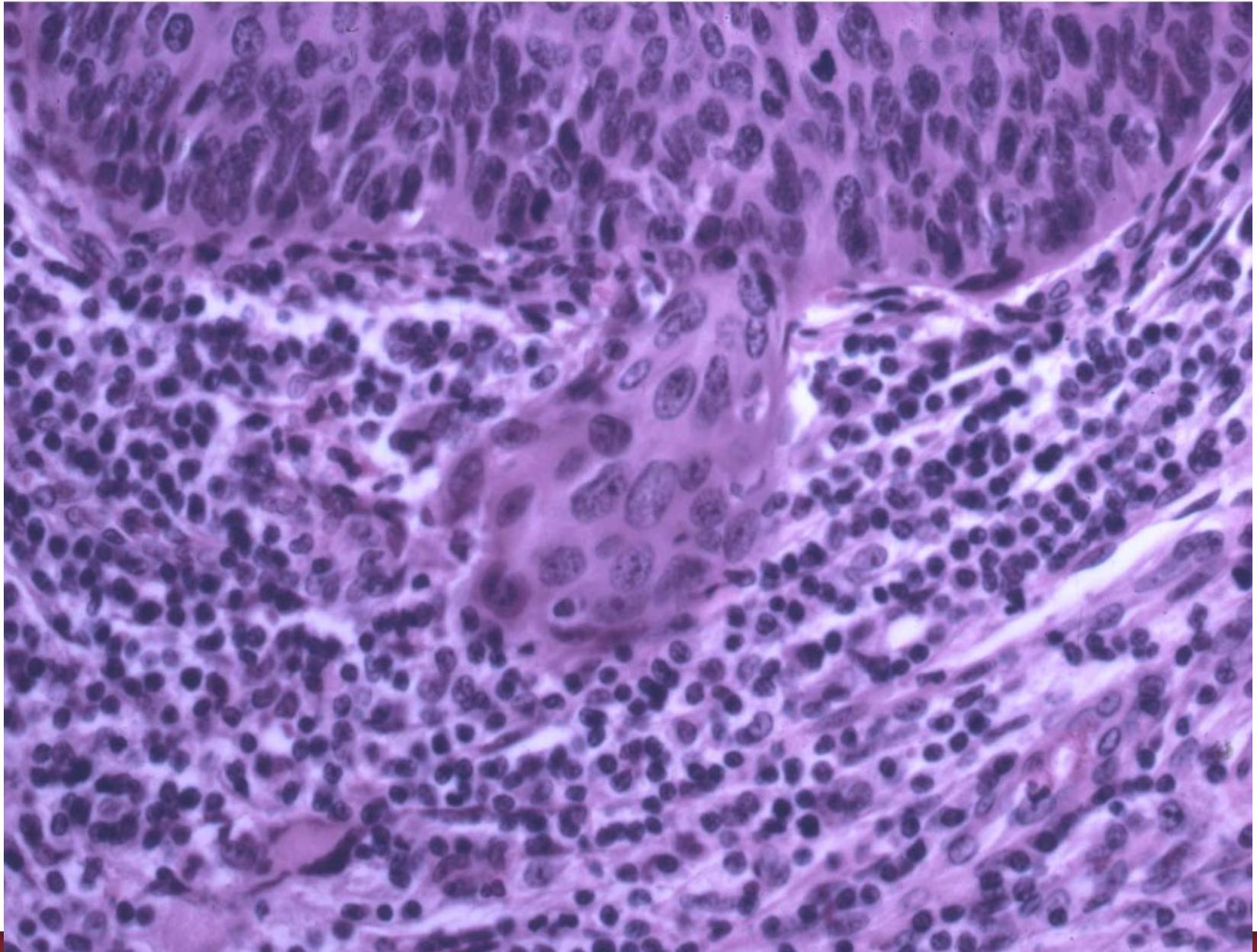


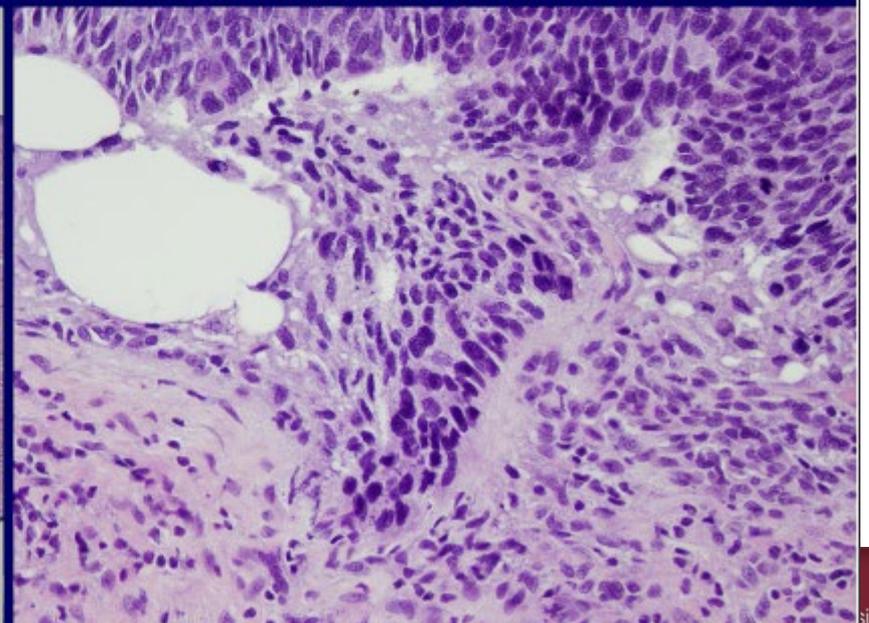
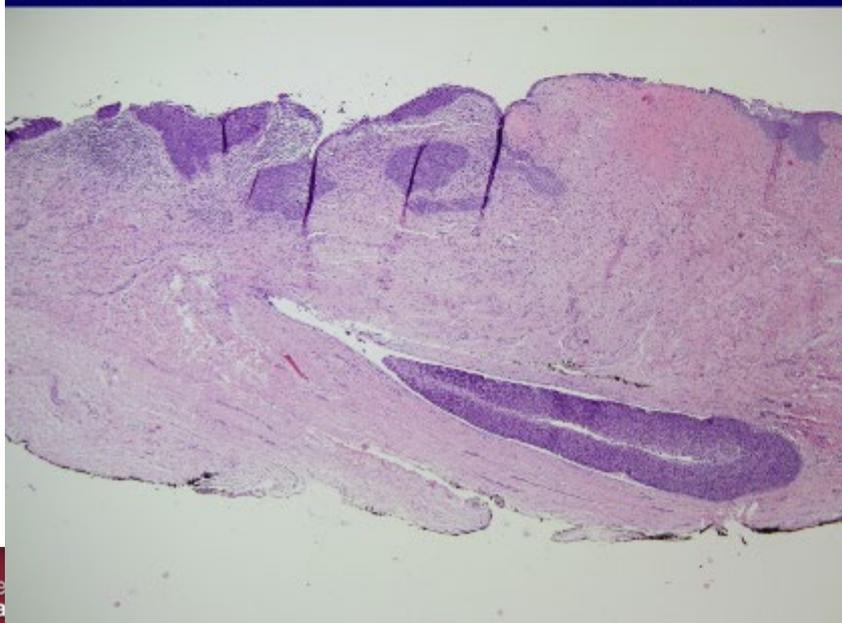
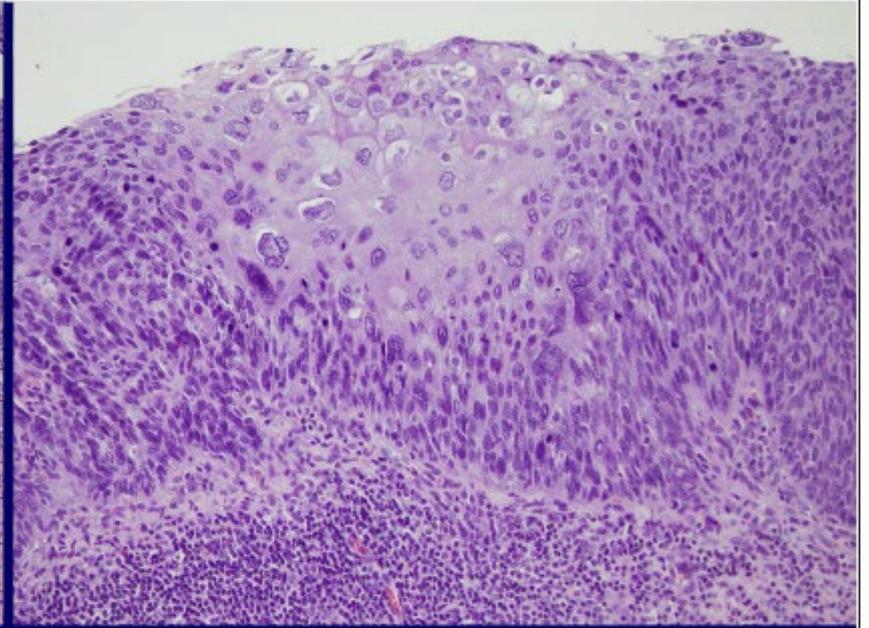
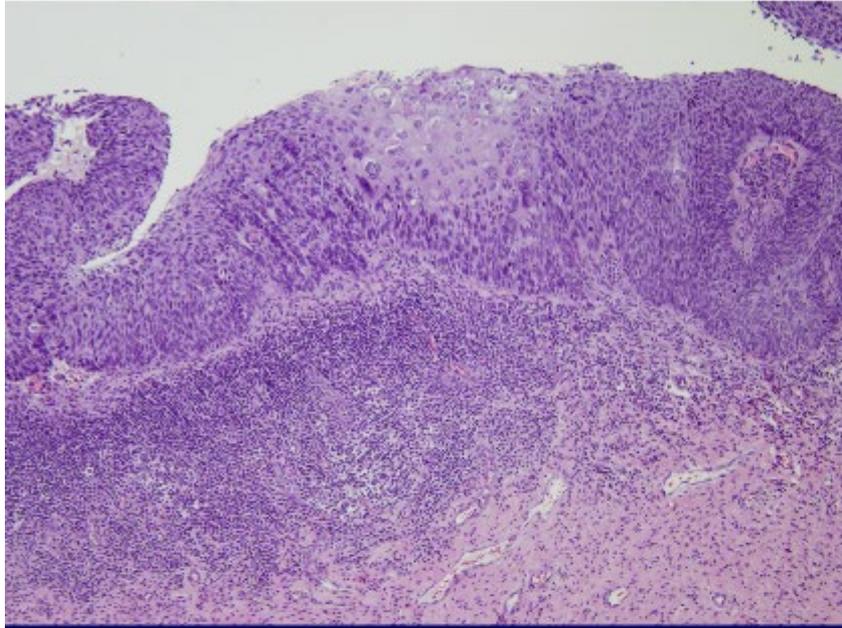
CD10



# CRITERIOS DE INVASIÓN

- Características morfológicas
  - Maduración de células epiteliales
    - Citoplasma eosinofílico abundante
  - Evidència d'activitat metabòlica
    - Nucléolos
- Discontinuidad de la membrana basal
  - Lenguas de epitelio
- Reacción estromal
  - Inflamación (puede ser granulomatosa)
  - Densa
  - Fibrosis / patrón arremolinado

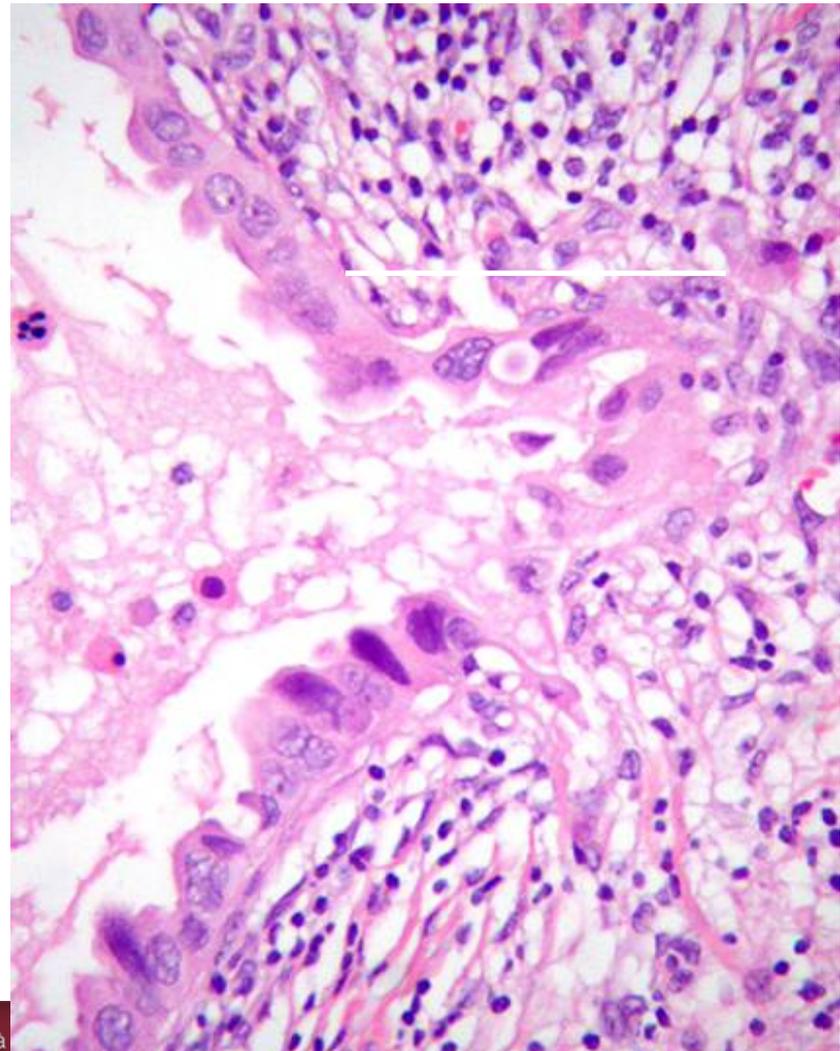
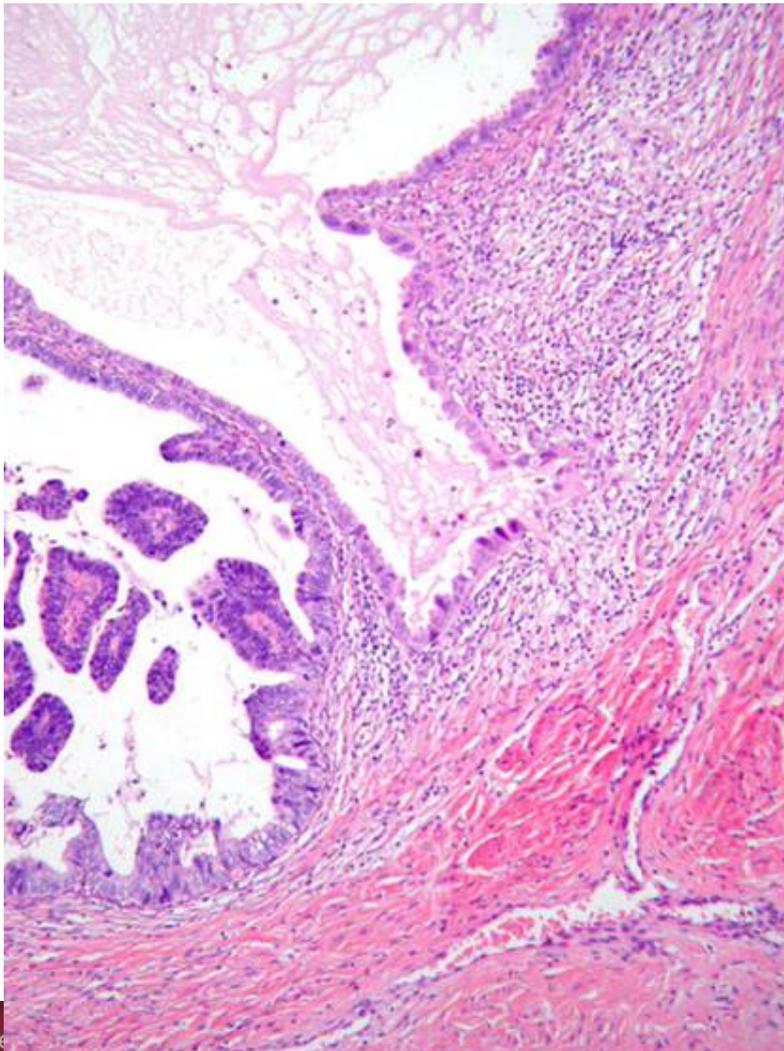


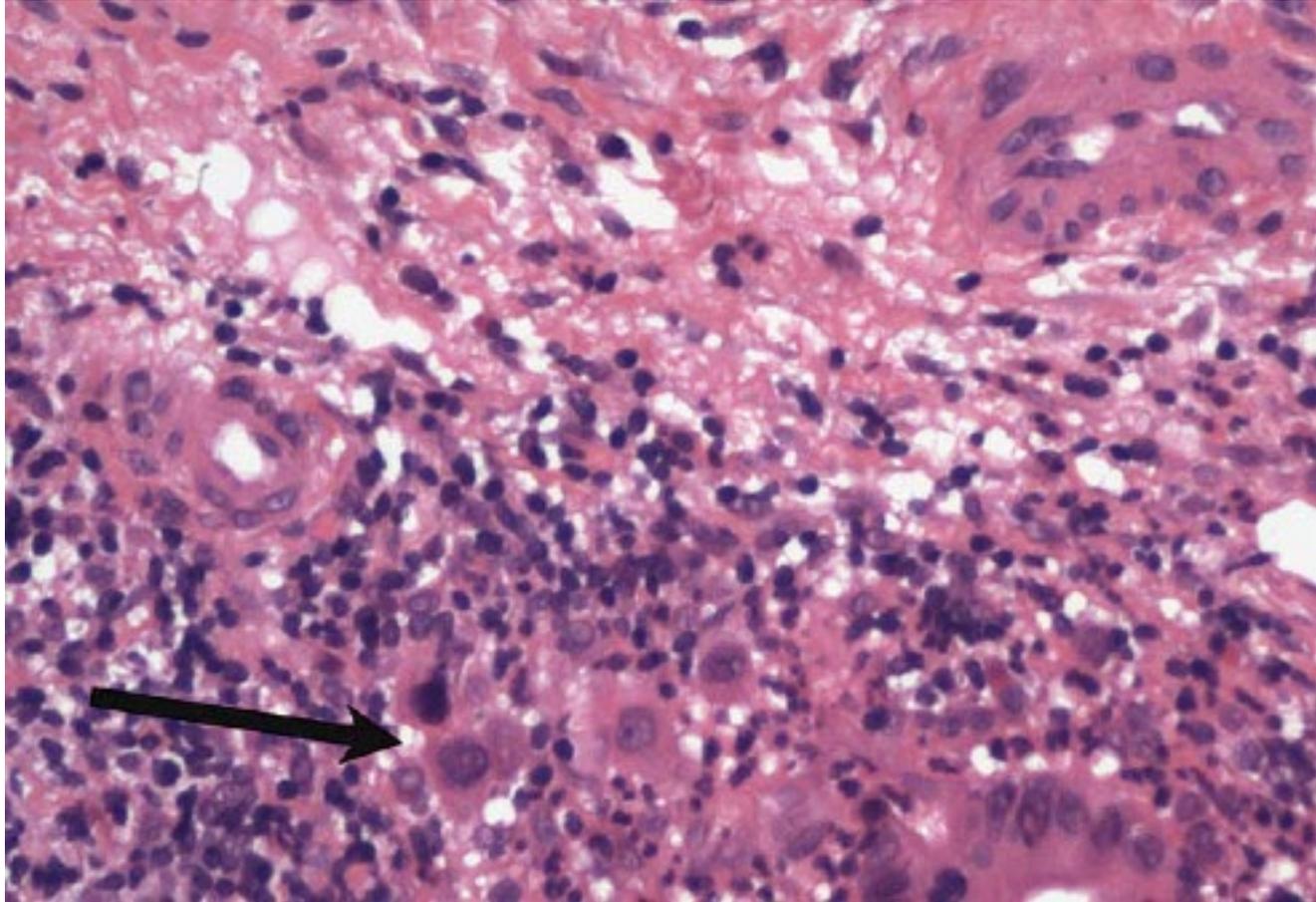


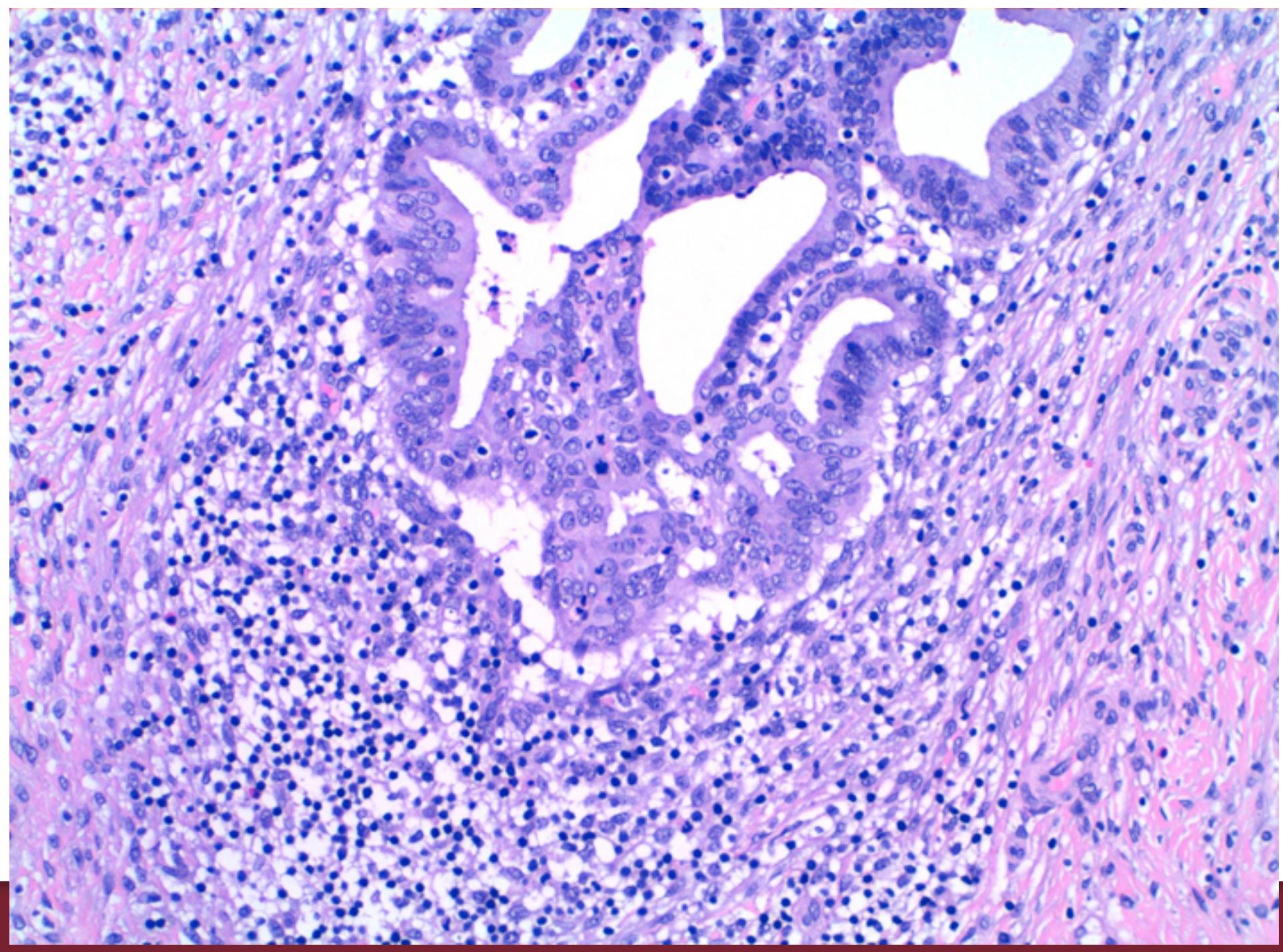
# ADC CRITERIOS DE INVASIÓN

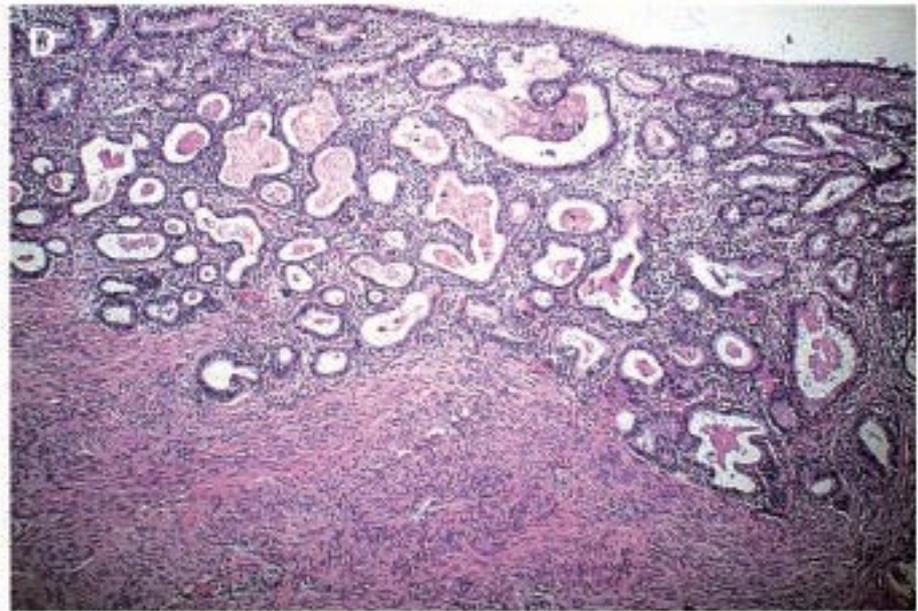
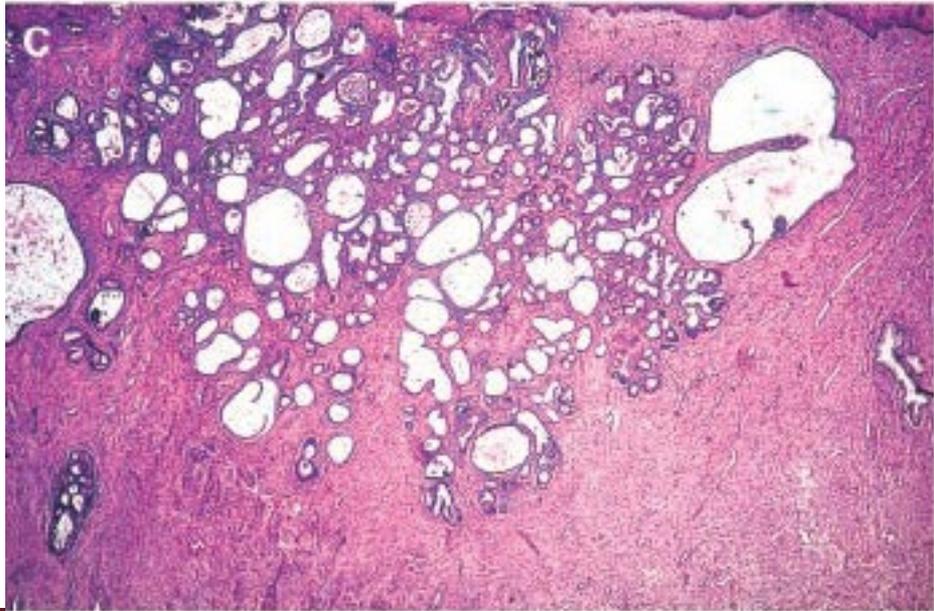
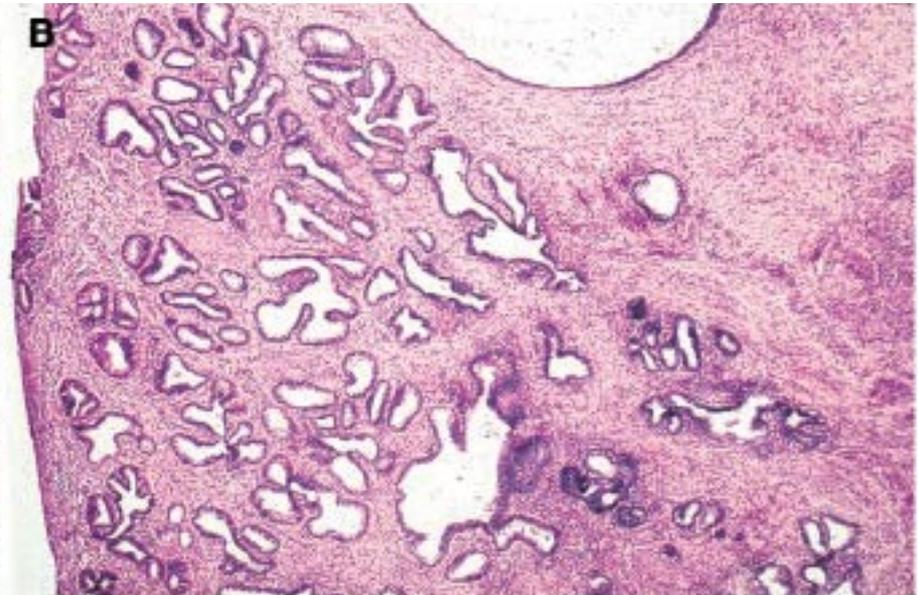
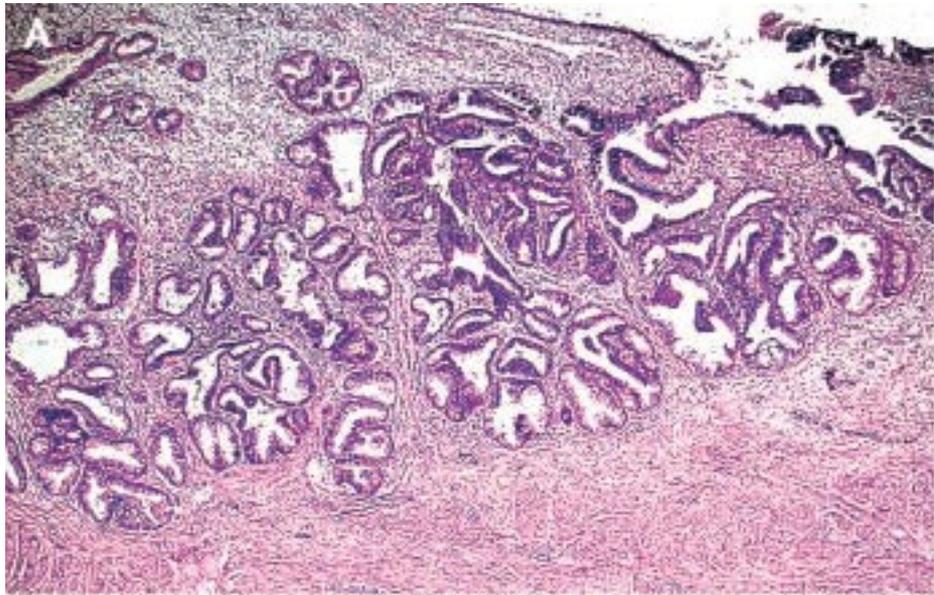
- Glándulas o nidos de aspecto infiltrativo
  - Glándulas atípicas más allá de la porción profunda de glándulas endocervicales normales
  - Glándulas demasiado complejas para ser AIS
  - Glándulas neoplásicas con reacción estromal
- 
- DIFÍCIL MEDICIÓN EXACTA DE LESIONES INFILTRANTES

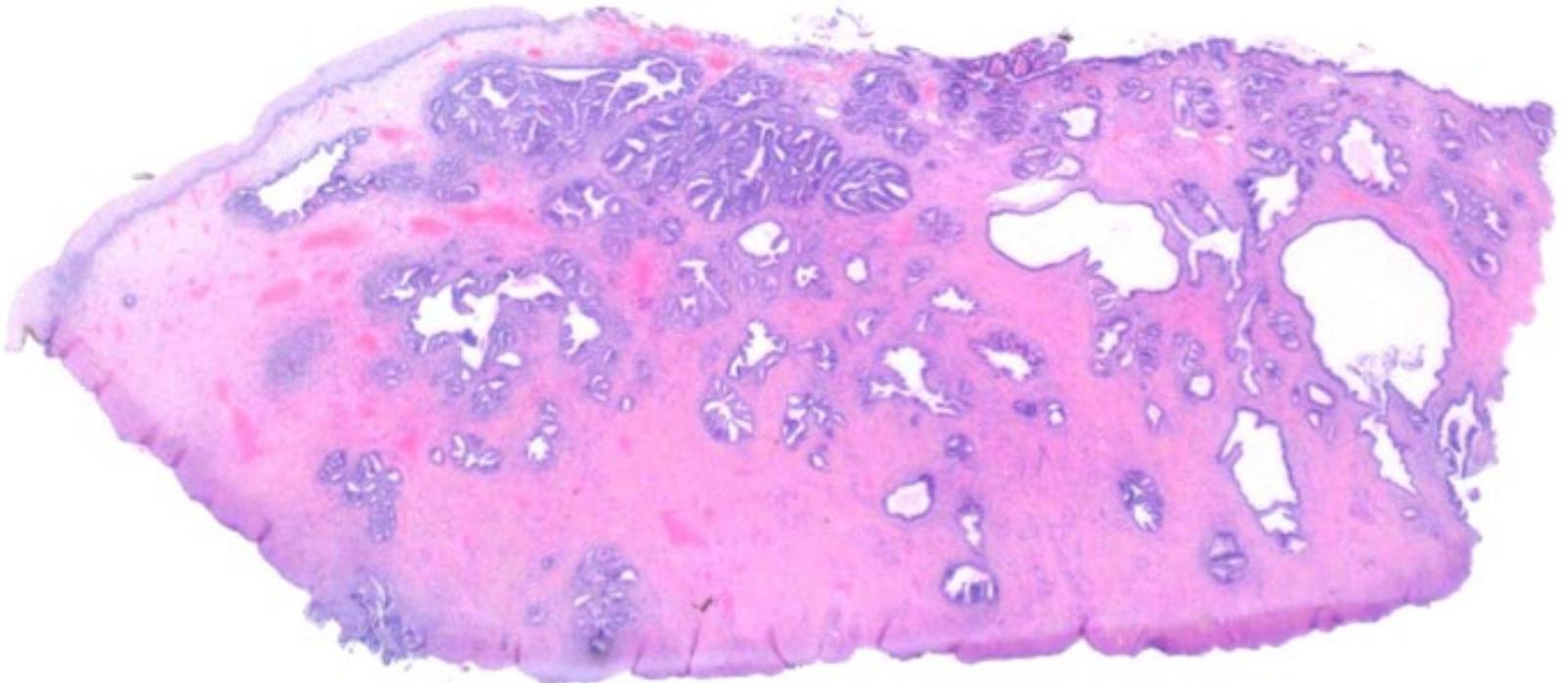
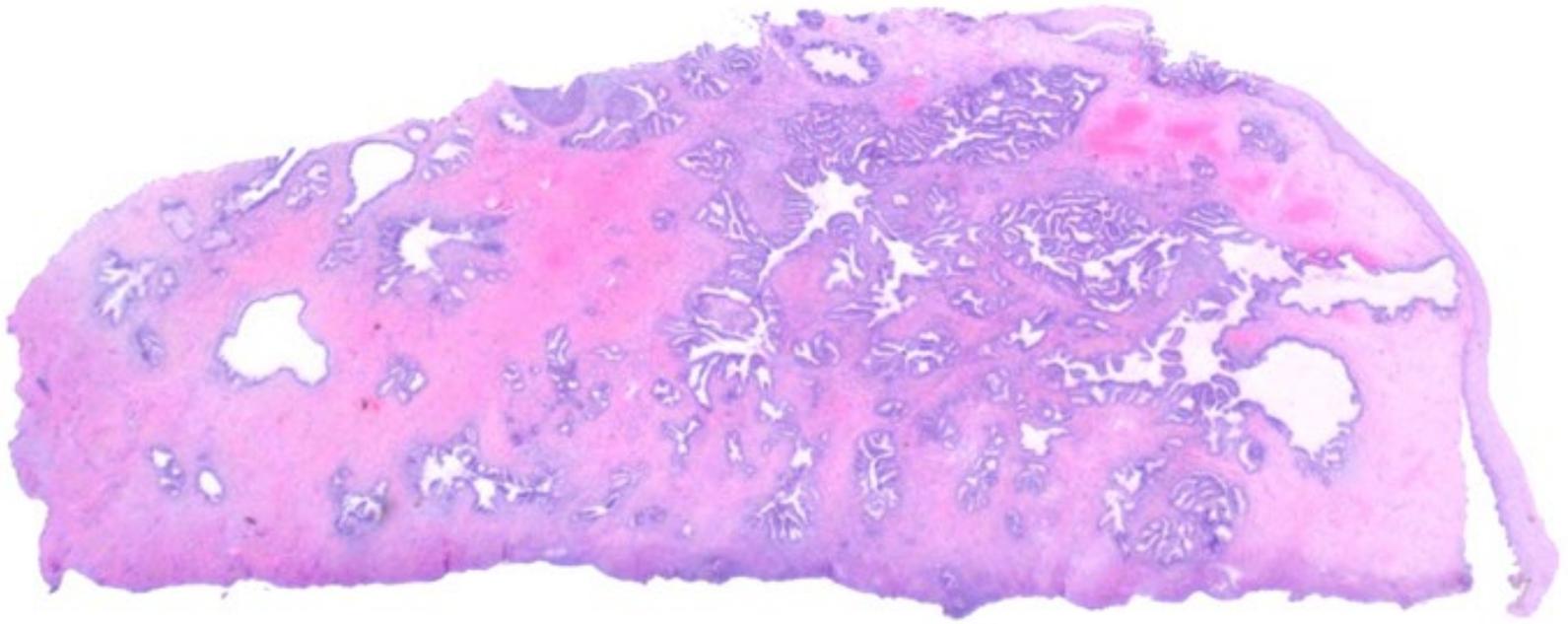
# ADENOCARCINOMA INFILTRANTE











## Original Article

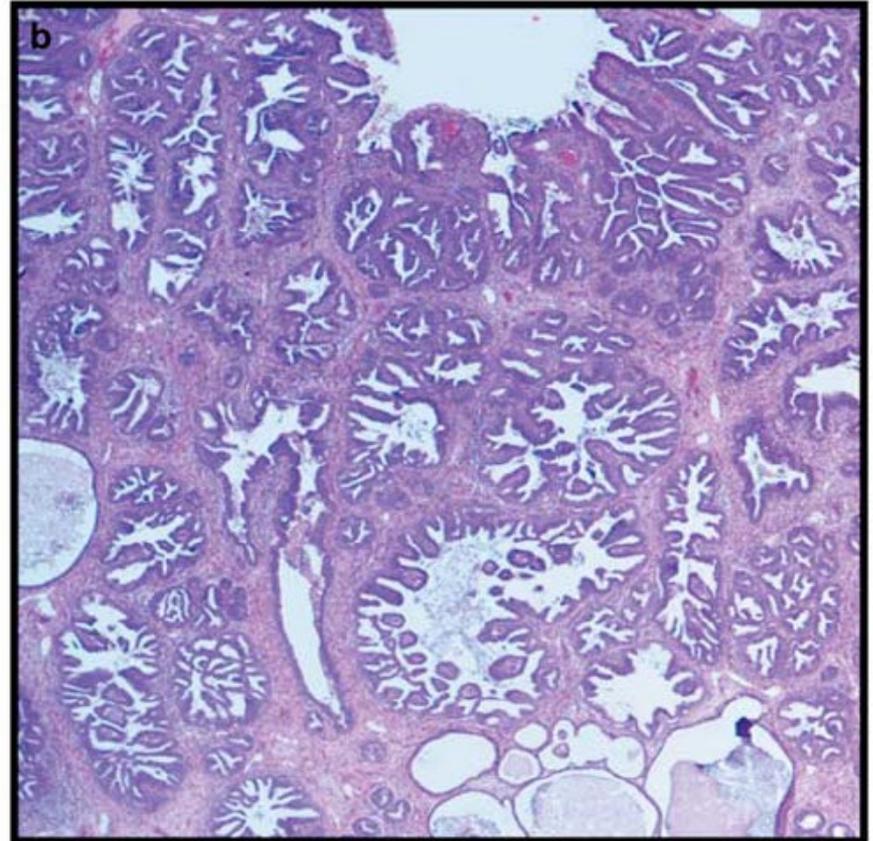
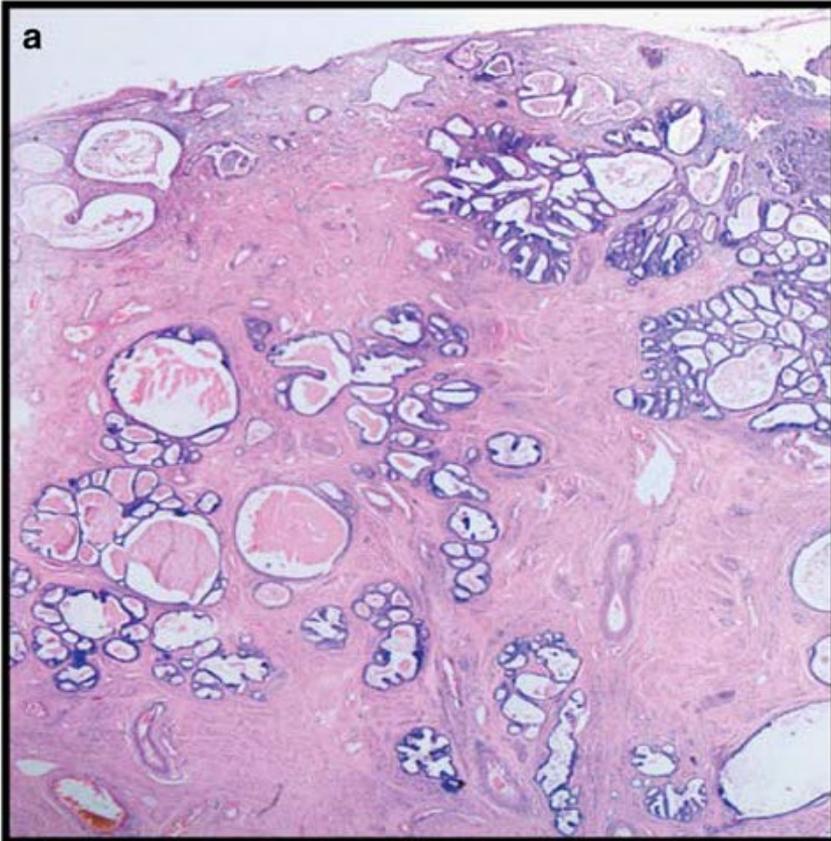
# Invasive Endocervical Adenocarcinoma: Proposal for a New Pattern-based Classification System With Significant Clinical Implications: A Multi-institutional Study

Andrea Diaz De Vivar, M.D., Andres A. Roma, M.D., Kay J. Park, M.D.,  
Isabel Alvarado-Cabrero, M.D., Golnar Rasty, M.D., Jose G. Chanona-Vilchis, M.D.,  
Yoshiki Mikami, M.D., Sung R. Hong, M.D., Brent Arville, D.O., Norihiro Teramoto, M.D.,  
Rouba Ali-Fehmi, M.D., Joanne K.L. Rutgers, M.D., Farah Tabassum, M.D.,  
Denise Barbuto, M.D., Irene Aguilera-Barrantes, M.D., Alexandra Shaye-Brown, M.D.,  
Dean Daya, M.D., and Elvio G. Silva, M.D.

**Table 1** Histologic criteria of the three Pattern Classifications

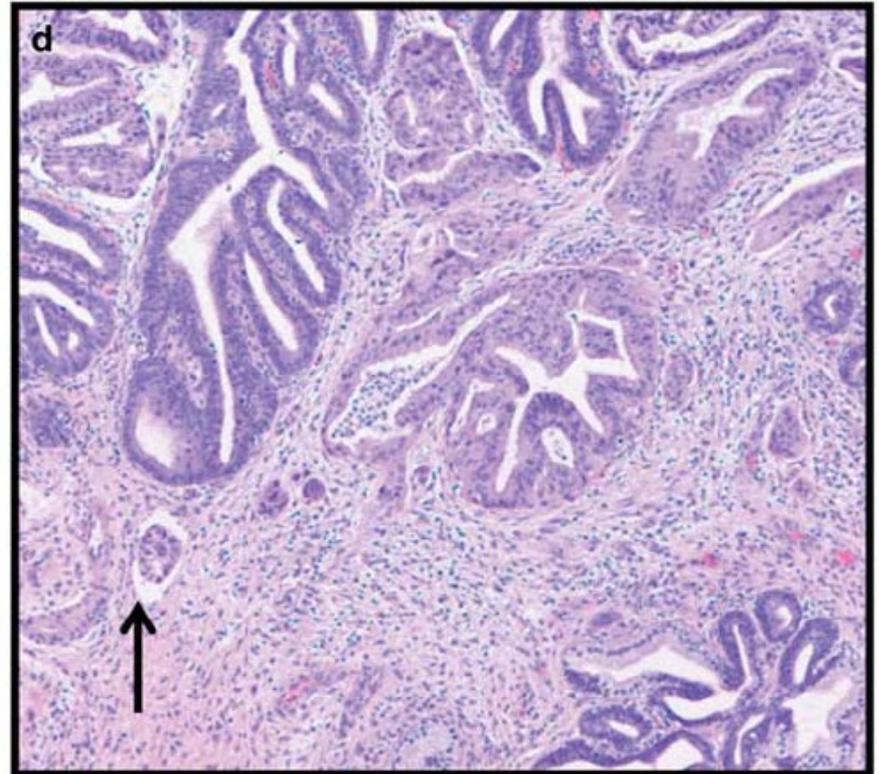
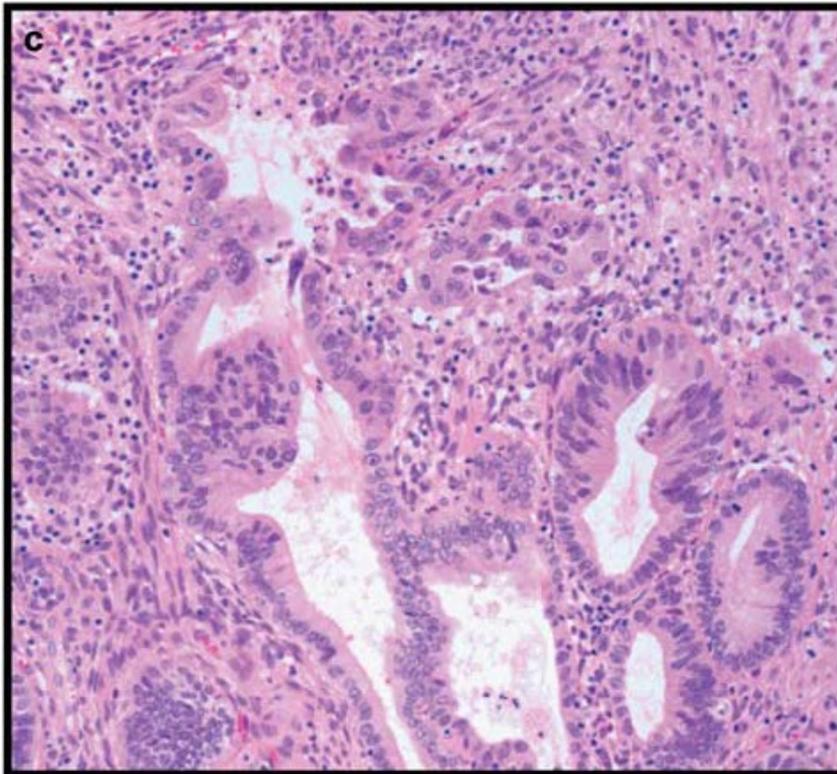
<i>Pattern classification</i>	<i>Criteria</i>
Pattern Classification-A	Well-demarcated glands with rounded contours, frequently forming groups No destructive stromal invasion No single cells or cell detachment No lymphovascular invasion Complex intraglandular growth acceptable, that is, cribriform, papillae Lack of solid growth, that is, architecturally well-moderately differentiated Depth of the tumor or relationship to large cervical vessels not relevant
Pattern Classification-B	Localized (limited, early) destructive stromal invasion arising from pattern A (well-demarcated) glands Individual or small groups of tumor cells, separated from the rounded gland, often in a focally desmoplastic or inflamed stroma Foci may be single, multiple, or linear at base of tumor Lymphovascular invasion $\pm$
Pattern Classification-C	Lack of solid growth, that is, architecturally well-moderately differentiated Diffuse destructive stromal invasion, characterized by diffusely infiltrative glands, with associated extensive desmoplastic response Confluent growth filling a 4 $\times$ field (5mm): glands, papillae (stroma only within papillae), or mucin lakes Glands often angulated or with a canalicular pattern, with interspersed open glands Solid, poorly differentiated component (architecturally high grade); nuclear grade is disregarded Lymphovascular invasion $\pm$

# PATRÓN A



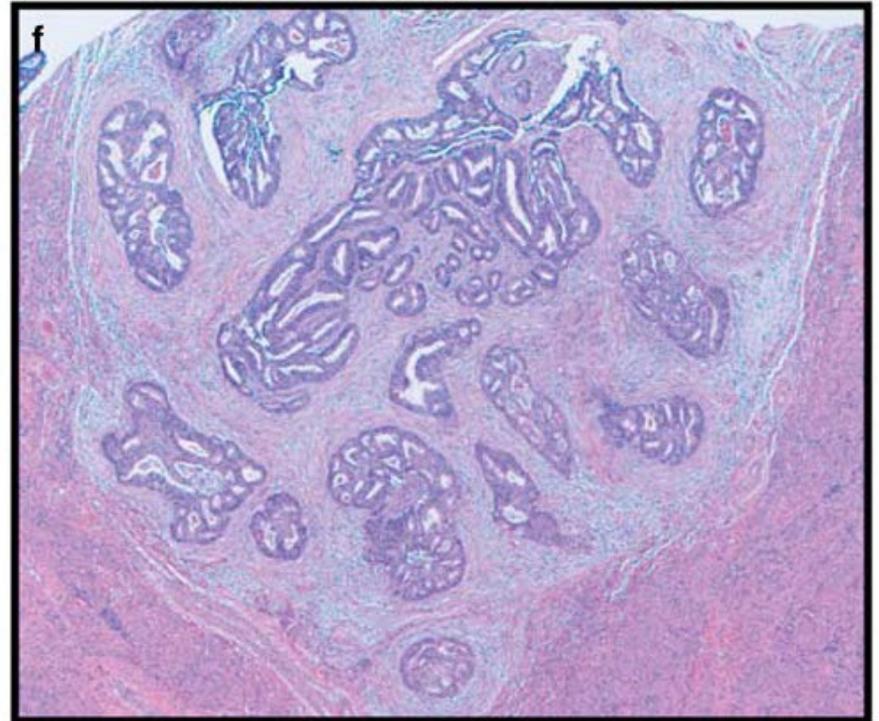
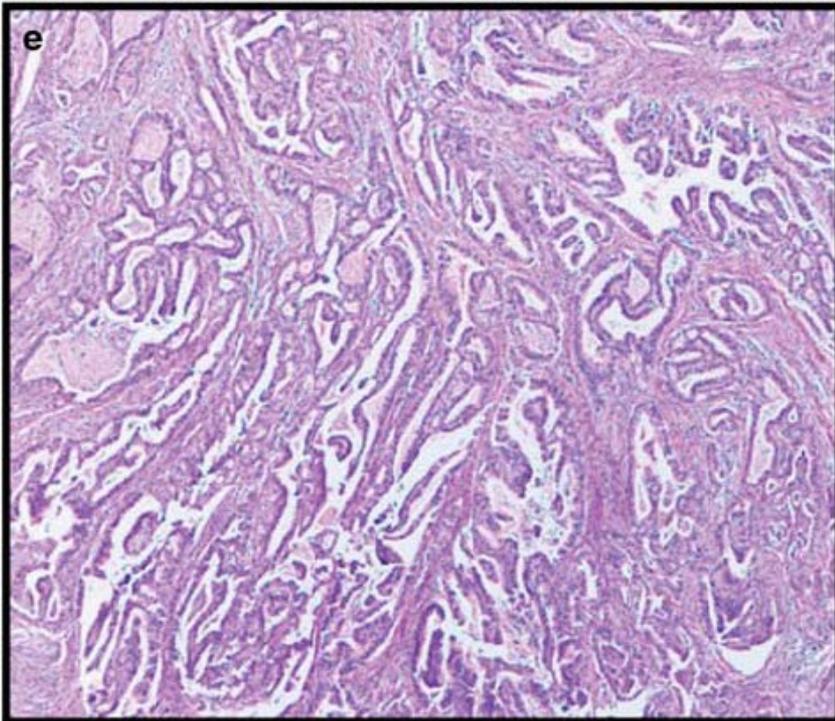
MODERN PATHOLOGY (2016) 29, 1083–1094

# PATRÓN B



MODERN PATHOLOGY (2016) 29, 1083–1094

# PATRÓN C



MODERN PATHOLOGY (2016) 29, 1083–1094

**TABLE 2.** Outcome data comparing the standard method of tumor evaluation (depth of invasion) versus the newly proposed pattern-based method

Method	N	DOI (mean in mm)	Patients with (+) LN	Total (+) LN/total resected LN	Recurrences	DOD	Stage I	Stages II–IV
Standard	352 (100%)	6.7	49 (13.9%)	78/6506	39 (11.4%)*	16 (4.6%)*	311 (88.3%)	41 (11.7%)
Pattern A	73 (20.7%)	3.8	0 (0%)	0/1333	0 (0%)	0 (0%)	73 (100%)	0 (0%)
Pattern B	90 (25.6%)	4.0	4 (4.4%)	5/1750	1 (1.2%)*	0 (0%)	86 (95.6%)	4 (4.4%)
Pattern C	189 (53.7%)	9.2	45 (23.8%)	73/3423	38 (22.1%)*	16 (8.8%)*	152 (80.4%)	37 (19.6%)

\*Percentages from available outcomes.

LN metastases:  $P < 0.001$  comparing Pattern A with B/C;  $P < 0.05$  comparing Pattern A with B;  $P < 0.0001$  comparing Pattern A with C.

Stage I versus II or higher:  $P < 0.005$  comparing Pattern A with B/C;  $P = 0.147$  comparing Pattern A with B;  $P < 0.0001$  comparing Pattern A with C.

DOD indicates died of disease; DOI, depth of invasion; LN, lymph node/s.

*Int J Gynecol Pathol Vol. 32, No. 6, November 2013*

**TABLE 3.** *Histologic features encountered in Pattern A in comparison with Patterns B and C*

Histologic features	Pattern A	Pattern B	Pattern C
Tumor differentiation (n = 338)			
Well	43 (58.9%)	39 (43.3%)	54 (28.6%)
Moderate	30 (41.1%)	47 (52.2%)	114 (60.3%)
Poor	0 (0%)	4 (4.5%)	21 (11.1%)
Tumor depth of invasion (n = 335)			
≤ 3 mm	34 (46.6%)	31 (34.5%)	20 (10.6%)
> 3–≤ 5 mm	19 (26%)	38 (42.2%)	29 (15.3%)
> 5 mm	20 (27.4%)	21 (23.3%)	140 (74.1%)
Lymph-vascular invasion	0/73 (0%)	24/90 (26.6%)	117/189 (61.9%)
Tumor size (mm)			
Range (mean)	2.5–42 (13.5)	0.7–65 (15.9)	1.2–87.5 (23.7)
Tumor thickness (mm)			
Range (mean)	1–19 (5.7)	1–63 (7.5)	0.7–40 (11.4)
Horizontal spread (mm)			
Range (mean)	1.5–20 (8.6)	2–30 (12.64)	1.2–30 (16.3)

Tumor size: Gross or clinical or #sections × 2.5 mm.

Tumor DOI:  $P < 0.05$  comparing Pattern A with B/C;  $P = 0.587$  comparing Pattern A with B;  $P < 0.05$  comparing Pattern A with C.

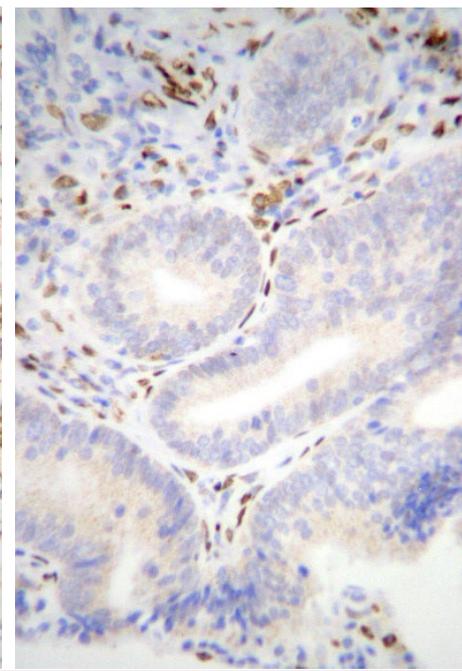
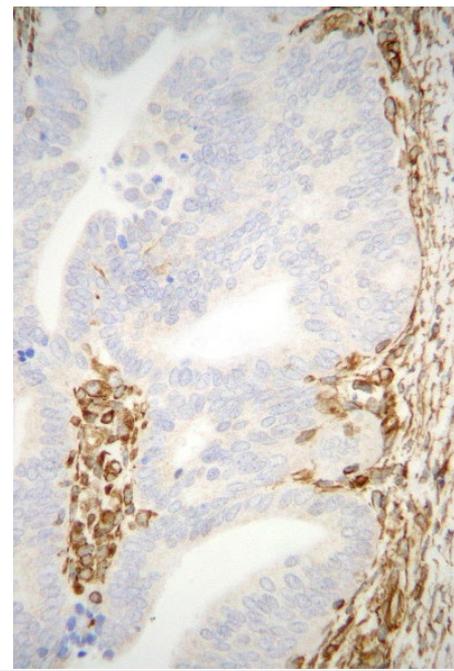
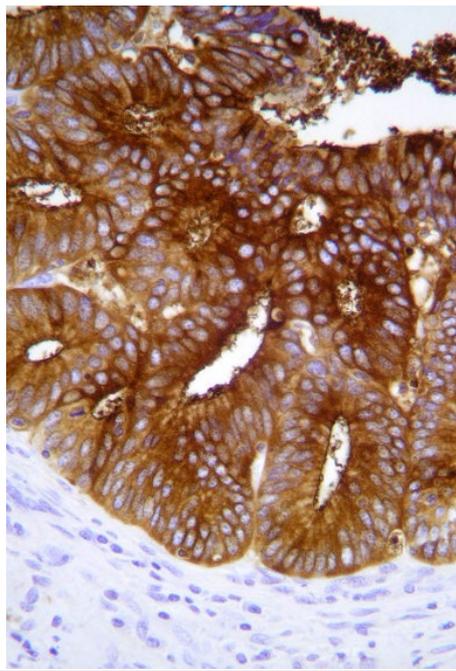
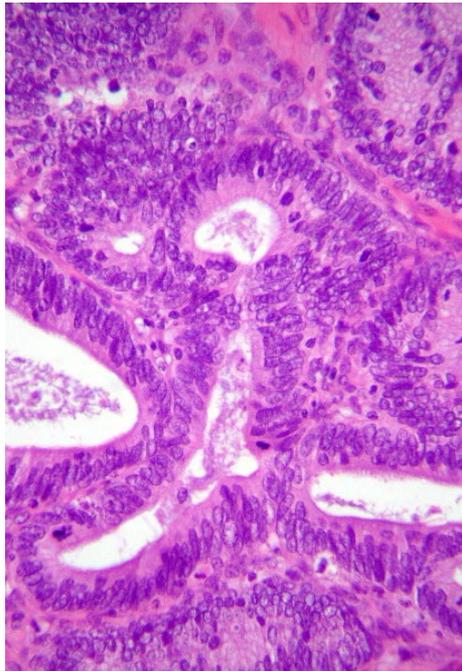
Lymph-vascular invasion:  $P < 0.05$  comparing Pattern A with B/C;  $P < 0.05$  comparing Pattern A with B;  $P < 0.05$  comparing Pattern A with C.

Tumor size:  $P < 0.05$  comparing Pattern A with B/C;  $P = 0.173$  comparing Pattern A with B;  $P < 0.05$  comparing Pattern A with C.

Horizontal spread:  $P < 0.05$  comparing Pattern A with B/C;  $P < 0.05$  comparing Pattern A with B;  $P < 0.05$  comparing Pattern A with C.

# ENDOCÉRVIX vs ENDOMETRIO

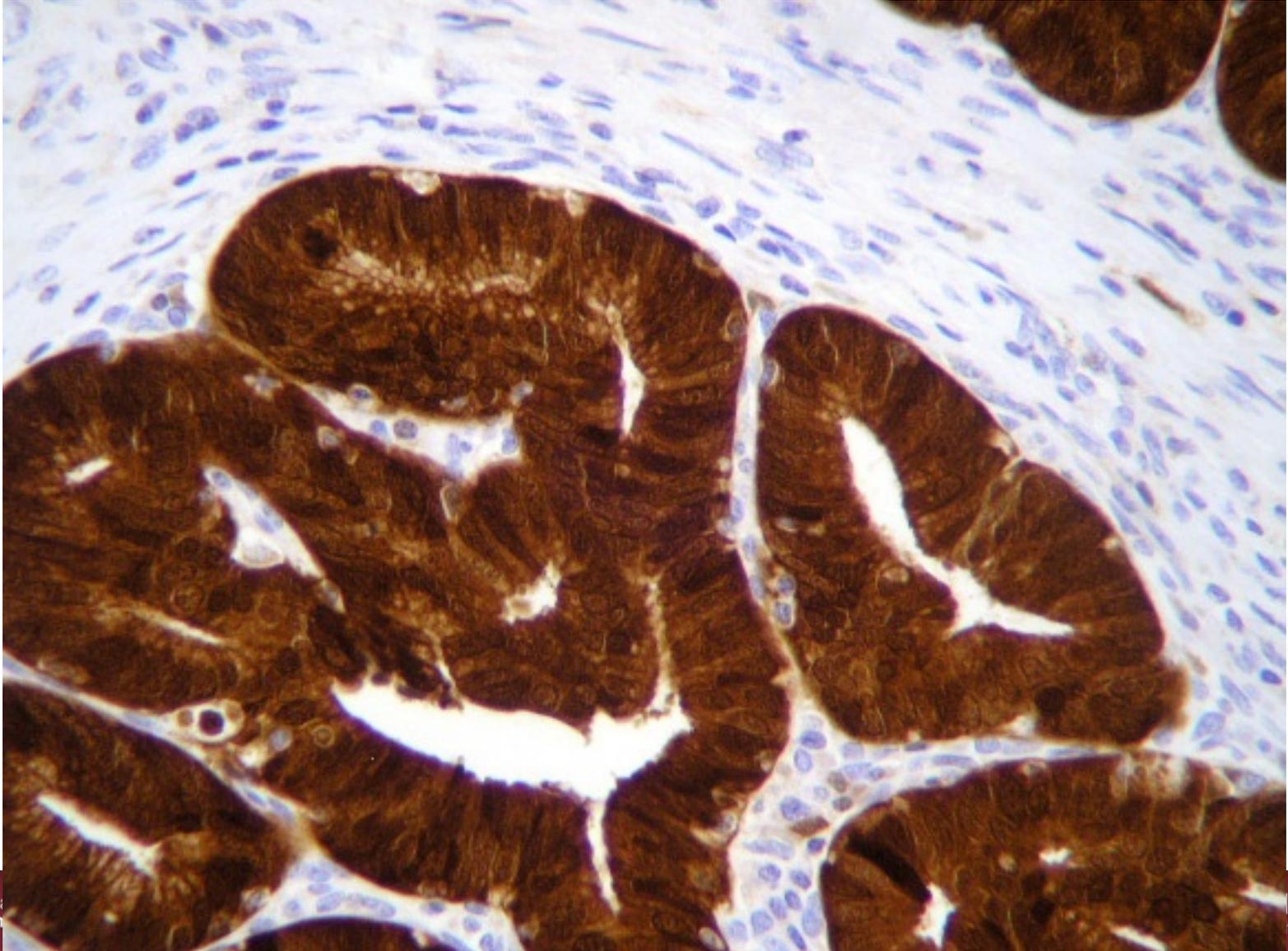
- LESIONES PRECURSORAS (ADC IN SITU / HIPERPLASIA COMPLEJA) Y CARCINOMAS
- ENDOCÉRVIX: CEA +, ER -, VIM -
- ENDOMETRIO: CEA -, ER +, VIM +



# PROTEINA P16

- INHIBIDORA DE CDK SOBRE-EXPRESADA EN CÉLULAS DE NEOPLASIAS RELACIONADAS CON INFECCIÓN POR HPV
- ES ÚTIL PARA DIFERENCIAR LESIONES REACTIVAS DE LESIONES PRE-NEOPLÁSICAS
- PUEDE ESTAR SOBRE-EXPRESADA EN TUMORES NO RELACIONADOS CON HPV (CARCINOMA SEROSO)
- ES ÚTIL PARA DIAGNÓSTICO DIFERENCIAL ENTRE ADC ENDOCERVICAL vs ENDOMETRIAL

# P16



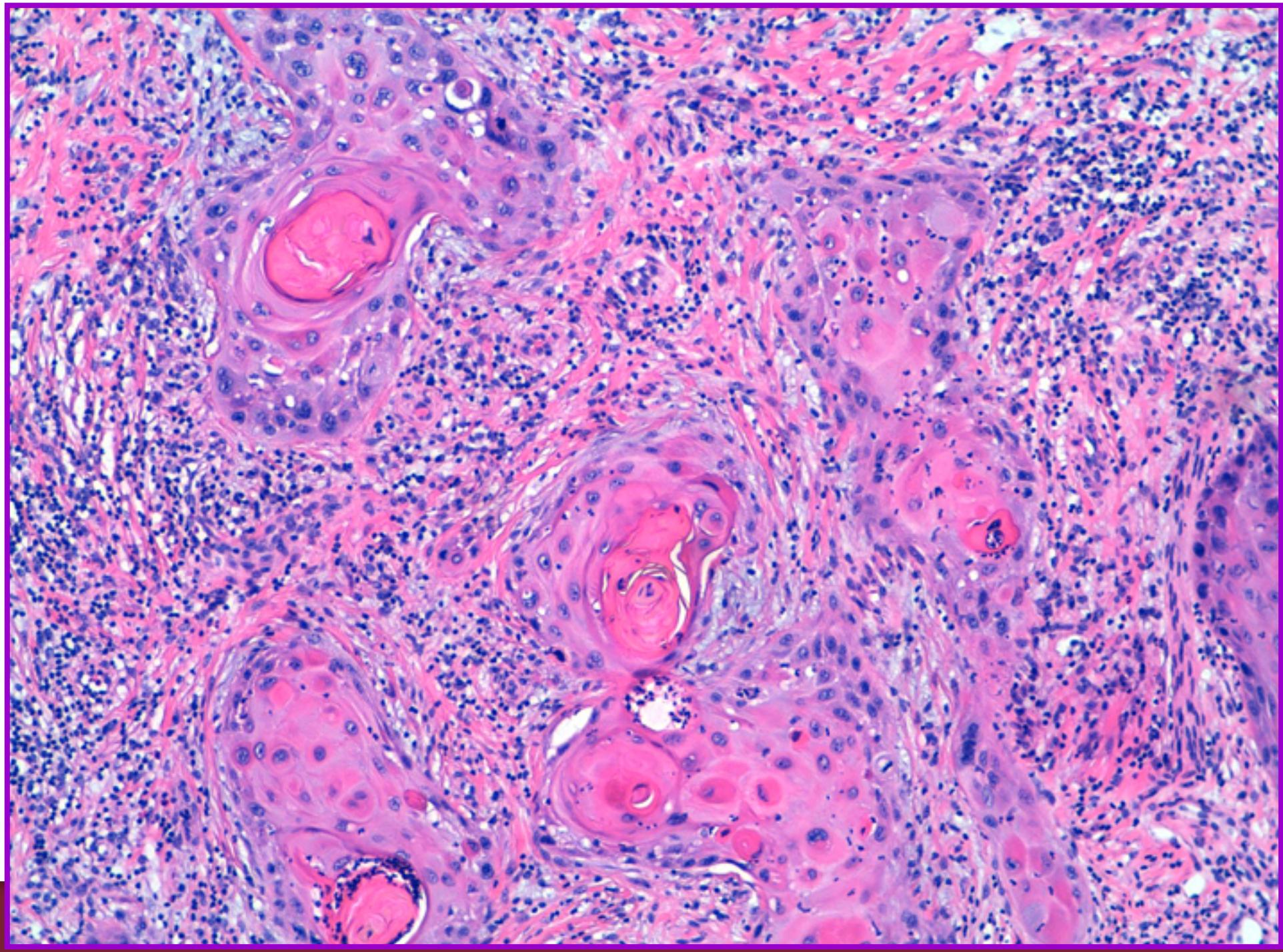
# CÁNCER DE VULVA

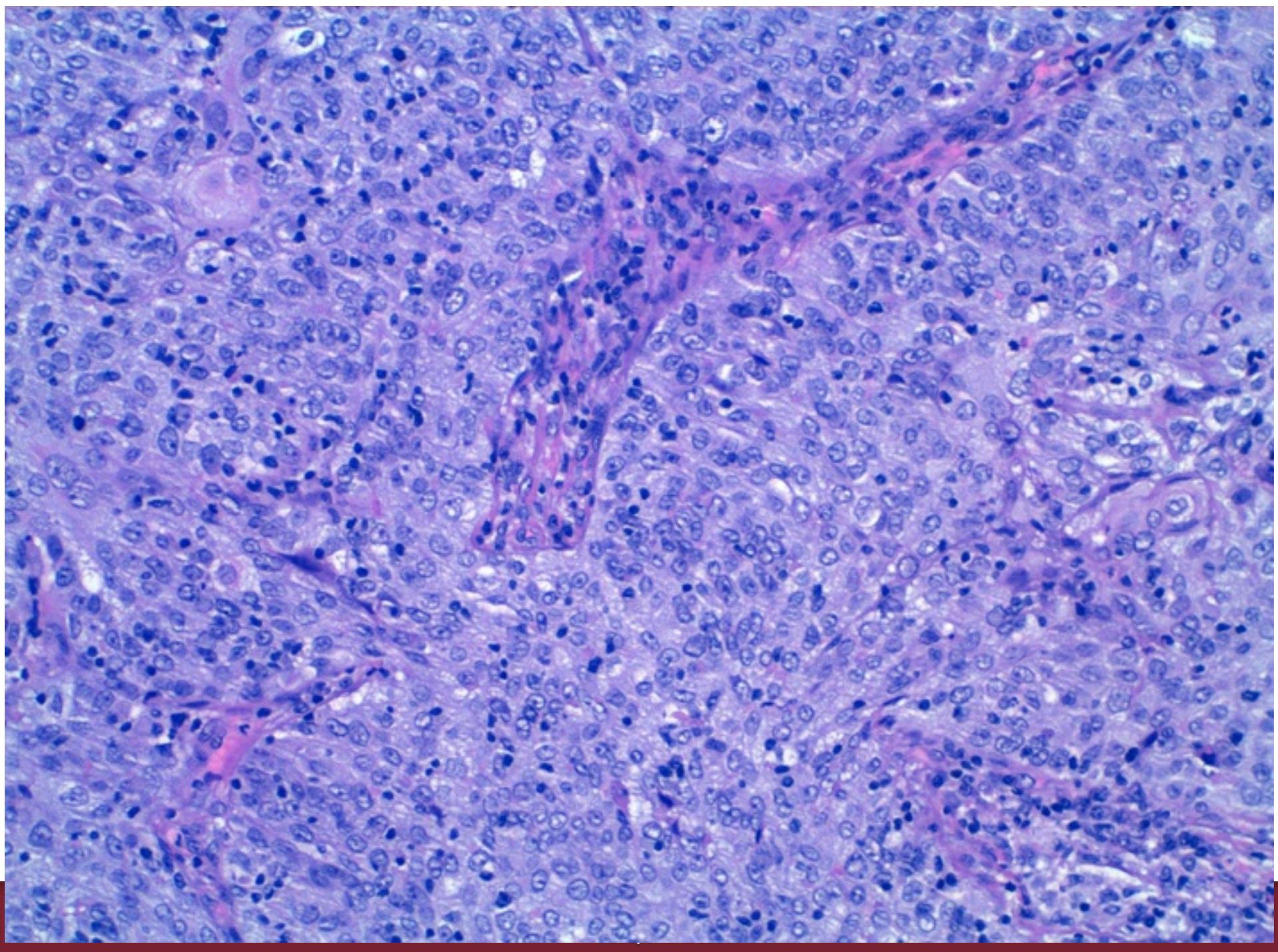
# TUMORES DE LA VULVA

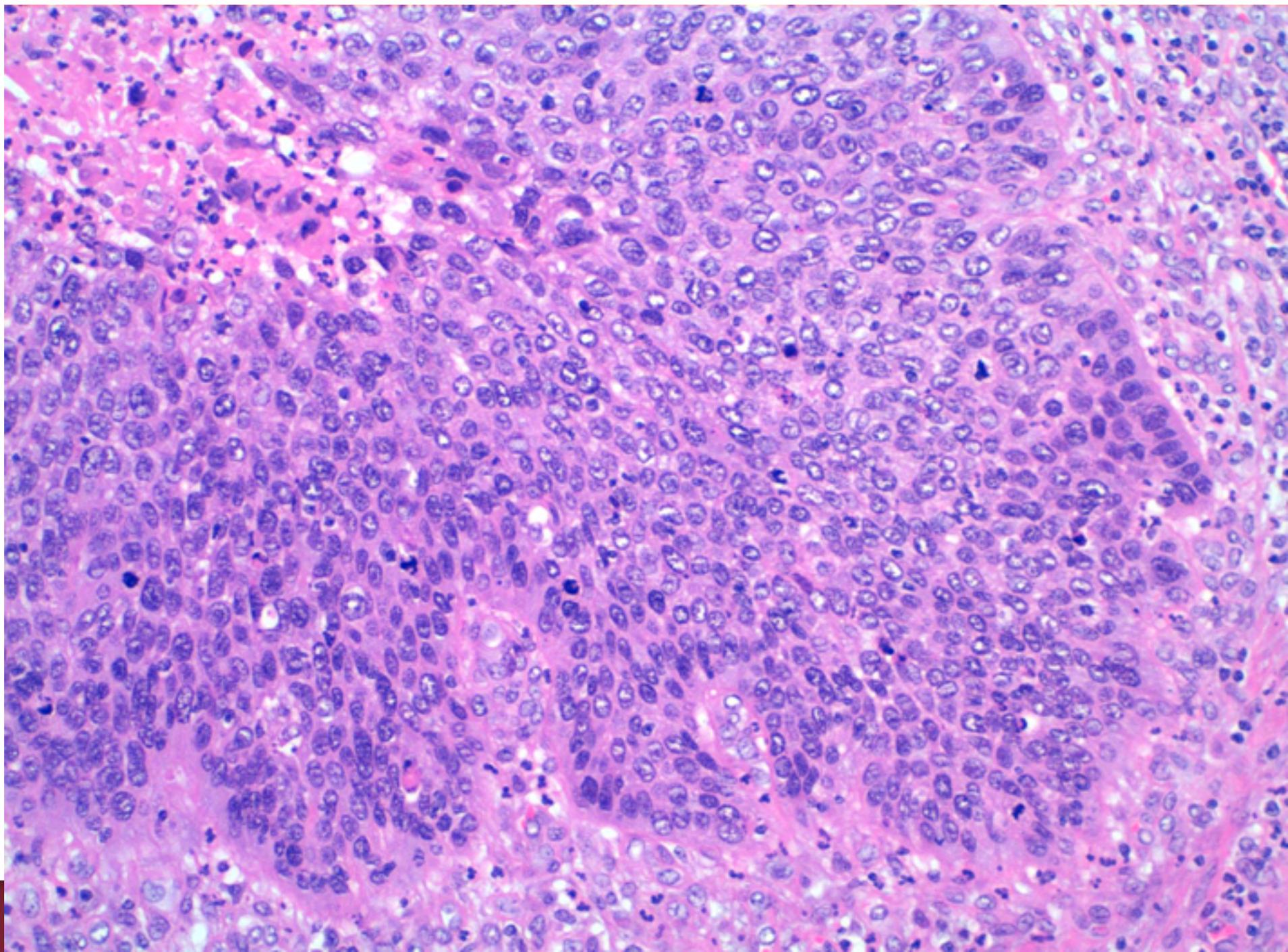
- TUMORES EPITELIALES
  - ESCAMOSOS
  - GLANDULARES
- TUMORS DE PARTES BLANDAS
- TUMORES MELANOCÍTICOS
- MISCELANEA
- TUMORES HEMATOPOYÉTICOS Y LINFOIDES
- TUMORS SECUNDARIS

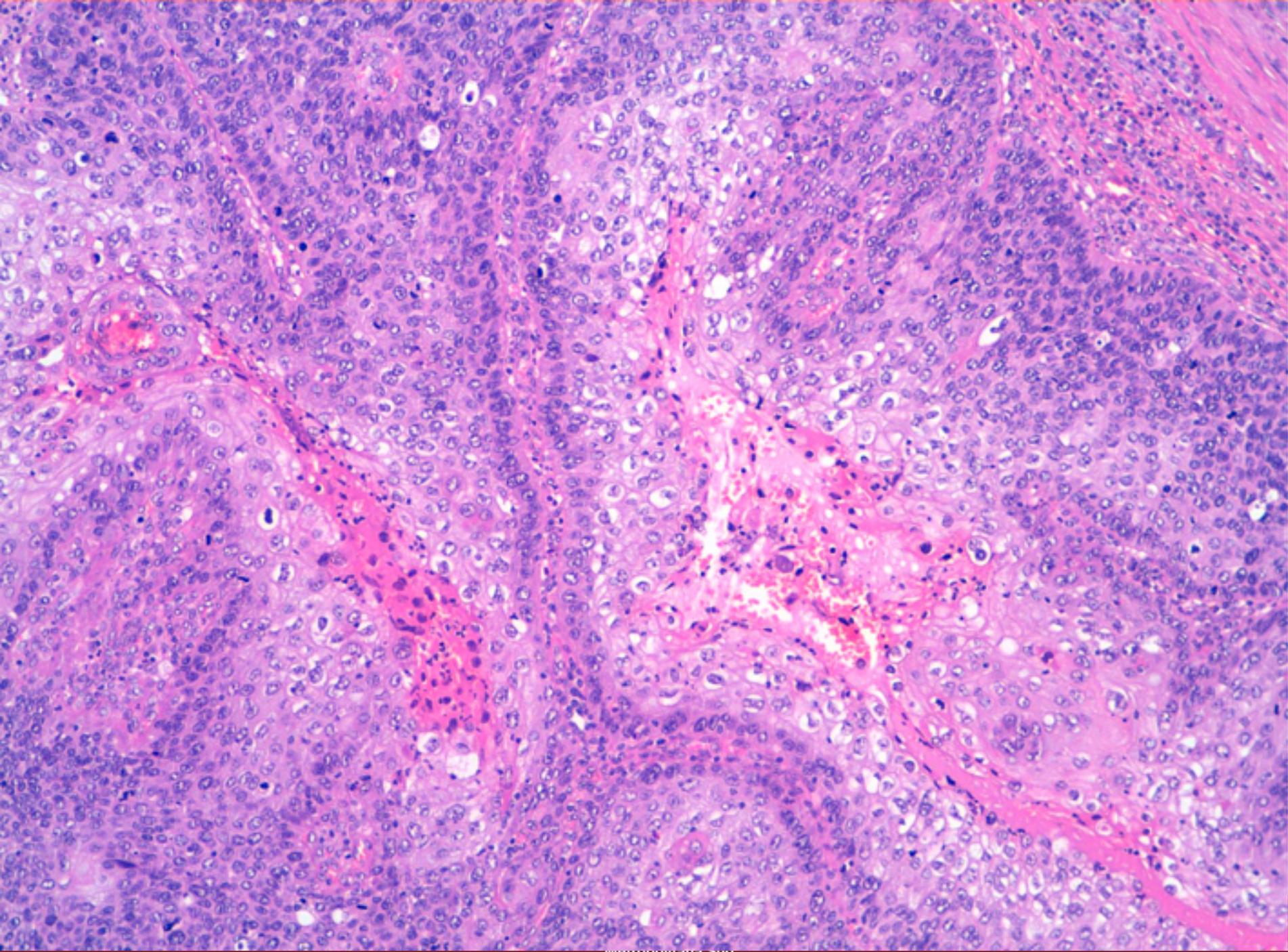
# CARCINOMAS ESCAMOSOS

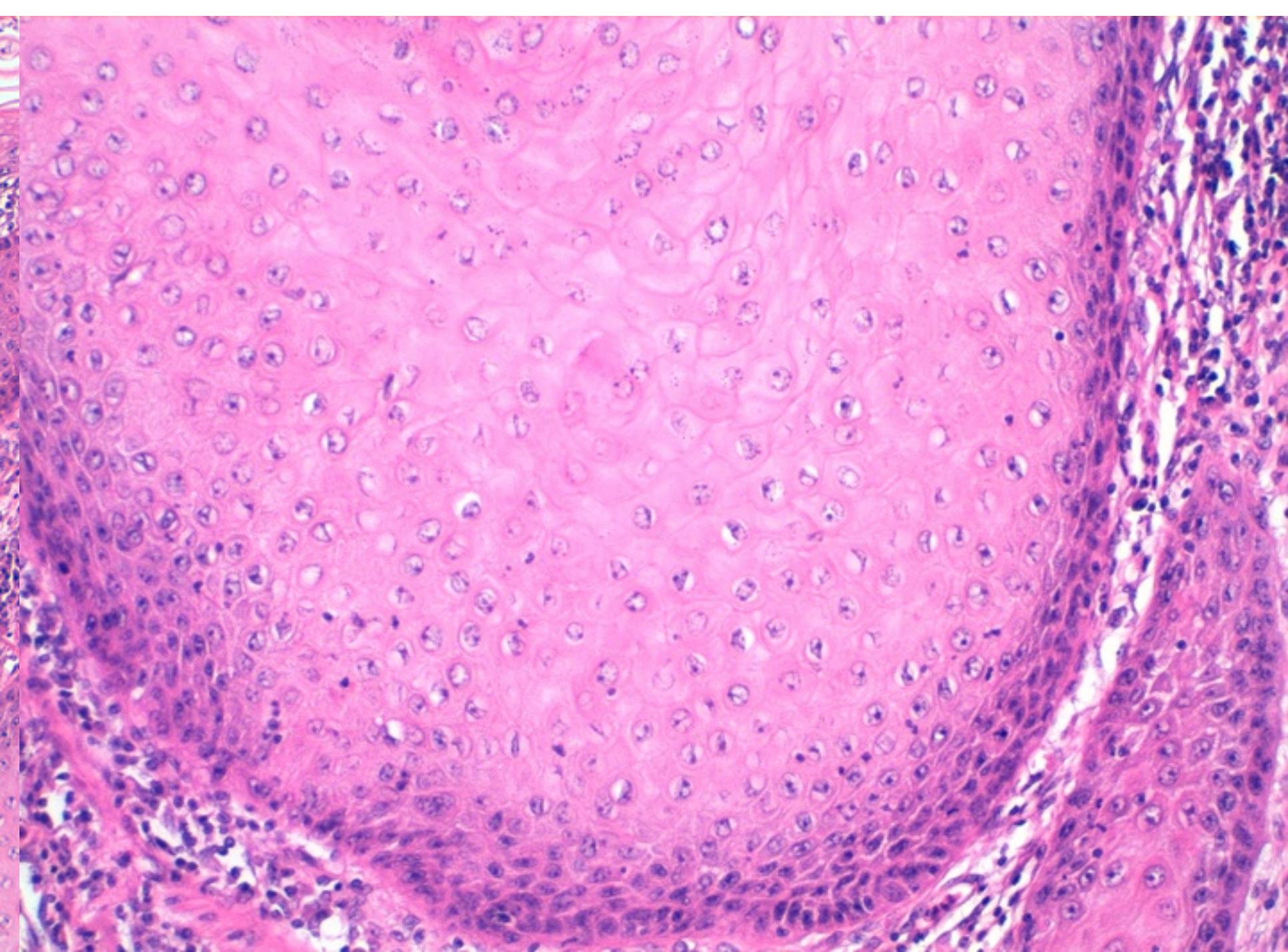
- CARCINOMA DE CÉLULAS ESCAMOSAS, NOS
  - QUERATINIZANTE
  - NO QUERATINIZANTE
  - BASALOIDE
  - CONDILOMATOSO (“WARTY”)
  - VERRUCOSO
- CARCINOMA DE CÉLULAS BASALES

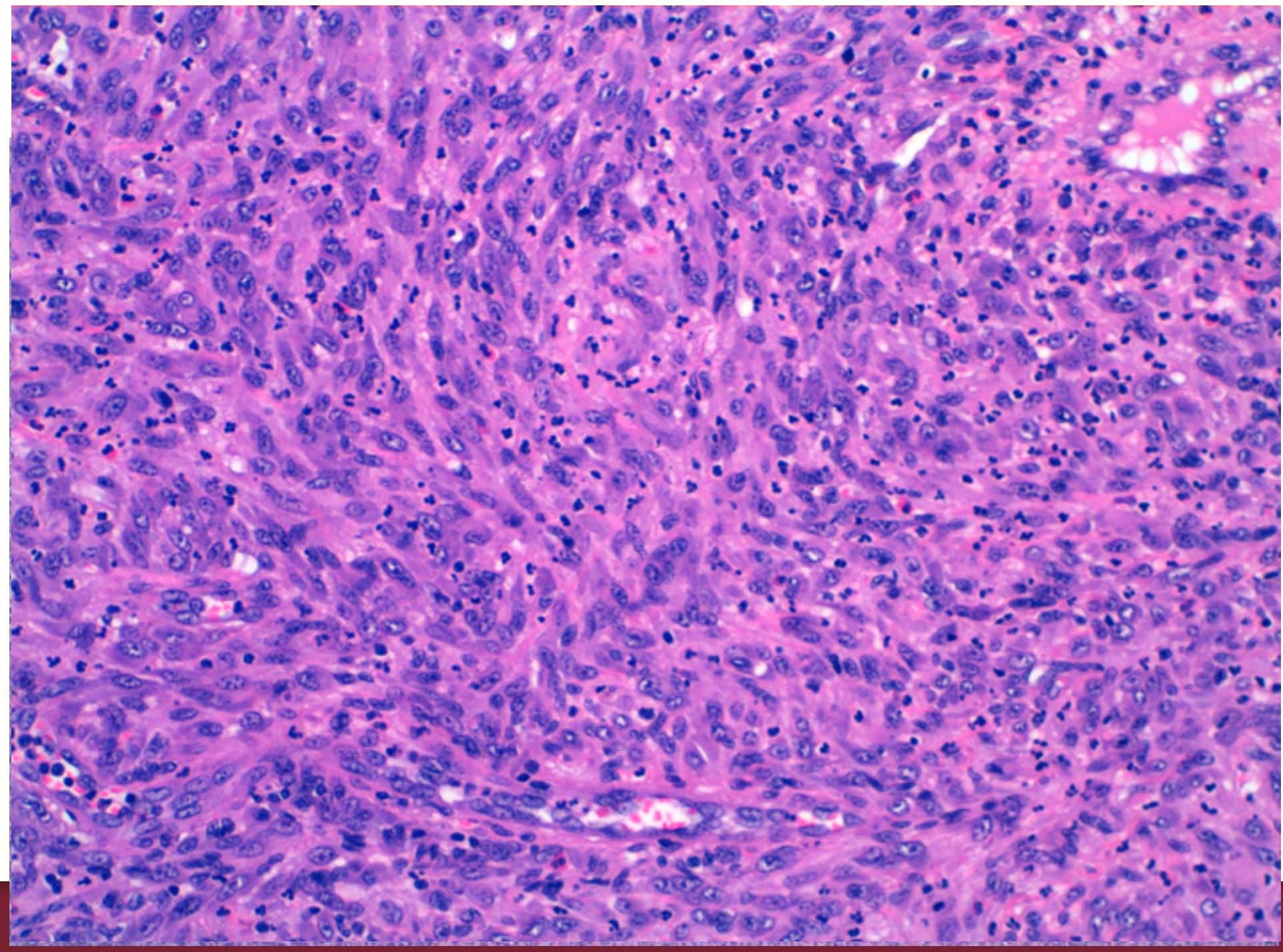








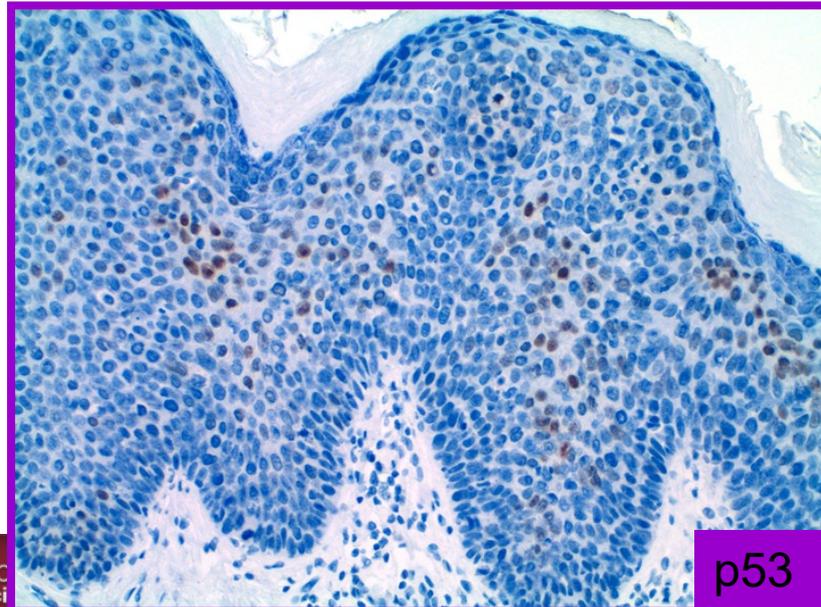
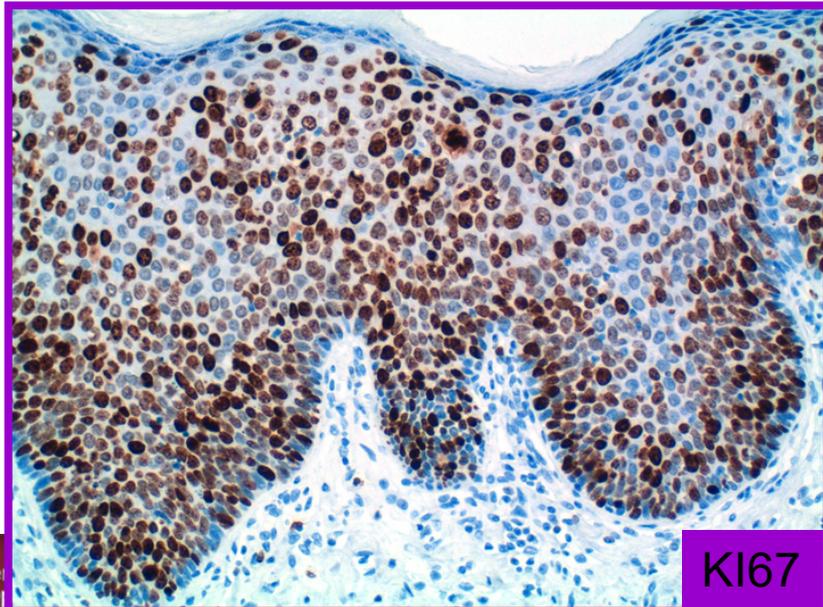
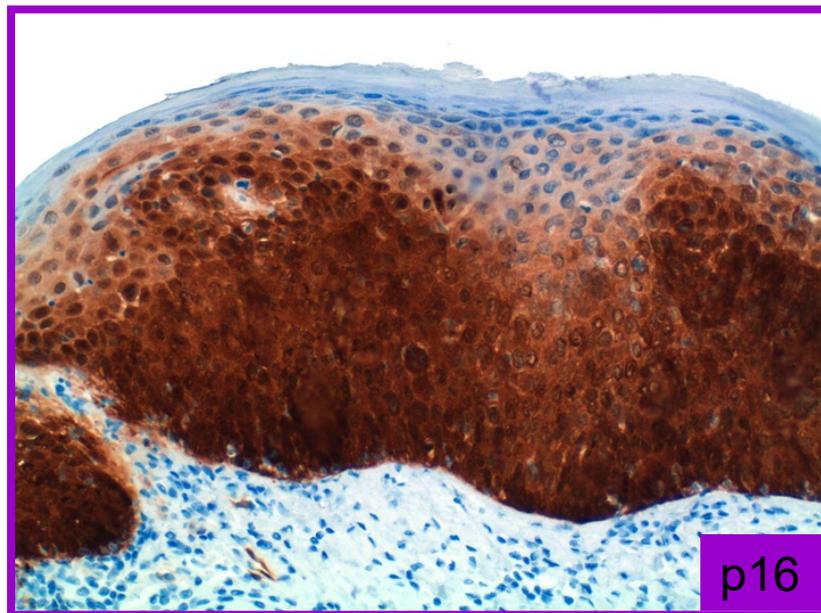
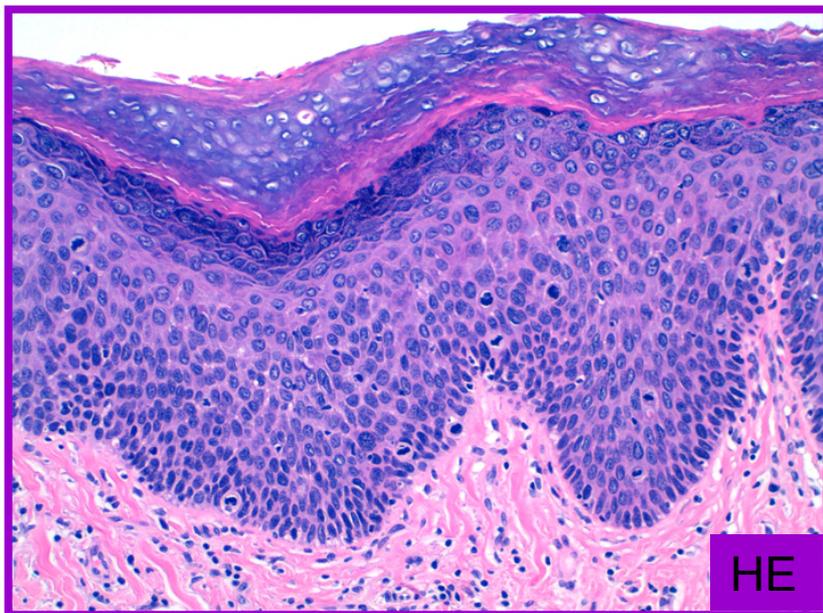




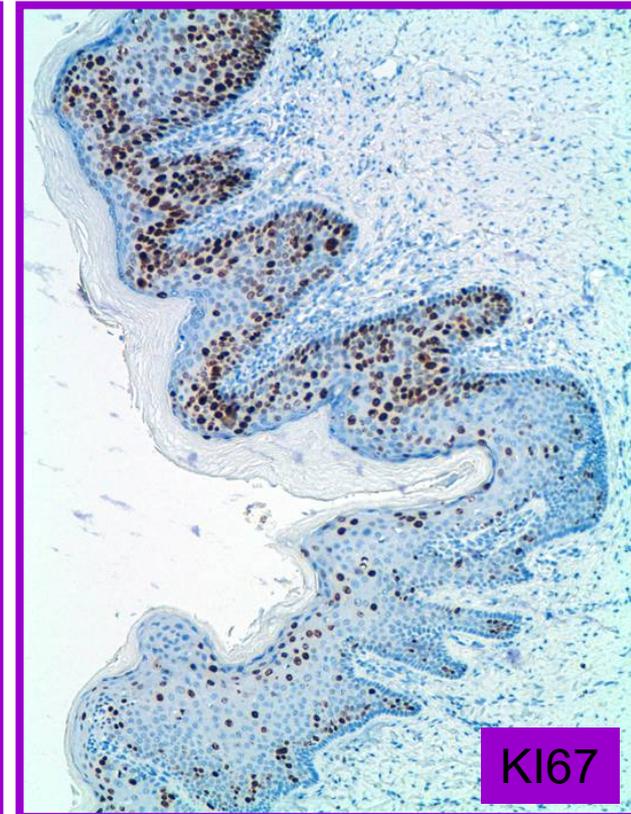
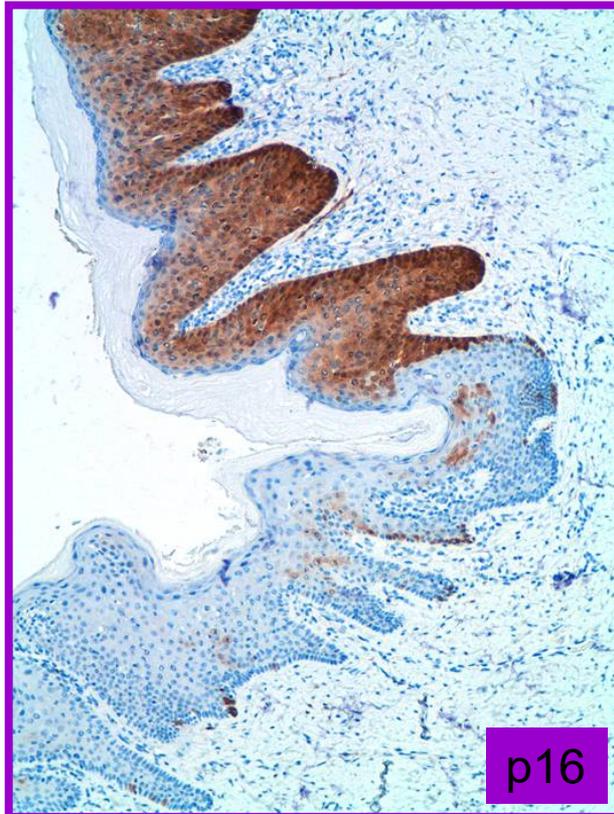
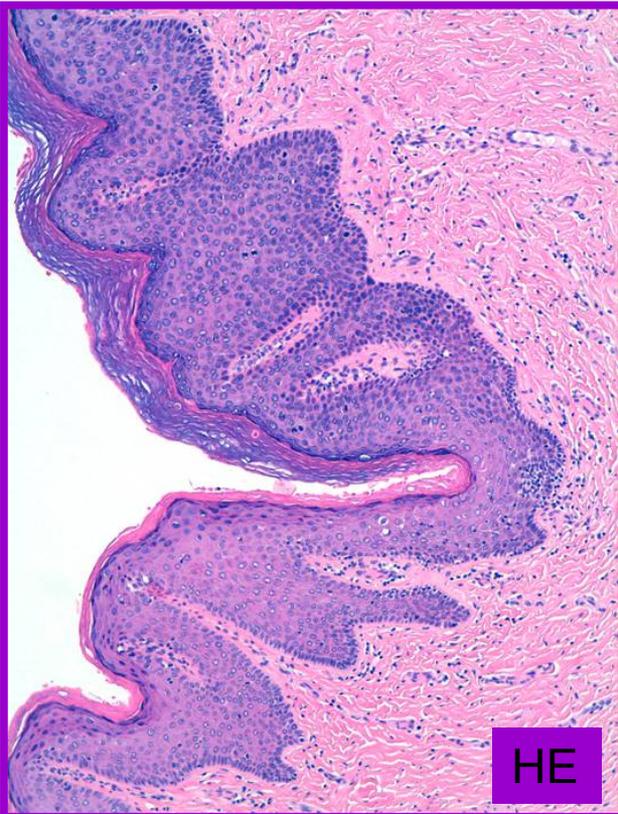
# LESIONES PRECURSORAS

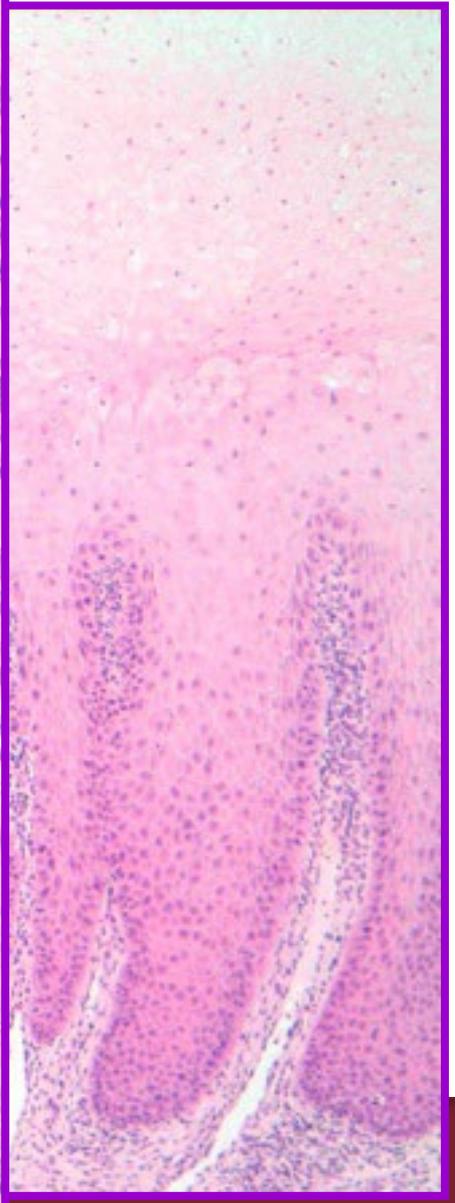
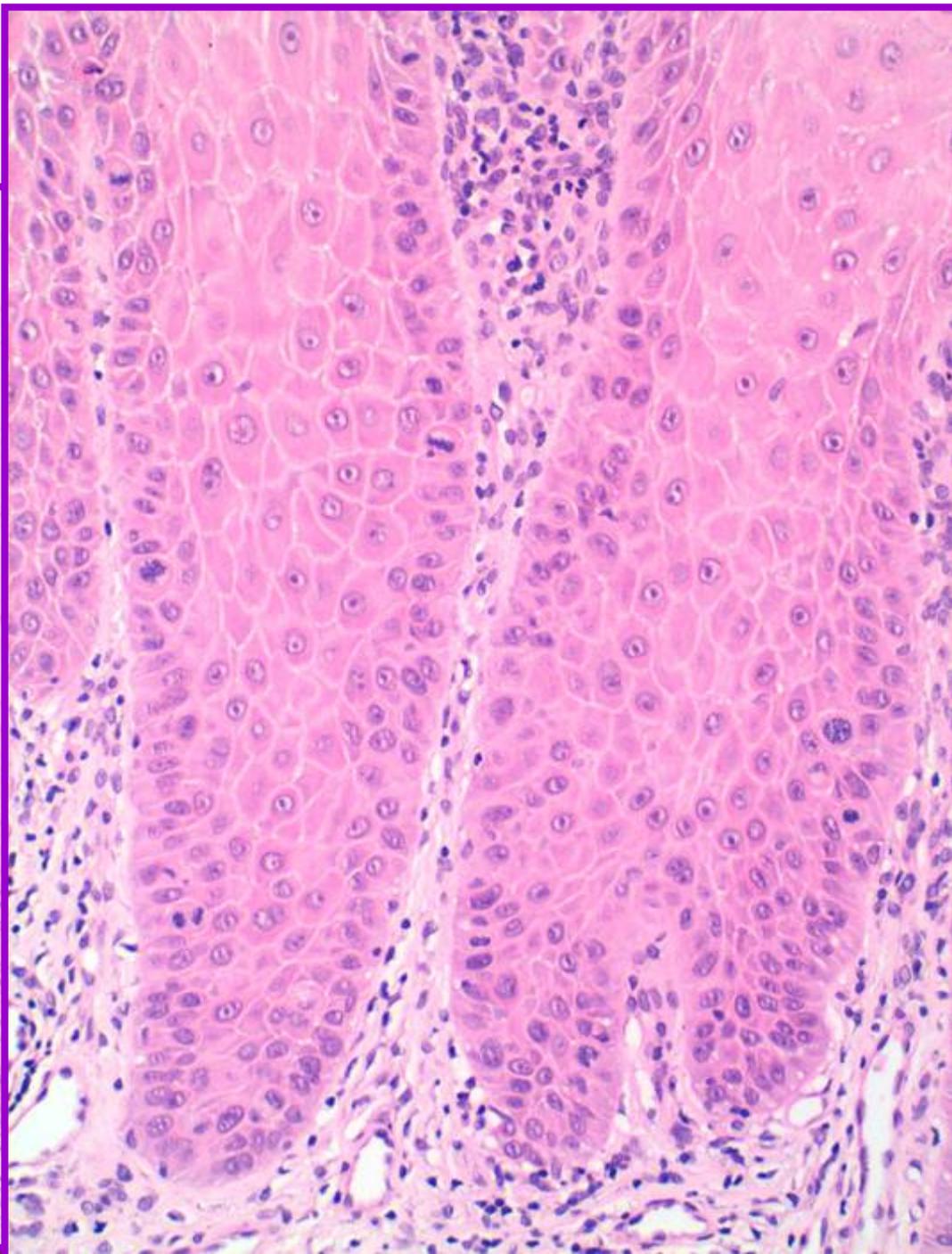
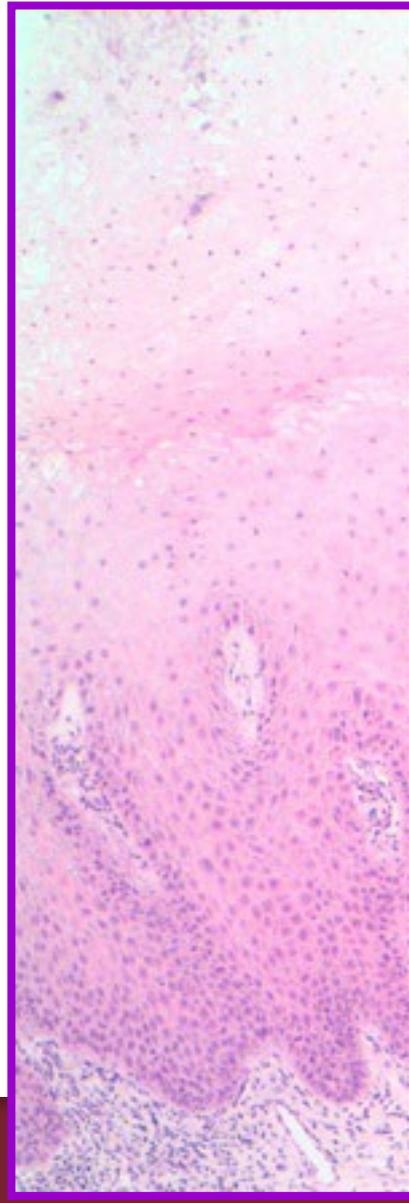
- VIN CLÁSICO (BASALOIDE / CONDILOMATOSO)
- VIN DIFERENCIADO

# VIN 3 PATRÓ BASALOIDE

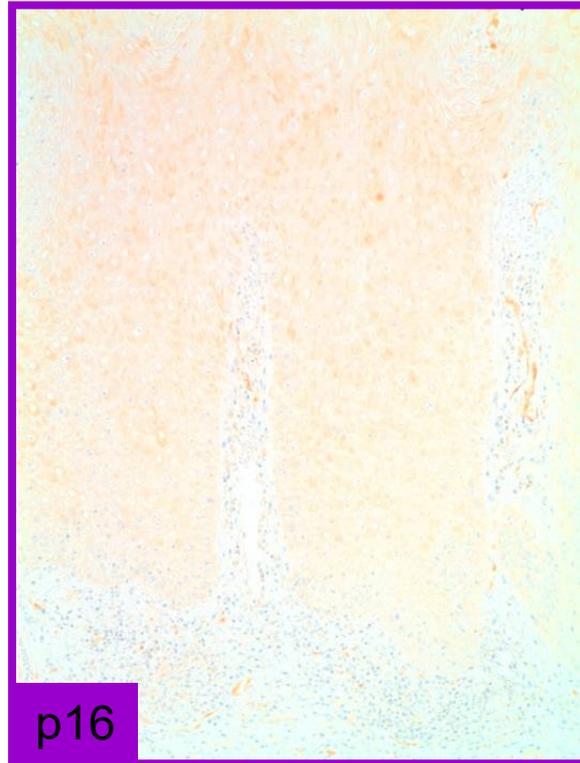
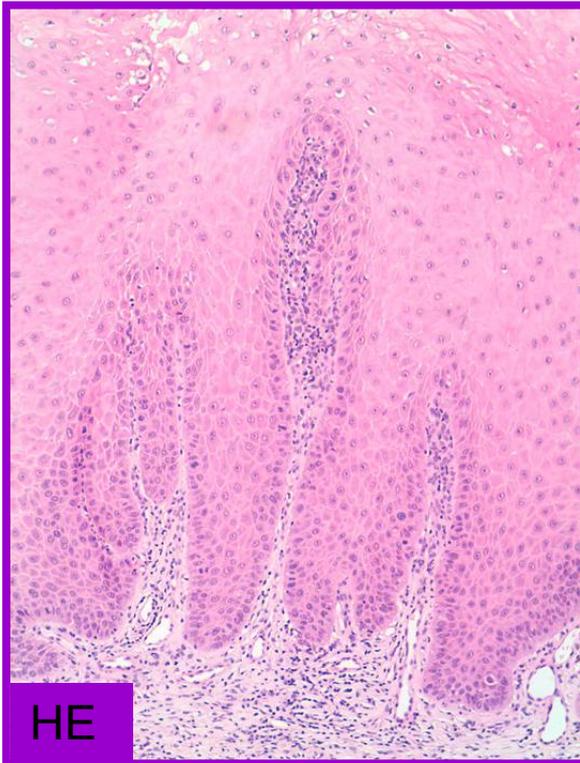


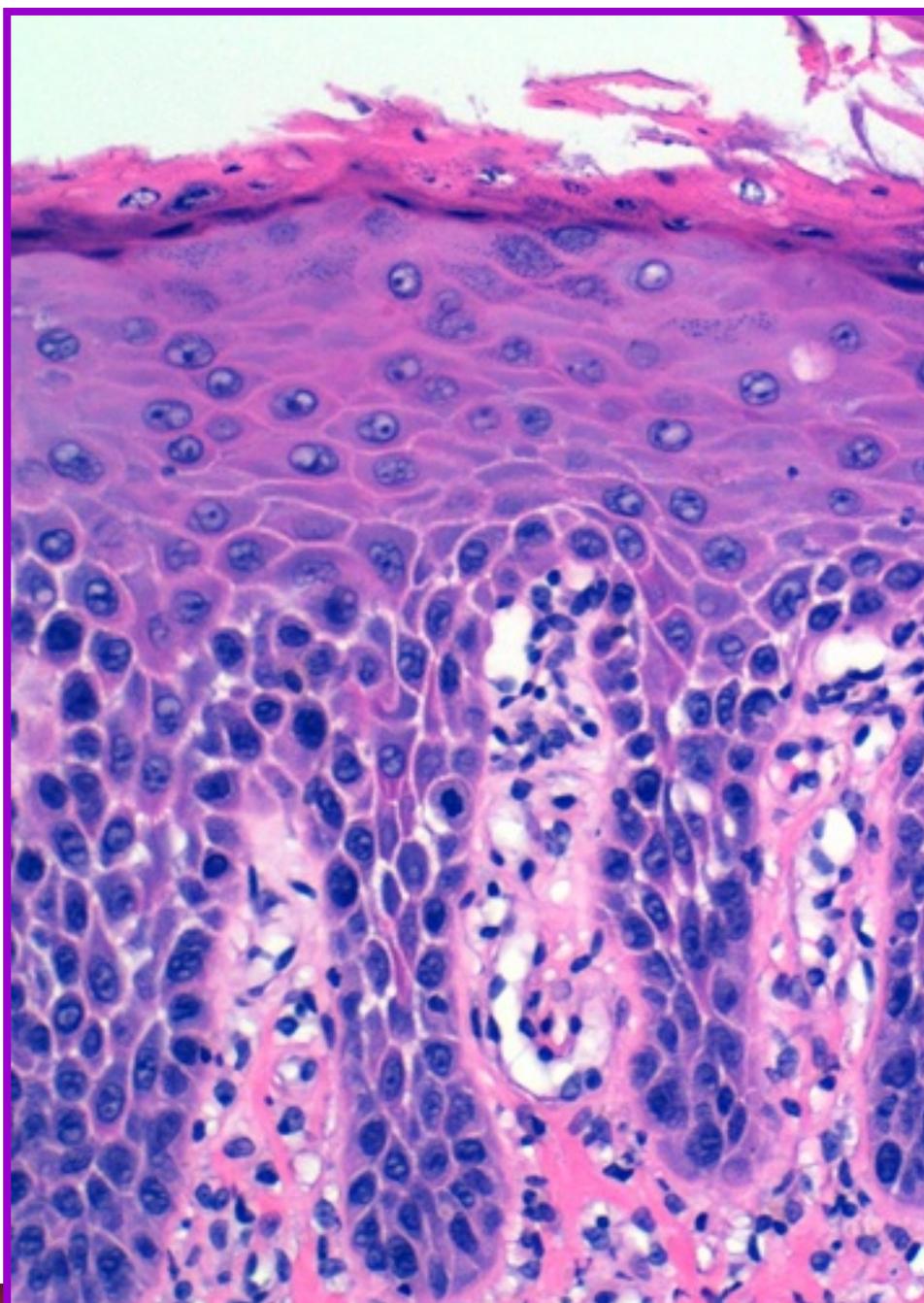
# VIN 3 PATRÓN BASALOIDE



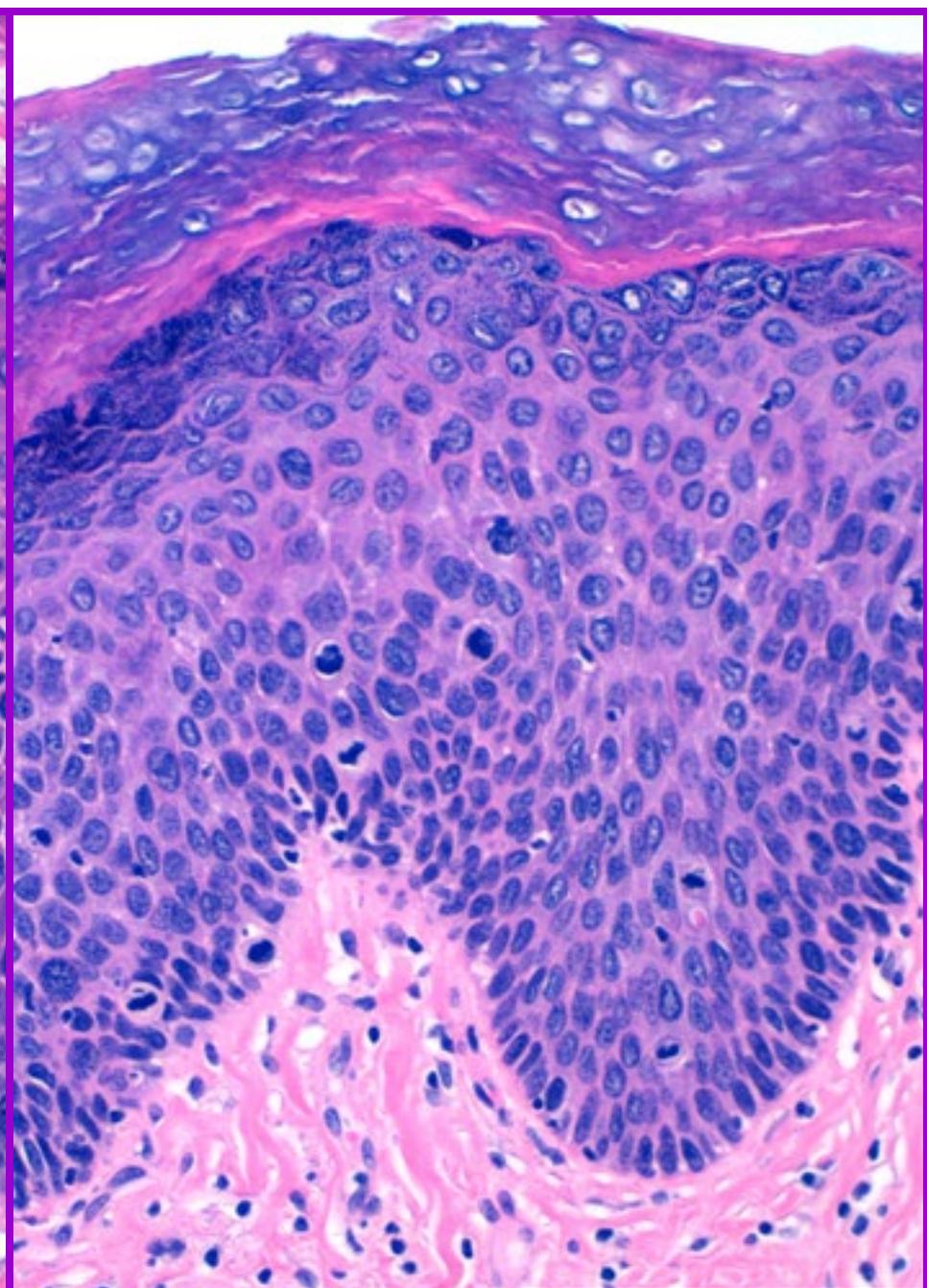


# VIN DIFERENCIADO

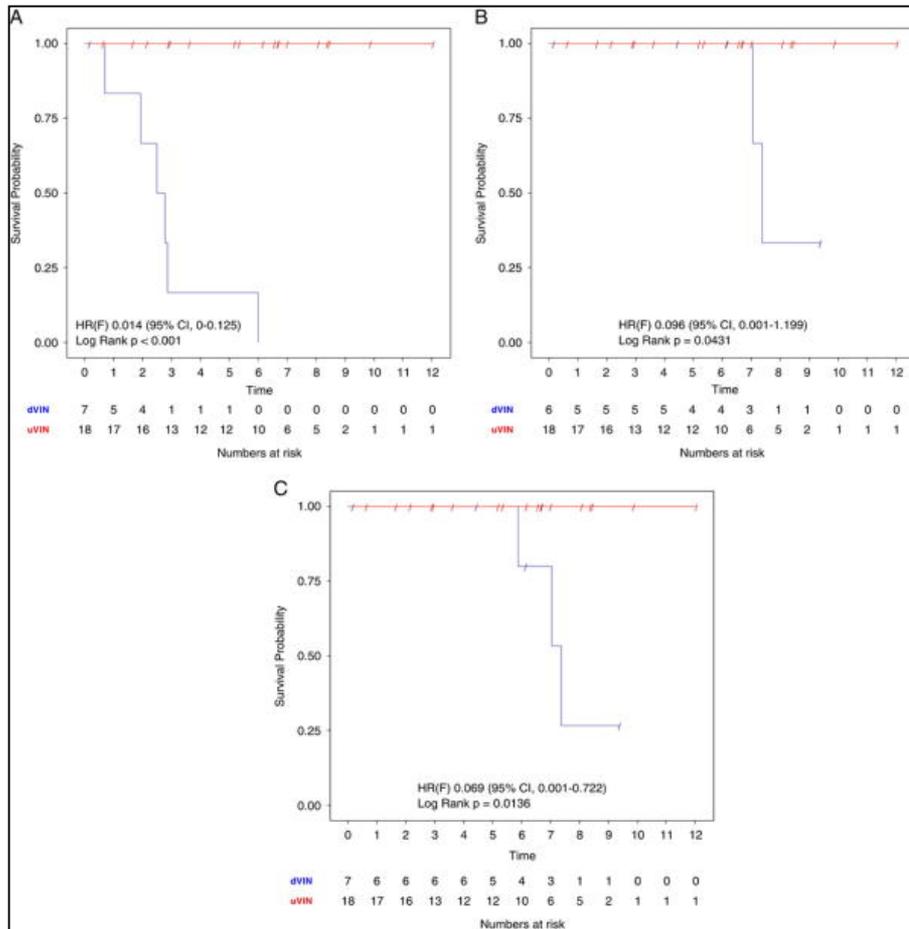




VIN DIFERENCIADO



VIN BASALOIDE



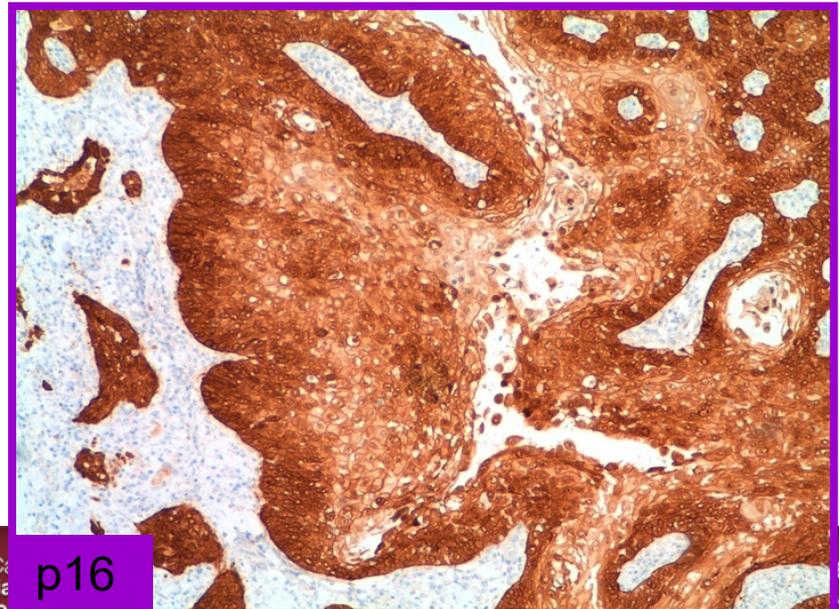
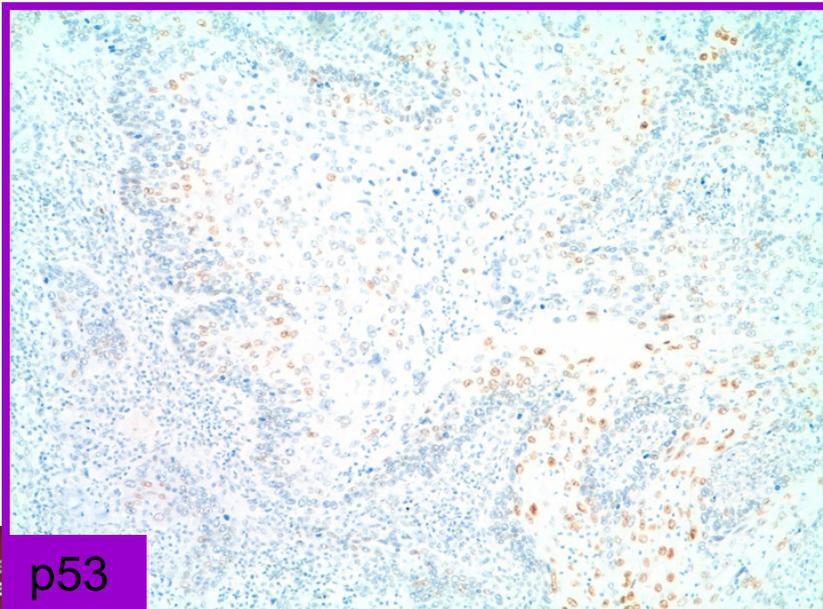
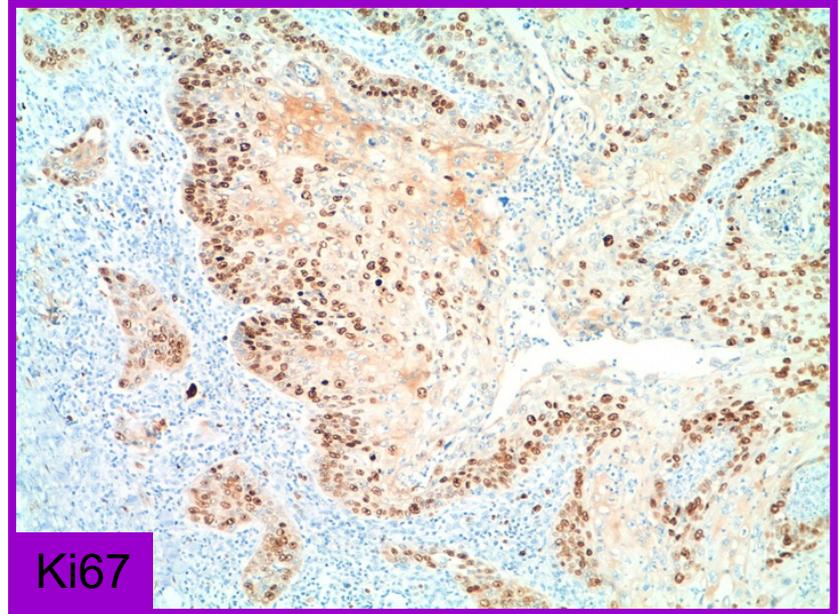
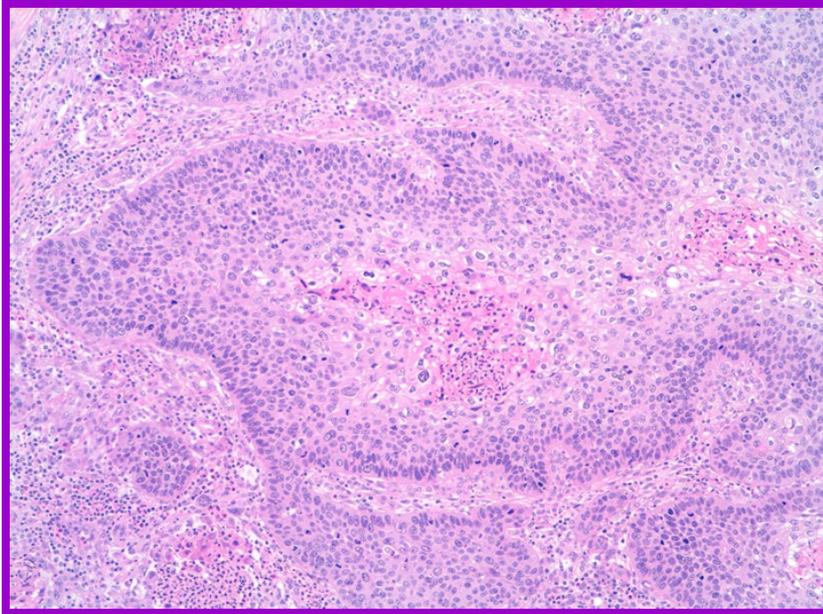
**HPV-independent Differentiated Vulvar Intraepithelial Neoplasia (dVIN) is Associated With an Aggressive Clinical Course.**

McAlpine, Jessica; Kim, So; Akbari, Ardalan; Eshragh, Sima; Reuschenbach, Miriam; von Knebel Doeberitz, Magnus; Prigge, Elena; Jordan, Suzanne; Singh, Naveena; Miller, Dianne; Gilks, C

International Journal of Gynecological Pathology.  
36(6):507-516, November 2017.  
DOI: 10.1097/PGP.0000000000000375

FIG. 4 . Kaplan-Meier survival analyses with log-rank statistic and hazard ratios shown for (A) progression-free survival, (B) disease-specific survival, and (C) overall Survival for cases of differentiated vulvar intraepithelial neoplasia (dVIN) only, without concurrent invasive squamous cell carcinoma (in blue) and HSIL(VIN3) (in red). The x axis is years from diagnosis, and the y axis represents the proportion of cases. Below the x axis the number of cases in both dVIN and HSIL(VIN3) cohorts are shown. CI indicates confidence interval; HR, hazard ratio.

# CARCINOMA ESCAMOSO CONDILOMATOSO



# CARCINOMA ESCAMOSO N.O.S.

