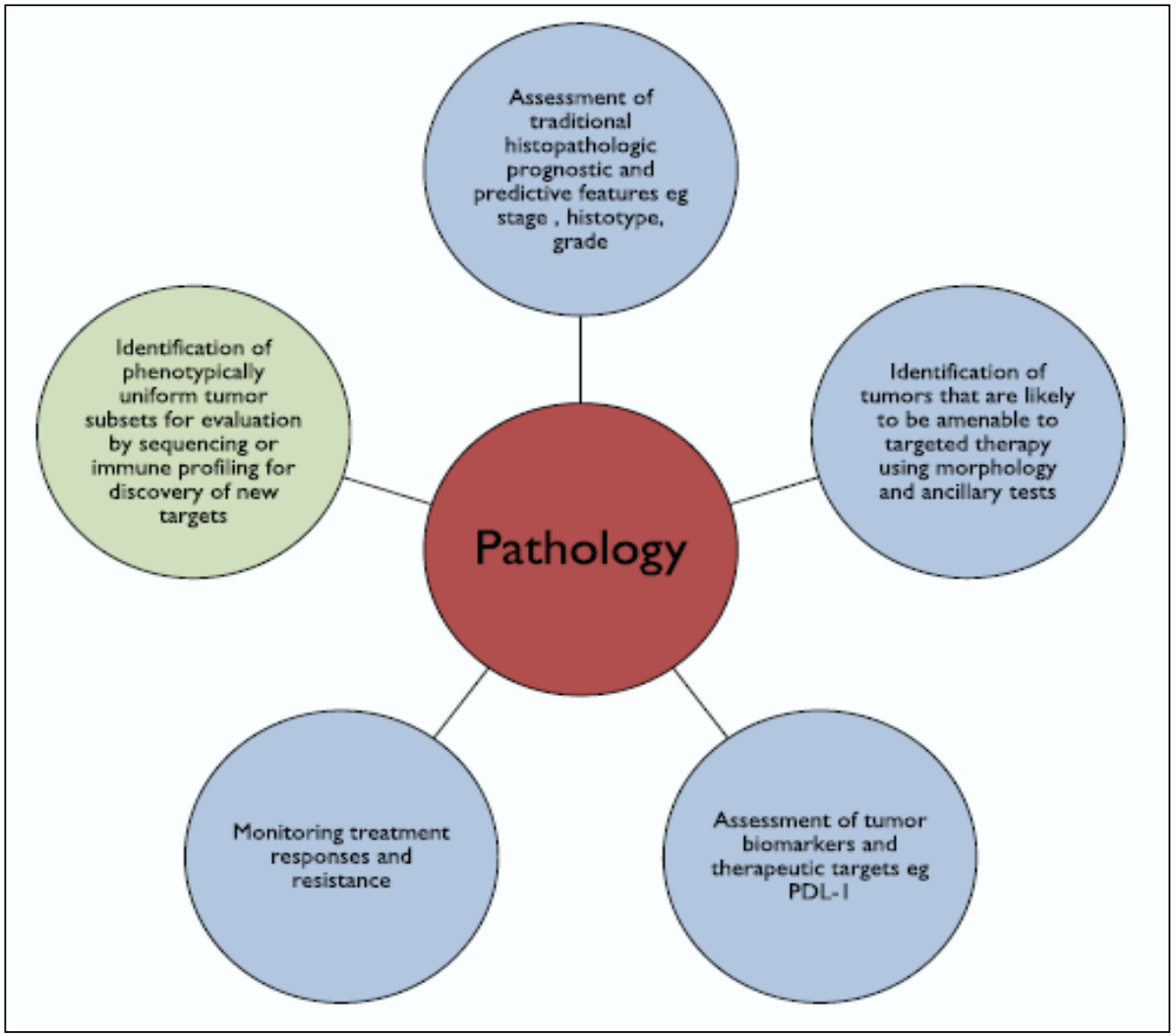
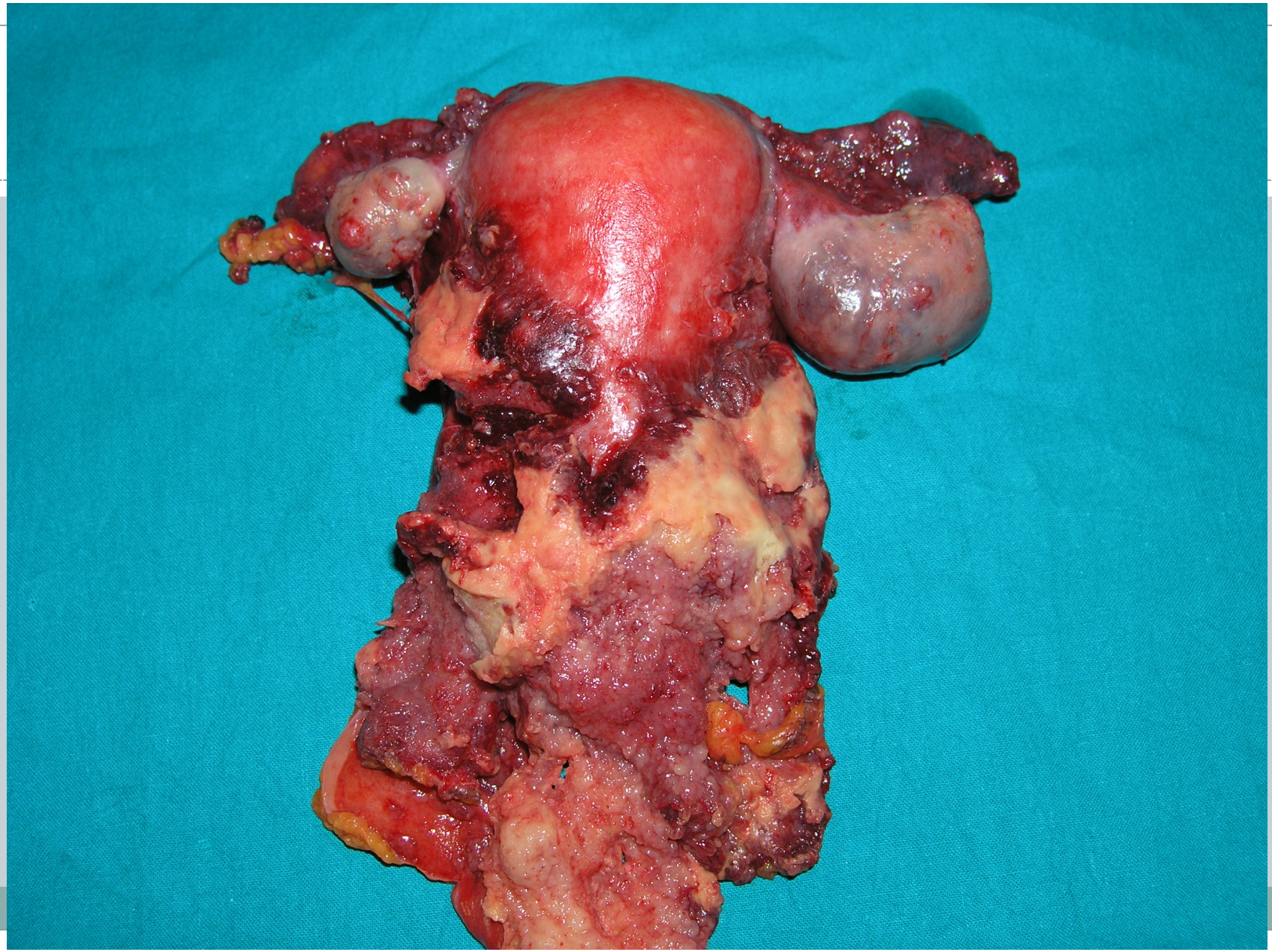
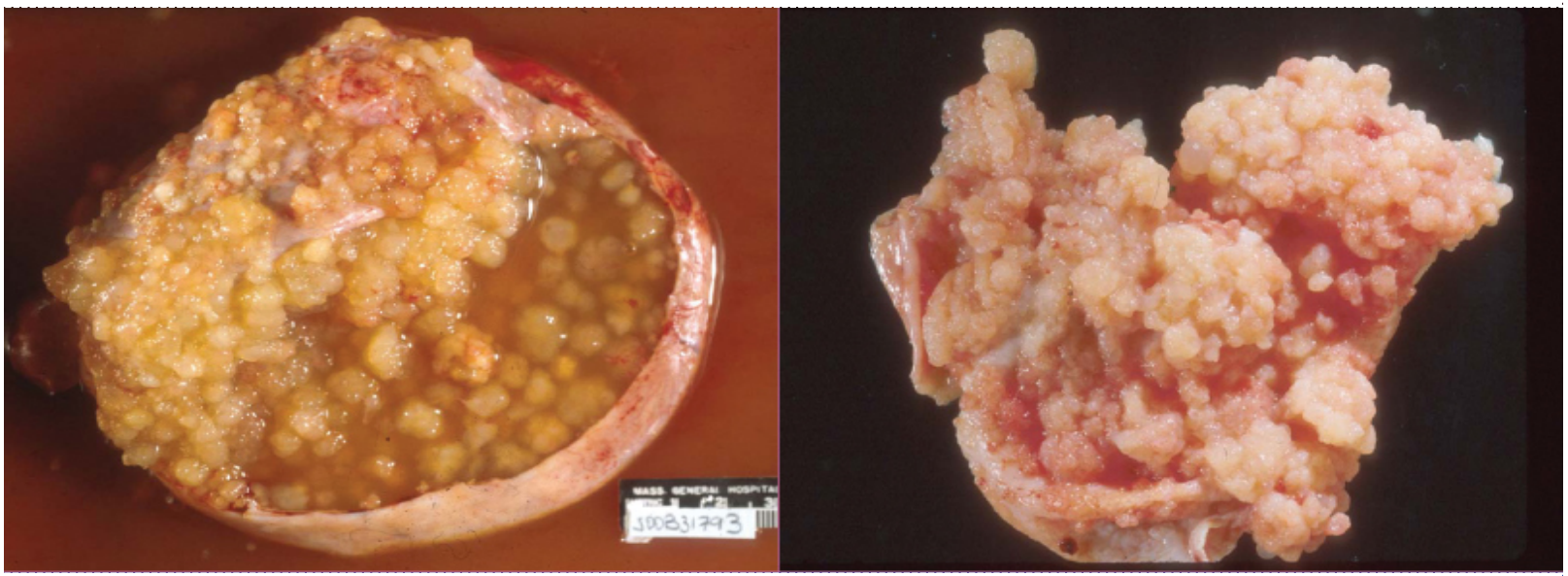
PATHOLOGY DRIVEN ONCOLOGY: learned clinical needs for modern treatments

Gian Franco Zannoni


Assessment of traditional histopathologic prognostic and predictive features eg stage , histotype, grade
Identification of phenotypically uniform tumor subsets for evaluation by sequencing or immune profiling for discovery of new targets
Identification of tumors that are likely to be amenable to targeted therapy using morphology and ancillary tests
Pathology
Monitoring treatment responses and resistance
Assessment of tumor biomarkers and therapeutic targets eg PDL-1

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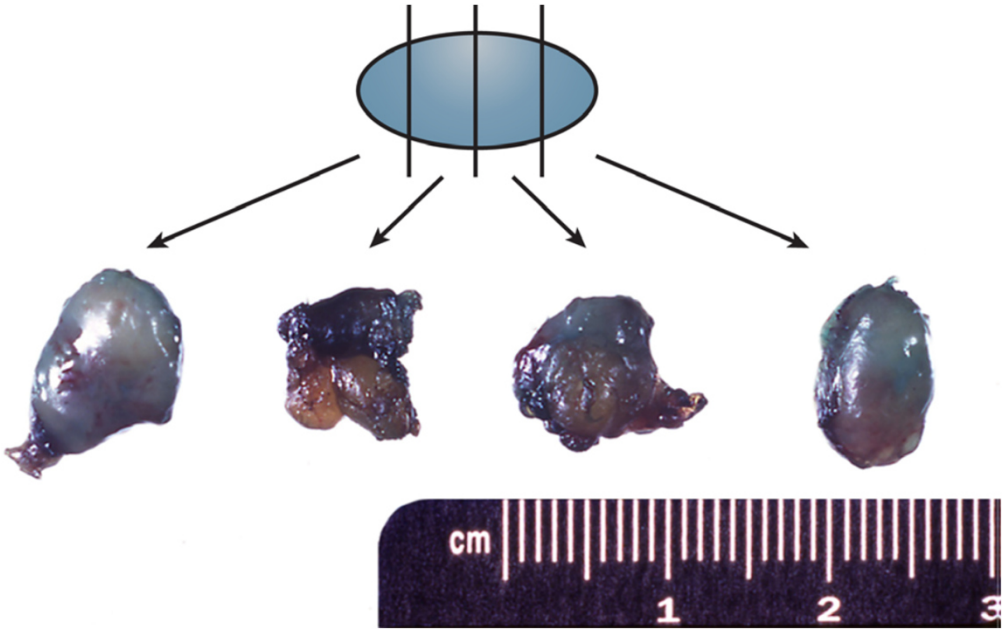
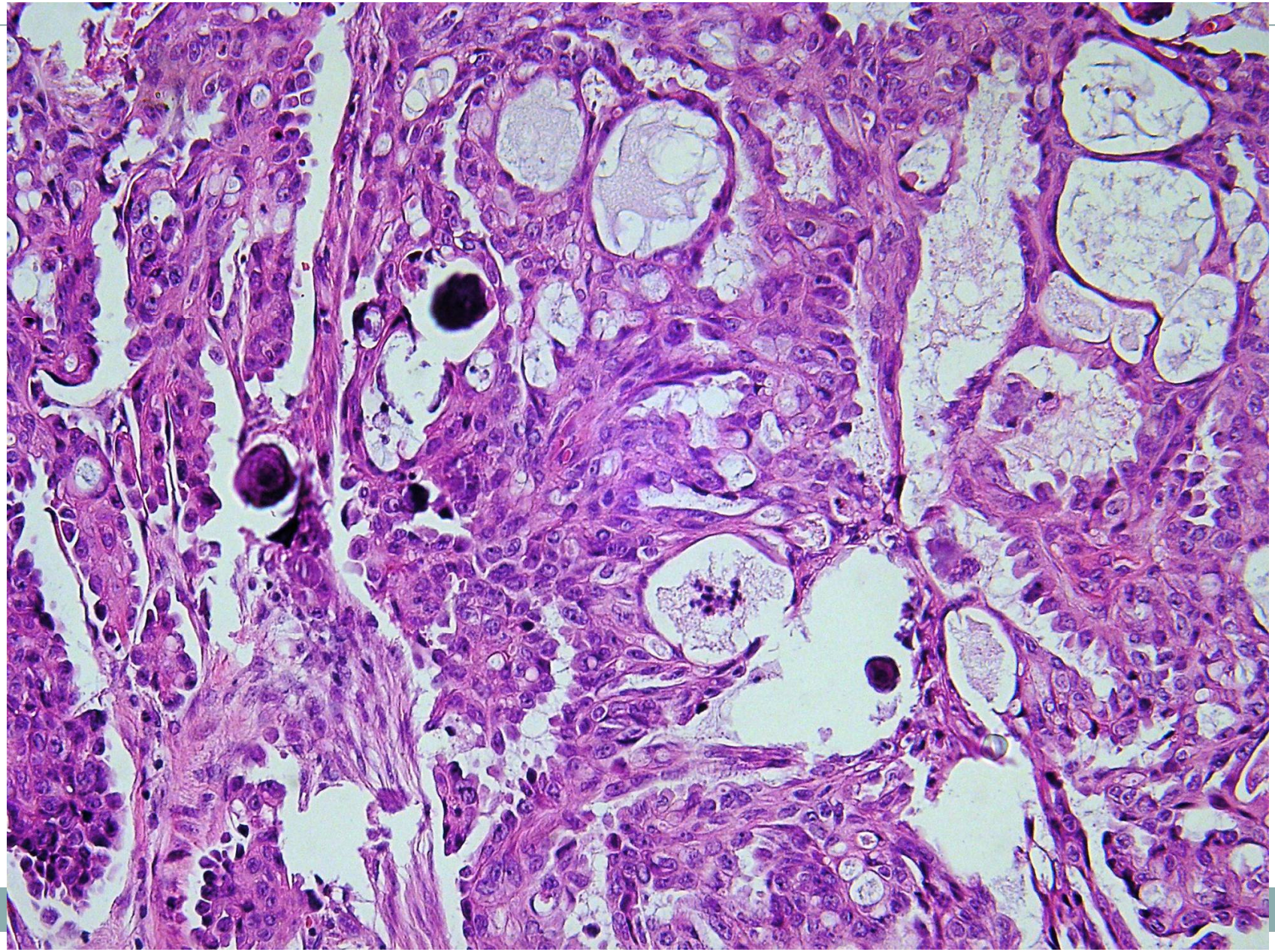
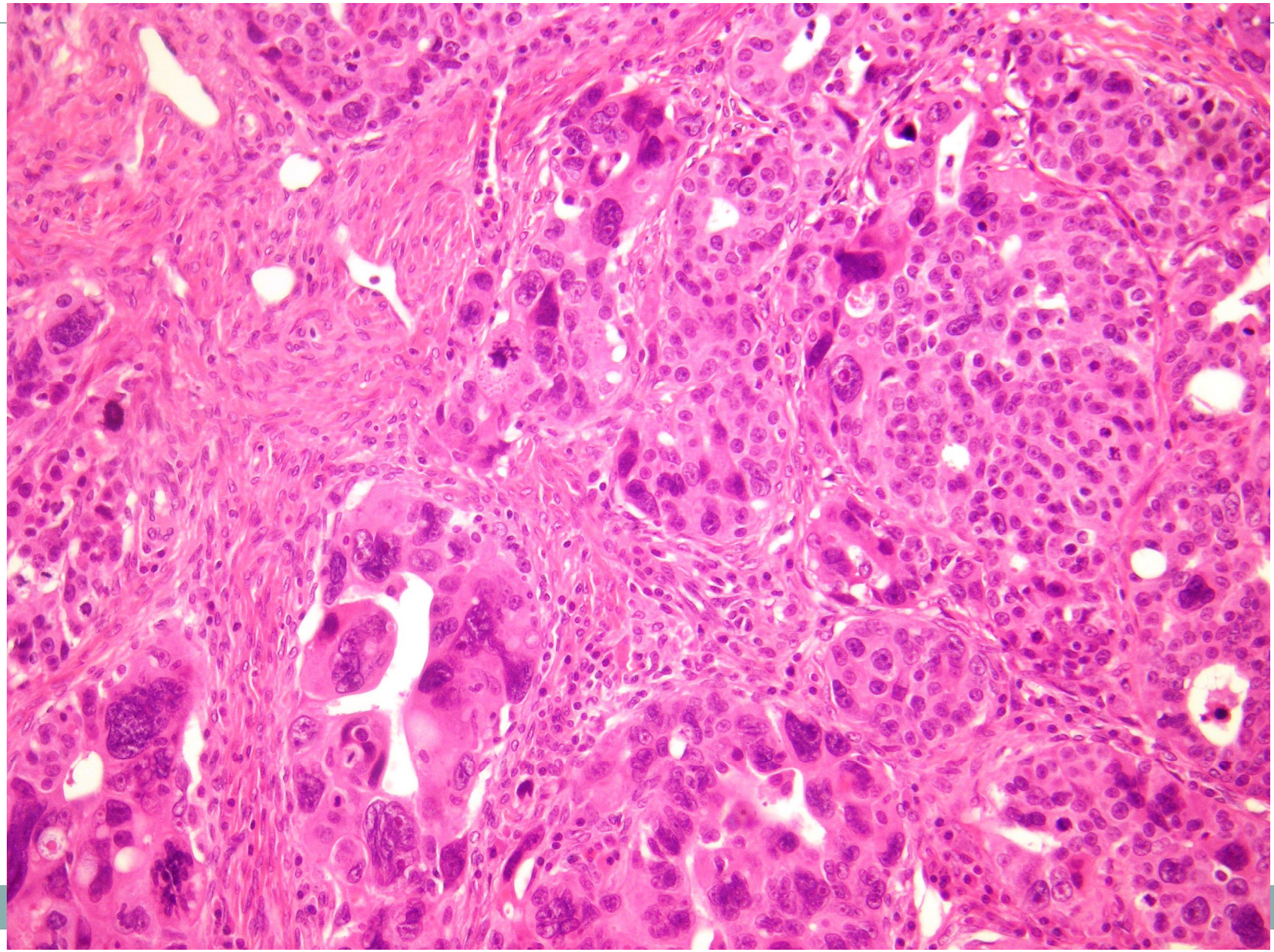


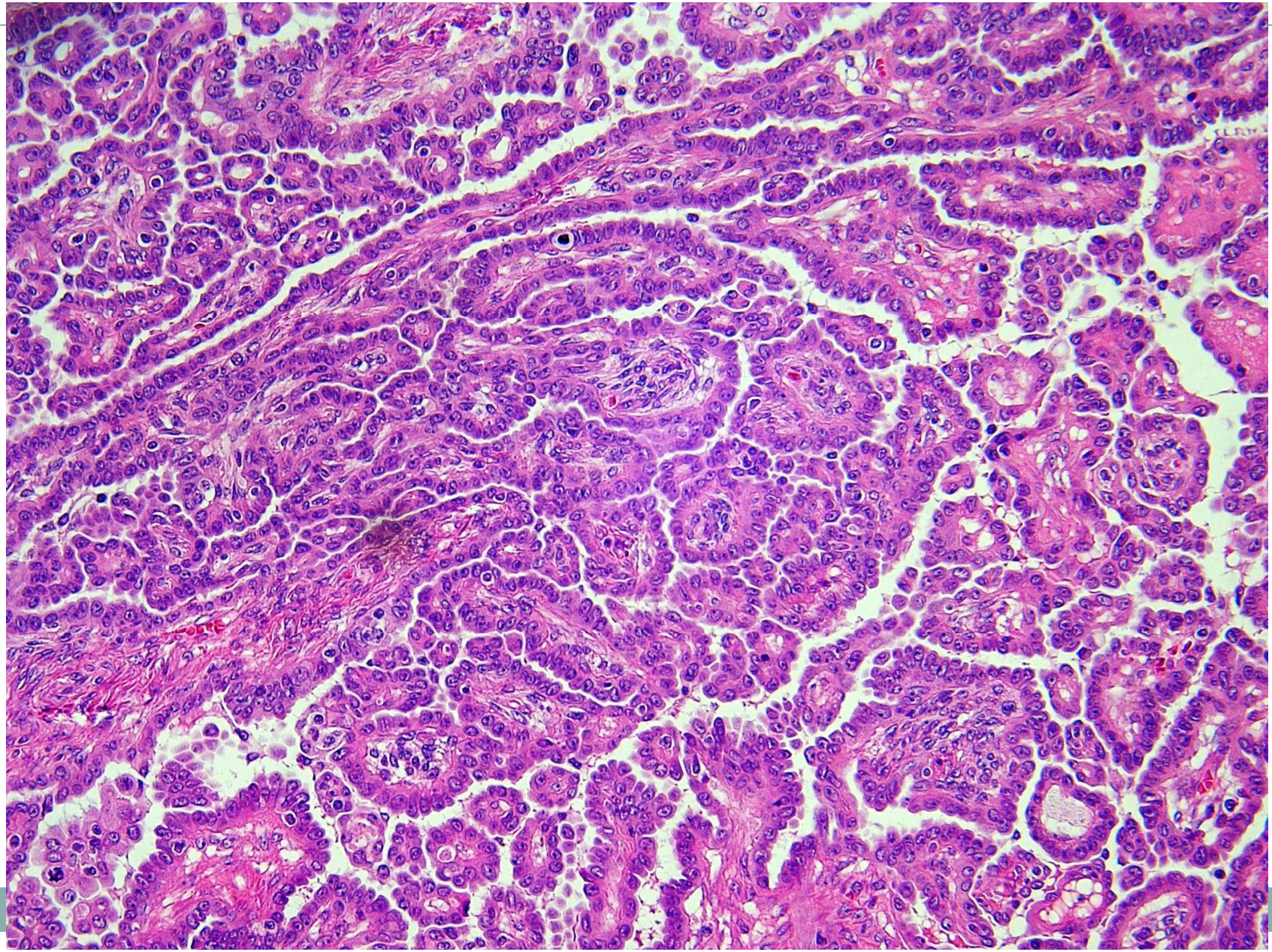
Gross evaluation of SLNs is the same, regardless of primary site.
LNs are thinly sectioned (≤2-mm-thick sections) perpendicular to the long axis.
This technique allows for maximum visualization of the LN surface area and subcapsular space

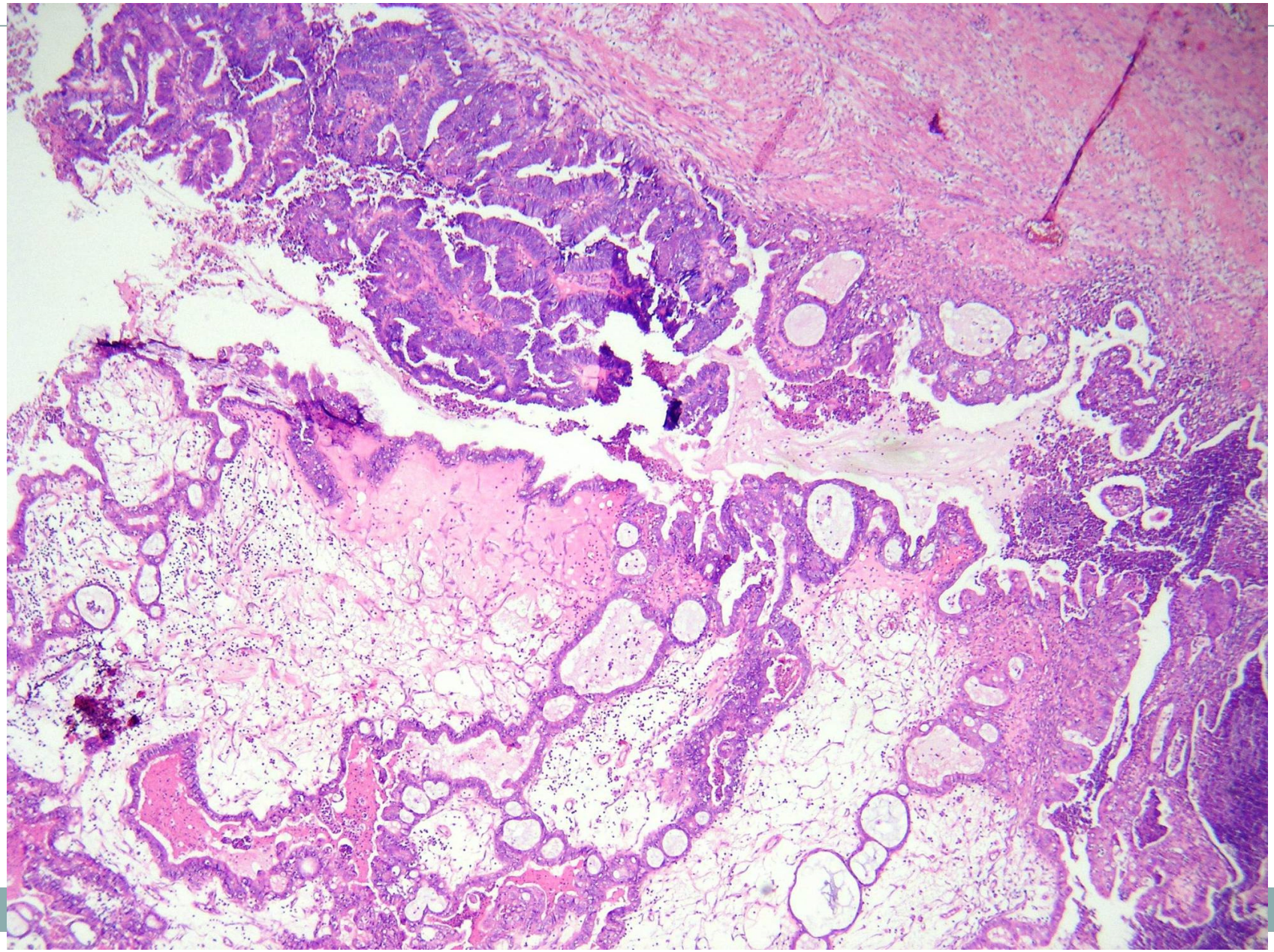
HISTOLOGY: the first step

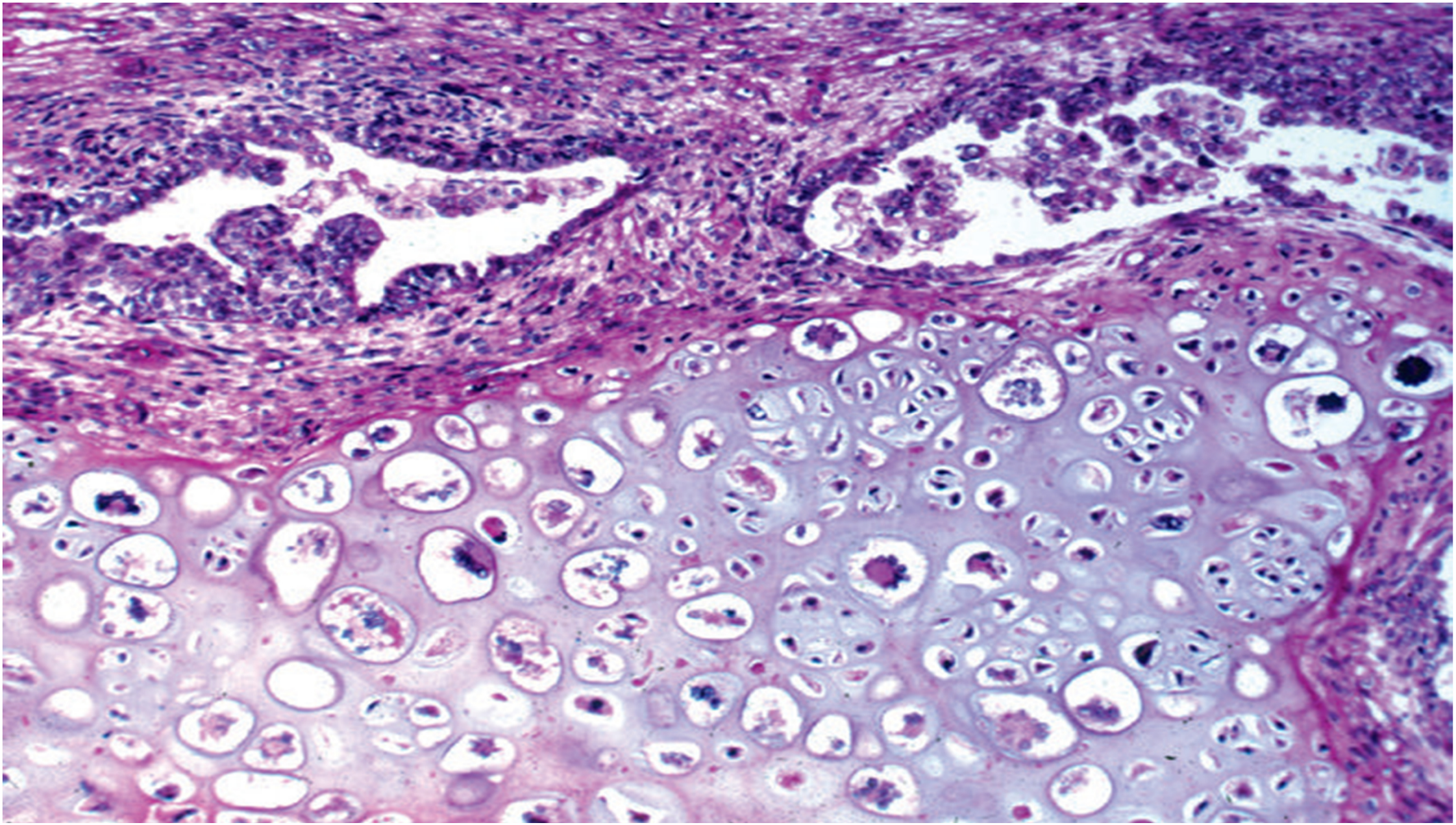
- Precise identification of histology
- Identify the correct pattern
- Use of immunoistochemestry
- Correlate with clinical information
- Assessment of prognostic factor

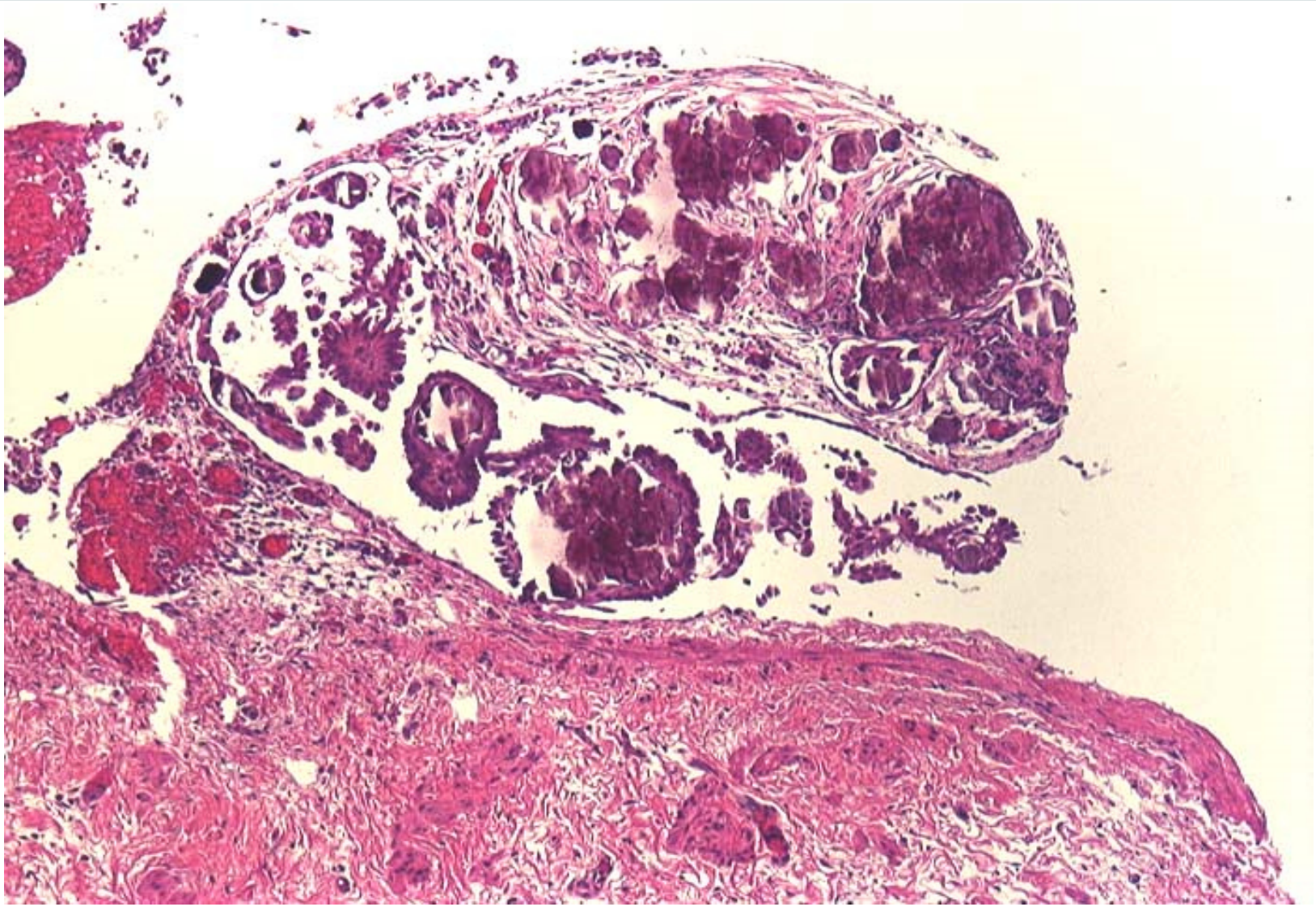


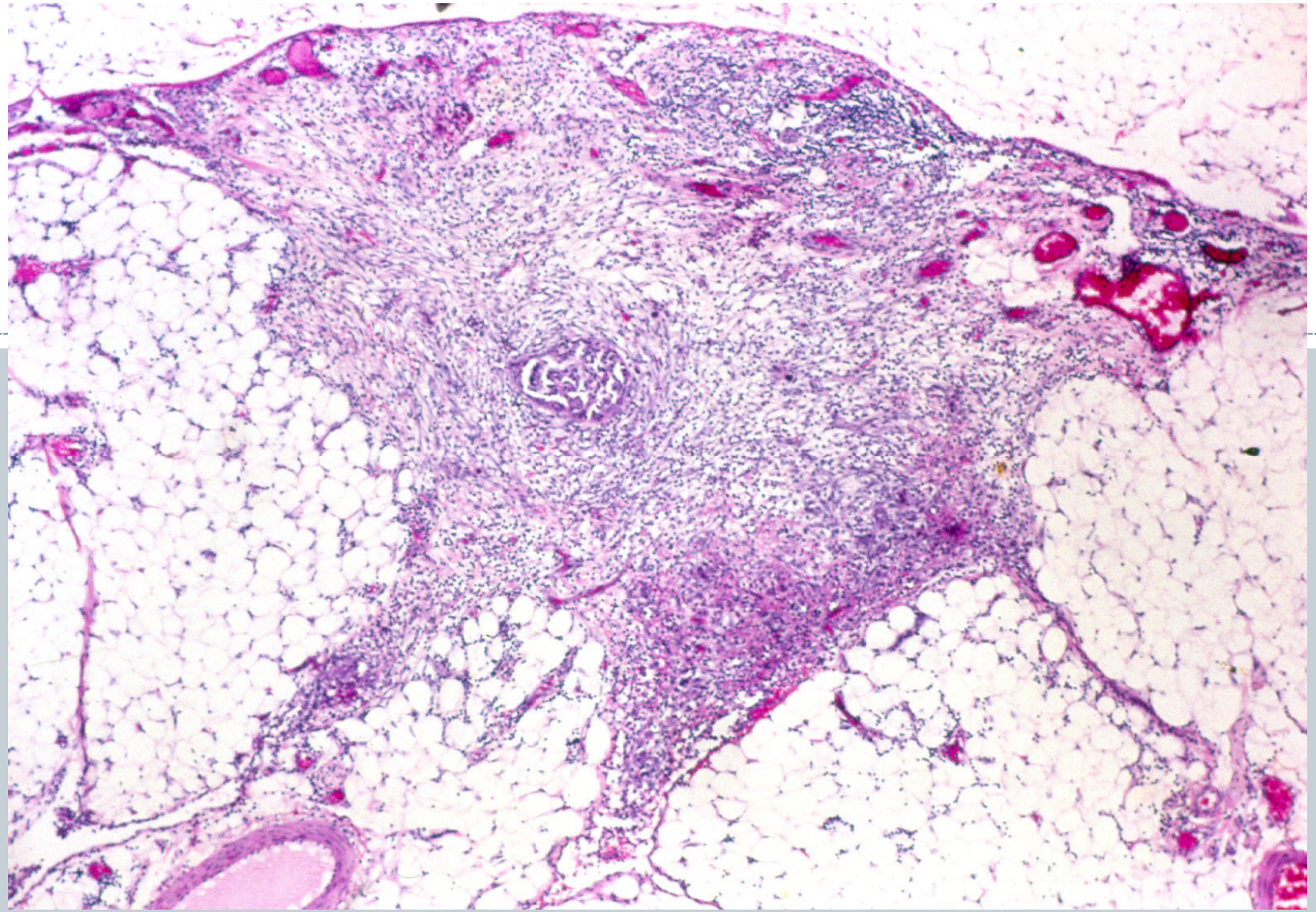


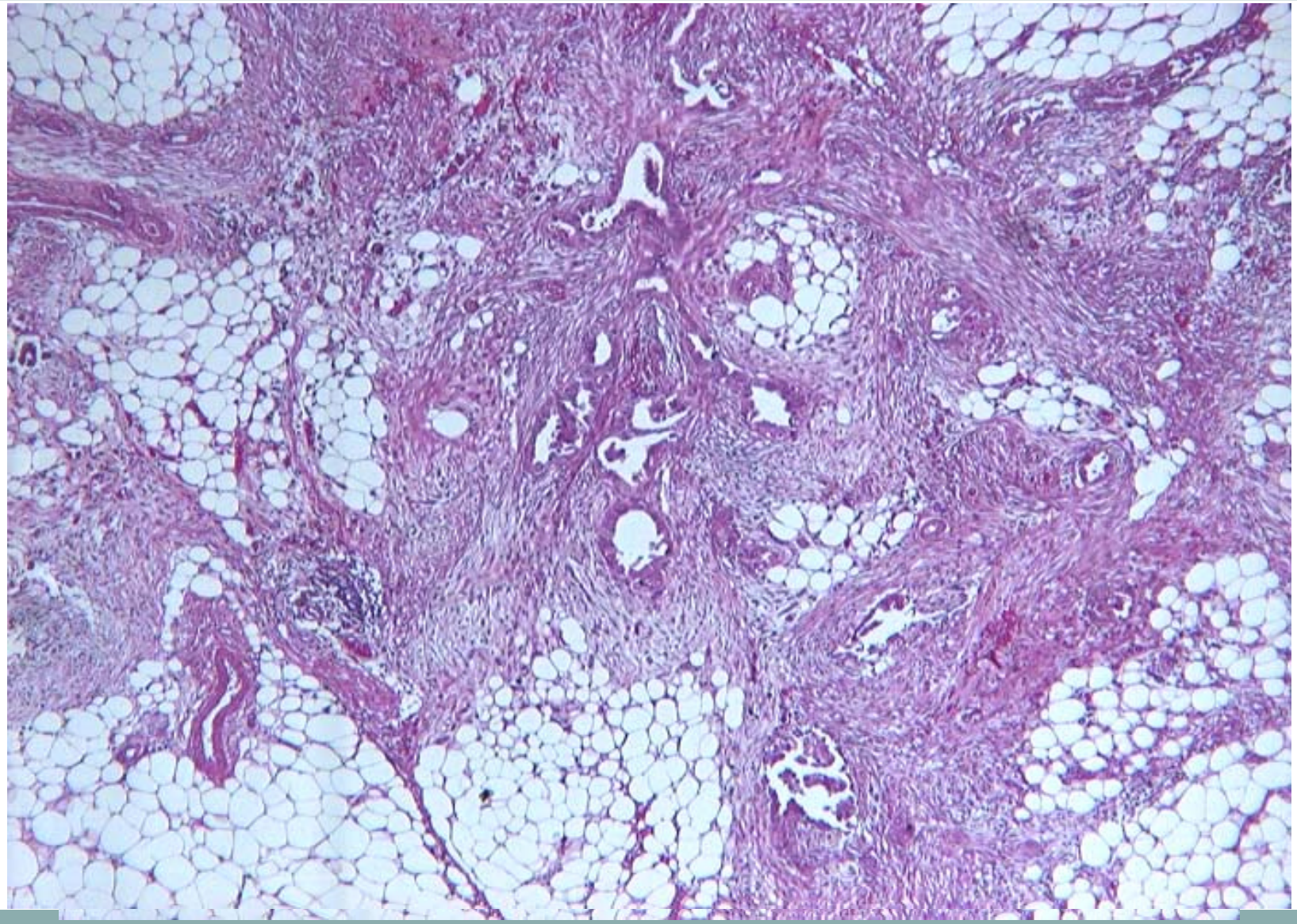


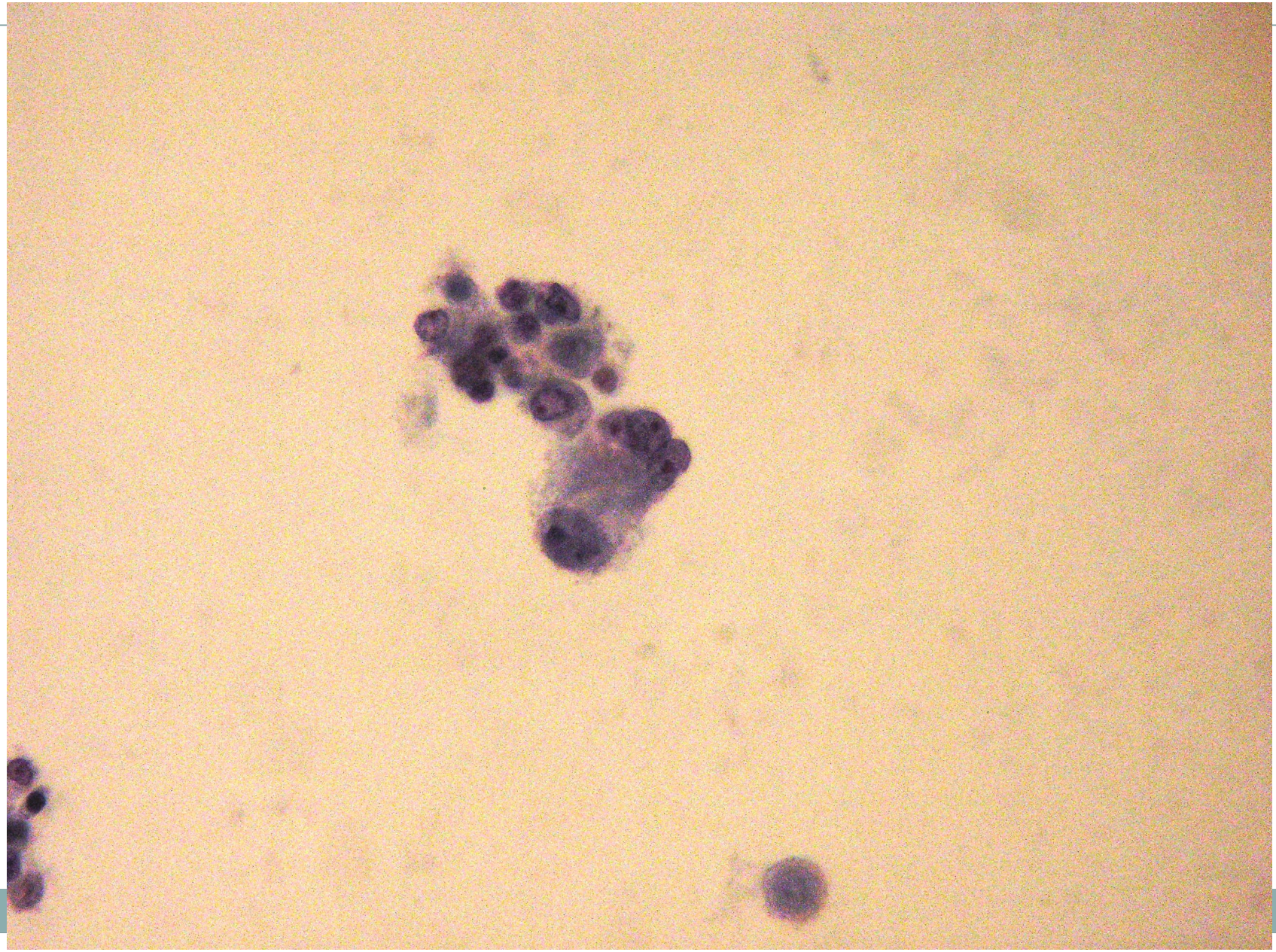


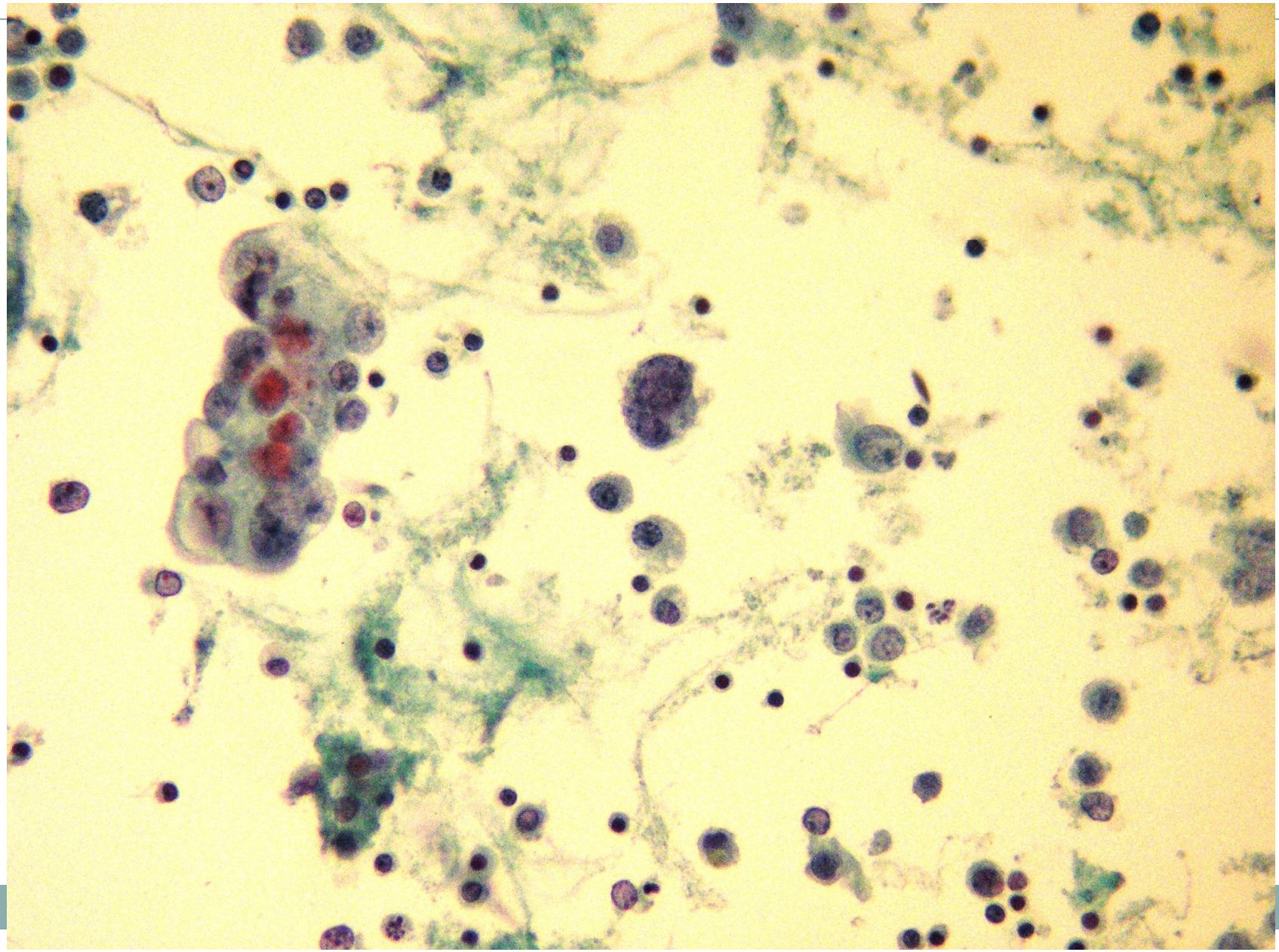


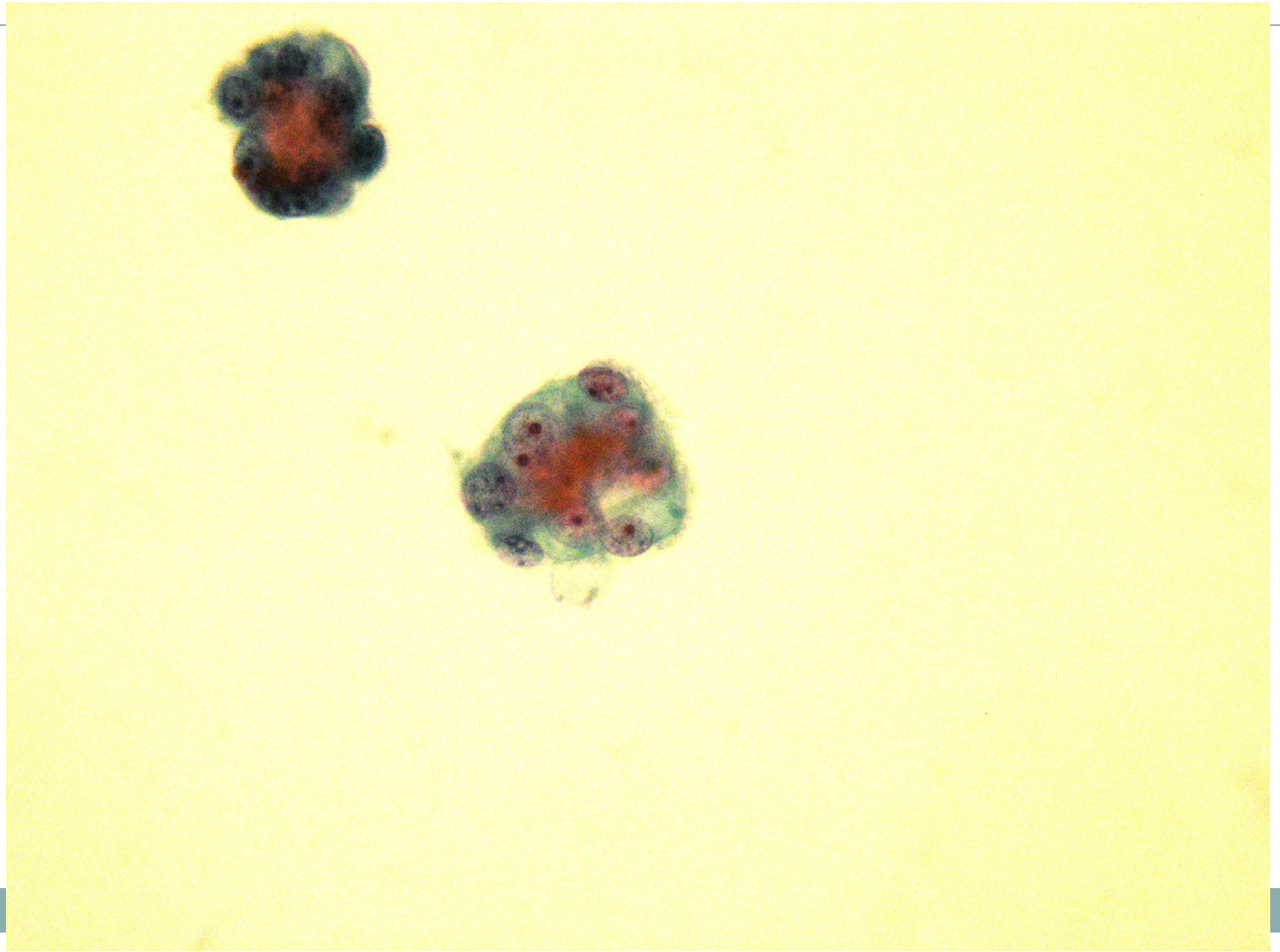


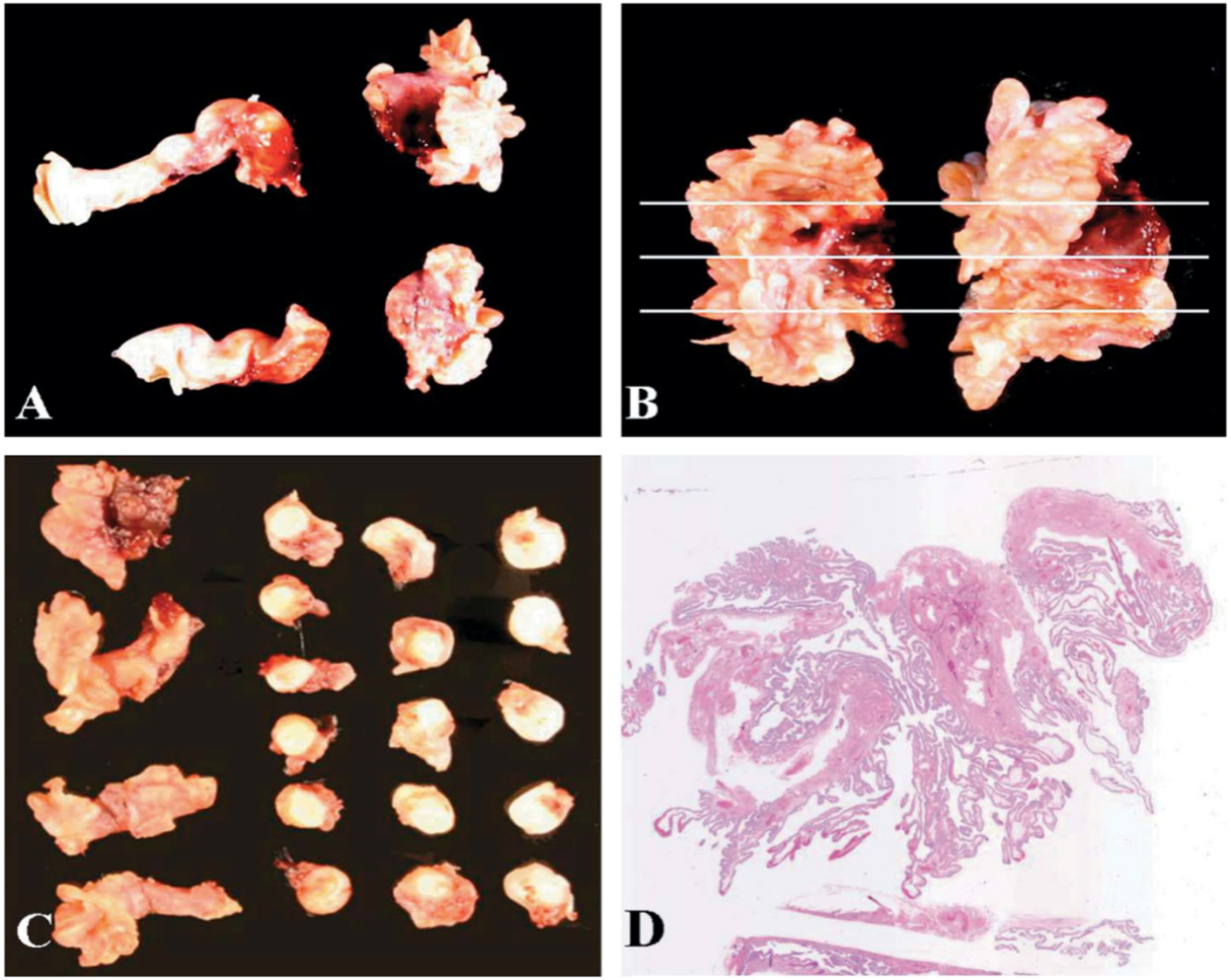








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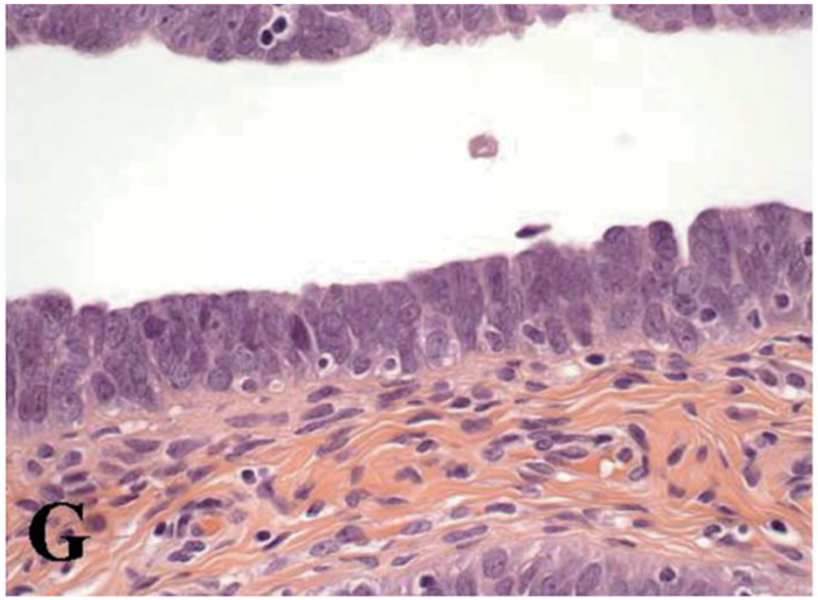
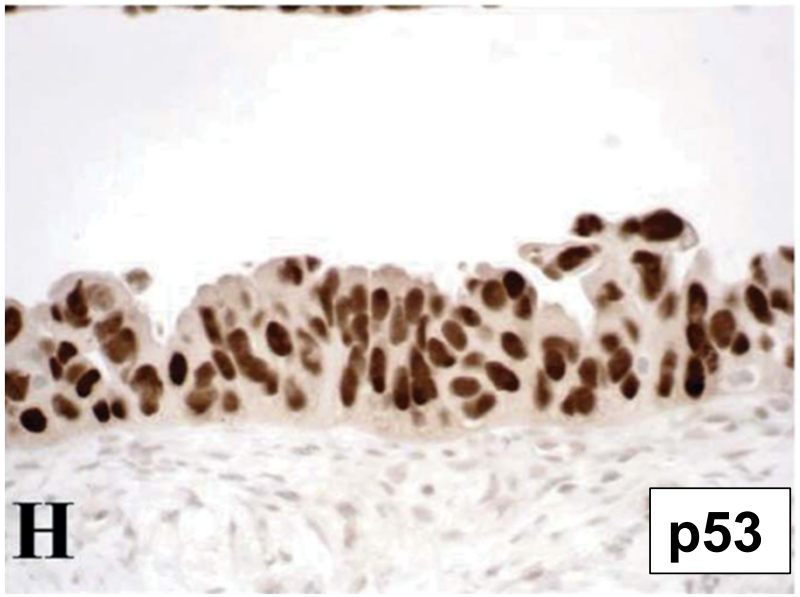
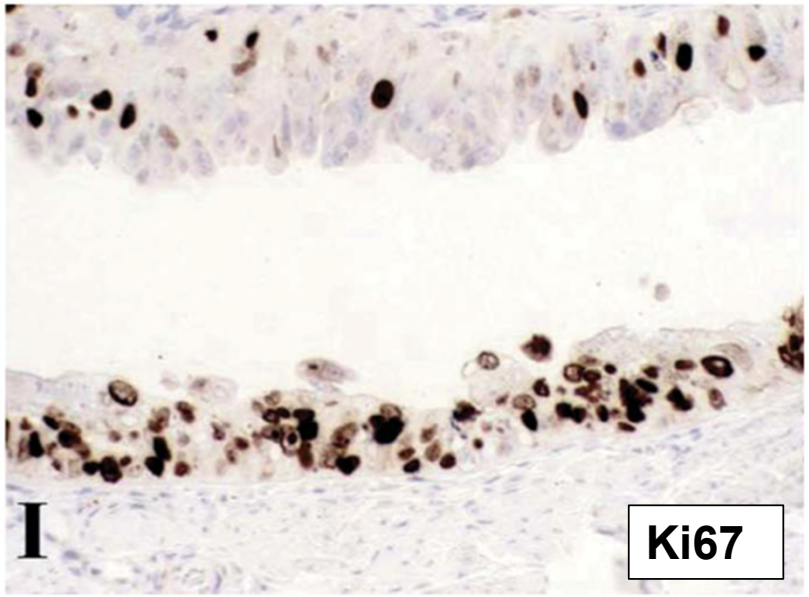






STIC
(Serous tubal in situ carcinoma)

In 40% of advanced HGSC

some studies have been demonstrated that STIC represents the early histologically detectable form of HGSC and it can disseminate to the ovary and metastasize

Am J Surg Pathol 2006; 30:230

STAGING: the second step

Table 1
2014 FIGO ovarian, fallopian tube, and peritoneal cancer staging system and corresponding TNM.

I	Tumor confined to ovaries or fallopian tube(s)	T1
IA	Tumor limited to one ovary (capsule intact) or fallopian tube, No tumor on ovarian or fallopian tube surface No malignant cells in the ascites or peritoneal washings	T1a
IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes No tumor on ovarian or fallopian tube surface No malignant cells in the ascites or peritoneal washings	T1b
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following: IC1 Surgical spill intraoperatively IC2 Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface IC3 Malignant cells present in the ascites or peritoneal washings	T1c
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp)	T2
IIA	Extension and/or implants on the uterus and/or fallopian tubes/and/or ovaries	T2a
IIB	Extension to other pelvic intraperitoneal tissues	T2b
III	Tumor involves one or both ovaries, or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	T3
IIIA	Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis	T1,T2,T3aN1
IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven)	
IIIA1(i)	Metastasis $\leq$ 10 mm in greatest dimension (note this is tumor dimension and not lymph node dimension)	T3a/T3aN1
IIIA1(ii)	Metastasis > 10 mm in greatest dimension	
IIIA 2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes	T3a/T3aN1
IIIB	Macroscopic peritoneal metastases beyond the pelvic brim $\leq$ 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes	T3b/T3bN1
III C	Macroscopic peritoneal metastases beyond the pelvic brim > 2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes (Note 1)	T3c/T3cN1
IV	Distant metastasis excluding peritoneal metastases Stage IV A: Pleural effusion with positive cytology Stage IV B: Metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity) (Note 2) (Note 1: includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ) (Note 2: Parenchymal metastases are Stage IV B)	Any T, Any N, M1 T3c/T3cN1)

Notes:
1. Includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ.
2. Parenchymal metastases are Stage IV B.

MOLECULAR pathway: the third step

- Pathogenesis
- Progression pathway
- Prognosis
- Target Therapy
- Response to therapy
- Familiar Syndrome

Morphologic patterns associated with *BRCA1* and *BRCA2* genotype in ovarian carcinoma

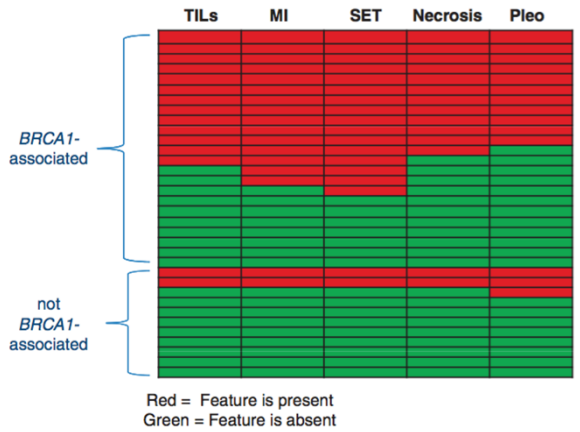
Robert A Soslow[1], Guangming Han[2], Kay J Park[1], Karuna Garg[1], Narciso Olvera[1], David R Spriggs[3], Noah D Kauff[3,4] and Douglas A Levine[5]

Morphological Features of HGSC BRCA1-related

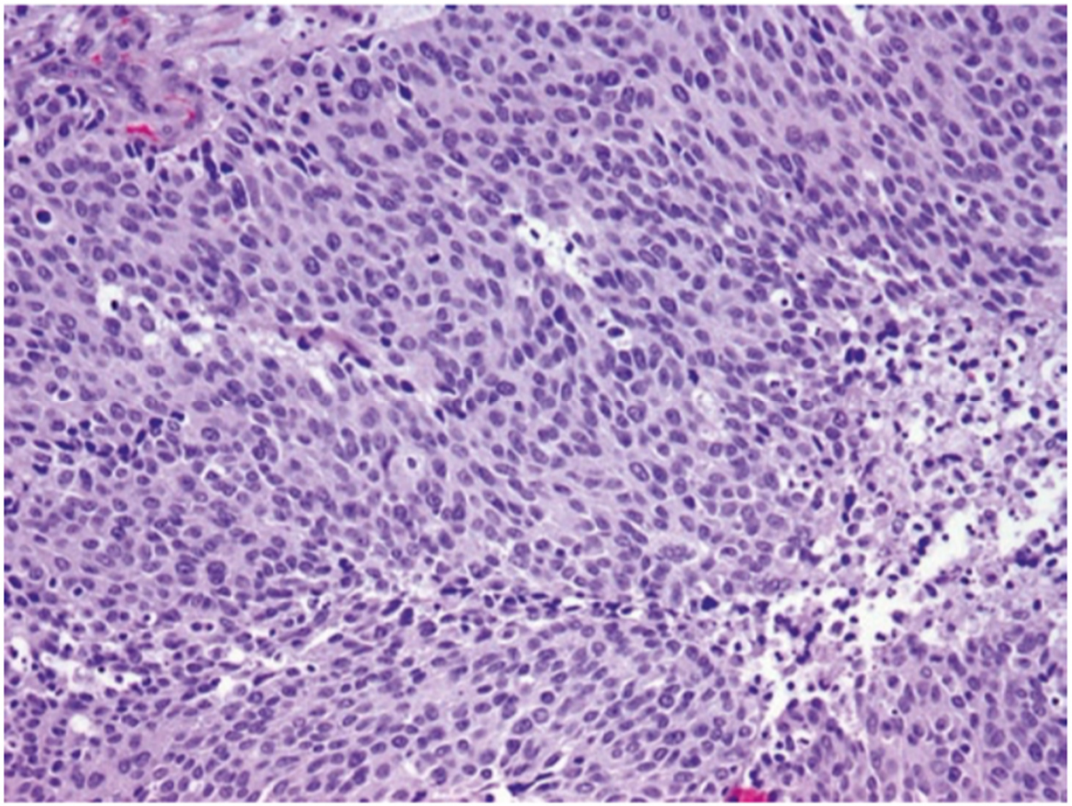
(both germline and somatic mutations)

- **SET** (Solid/pseudoEndometrioid/Transitional) pattern
- **Tumor infiltranting lymphocytes** (TIL)
- **Tubal involvement**
- Severe Pleomorphism
- Higher Mitotic Count
- Frequent necrosis (geographical/comedo)

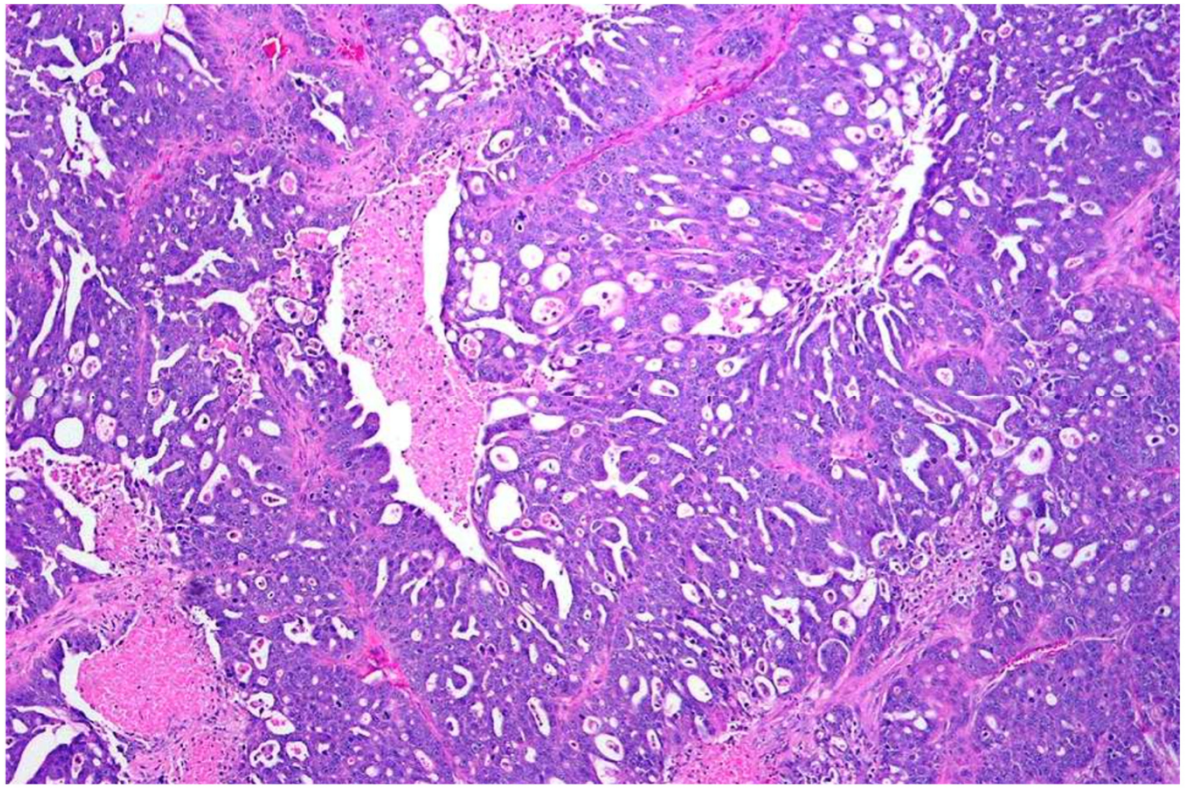
BRCA2-associated HGSC tends to have less-pronounced TIL and necrosis



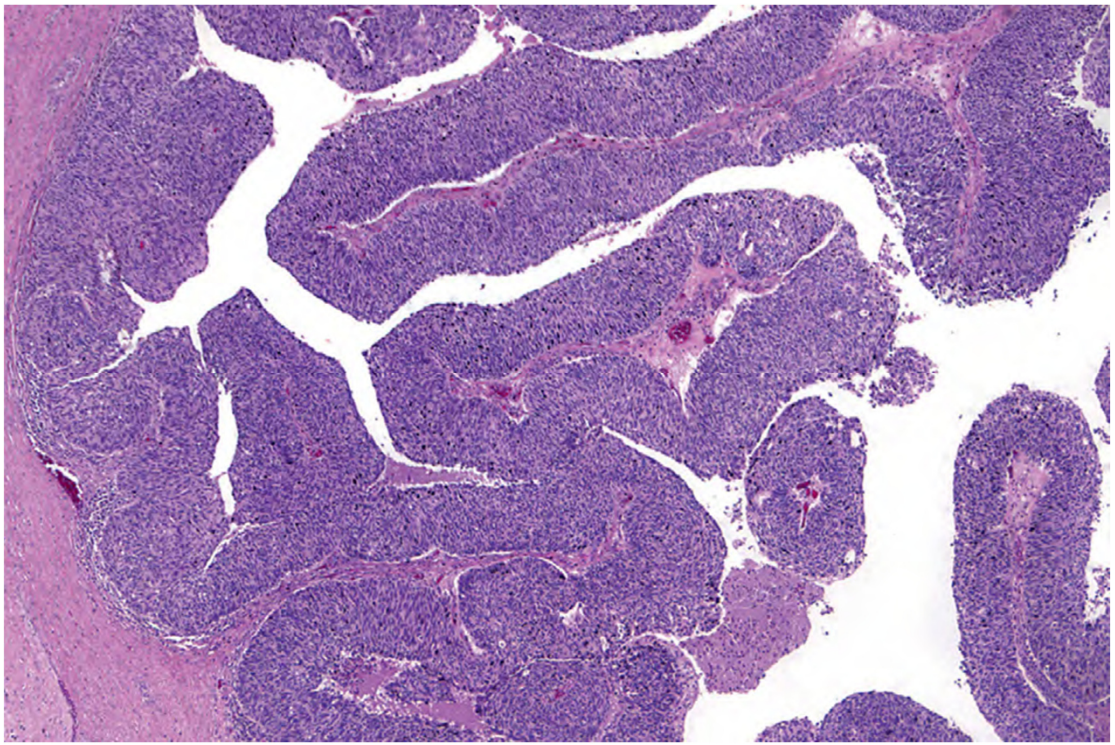
Modern Pathology 2012; 25:625



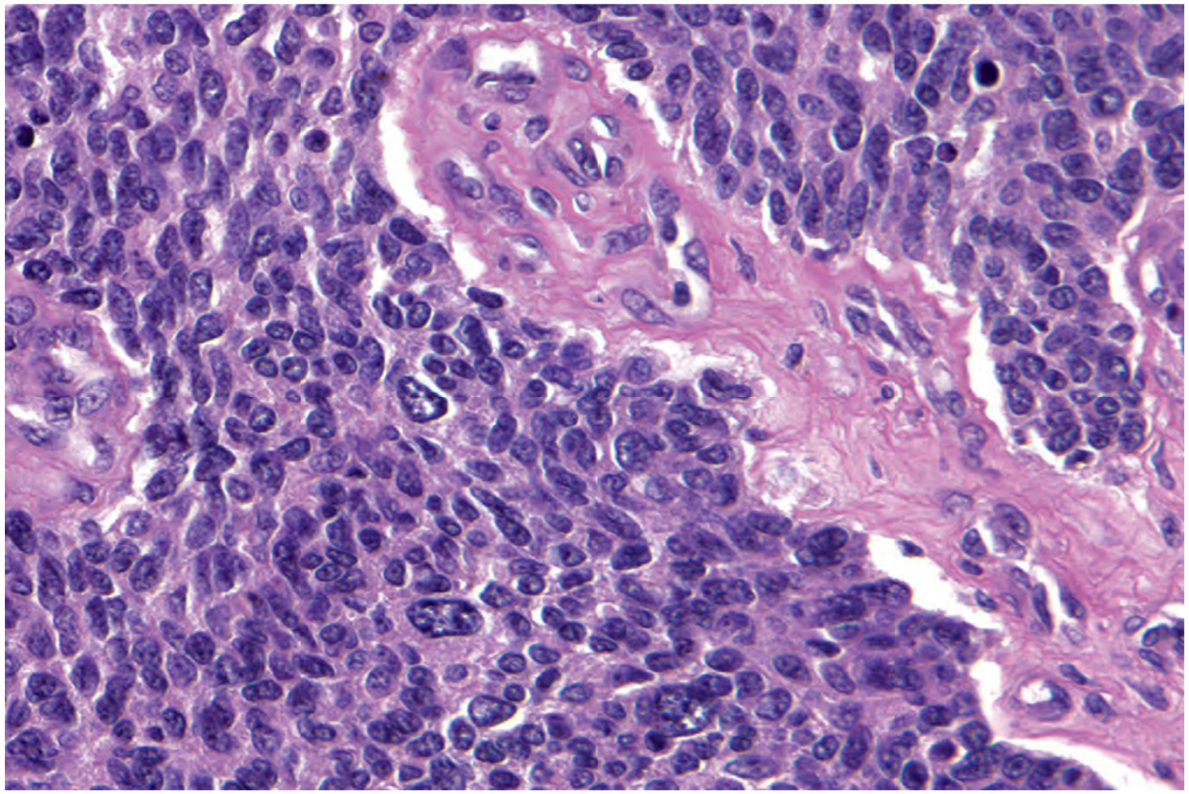
SET Solid



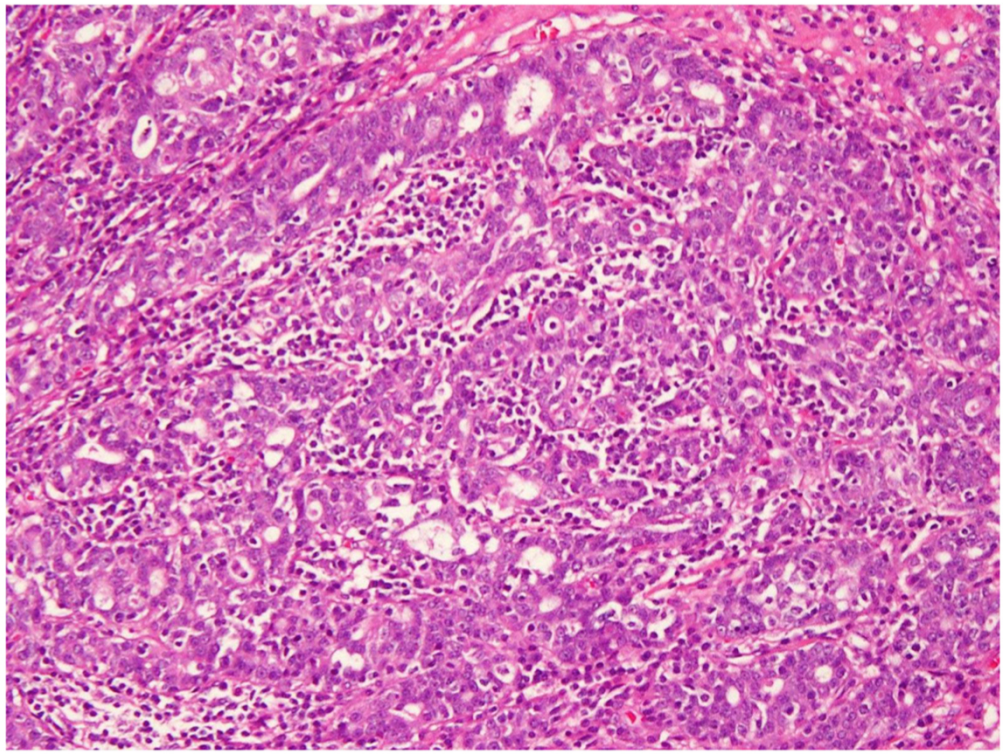
SET pseudo-Endometriod



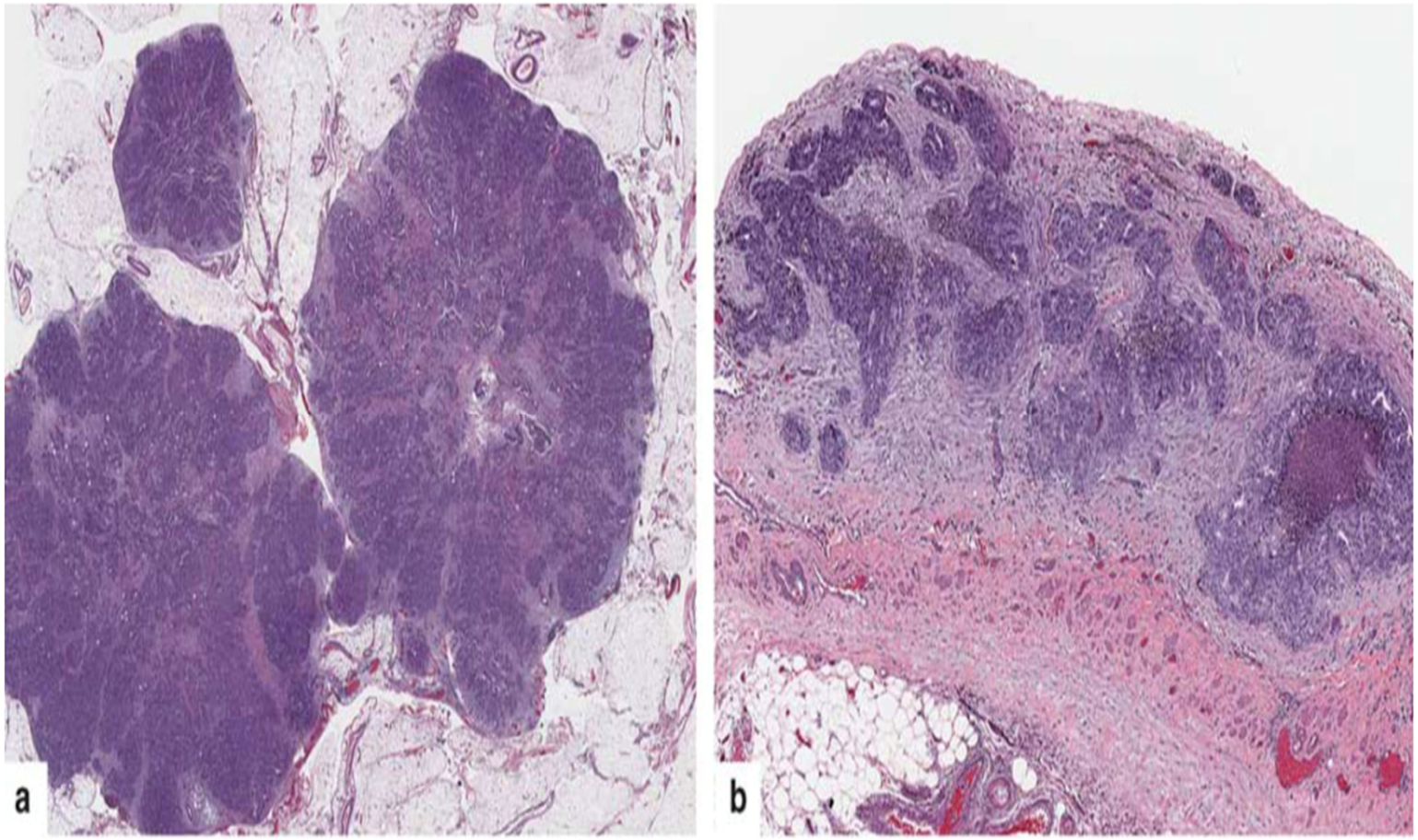
SET-Transitional



SET-Transitional



TIL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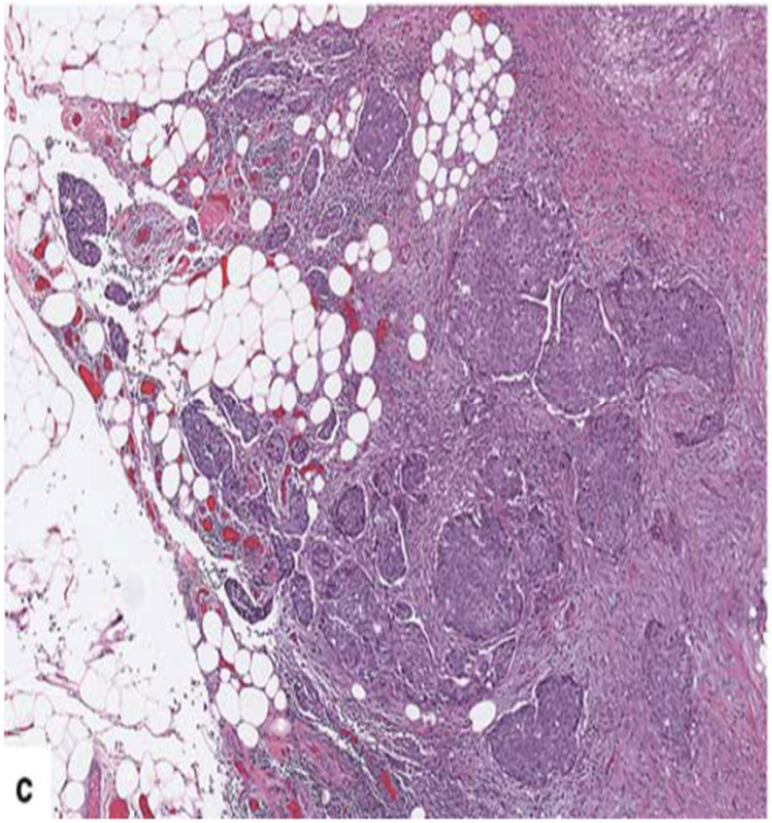
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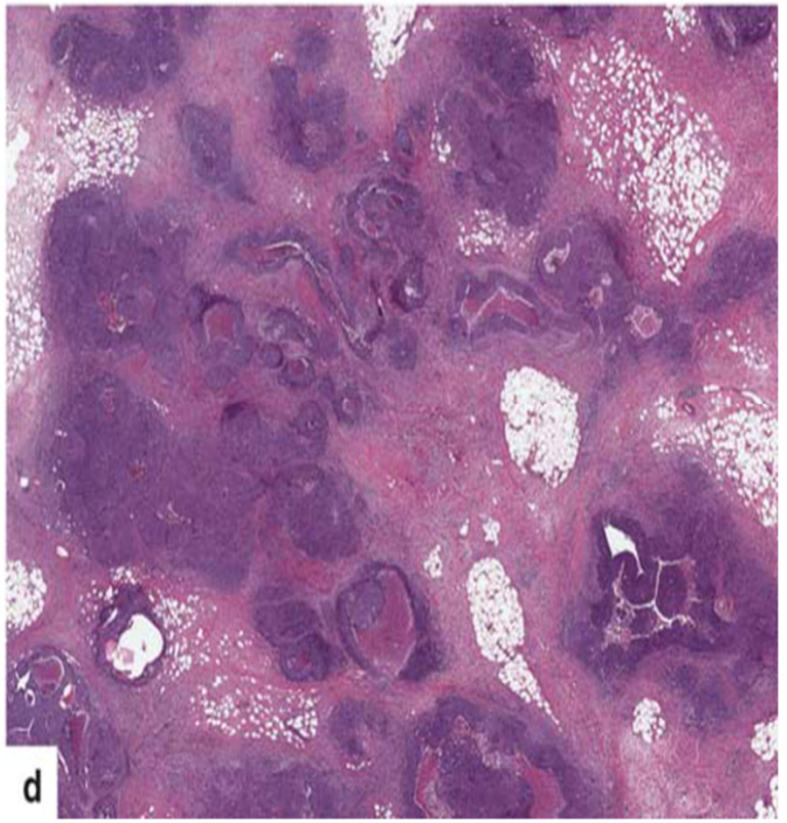
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Role of modern pathologist

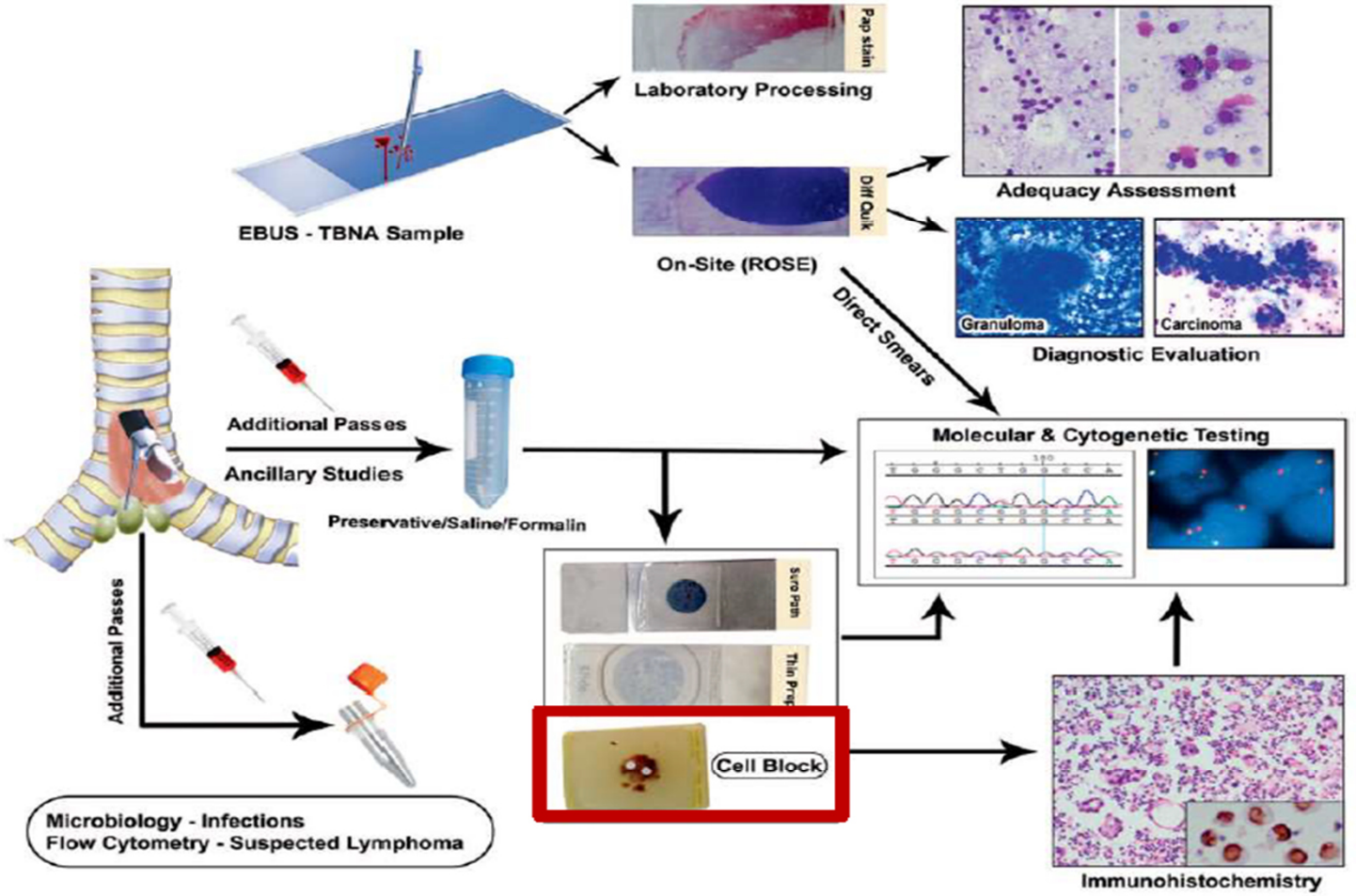

Figure 2. *Schematic diagram to show purpose and algorithmic flow of rapid on-site evaluation (ROSE) for endobronchial ultrasound–guided transbronchial needle aspirate (EBUS-TBNA) specimens.*

Jain D et al. Rapid On-Site Evaluation of Endobronchial Ultrasound-Guided Transbronchial Needle Aspirations for the Diagnosis of Lung Cancer: A Perspective From Members of the Pulmonary Pathology Society. Arch Pathol Lab Med. 2018 Feb;142(2):253-262.

A predictive biomarker indicates the likely benefit to the patient from the treatment, compared to their condition at baseline

Ruberg S.J., Shen L. (2015) Personalized medicine: four perspectives of tailored medicine. *Stat. Biopharm. Res.*, 7, 214–229.

A biomarker is predictive if the treatment effect (experimental compared with control) is different for biomarker-positive patients compared with biomarker-negative patients.

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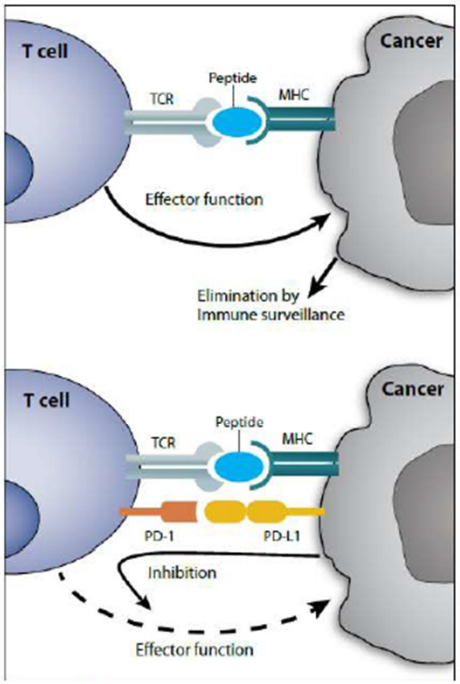
JOURNAL OF CLINICAL ONCOLOGY

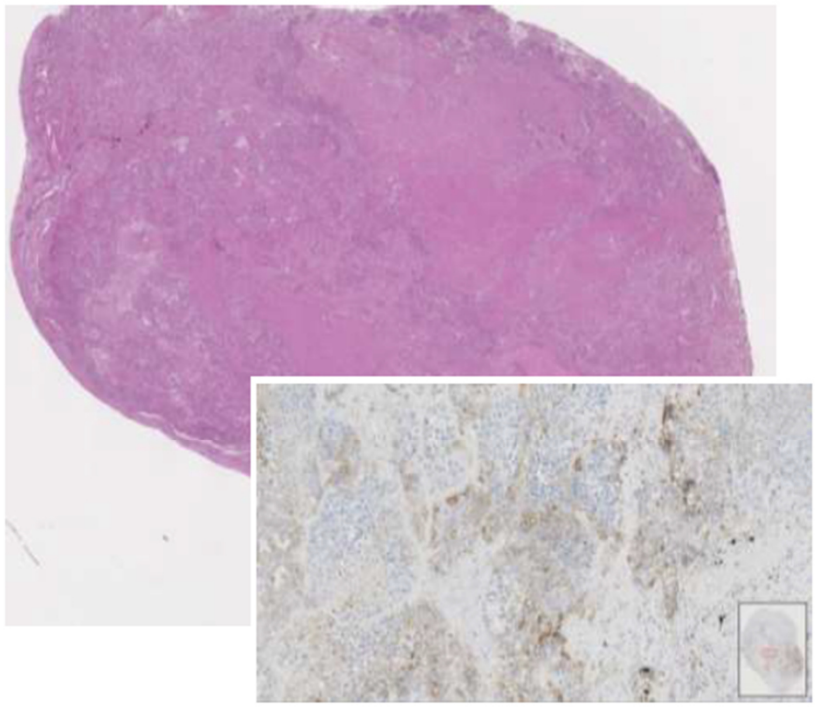
STATISTICS IN BRIEF

Biomarker: Predictive or Prognostic?

Karla V. Ballman

PD-L1 detection with immunohistochemistry (IHC) is the only predictive biomarker available to date for PD-L1/PD1 immunotherapy





IASLC ATLAS OF PD-L1 IMMUNOHISTOCHEMISTRY TESTING IN LUNG CANCER

ISBN: 978-0-9832958-7-7

Journal of *Personalized Medicine*

MDPI

Review

Atlas of PD-L1 for Pathologists: Indications, Scores, Diagnostic Platforms and Reporting Systems

Stefano Marletta [1,2], Nicola Fusco [3], Enrico Munari [4], Claudio Luchini [1], Alessia Cimadamore [5], Matteo Brunelli [1], Giulia Querzoli [6], Maurizio Martini [7], Elena Vigliar [8], Romano Colombari [9], Ilaria Girolami [10], Fabio Pagni [11] and Albino Eccher [6,*]

Table 1. Currently approved therapeutic indications, clones and scoring systems for immunohistochemical evaluation of PD-L1 status.

Tumor	Indications	Scoring System (Clones) and Therapeutic Guidelines
Lung cancer	1L/2L in stage IV NSCL or diffuse SCLC	TPS $\geq$ 1% (22C3, SP142, SP263) and IC $\geq$ 10% (SP142) *
GE cancer	1L or following lines in stage IV	CPS $\geq$ 1 (22C3, 28-8)
Colon and pancreas cancer	1L or following lines in stage IV MSI-H	IC $\geq$ 1% (28-8) (registration trial Check-Mate 142)
Breast cancer	1L or following lines in stage IV TNBC	IC $\geq$ 1% (SP142)
Urothelial carcinoma	1L platinum-unfit, 2L platinum-fit both in stage IV	CPS > 10 (22C3) and IC $\geq$ 5% (SP142)
Kidney cancer	1L in stage IV RCC	Therapy given regardless of PD-L1 status (22C3, SP142, SP263)
Melanoma	1L in stage IV melanoma	TPS $\geq$ 1% (22C3, 28-8, SP263) and MEL score > 2 (22C3)
HNSCC	1L in recurrent or stage IV HNSCC +/− platinum	CPS $\geq$ 1 (22C3, SP263) or regardless of PD-L1 status (+ platinum)

* use of specific scoring systems for each clone is recommended by FDA but not by EMA. Abbreviations: 1L: first line, 2L: second line, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, TPS: tumor proportion score, IC: immune cell score, GE: gastro-esophageal, CPS: combined proportion score, MSI-H: high microsatellite instability, NA: not available, TNBC: triple-negative breast cancer, RCC: renal cell carcinoma, HNSCC: head and neck squamous cell carcinoma.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma

J. Larkin, V. Chiarion-Sileni, R. Gonzalez, J.J. Grob, C.L. Cowey, C.D. Lao, D. Schadendorf, R. Dummer, M. Smylie, P. Rutkowski, P.F. Ferrucci, A. Hill, J. Wagstaff, M.S. Carlino, J.B. Haanen, M. Maio, I. Marquez-Rodas, G.A. McArthur, P.A. Ascierto, G.V. Long, M.K. Callahan, M.A. Postow, K. Grossmann, M. Sznol, B. Dreno, L. Bastholt, A. Yang, L.M. Rollin, C. Horak, F.S. Hodi, and J.D. Wolchok

N ENGL J MED 373;1 NEJM.ORG JULY 2, 2015

PD-L1 positivity was defined as at least 5% of tumor cells showing PD-L1 staining of any intensity on the cell surface in a section containing at least 100 tumor cells that could be evaluated.

Dako

An Agilent Technologies Company

PD-L1 IHC 28-8 pharmDx

CONCLUSIONS

Among previously untreated patients with metastatic melanoma, nivolumab alone or combined with ipilimumab resulted in significantly longer progression-free survival than ipilimumab alone. In patients with PD-L1–negative tumors, the combination of PD-1 and CTLA-4 blockade was more effective than either agent alone. (Funded by Bristol-Myers Squibb; CheckMate 067 ClinicalTrials.gov number, NCT01844505.)

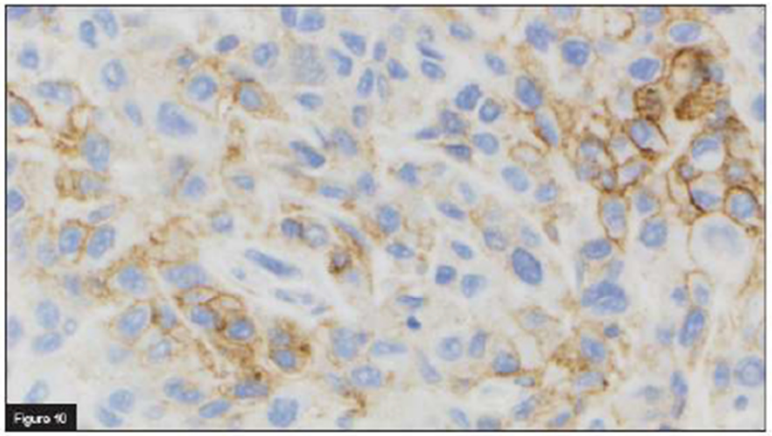


Figure 10

PD-L1 IHC 28-8 pharmDx Melanoma Interpretation Manual - US Version

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer

J. Cortes, H.S. Rugo, D.W. Cescon, S.-A. Im, M.M. Yusof, C. Gallardo, O. Lipatov, C.H. Barrios, J. Perez-Garcia, H. Iwata, N. Masuda, M. Torregroza Otero, E. Gokmen, S. Loi, Z. Guo, X. Zhou, V. Karantza, W. Pan, and P. Schmid, for the KEYNOTE-355 Investigators*

CONCLUSIONS

Among patients with advanced triple-negative breast cancer whose tumors expressed PD-L1 with a CPS of 10 or more, the addition of pembrolizumab to chemotherapy resulted in significantly longer overall survival than chemotherapy alone. (Funded by Merck Sharp and Dohme; KEYNOTE-355 ClinicalTrials.gov number, NCT02819518.)

Table 2. FDA-approved PD-L1 assays in clinical practice.

ICI	PD-L1 Assay	PD-L1 Score	Setting	Therapy	References
Pembrolizumab	22C3 (pharmDx)	CPS $\geq$ 10	Unresectable/metastatic TNBC	Pembrolizumab plus chemotherapy	Cortes, 2022 [40]
		CPS $\geq$ 1/regardless of PDL1 status	high-risk early-stage (NAD/AD)	Pembrolizumab plus chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant therapy	Downs-Canner, 2023 [41]
Atezolizumab	SP142 (Ventana)	IC score $\geq$ 1	Unresectable/metastatic TNBC	Atezolizumab plus nab-paclitaxel	Emens, 2021 [42]
		Regardless of IC	NAD	Atezolizumab	Mittendorf, 2020 [43]

Abbreviations: ICI—immune checkpoint inhibitor; TNBC—triple-negative breast cancer; NAD—neoadjuvant chemotherapy; AD—adjuvant chemotherapy; CPS—combined proportion score; IC—immune cell score.

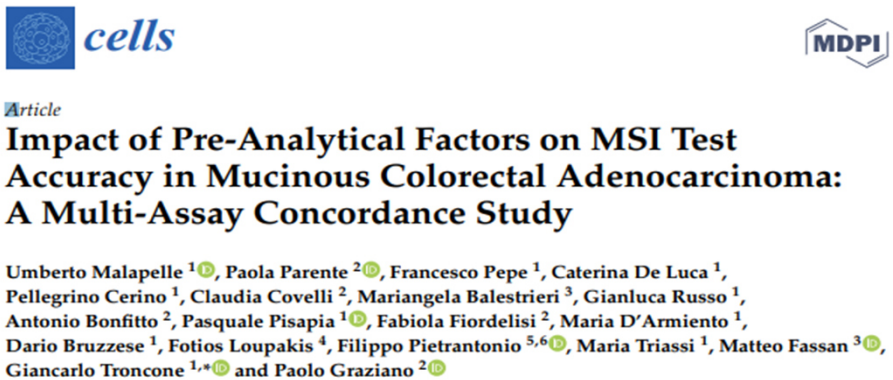
Table 3. Therapeutic approach in advanced TNBC based on PD-L1 IHC.

PD-L1 Status	FDA-Approved PD-L1 Scores	Therapy	Relevant Clinical Trials
PD-L1-negative	CPS < 10 (22C3) IC < 1 (SP142)	No Immunotherapy	
PD-L1-positive	CPS < 10 IC score $\geq$ 1%	Atezolizumab plus Nab-paclitaxel	IMpassion130 [42]
PD-L1-positive	CPS $\geq$ 10 IC score $\geq$ 1%	Pembrolizumab/Atezolizumab plus chemotherapy (Nab.paclitaxel or Carbo/Gem or paclitaxel)	Keynote-355 [40] Keynote-522 [41] IMpassion130 [42]
PD-L1-positive	CPS $\geq$ 10 IC score < 1%	Pembrolizumab plus chemotherapy (Nab.paclitaxel or Carbo/Gem or paclitaxel)	Keynote-355 [40] Keynote-522 [41]

Abbreviations: CPS—combined proportion score; IC—immune cell score.

Pre-analytical phase issues

- use of a 10% formalin buffer
- the duration of fixation
- storage of unstained slides
- storage of tissue blocks under controlled conditions (temperature, humidity, light)



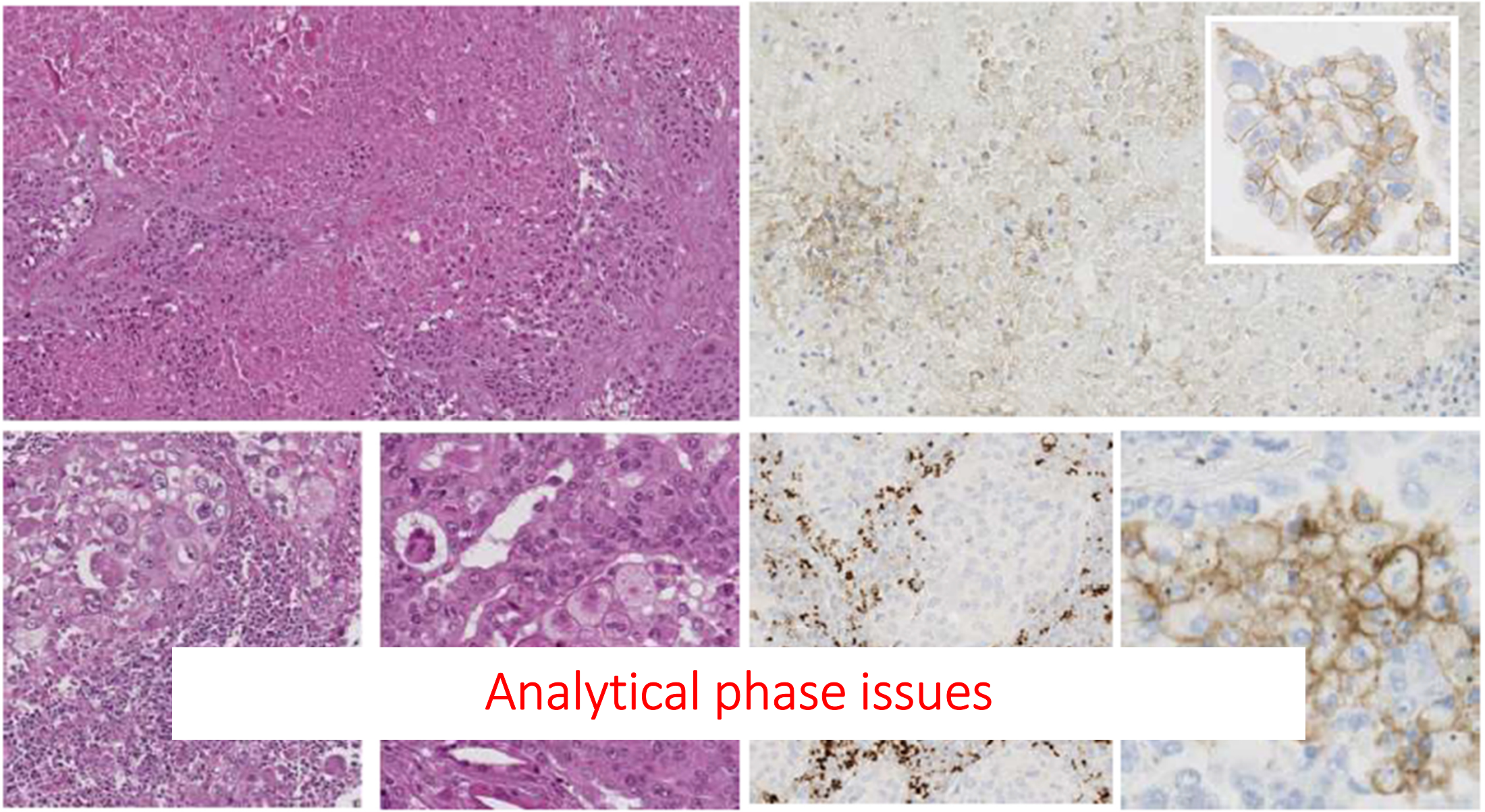
cells

MDPI

Article

Impact of Pre-Analytical Factors on MSI Test Accuracy in Mucinous Colorectal Adenocarcinoma: A Multi-Assay Concordance Study

Umberto Malapelle [1], Paola Parente [2], Francesco Pepe [1], Caterina De Luca [1], Pellegrino Cerino [1], Claudia Covelli [2], Mariangela Balestrieri [3], Gianluca Russo [1], Antonio Bonfitto [2], Pasquale Pisapia [1], Fabiola Fiordelisi [2], Maria D'Armiento [1], Dario Bruzzese [1], Fotios Loupakis [4], Filippo Pietrantonio [5,6], Maria Triassi [1], Matteo Fassan [3], Giancarlo Troncone [1,*] and Paolo Graziano [2]



Analytical phase issues

Sampling issues

Small tissue sample (biopsy, CYTOLOGY)

Resection specimen

Published in final edited form as:
J Am Soc Cytopathol. 2018 ; 7(3): 133–141. doi:10.1016/j.jasc.2018.02.003.

PD-L1 testing using the clone 22C3 pharmDx kit for selection of patients with non–small cell lung cancer to receive immune checkpoint inhibitor therapy: are cytology cell blocks a viable option?

Vanda F. Torous, MD[1], **Deepa Rangachari, MD**[2], **Benjamin P. Gallant**[2], **Meghan Shea, MD**[2], **Daniel B. Costa, MD, PhD**[2], and **Paul A. VanderLaan, MD, PhD**[1,*]

In a large cohort of lung cancer patients, cytology cell block specimens show similar testing characteristics to surgical pathology biopsy specimens.

Table 2

PD-L1 expression stratified by specimen type and clinically relevant tumor proportion score (TPS) cutoff values

PD-L1 TPS	Overall (n=232)	Cytology Cell-block Specimen (n=94)	Surgical Pathology Specimen (n=138)	p-value
<1% PD-L1 TPS	87 (37.5%)	35 (37.2%)	52 (37.7%)	0.4
1–49% PD-L1 TPS	55 (23.7%)	20 (21.3%)	35 (25.3%)	
≥50% PD-L1 TPS	81 (34.9%)	33 (35.1%)	48 (34.8%)	
Failed analysis	9 (3.9%)	6 (6.4%)	3 (2.2%)	

P-value via Fisher's exact test.

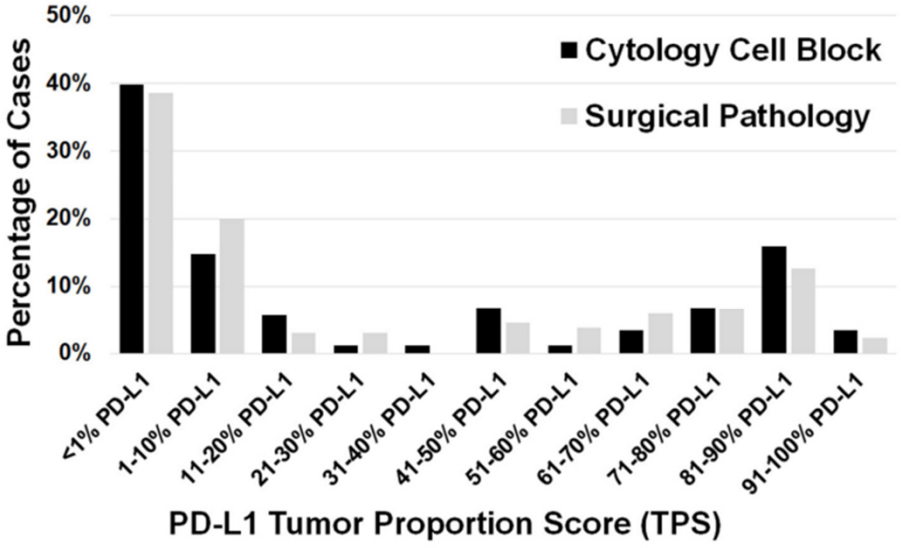


Figure 1.
PD-L1 expression stratified by specimen type and increasing 10%-increments of tumor proportion score (TPS).

ORIGINAL ARTICLE

PD-L1 Immunohistochemistry Comparability Study in Real-Life Clinical Samples: Results of Blueprint Phase 2 Project

81 samples

- 21 resections
- 20 core needle or bronchial biopsy samples
- 18 tumor-positive lymph node excision biopsy
- **22 cytological cell blocks**

24 experienced pulmonary pathologists *IASLC Pathology Committee members*
15 countries across five continents

- highly comparable staining by the 22C3, 28–8 and SP263 assays
- less sensitivity with the SP142 assay
- higher sensitivity with the 73–10 assay to detect PD-L1 expression on TCs
- Glass slide and digital image scorings were highly concordant

strong reliability among pathologists in TC PD-L1 scoring with all assays
poor reliability in IC PD-L1 scoring
good agreement in assessing PD-L1 status on cytological cell block

FOCUS ON MMRd/MSI

Endometrial Cancer

cancers MDPI

Review

New Pathological and Clinical Insights in Endometrial Cancer in View of the Updated ESGO/ESTRO/ESP Guidelines

Angela Santoro [1], Giuseppe Angelico [1], Antonio Travaglino [1], Frediano Inzani [1], Damiano Arciuolo [1], Michele Valente [1], Nicoletta D'Alessandris [1], Giulia Scaglione [1], Vincenzo Fiorentino [1], Antonio Raffone [2] and Gian Franco Zannoni [1,3,*]

Int. J. Mol. Sci. 2022, 23, 11684. https://doi.org/10.3390/ijms231911684 https://www.mdpi.com/journal/ijms

International Journal of Molecular Sciences MDPI

Review

TCGA Molecular Prognostic Groups of Endometrial Carcinoma: Current Knowledge and Future Perspectives

Damiano Arciuolo [1,2], Antonio Travaglino [1,3], Antonio Raffone [4], Diego Raimondo [4], Angela Santoro [1], Daniela Russo [3], Silvia Varricchio [3], Paolo Casadio [4], Frediano Inzani [1], Renato Seracchioli [4], Antonio Mollo [5], Massimo Mascolo [3,*] and Gian Franco Zannoni [1,2]

Table 3. Prevalence of the 4 TCGA molecular prognostic groups across different histotypes of endometrial carcinoma.

Molecular Prognostic Group	LG-EEC	HG-EEC	SC	CCC	Mixed	UDC/DDC	CS	NEC ***	MLC
POLE-mutated	6.2%	12.1%	0% *	3.8%	5.6%	12.4%	5.3%	7.1%	0%
MMR-deficient	24.7%	39.7%	0% *	9.8%	33.3%	44%	7.3%	42.9%	0%
p53-abnormal	4.7%	21.3%	100% **	42.5%	61.1%	18.6%	73.9%	35.7%	0%
NSMP	63.5%	28%	0% *	40.9%	0%	25%	13.5%	14.3%	100%

LG-EEC: low-grade endometrioid carcinoma; HG-EEC: high-grade endometrioid carcinoma; SC: serous carcinoma; CCC: clear-cell carcinoma; Mixed: mixed carcinoma; UDC/DDC: undifferentiated/dedifferentiated carcinoma; CS: carcinosarcoma; NEC: neuroendocrine carcinoma; MLC: mesonephric-like carcinoma. * Endometrial carcinomas with a serous morphology and POLE mutation or MMR deficiency are diagnosed as serous-like high-grade endometrioid carcinoma. ** Serous carcinomas with normal p53 expression in the presence of TP53 mutation, or with no TP53 mutation but with high copy-number variation, may rarely occur. *** The only published series of endometrial neuroendocrine carcinoma assessed with the TCGA classifier was constituted of 4 pure neuroendocrine carcinomas and 10 mixed carcinomas with a neuroendocrine component [30].

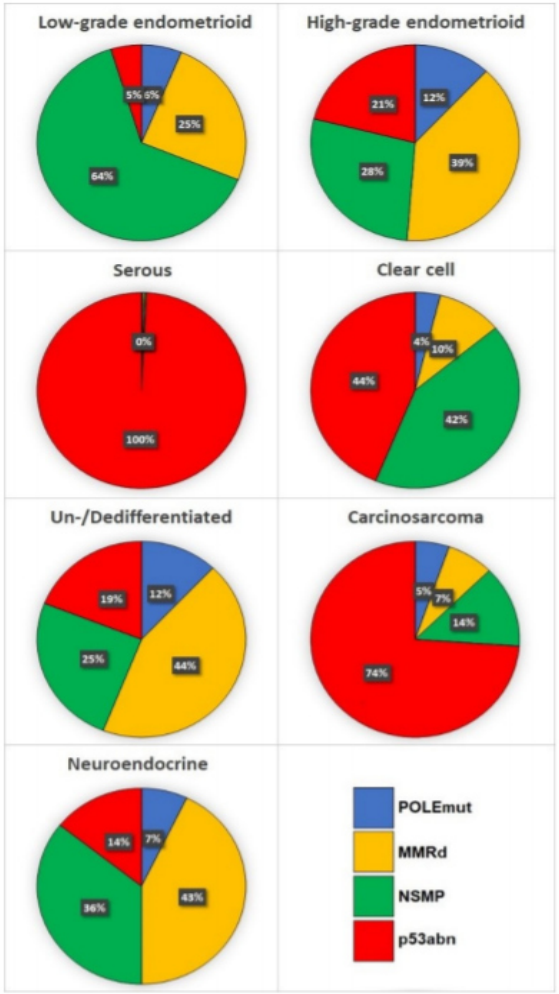


Figure 1. Distribution of TCGA molecular groups according to endometrial carcinoma histotype.

ASCO
752 Volume 40, Issue 7
Journal of Clinical Oncology

original reports

Pembrolizumab in Patients With Microsatellite Instability–High Advanced Endometrial Cancer: Results From the KEYNOTE-158 Study

David M. O'Malley, MD[1]; Giovanni Mendonca Bariani, MD[2]; Philippe A. Cassier, MD[3]; Aurelien Marabelle, MD, PhD[4]; Aaron R. Hansen, MBBS[5]; Ana De Jesus Acosta, MD[6]; Wilson H. Miller Jr, MD, PhD[7,8]; Tamar Safra, MD[9,10]; Antoine Italiano, MD, PhD[11,12]; Linda Mileshkin, MBBS[13]; Lei Xu, PhD[14]; Fan Jin, MD[14]; Kevin Norwood, MD[14]; and Michele Maio, MD[15]

CONCLUSION Pembrolizumab demonstrated robust and durable antitumor activity and encouraging survival outcomes with manageable toxicity in patients with previously treated, advanced MSI-H/dMMR endometrial cancer.

MERCK

Media > News releases > News release

FDA Approves Merck's KEYTRUDA® (pembrolizumab) for Patients With MSI-H/dMMR Advanced Endometrial Carcinoma, Who Have Disease Progression Following Prior Systemic Therapy in Any Setting and Are Not Candidates for Curative Surgery or Radiation

The objective response rate (ORR) was 46% (95% CI, 35-56) for patients who received KEYTRUDA, including a complete response rate of 12% and a partial response rate of 33%, at a median follow-up time of 16.0 months (range, 0.5 to 62.1 months).

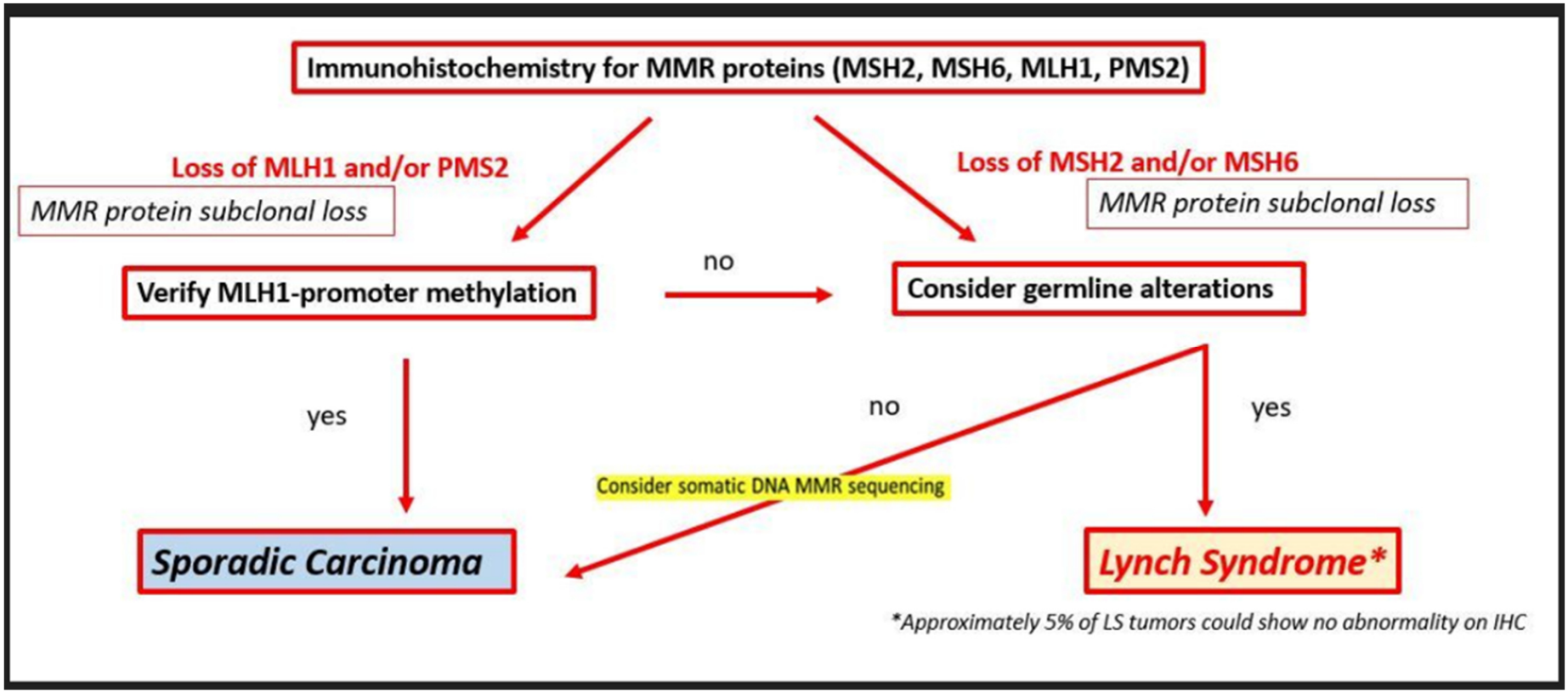
Of the responding patients (n=41), 68% had responses lasting 12 months or longer, and 44% had responses lasting 24 months or longer. Median duration of response (DOR) was not reached (range, 2.9 to 55.7+ months).

On April 22, 2021, the U.S. **Food and Drug Administration (FDA) granted accelerated approval to Jemperli (dostarlimab)** for treating patients with recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing chemotherapy

Dostarlimab (Jemperli), anti PD1 monotherapy, induced durable antitumor activity in advanced or recurrent EC among patients with mismatch repair deficient (dMMR)/microsatellite instability–high (MSI-H) or mismatch repair proficient (MMRp)/mismatch stable (MSS) disease, according to data from 2 expansion cohorts in the GARNET trial (NCT02715284) presented at the 2022 ASCO Annual Meeting

dMMR/MSI-H was associated with better outcomes: *a higher response rate and longer PFS and OS*. Safety was consistent with other PD-1 antibodies.

Oaknin A, Pothuri B, Gilbert L, et al. Dostarlimab in advanced/recurrent (AR) mismatch repair deficient/microsatellite instability–high or proficient/stable (dMMR/MSI-H or MMRp/MSS) endometrial cancer (EC): The GARNET study. J Clin Oncol. 2022;40(suppl 16):5509. doi:10.1200/JCO.2022.40.16_suppl.5509


Immunohistochemistry for MMR proteins (MSH2, MSH6, MLH1, PMS2)
Loss of MLH1 and/or PMS2
MMR protein subclonal loss
Loss of MSH2 and/or MSH6
MMR protein subclonal loss
Verify MLH1-promoter methylation
no
Consider germline alterations
yes
no
yes
Consider somatic DNA MMR sequencing
Sporadic Carcinoma
Lynch Syndrome*
*Approximately 5% of LS tumors could show no abnormality on IHC

PATHOLOGICA 2022;114:189-198;
DOI: 10.32074/1591-951X-775

Guidelines

Biomarker characterization in endometrial cancer in Italy: first survey data analysis

Gian Franco Zannoni[1,2], Angela Santoro[2], Nicoletta D'Alessandris[2], Giulia Scaglione[2], Frediano Inzani[2], Giuseppe Angelico[3], Emma Bragantini[4], Alessia Piermattei[2], Federica Cianfrini[2] Brigitte Bisaro[5], Matteo Fassan[6] and Members of PAGINE (SIAPEC) - Collaborators*

- 41 participating laboratories
- 42% of market share estimated (Q1 2021)
- Public/Academic hospital pathology labs
- Information collected through questionnaire

- 1

FOCUS ON HER2

Virchows Archiv
https://doi.org/10.1007/s00428-023-03656-w

REVIEW AND PERSPECTIVES

Standardized pathology report for HER2 testing in compliance with 2023 ASCO/CAP updates and 2023 ESMO consensus statements on HER2-low breast cancer

Mariia Ivanova[1] · Francesca Maria Porta[1] · Marianna D'Ercole[1] · Carlo Pescia[1] · Elham Sajjadi[1,2] · Giulia Cursano[1] · Elisa De Camilli[1] · Oriana Pala[1] · Giovanni Mazzarol[1] · Konstantinos Venetis[1] · Elena Guerini-Rocco[1,2] · Giuseppe Curigliano[2,3] · Giuseppe Viale[1] · Nicola Fusco[1,2]

Received: 20 July 2023 / Revised: 3 September 2023 / Accepted: 13 September 2023

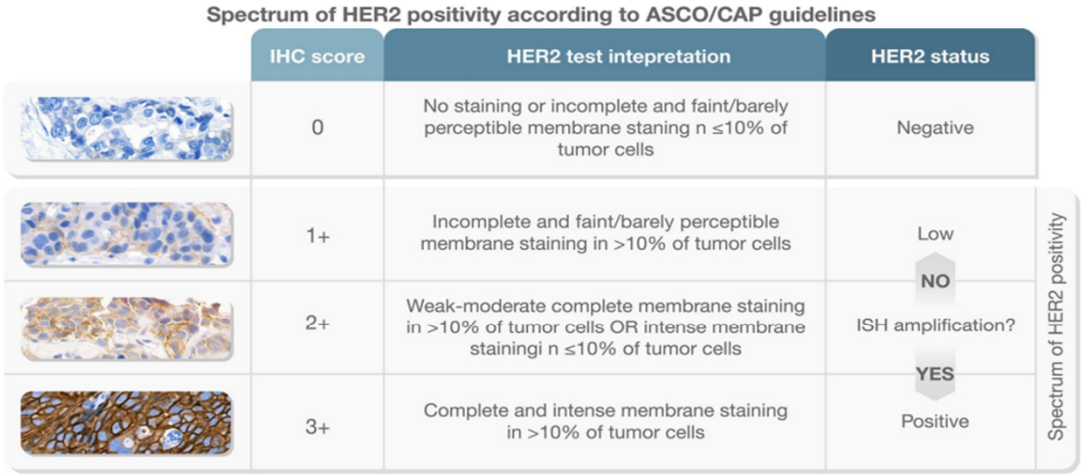


Fig. 1 Spectrum of HER2 positivity according to ASCO/CAP guidelines. Comprehensive visual representation of HER2 expression levels in BC depicting the final HER2 status through pathological interpretation and scoring. IHC, immunohistochemistry; ISH, in situ hybridization. Breast Biomarker Reporting, CAP Cancer Protocol Templates, v v1.5.0.1 (March 2023), available at: https://documents.cap.org/documents/Breast.Bmk_1.5.0.1.REL_CAPCP.pdf

Chemotherapy Response Score: Development and Validation of a System to Quantify Histopathologic Response to Neoadjuvant Chemotherapy in Tubo-Ovarian High-Grade Serous Carcinoma

Steffen Böhm, Asma Faruqi, Ian Said, Michelle Lockley, Elly Brockbank, Arjun Jeyarajah, Amanda Fitzpatrick, Darren Ennis, Thomas Dowe, Jennifer L. Santos, Linda S. Cook, Anna V. Tinker, Nhu D. Le, C. Blake Gilks, and Naveena Singh

Table 3. Criteria for the Chemotherapy Response Score

CRS 1	No or minimal tumor response. Mainly viable tumor with no or minimal regression-associated fibroinflammatory changes, limited to a few foci; cases in which it is difficult to decide between regression and tumor-associated desmoplasia or inflammatory cell infiltration.
CRS 2	Appreciable tumor response amid viable tumor that is readily identifiable. Tumor is regularly distributed, ranging from multifocal or diffuse regression-associated fibroinflammatory changes with viable tumor in sheets, streaks, or nodules to extensive regression-associated fibroinflammatory changes with multifocal residual tumor, which is easily identifiable.
CRS 3	Complete or near-complete response with no residual tumor OR minimal irregularly scattered tumor foci seen as individual cells, cell groups, or nodules up to 2 mm maximum size. Mainly regression-associated fibroinflammatory changes or, in rare cases no or very little residual tumor in the complete absence of any inflammatory response. It is advisable to record whether there is no residual tumor or whether there is microscopic residual tumor present.

NOTE. Regression-associated fibroinflammatory changes consist of fibrosis associated with macrophages, including foam cells, mixed inflammatory cells, and psammoma bodies, as distinguished from tumor-related inflammation or desmoplasia.

Three-tier chemotherapy response score based on omental assessment of residual disease which predicted progression-free survival (PFS) and overall survival (OS)

J Clin Oncol 2015; 33:2457-2463.

Pathological Chemotherapy Response Score in Patients Affected by High Grade Serous Ovarian Carcinoma: The Prognostic Role of Omental and Ovarian Residual Disease

*Angela Santoro[1], Giuseppe Angelico[1], Alessia Piermattei[1], Frediano Inzani[1], Michele Valente[1], Damiano Arciuolo[1], Saveria Spadola[1], Antonino Mulè[1], Piercarlo Zorzato[2], Anna Fagotti[2,3], Giovanni Scambia[2,3] and Gian Franco Zannoni[1,4]**

PROGNOSTIC IMPACT OF OVARIAN AND OMENTAL CRS

161 women with advanced stage III-IV tubo-ovarian HGSC treated with NACT and interval debulking surgery.

Front. Oncol 2019; 9:778.

frontiers in Oncology

SYSTEMATIC REVIEW
published: 10 February 2022
doi: 10.3389/fonc.2022.814989

Assessing Post-Treatment Pathologic Tumor Response in Female Genital Tract Carcinomas: An Update

Frediano Inzani[1], *Damiano Arciuolo*[1], *Giuseppe Angelico*[1], *Angela Santoro*[1], *Antonio Travaglino*[1], *Nicoletta D'Alessandris*[1], *Giulia Scaglione*[1], *Michele Valente*[1], *Federica Cianfrini*[1], *Antonio Raffone*[3,4] *and Gian Franco Zannoni*[1,2*]

- **Multidisciplinary approach in diagnostic procedure**
- **Knownledge of advantages and limitations of molecular diagnostic approach**
- **Remember the CLINICAL use of pathological diagnosis**

PRECISION MEDICINE START FROM H&E