The British Association of Gynaecological Pathologists

Lecturer – Dr Carlos Parra-Herran

Dr. Carlos Parra-Herran is a gynaecologic pathologist at Brigham and Women's Hospital.

Completed medical school training at Univesidad Nacional de Colombia.

Completed his residency at Jackson Memorial Hospital, followed by subspecialty training at Brigham and Women's Hospital (Boston) and Sunnybrook Health Sciences Centre (Toronto).

Has authored >120 peer-reviewed journal articles as well as multiple book chapters.

Has edited 3 reference textbooks in gynecologic pathology.

Serves as teaching faculty for continuing medical education at USCAP and BAGP.

Serves as a member of the USCAP education committee.

Is the current president of the Latin American Pathology Foundation (LAPF).

LECTURE

Friday 29 November 2024 – HPV-Independent vulvar squamous lesions

The British Association of Gynaecological Pathologists

Speaker disclosures

Choose one

- ❑ I have no financial conflicts of interest to disclose

HPV-INDEPENDENT SQUAMOUS LESIONS OF THE VULVA

Carlos Parra-Herran MD

Pathologist, Brigham and Women's Hospital

Associate Professor, Harvard Medical School, Boston MA US

CONFLICT OF INTEREST STATEMENT

- I have no conflicts of interests or financial relations to disclose

OUTLINE

- HPV-independent squamous lesions
  - *Proposed classifications*
  - *Proposed definitions*
  - *Differential Diagnosis*

International Agency for Research on Cancer

World Health Organization

Female Genital Tumours

Squamous cell tumours and precursors

- Squamous intraepithelial lesions, HPV-associated, of the vulva
- Vulvar intraepithelial neoplasia, HPV-independent
- Squamous cell carcinoma, HPV-associated, of the vulva
- Squamous cell carcinoma, HPV-independent, of the vulva
- Squamous cell carcinoma NOS of the vulva
- Basal cell carcinoma

VULVAR SQUAMOUS PRECURSORS

- Vulvar intraepithelial neoplasia, HPV-independent
  - *Differentiated type*
  - *Differentiated exophytic vulvar intraepithelial lesion*

HPV-INDEPENDENT VIN

- Does not require grading
  - *dVIN is high-grade by definition*
  - *vaVIN has no proposed grading to date*
- Usually in post-menopausal women (70-80 years)
- Chronic inflammatory conditions
  - *Lichen sclerosus*
  - *Lichen simplex chronicus*

J Clin Pathol 2014;67(4):290-4
Mod Pathol 2010;23:404-12
Mod Pathol 2011;24(2):297-305
Int J Gynecol Cancer 2003;89:2249-53

HPV-INDEPENDENT VIN DIFFERENTIATED TYPE

- Rare (5-10% of all VINs)
- Prospective diagnosis is rare!
  - *Misdiagnosis as reactive condition*
  - *Poor to moderate reproducibility among pathologists*

HPVpos VSCC	HPVneg/p53wt VSCC	HPVneg/p53mut VSCC
($n = 75, 18\%$)	($n = 63, 15\%$)	($n = 275, 66\%$)

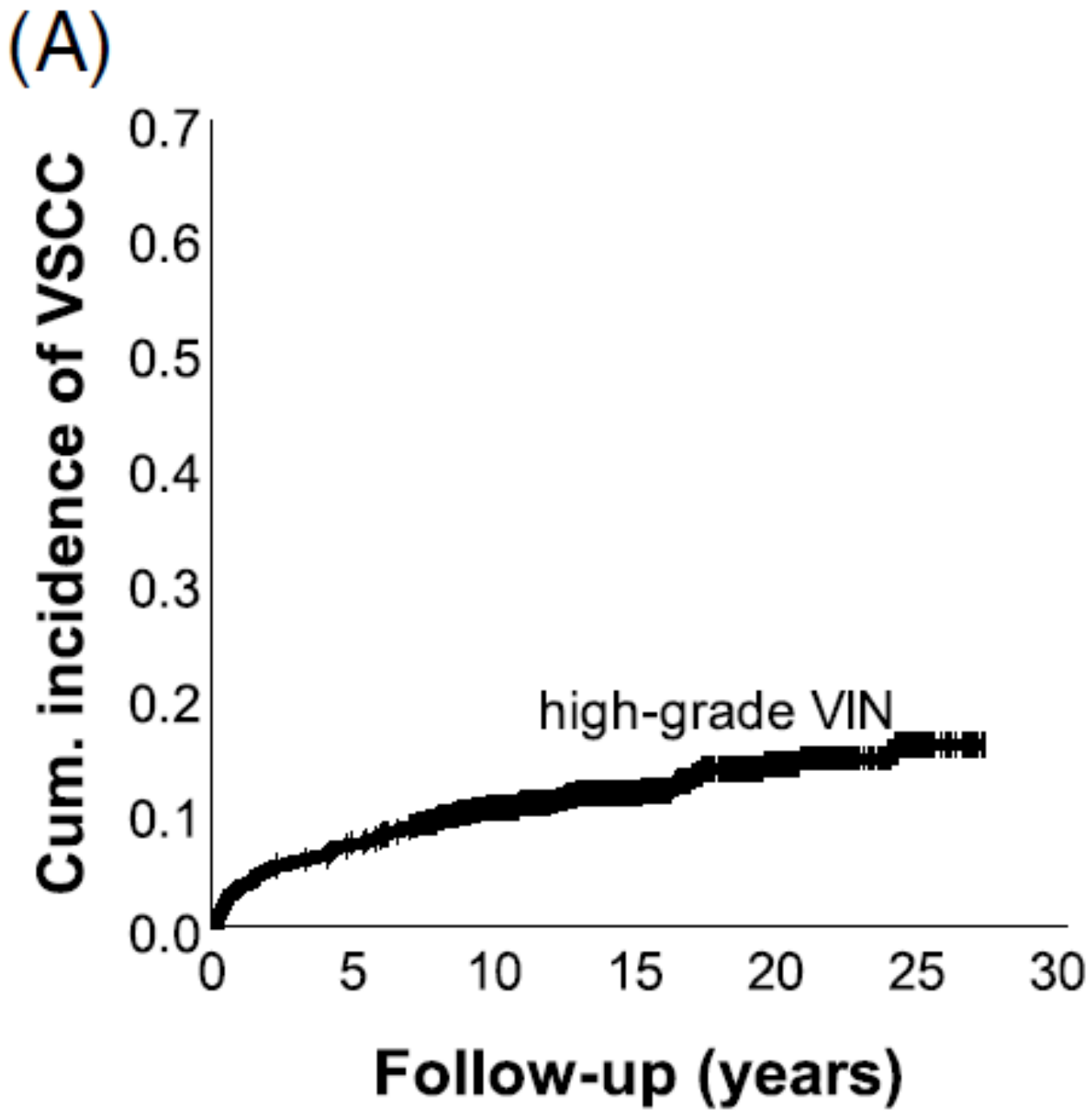
Mod Pathol 2011;24:297-305
Virchows Arch 2021;479:305-315

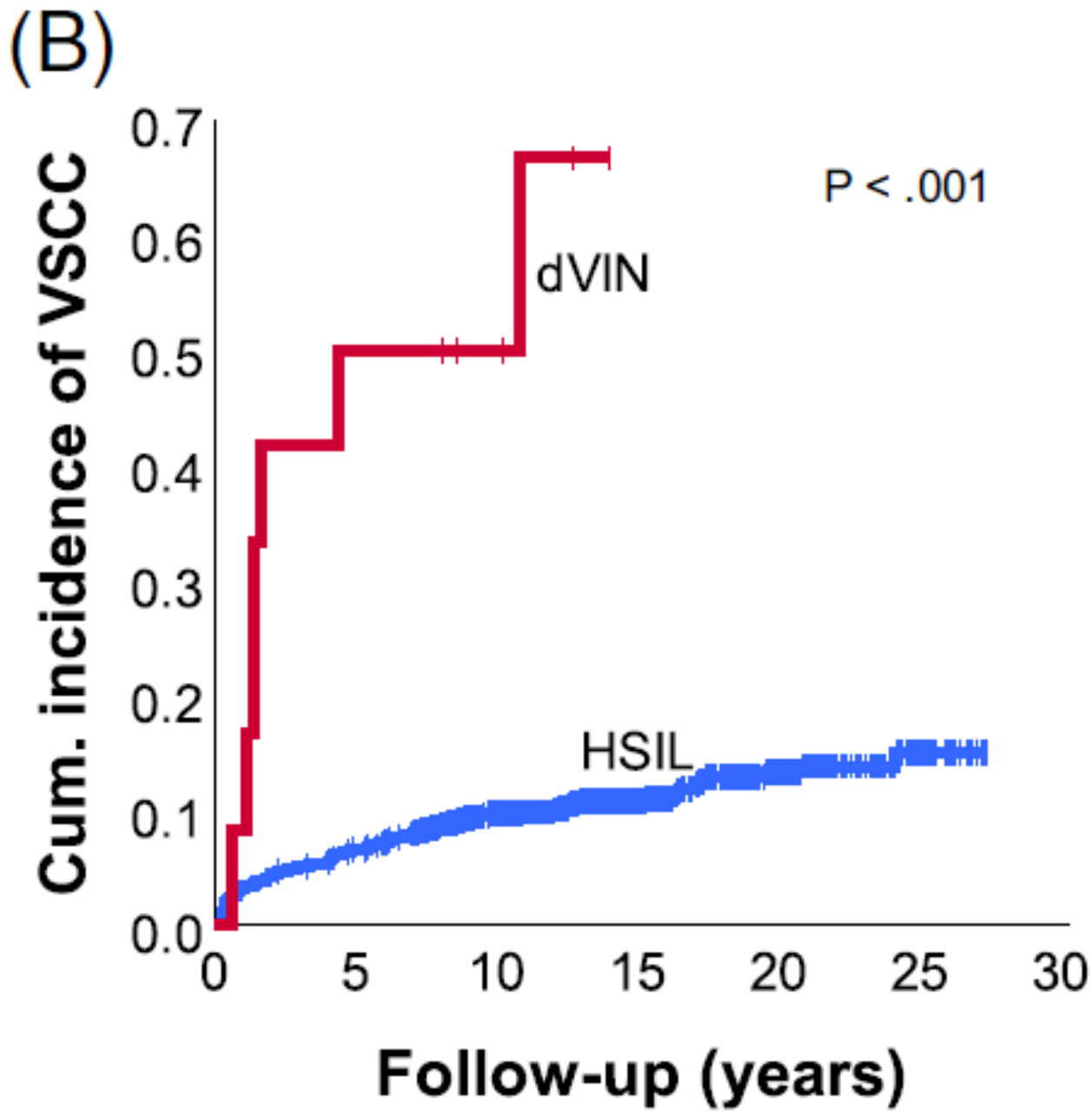
Mod Pathol 2013;26:874-880
Gynecol Oncol 2020;159:649-656

HPV-INDEPENDENT DIFFERENTIATED VIN

- Median time to progression to VSCC: 9–23 months
- 10-year cumulative VSCC risk: 50%
  - *Compared to 10% for HSIL*
- Absolute risk for primary SCC: 33-86%
  - *Compared to 3-10% cancer risk for HSIL*

Cancers 2021;13:6170
Int. J. Cancer 2020;148:90–98



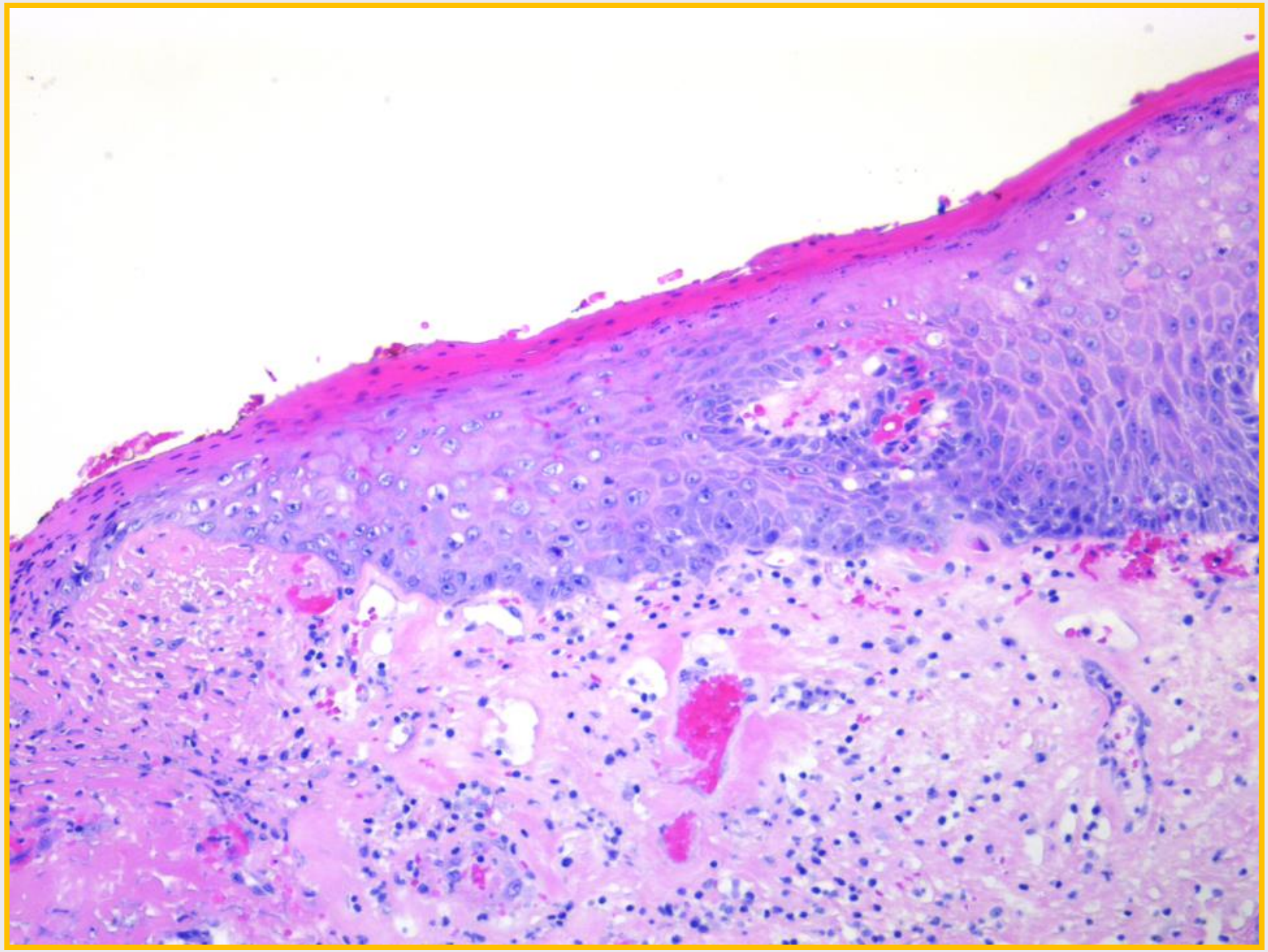


Int. J. Cancer 2020;148:90–98

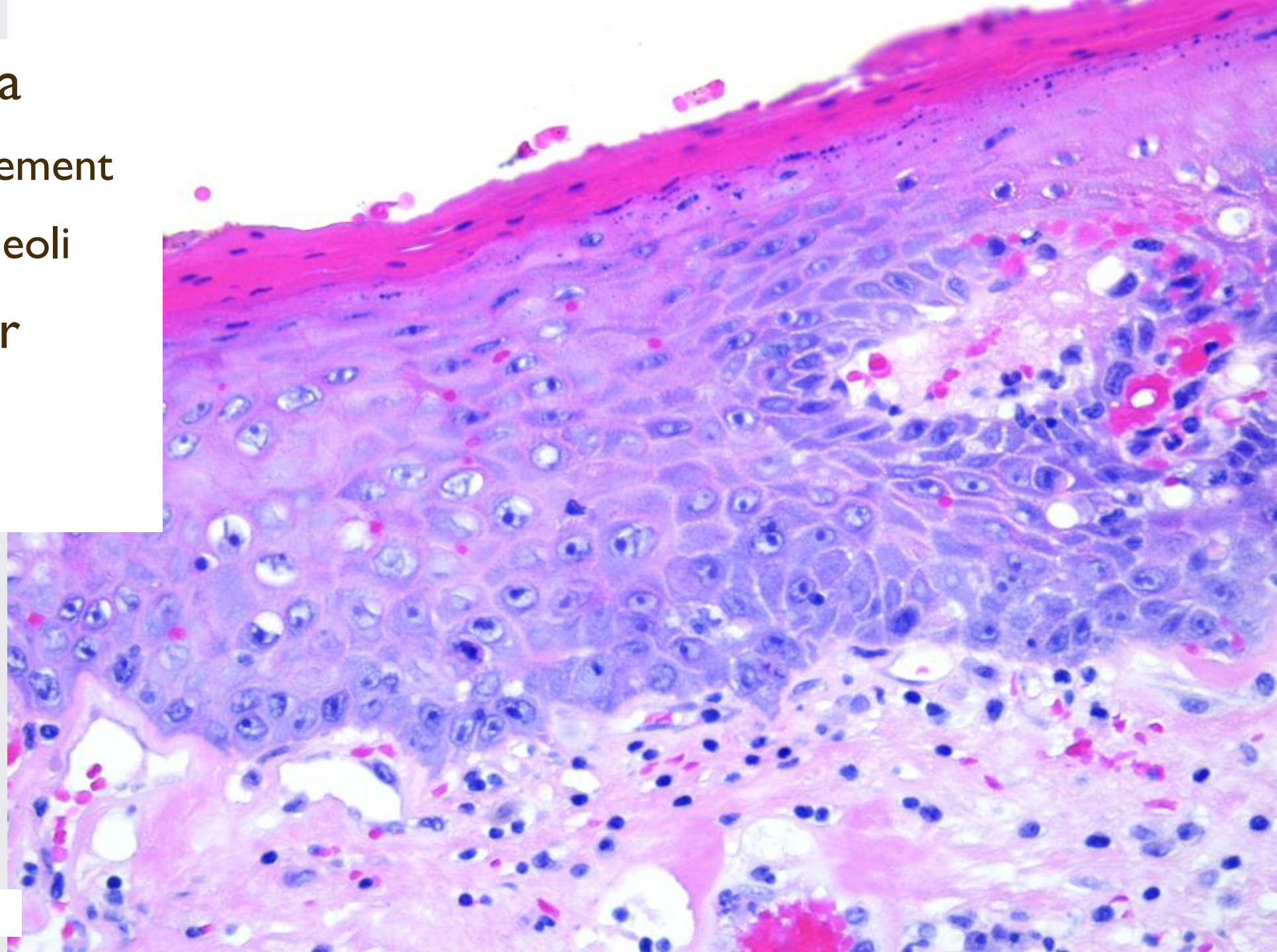
Retained overall organization and maturation

Atypia discernable under × 100

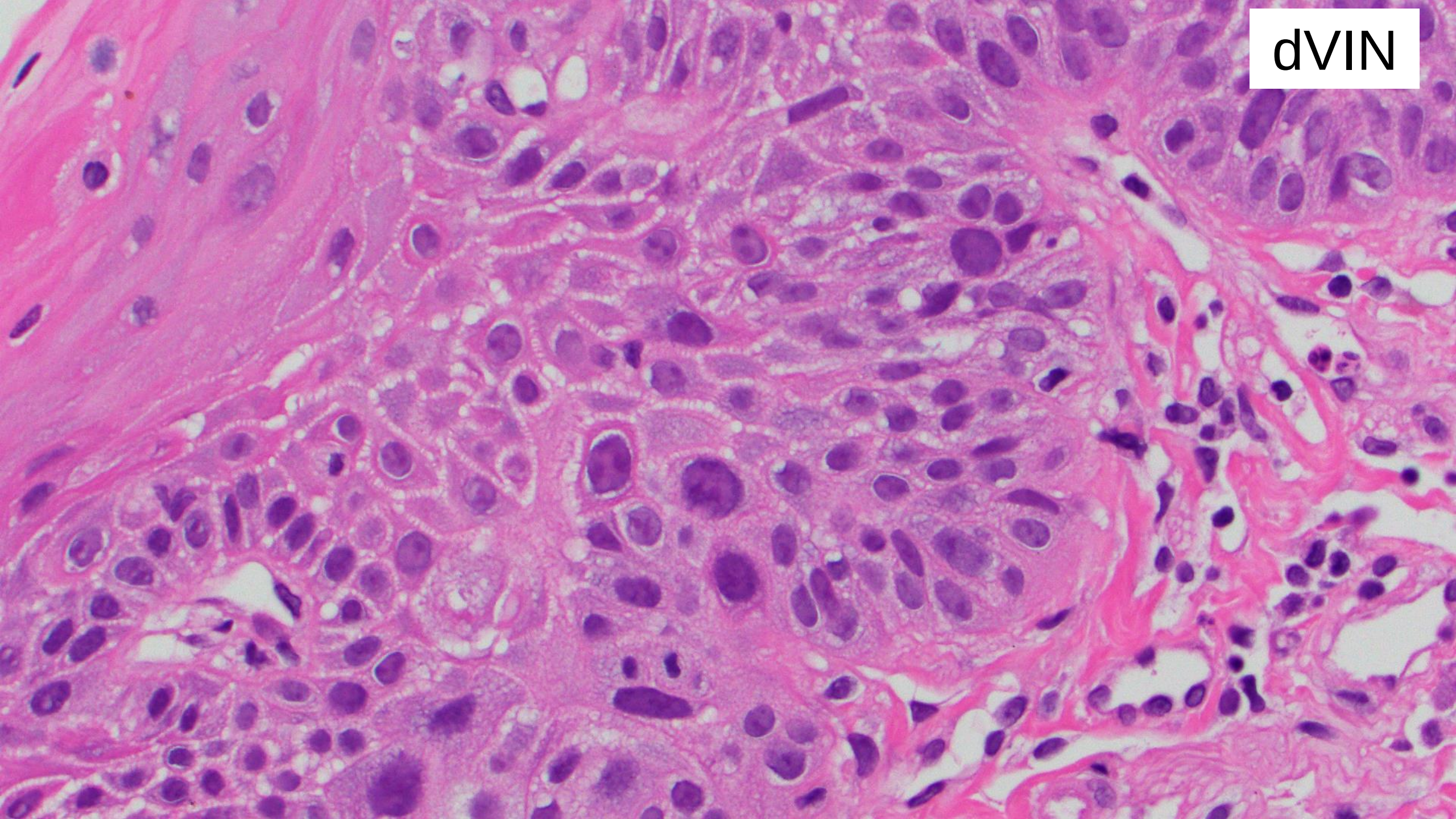
dVIN

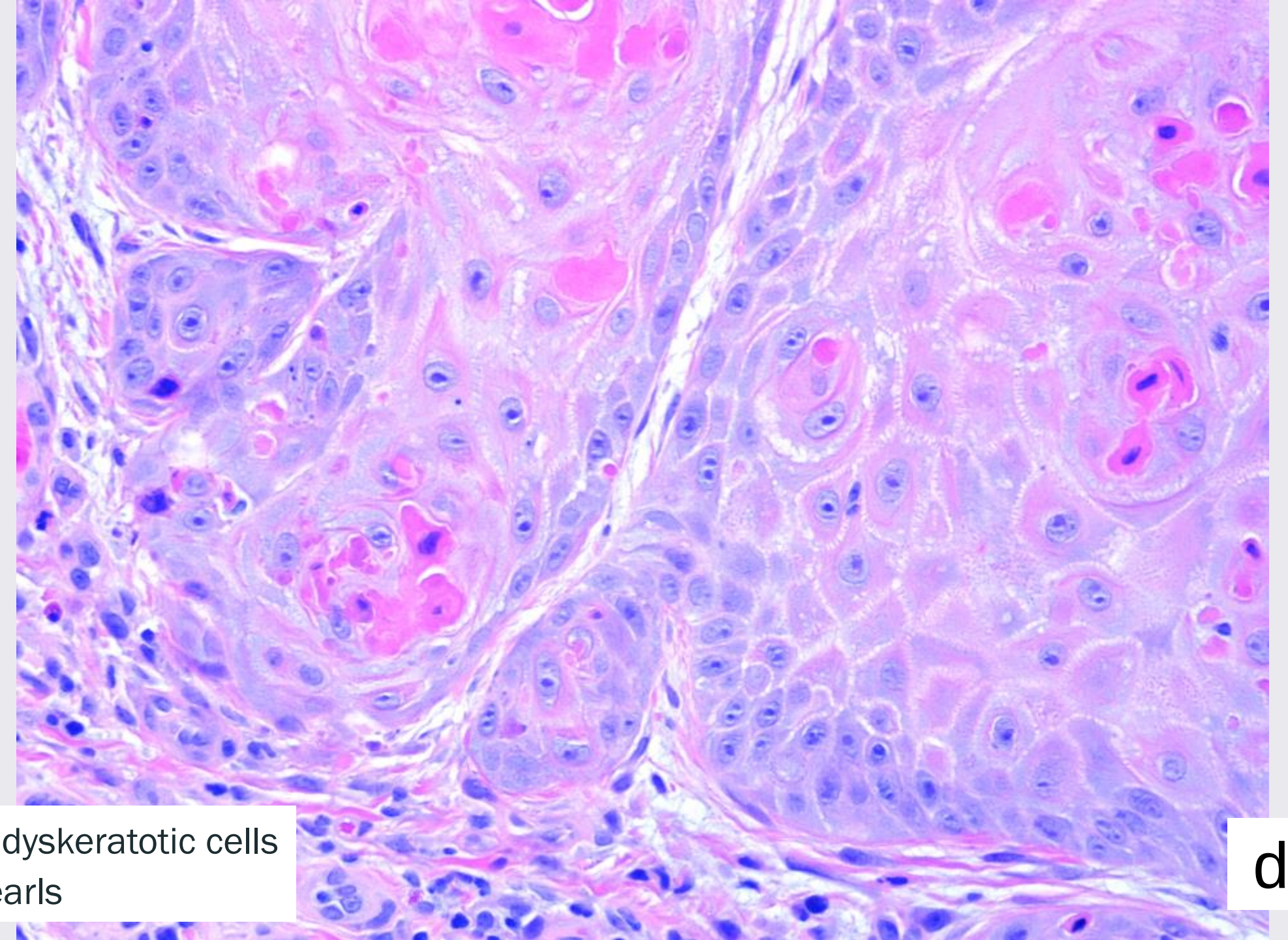


- Basal cell atypia
  - Nuclear enlargement
  - Prominent nucleoli
- Altered cellular alignment
- Parakeratosis



Virchows Arch 2021;479:305-315

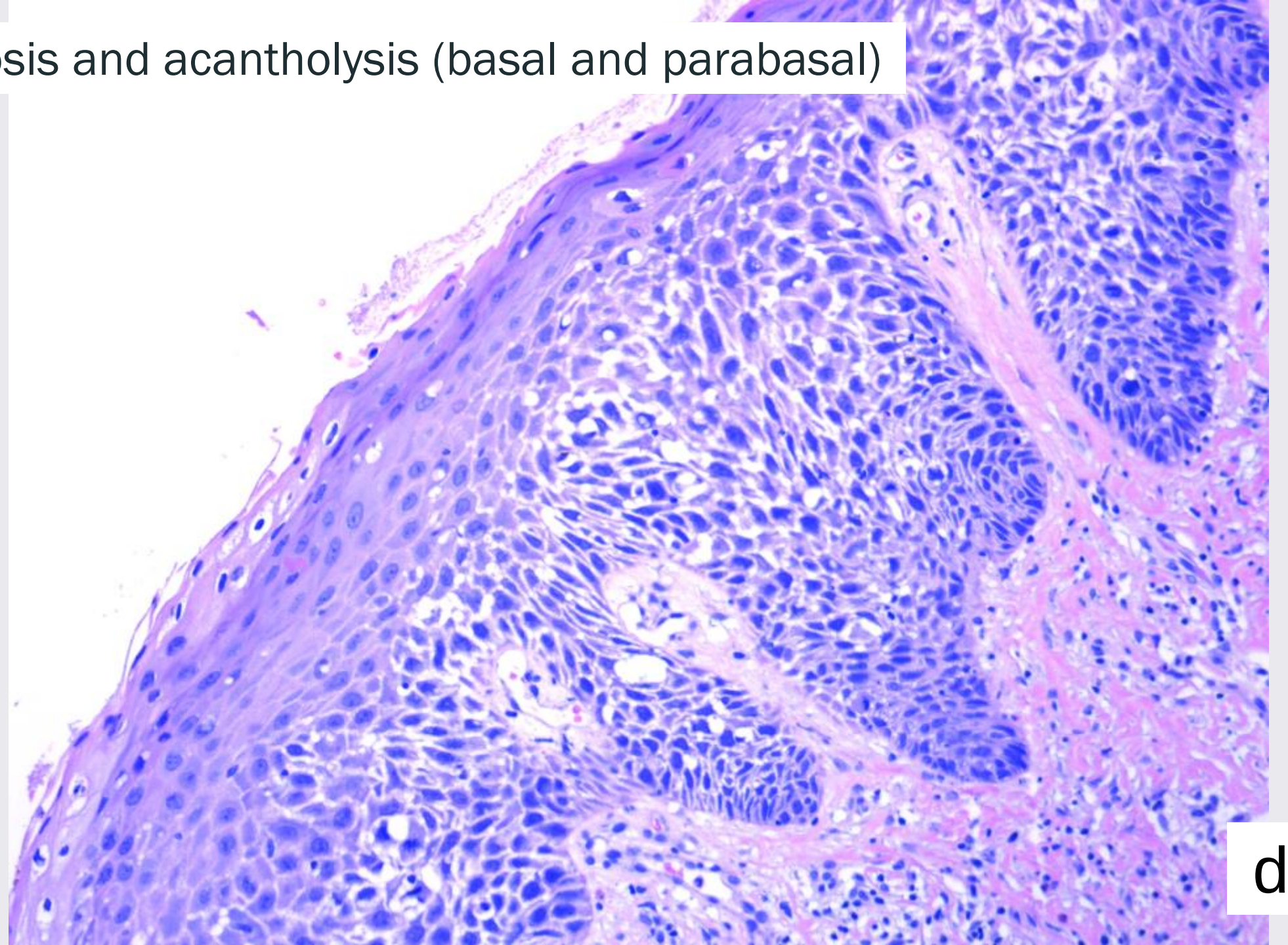

dVIN



Individual dyskeratotic cells
Keratin pearls

dVIN

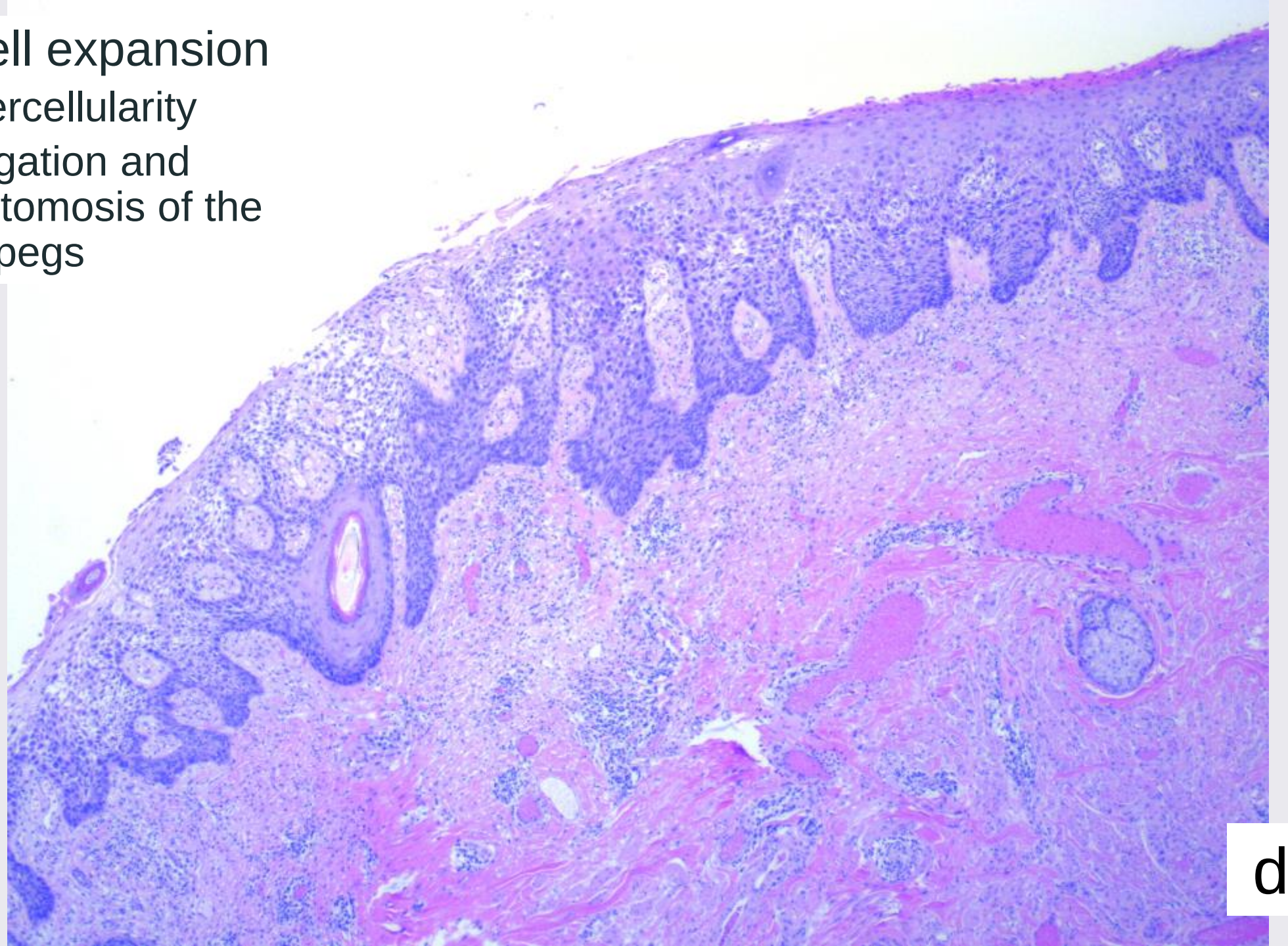
Spongiosis and acantholysis (basal and parabasal)



dVIN

Basal cell expansion

- Hypercellularity
- Elongation and anastomosis of the rete pegs



dVIN

Interobserver Agreement Across Subspecialties for Diagnosis of Differentiated Vulvar Intraepithelial Neoplasia and Predictive Values of 20 Histologic Features

Shula A. Schechter, MD; May P. Chan, MD; Selvaraj Muthusamy, MBBS, PhD; Stephanie L. Skala, MD; Grace Y. Wang, MD

Table 1. Logistic Regression for Prediction of Differentiated Vulvar Intraepithelial Neoplasia (dVIN) and Progression to Squamous Cell Carcinoma (SCC)

	Coefficient[a]	*P* Value[a]	Coefficient[b]	*P* Value[b]
Keratin pearls	1.95	<.001	1.96	<.001
Basal pleomorphism	1.97	<.001	1.20	<.001
Basal layer disarray	0.91	<.001	1.08	<.001
Parakeratosis	0.67	<.001	0.83	<.001
Epidermal thickness	0.76	.002	1.05	<.001
Hypergranulosis	0.39	.05	0.67	<.001
Lichenoid inflammation	0.63	.20	0.69	.002
Anastomosing rete	0.20	.35	−0.04	.84
Elongated rete	0.07	.78	0.26	.42
Homogenized dermal collagen	−0.87	<.001	−0.78	.003

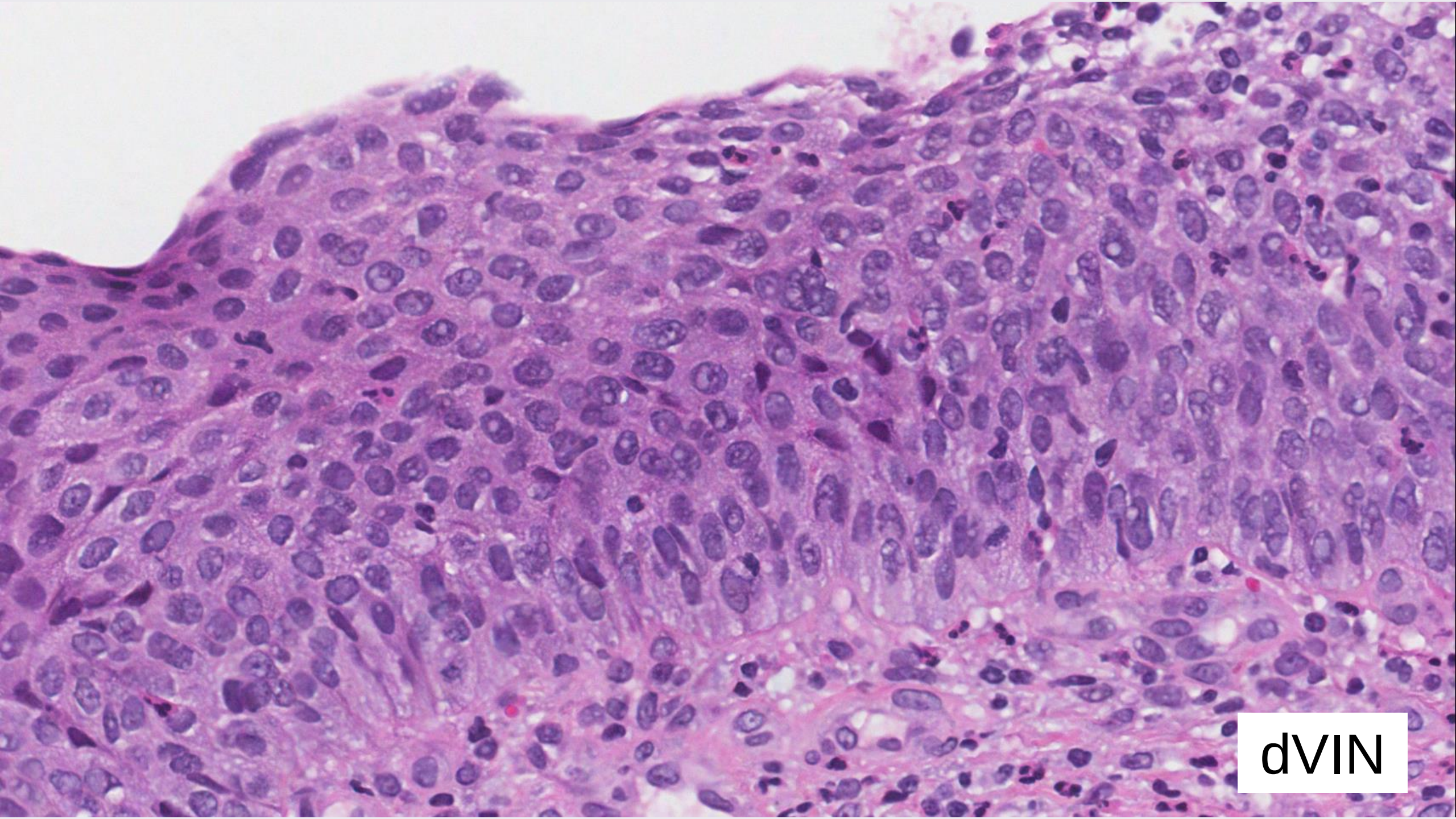
[a] Coefficient and *P* values for prediction of dVIN.
[b] Coeffcient and *P* values for prediction of progression to SCC.

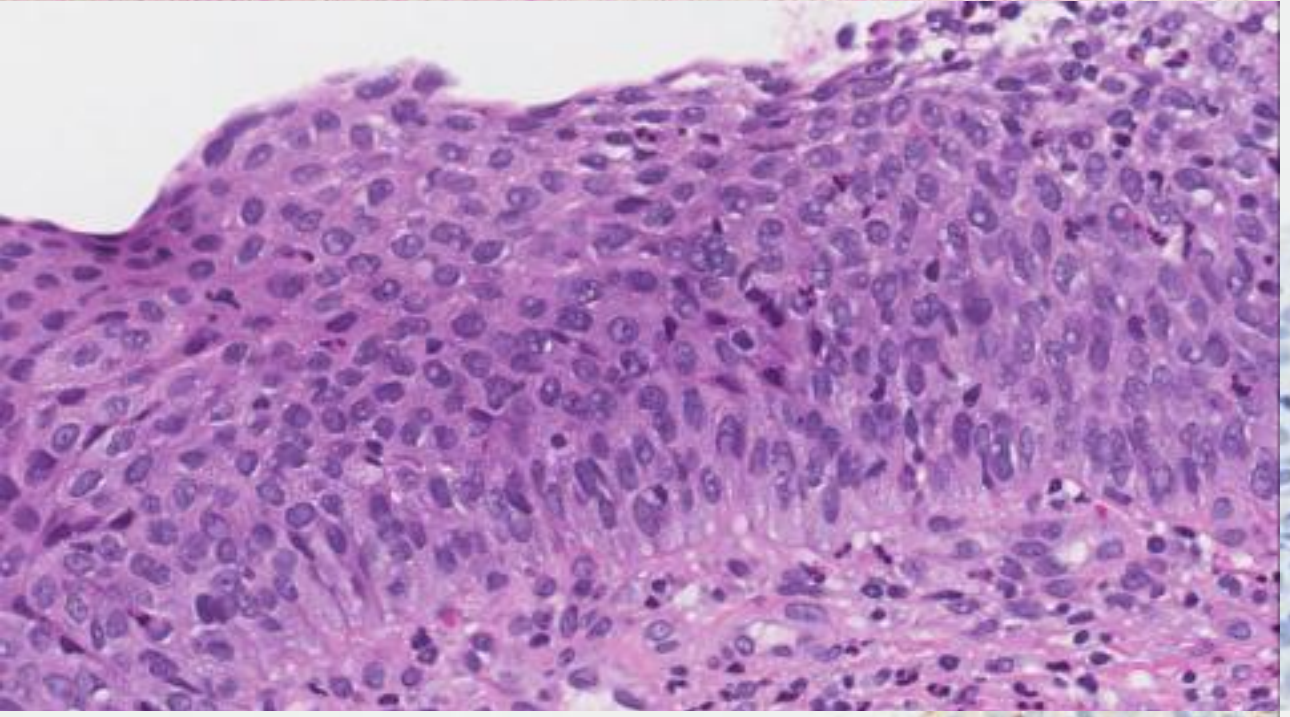
Arch Pathol Lab Med 2023 PMID 36821250

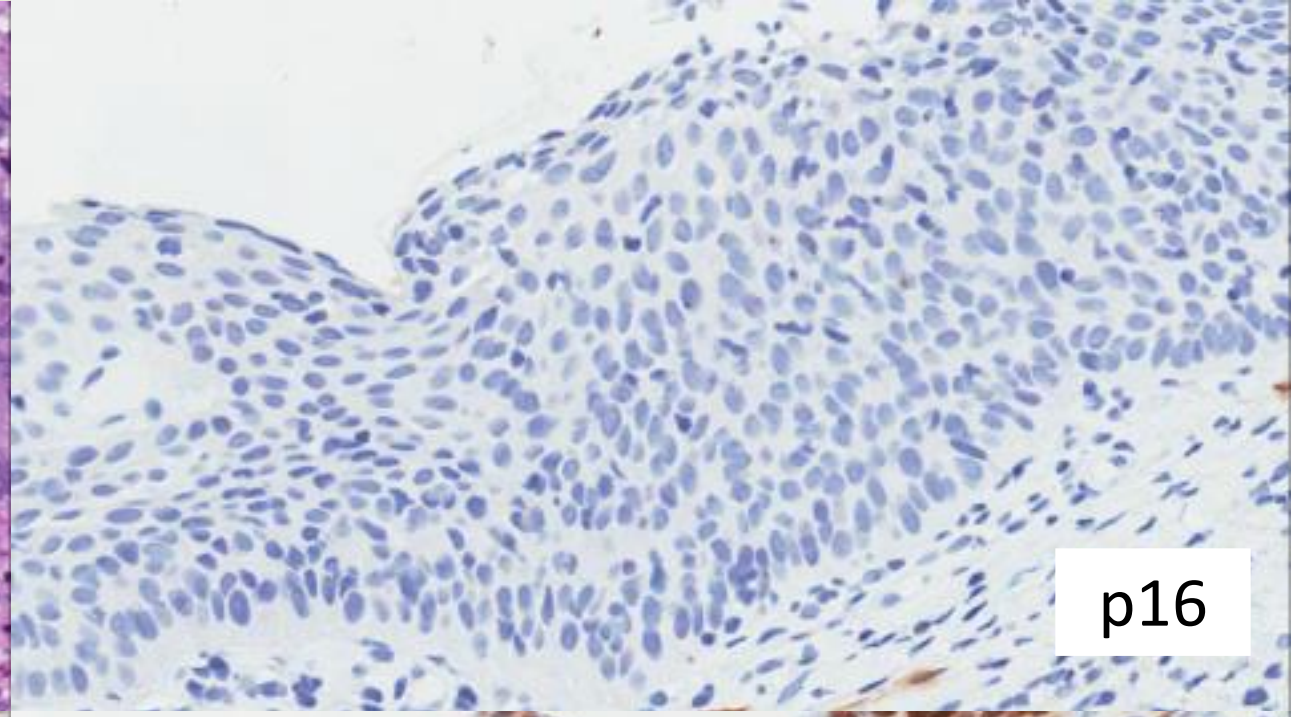
HPV-INDEPENDENT VIN DIFFERENTIATED TYPE

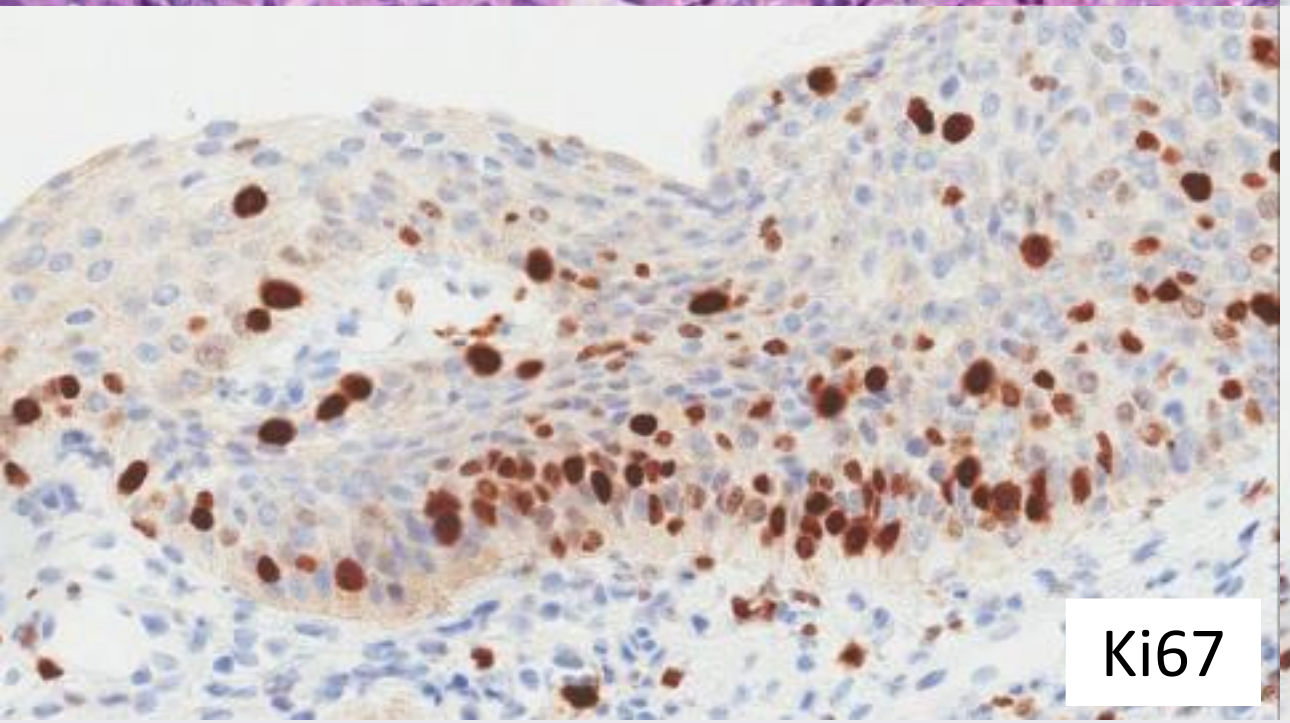
- HSIL-like / Basaloid dVIN
  - *10-20% of cases*
  - *Immature appearance*
  - *Overlap with HSIL*

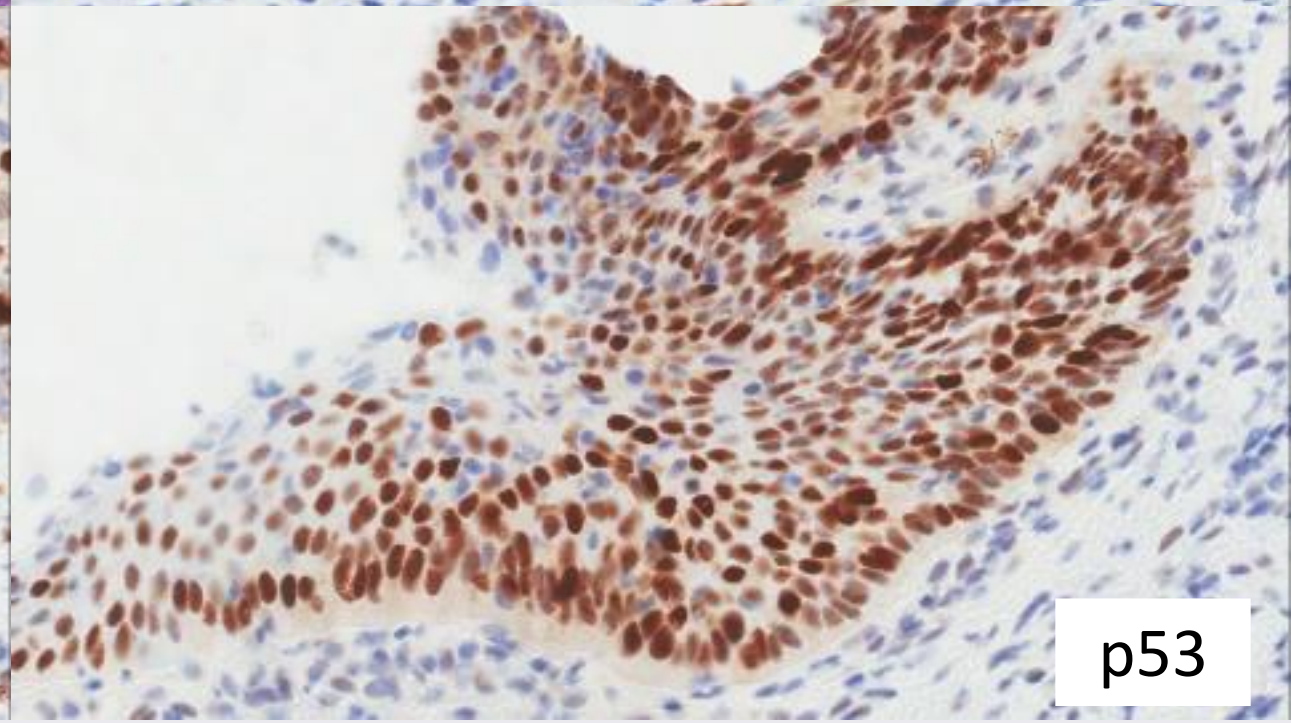
Am J Surg Pathol 2009;33(11):1659-65
Am J Surg Pathol 2020;44:1506–1514


dVIN




p16


Ki67


p53

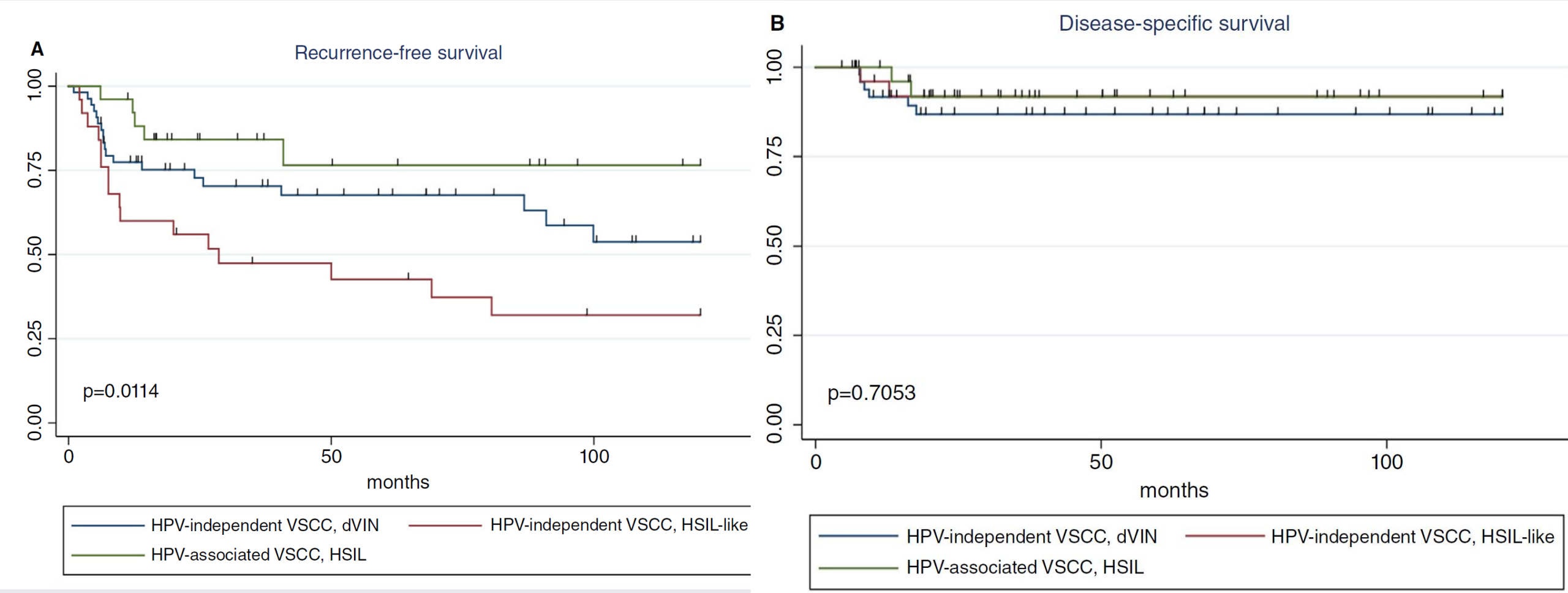
Vulvar squamous cell carcinoma arising on human papillomavirus-independent precursors mimicking high-grade squamous intra-epithelial lesion: a distinct and highly recurrent subtype of vulvar cancer

Histopathology 2023;82:731-44

Núria Carreras-Dieguez,[1] Adela Saco,[2] Marta del Pino,[1] Clàudia Pumarola,[1] Ricardo López del Campo,[2] Carolina Manzotti,[2,3] Adriana Garcia,[2] Lorena Marimon,[2,3] Sherley Diaz-Mercedes,[2,3] Pere Fuste,[1] Maria Teresa Rodrigo-Calvo,[2] Naiara Vega,[2] Aureli Torné[1,4] & Natalia Rakislova[2,3]

	HPV-associated VSCC with adjacent HSIL (n = 26)	HPV-independent VSCC with adjacent dVIN (n = 54)	HPV-independent VSCC with adjacent HSIL-like lesion (n = 25)	P
Mean follow-up (months)	52.5 ± 38.5	56.7 ± 43.8	65.6 ± 44.2	0.49
Recurrence of VSCC [n (%)]	5 (19.2%)	19 (35.0%)	16 (64.0%)	**<0.001**
Mean time to recurrence (months)	17.2 ± 13.6	32.9 ± 42.0	40.78 ± 46.1	0.31
Deaths due to VSCC [n (%)]	2 (7.6%)	8 (14.8%)	4 (16.0%)	0.61
Median time to death (months)	15.01 ± 2.4	11.2 ± 4.5	10.4 ± 3.5	0.61

Histopathology 2023;82:731-44



IMMUNOHISTOCHEMISTRY

HPV-independent VIN (dVIN)	HPV-associated lesions (HSIL)
■ P16 negative or patchy	■ P16 overexpression
■ Abnormal p53 staining	■ Wild type p53 pattern

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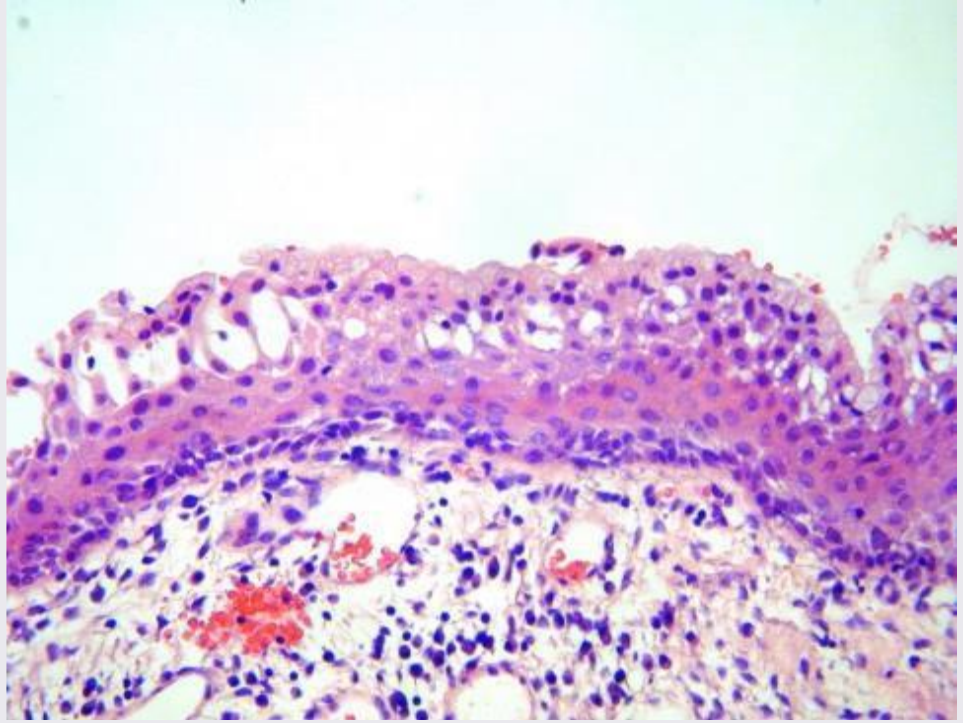
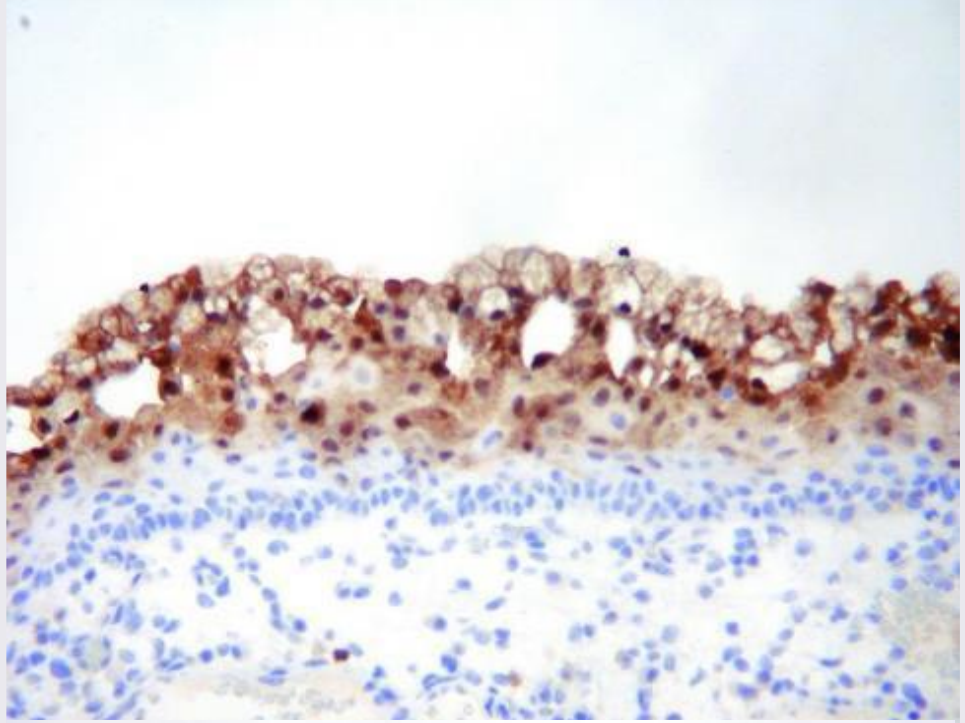
Interpretation of p16 Immunohistochemistry In Lower Anogenital Tract Neoplasia

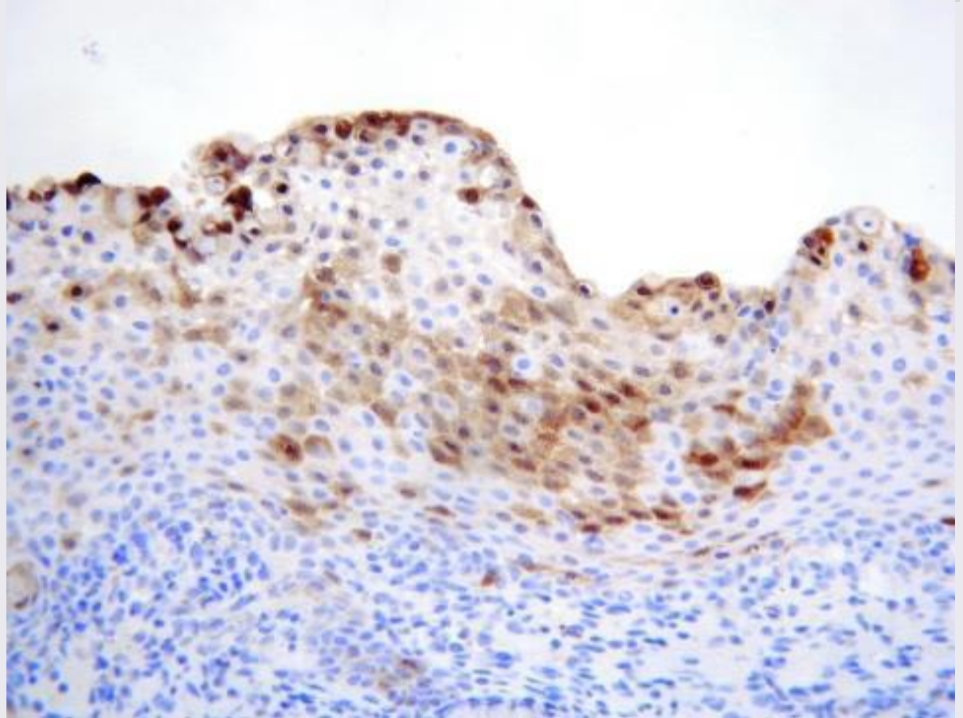
Authors: Naveena Singh[1], C Blake Gilks[2], Richard Wing-Cheuk Wong[3], W Glenn McCluggage[4], C Simon Herrington[5]

[1]Barts Health NHS Trust, London, UK; [2]Vancouver General Hospital [3]Pamela Youde Nethersole Eastern Hospital, Hong Kong, [4]Belfast Health and Social Care Trust, Belfast, UK; [5]University of Edinburgh

The British Association of Gynaecological Pathologists
https://www.thebagp.org/resources/bagp-guidance-documents/ Accessed 8/4/2024

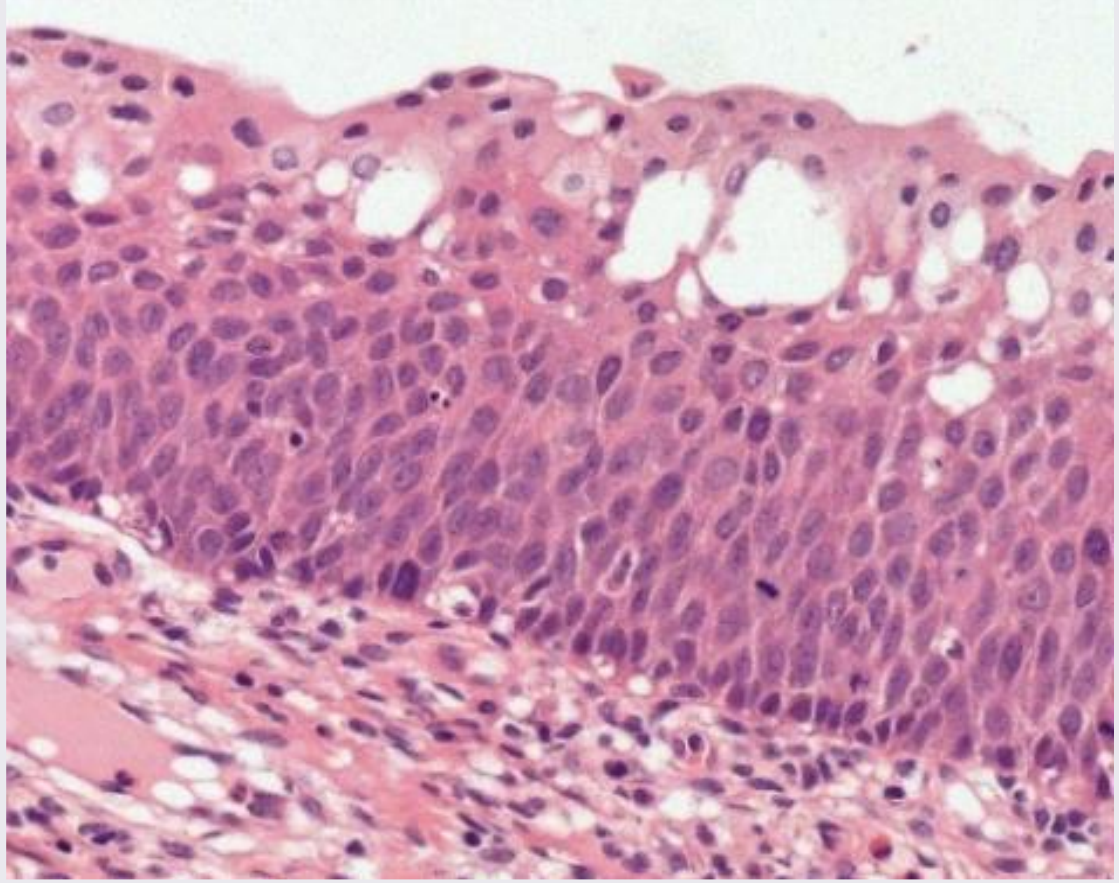


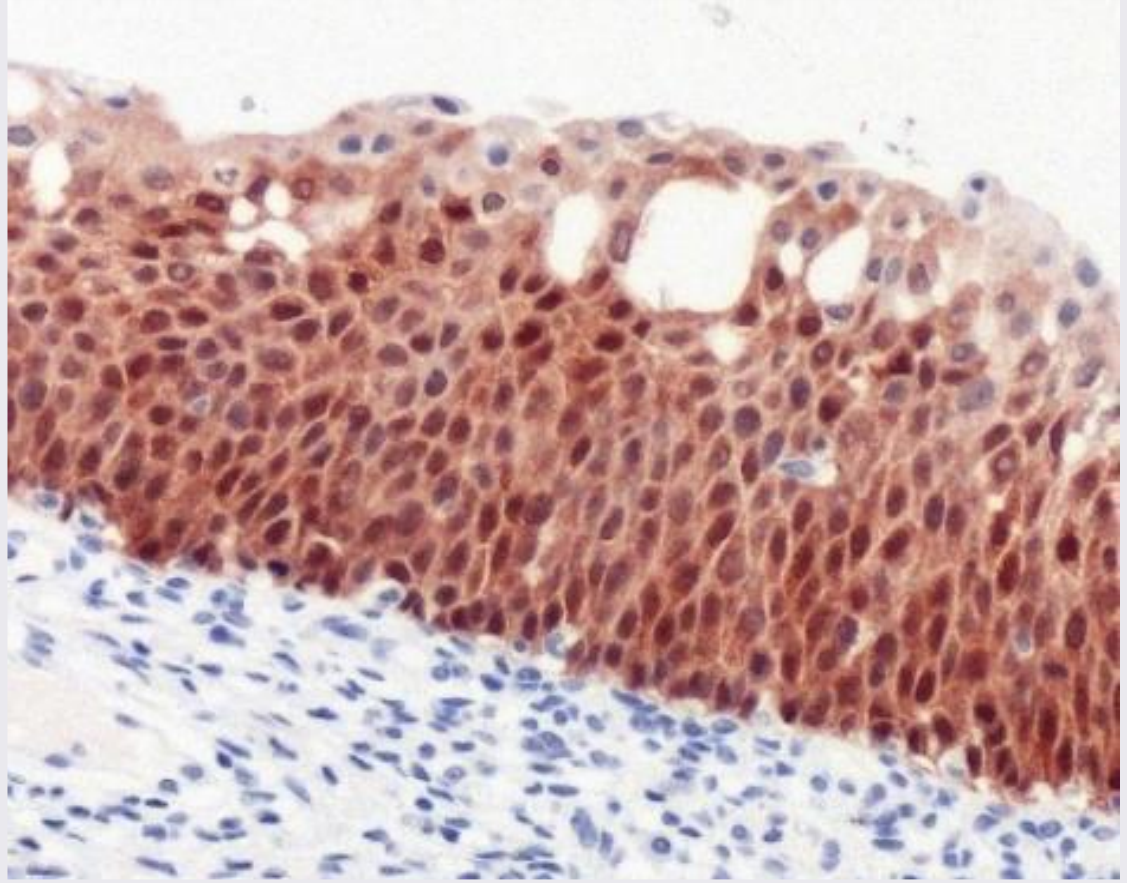




Normal squamous epithelium is negative for 16 or shows patchy staining

The British Association of Gynaecological Pathologists
https://www.thebagp.org/resources/bagp-guidance-documents/
Accessed 8/4/2024

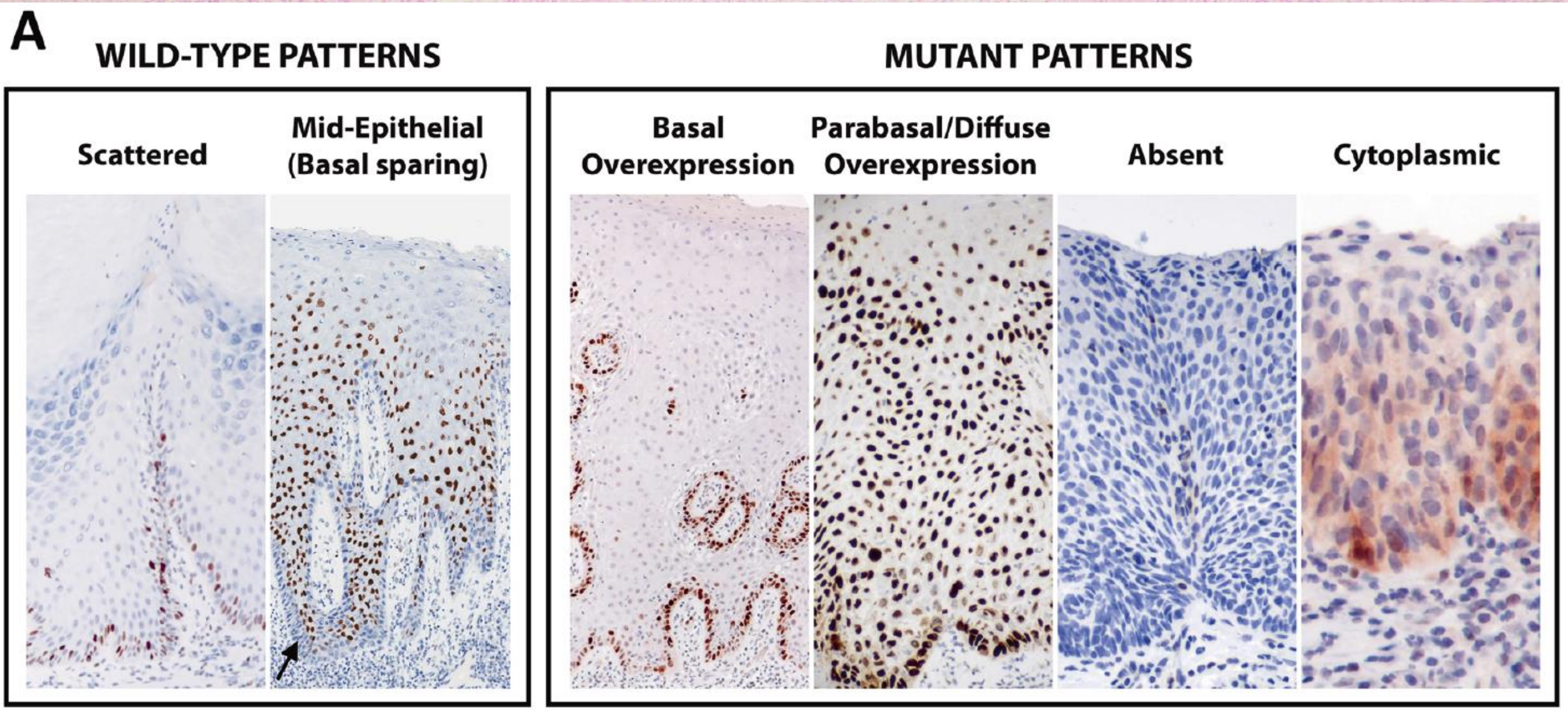




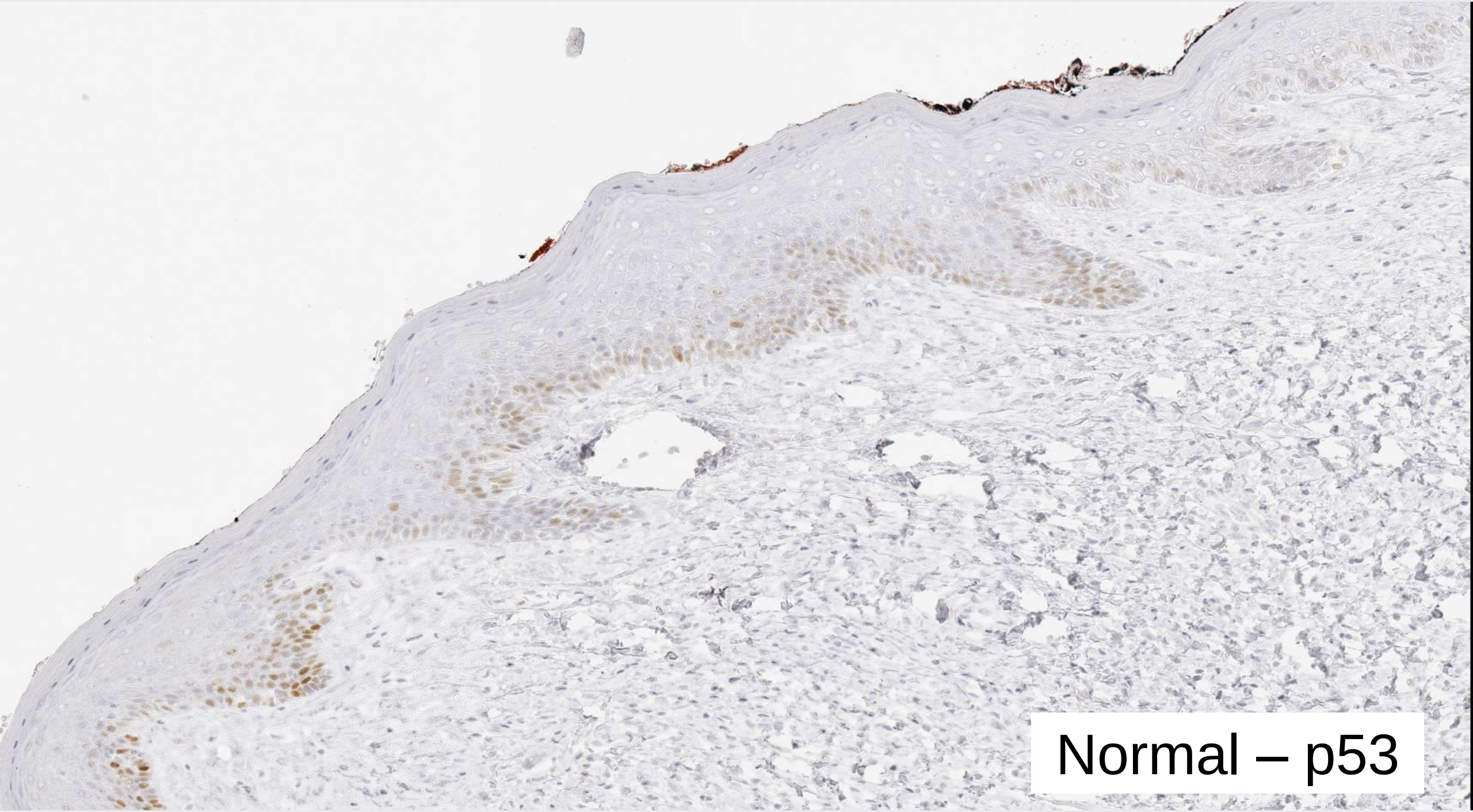
Abnormal expression = Strong and diffuse, nuclear and cytoplasmic, at least in basal third

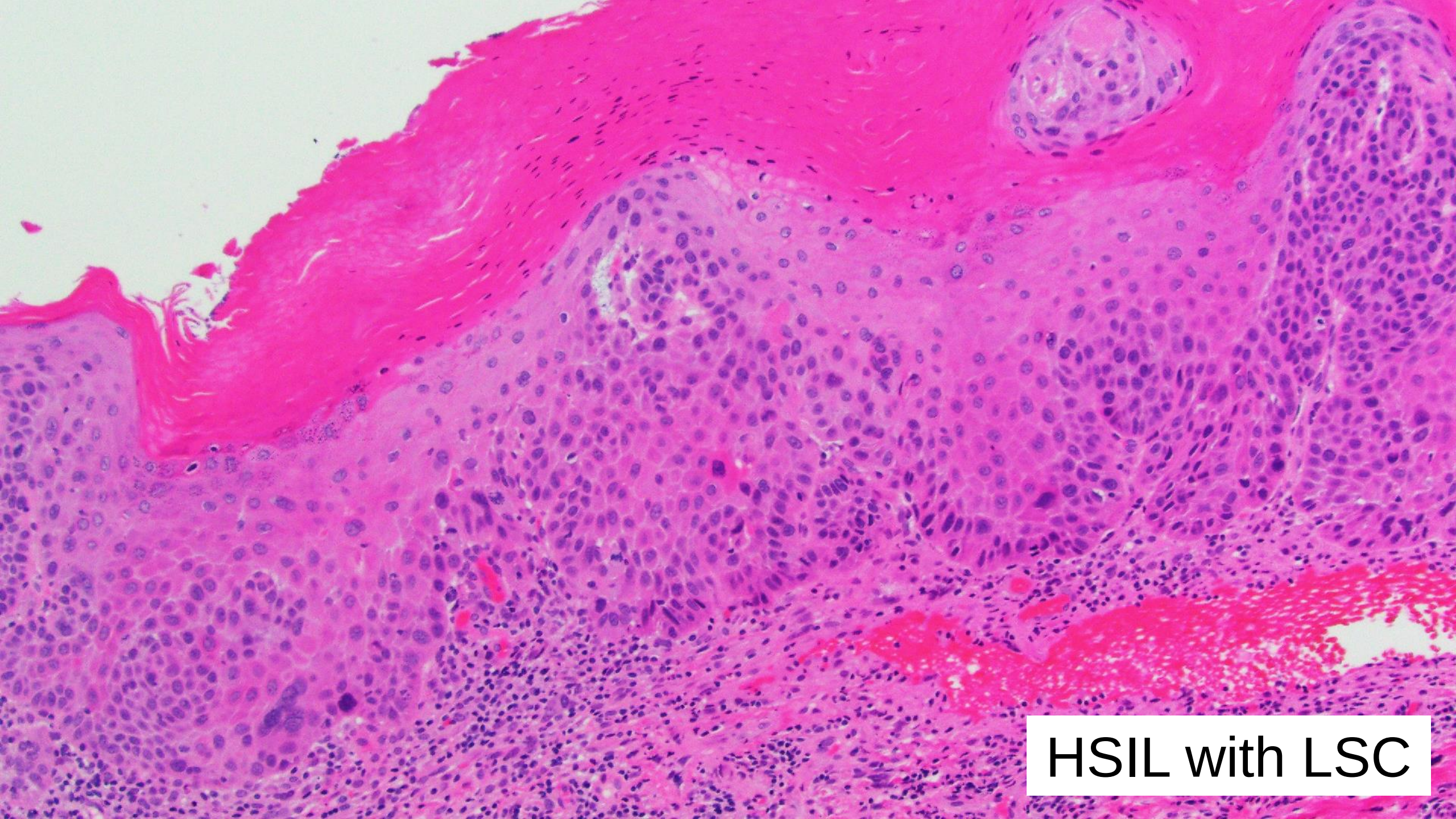
At least 6 cells (should correlate with abnormal population)

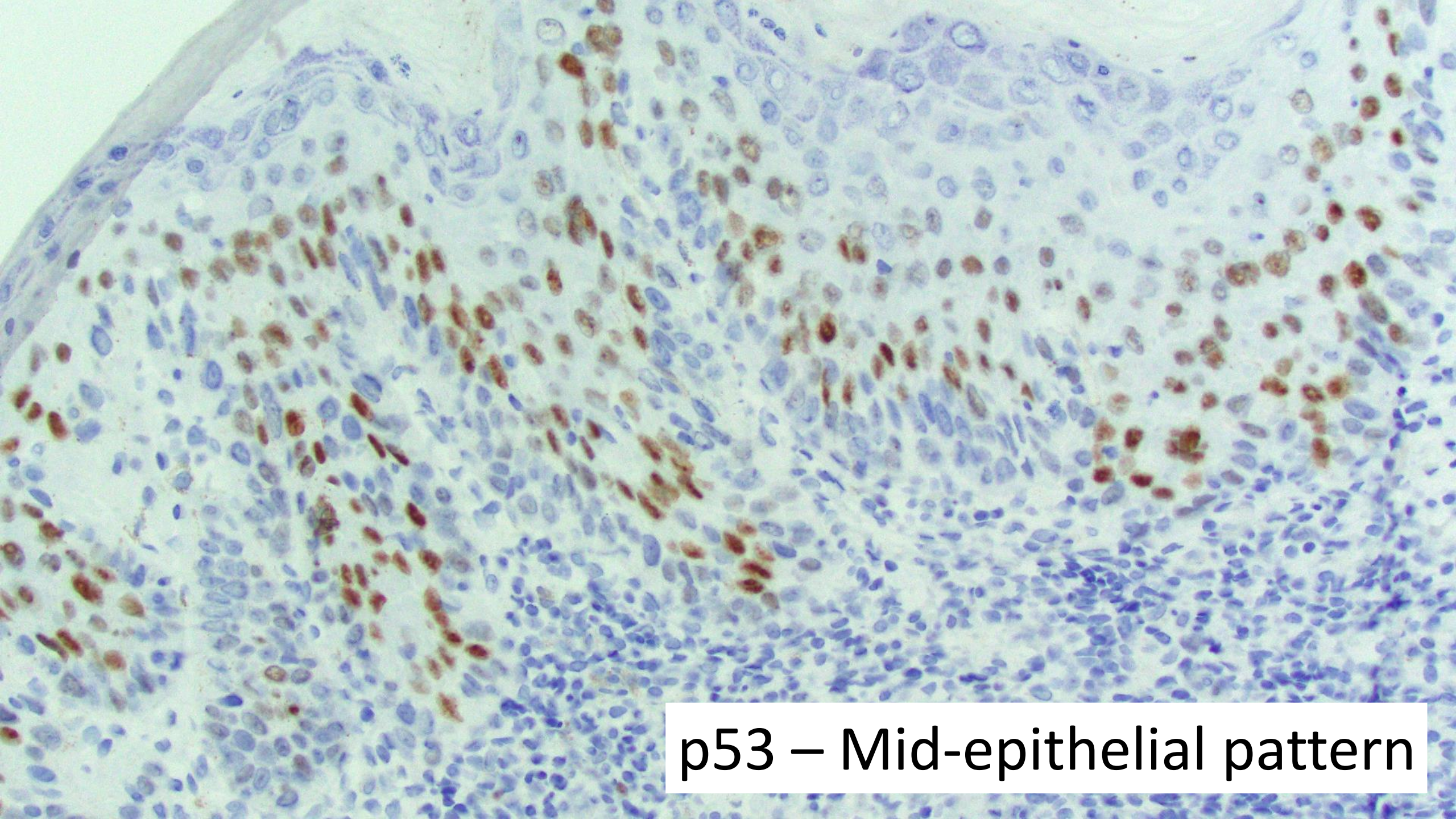
The British Association of Gynaecological Pathologists
https://www.thebagp.org/resources/bagp-guidance-documents/ Accessed 8/4/2024

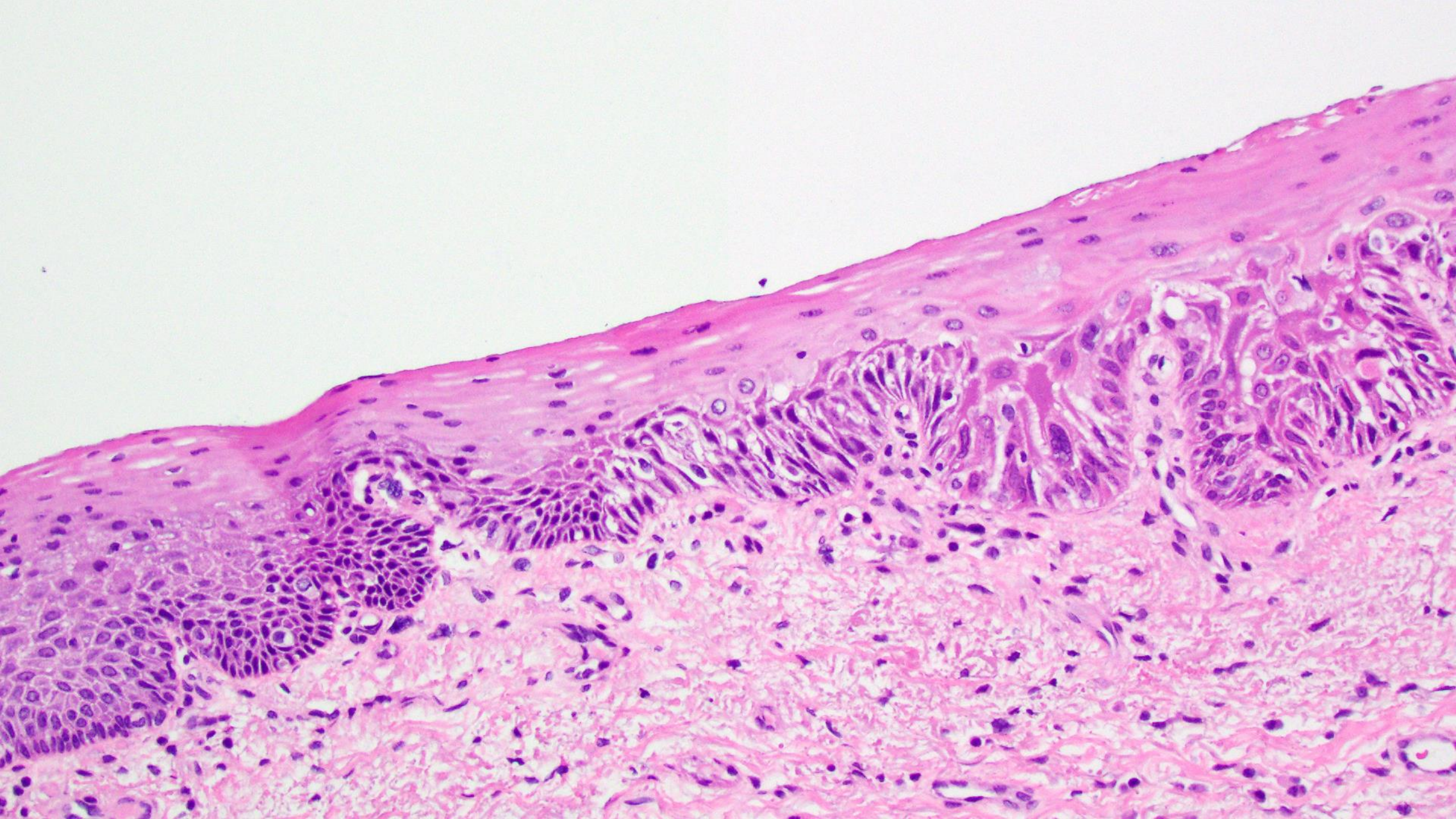


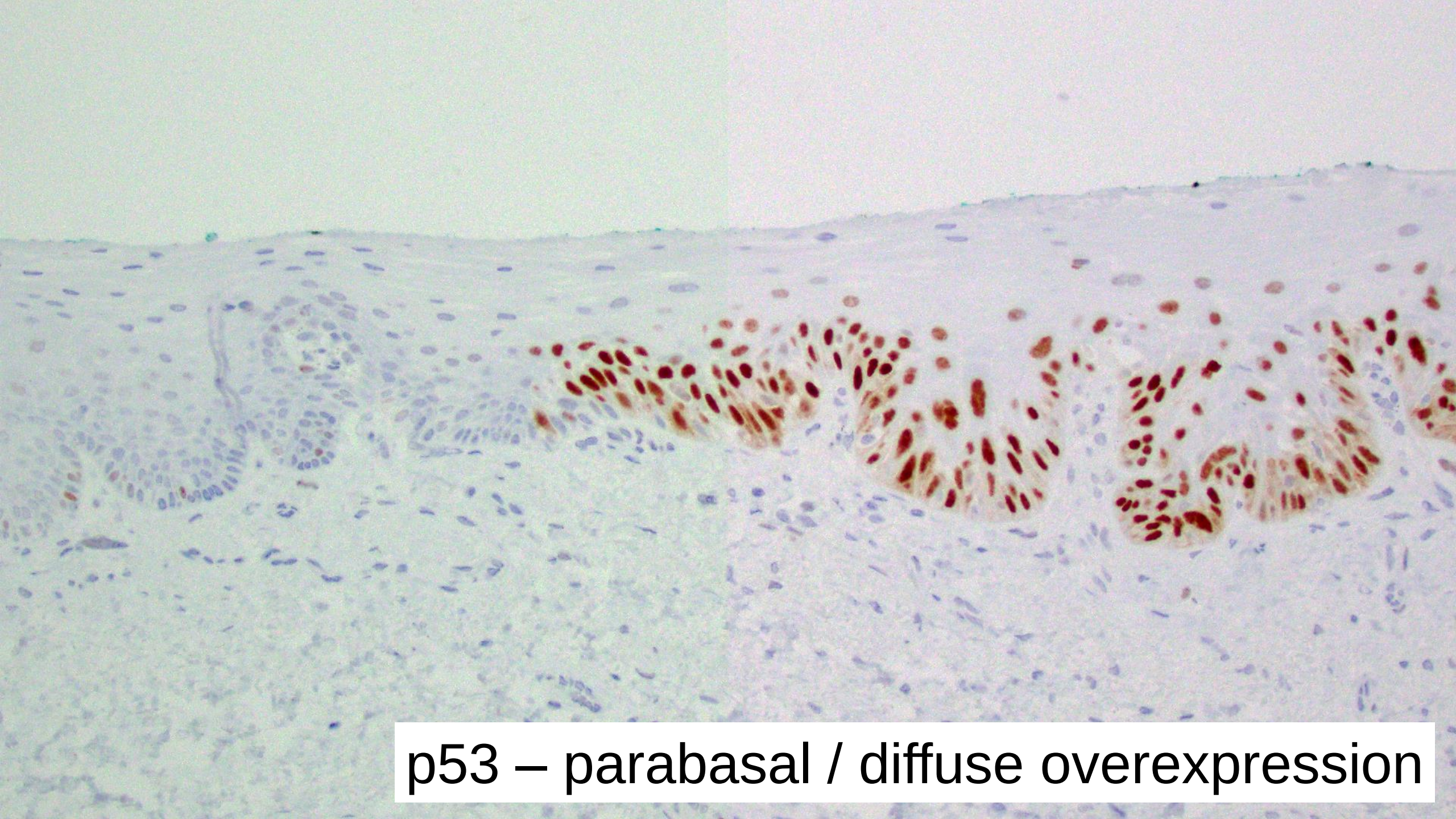
Mod Pathol 2020 PMID: 32203095

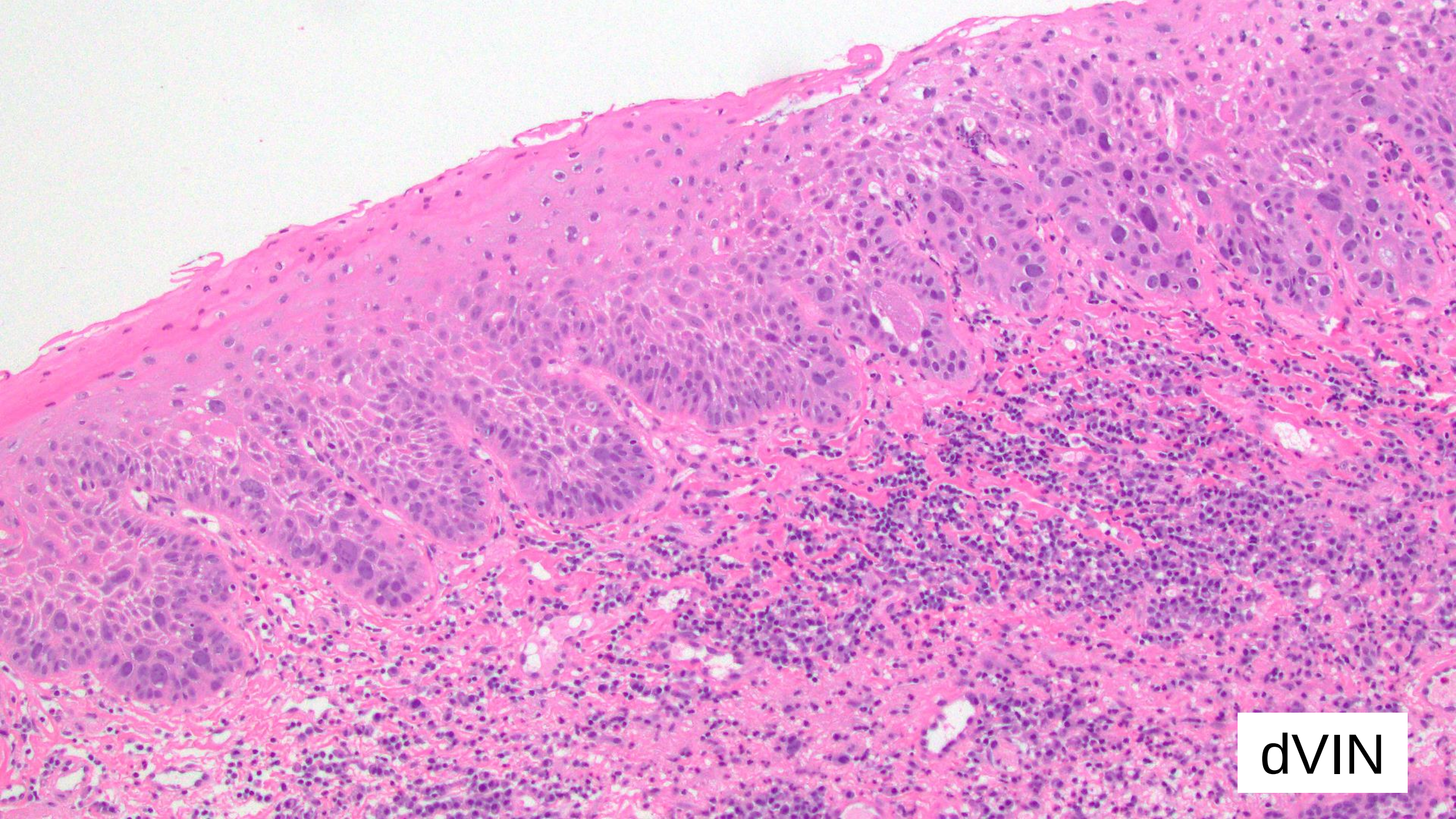

Normal – p53

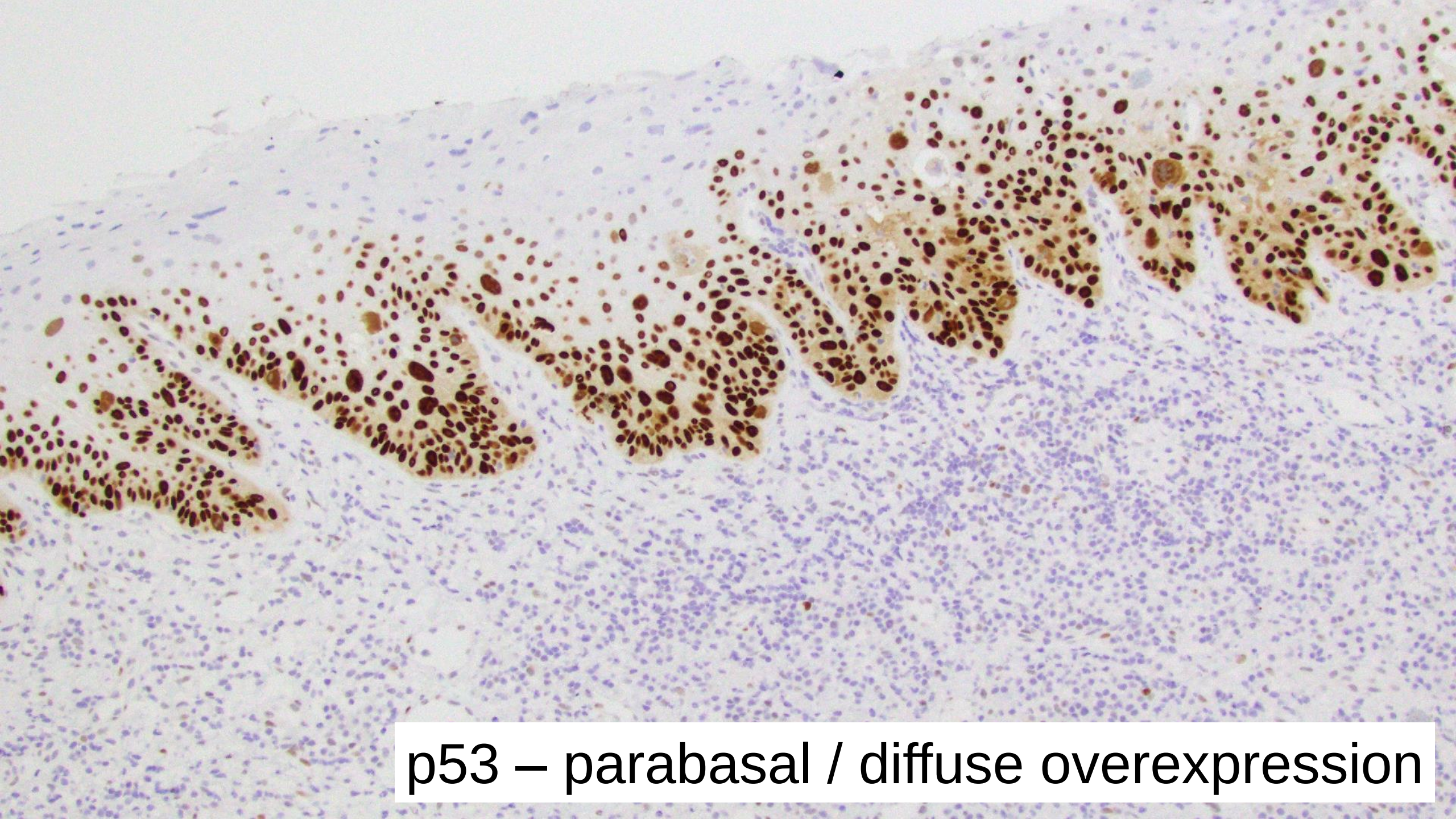

HSIL with LSC

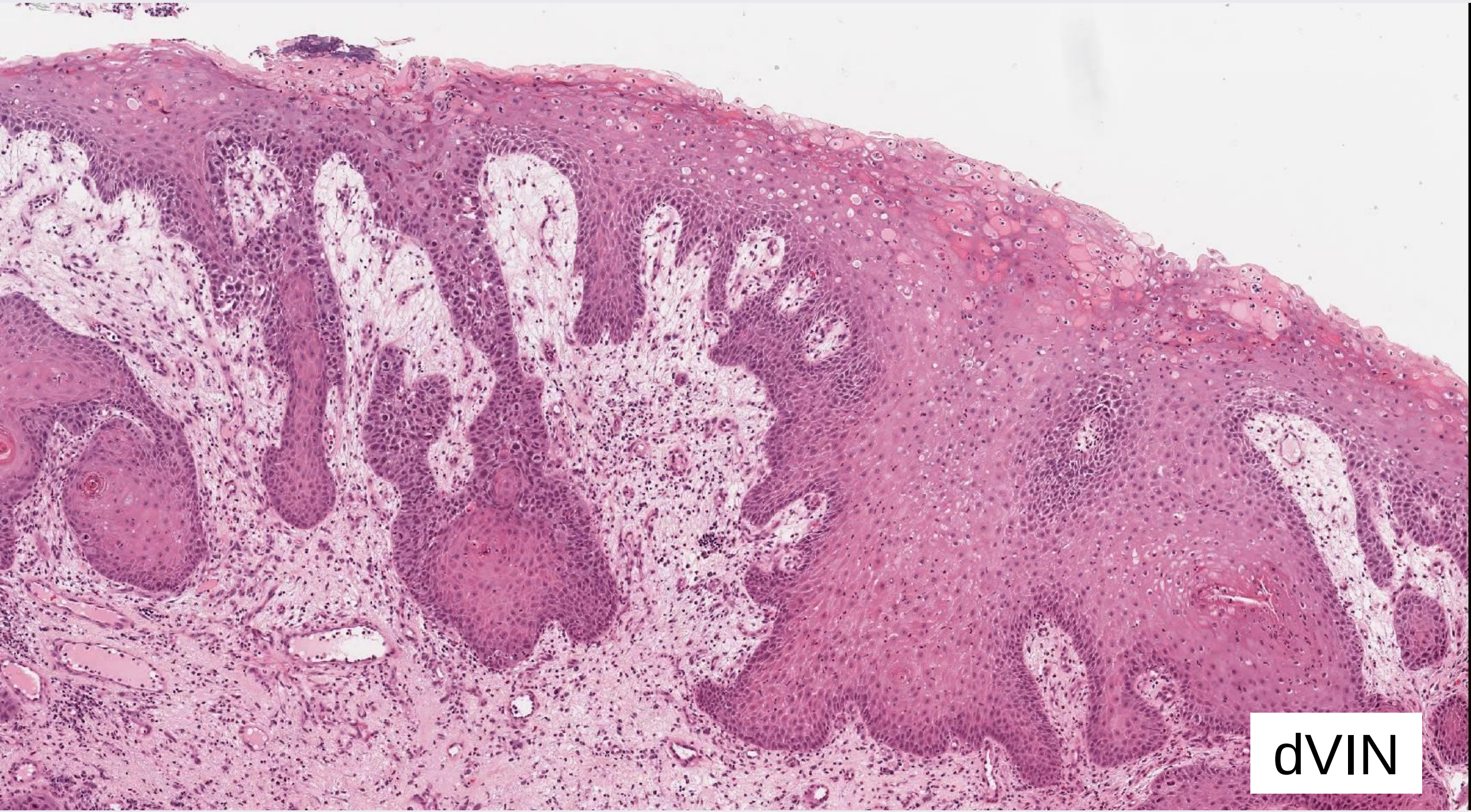

p53 – Mid-epithelial pattern

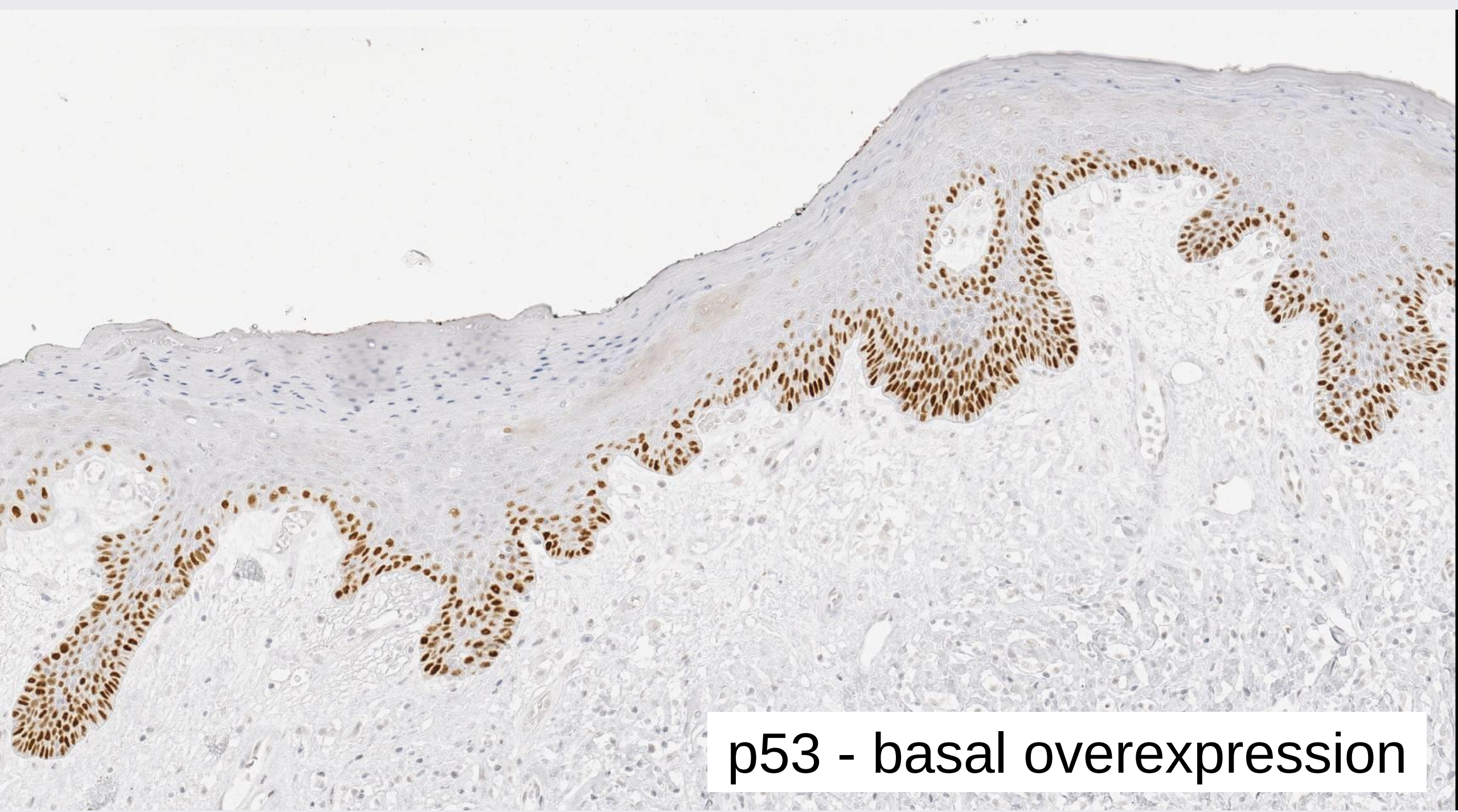


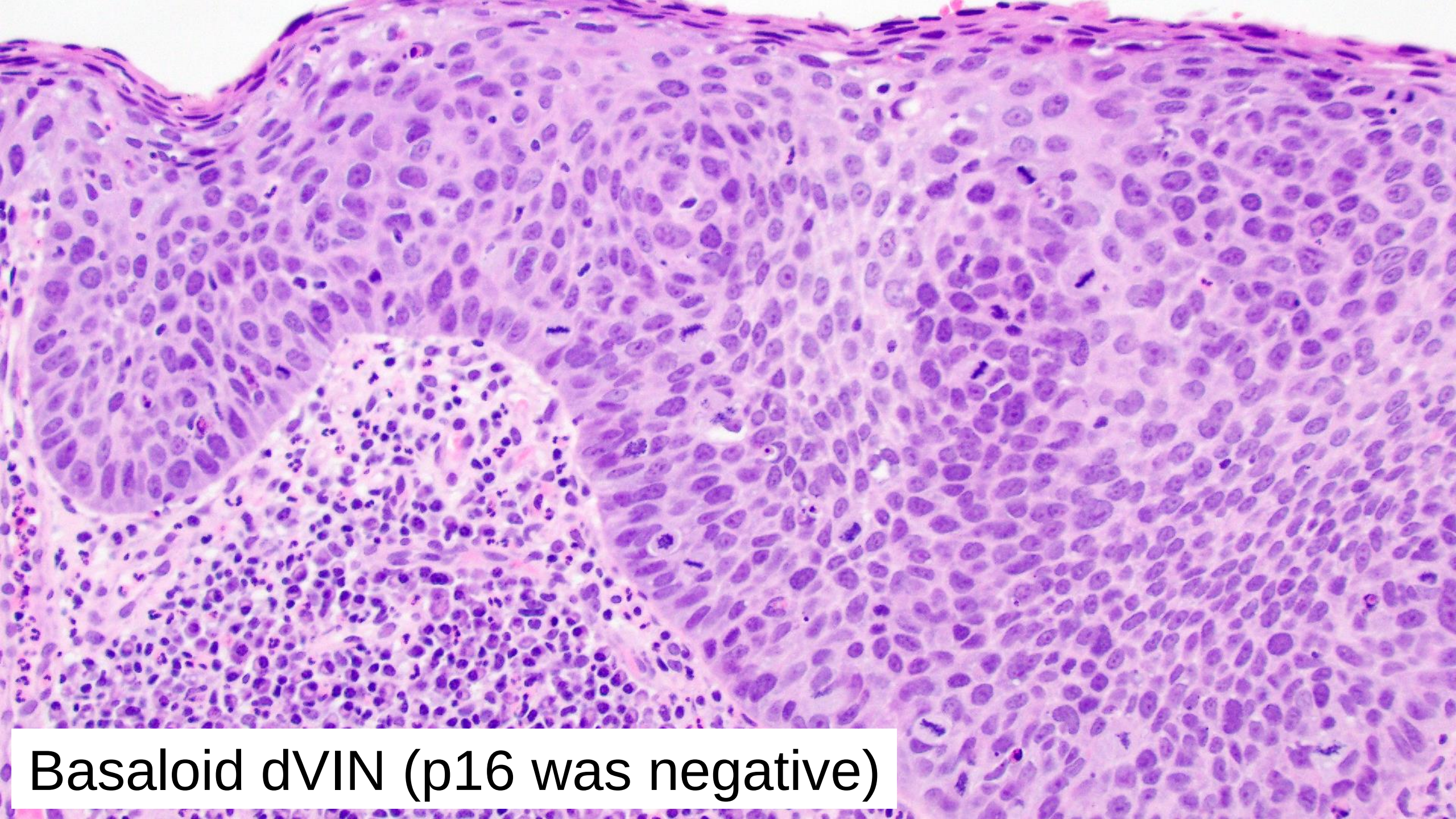

p53 – parabasal / diffuse overexpression

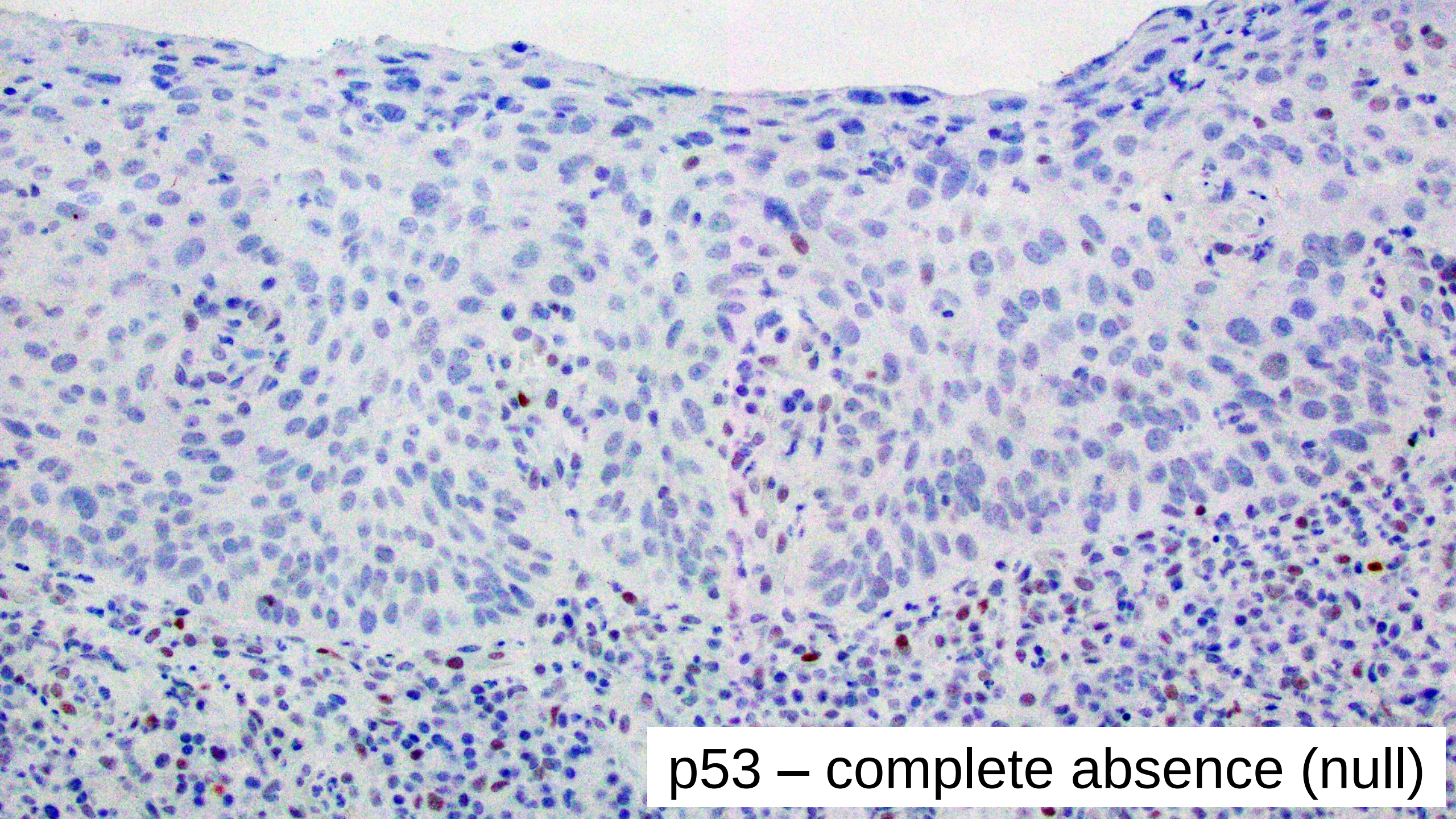

dVIN


p53 – parabasal / diffuse overexpression


dVIN


p53 - basal overexpression


Basaloid dVIN (p16 was negative)

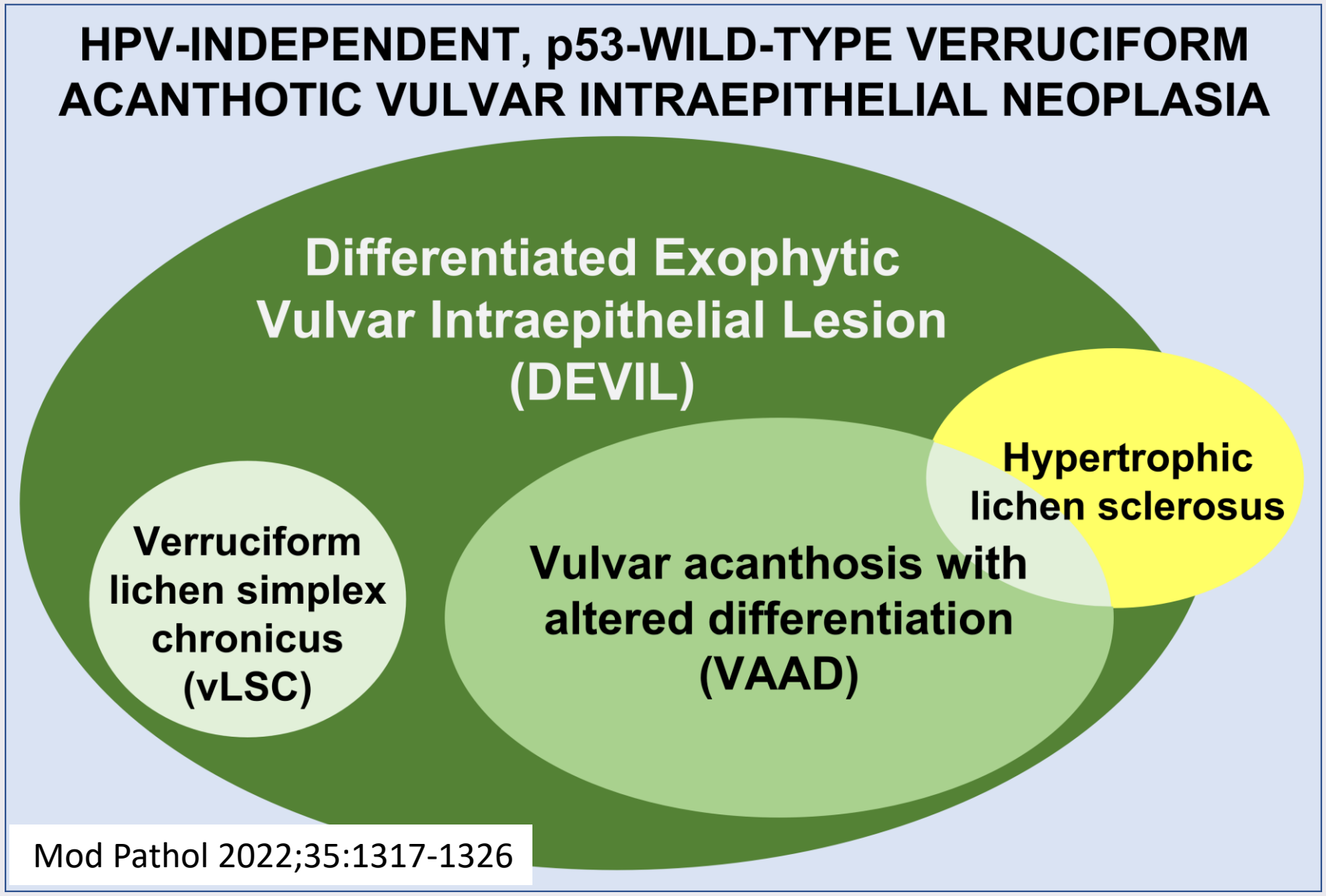

p53 – complete absence (null)

Can dVIN be p53-wild type?

- *Is dVIN an H&E-only diagnosis?*
- Increasingly debatable
- Only if H&E is convincing
- dVIN is not a reproducible diagnosis

Is dVIN the best nomenclature?

HPV-INDEPENDENT p53 WT VIN



Mod Pathol 2022;35:1317-1326

- Association with HPV-independent SCCs
  - Verrucous
  - Conventional

Am J Surg Pathol 2004;28:638-643
Mod Pathol 2017;30:448-458
Mod Pathol 2020;33(S2):1004-1005

Histopathology 2021, 79, 975–988. DOI: 10.1111/his.14451

DEVIL, VAAD and vLSC constitute a spectrum of HPV-independent, p53-independent intra-epithelial neoplasia of the vulva

Simon F Roy,[1,2] Jahg Wong,[1,2] Cécile Le Page,[1] Danh Tran-Thanh,[1] Maroie Barkati,[3] Annick Pina,[4] Vincent Quoc-Huy Trinh[5] & Kurosh Rahimi[1,2]

Table 3. Outcomes of patients with verruciform precursor lesions without invasive carcinoma at initial diagnosis.

	VAAD (n = 11)	DEVIL (n = 5)	Verruciform lichen simplex chronicus (n = 11)	Total (n = 27)	P-value
Median follow-up (months, IQR)	30.2 (14.6–79.4)	28.1 (11.9–41.7)	41.1 (10–82.7)	33 (14.6–61.6)	0.804
Recurrence of verruciform lesion	7 (64%)	3 (60%)	2 (18%)	12 (44%)	0.074
Median recurrence of verruciform lesion time (months, 95% CI)*	9.6 (0–42.1)	7.5 (6.2–8.8)	67.1 (48.2–86.0)**	36.0 (24.2–47.8)	0.082***
Progression to SCC	5 (46%)	2 (40%)	3 (27%)	10 (37%)	0.669
Median progression to squamous cell carcinoma time (months, 95% CI)	63.7 (1.5–125.8)	42.5 (17.7–53.0)	56.9 (34.3–79.5)**	42.5 (18.6–66.3)	0.782***

* IQR not calculable, 95% confidence interval shown instead.

** Media not calculable, mean shown instead.

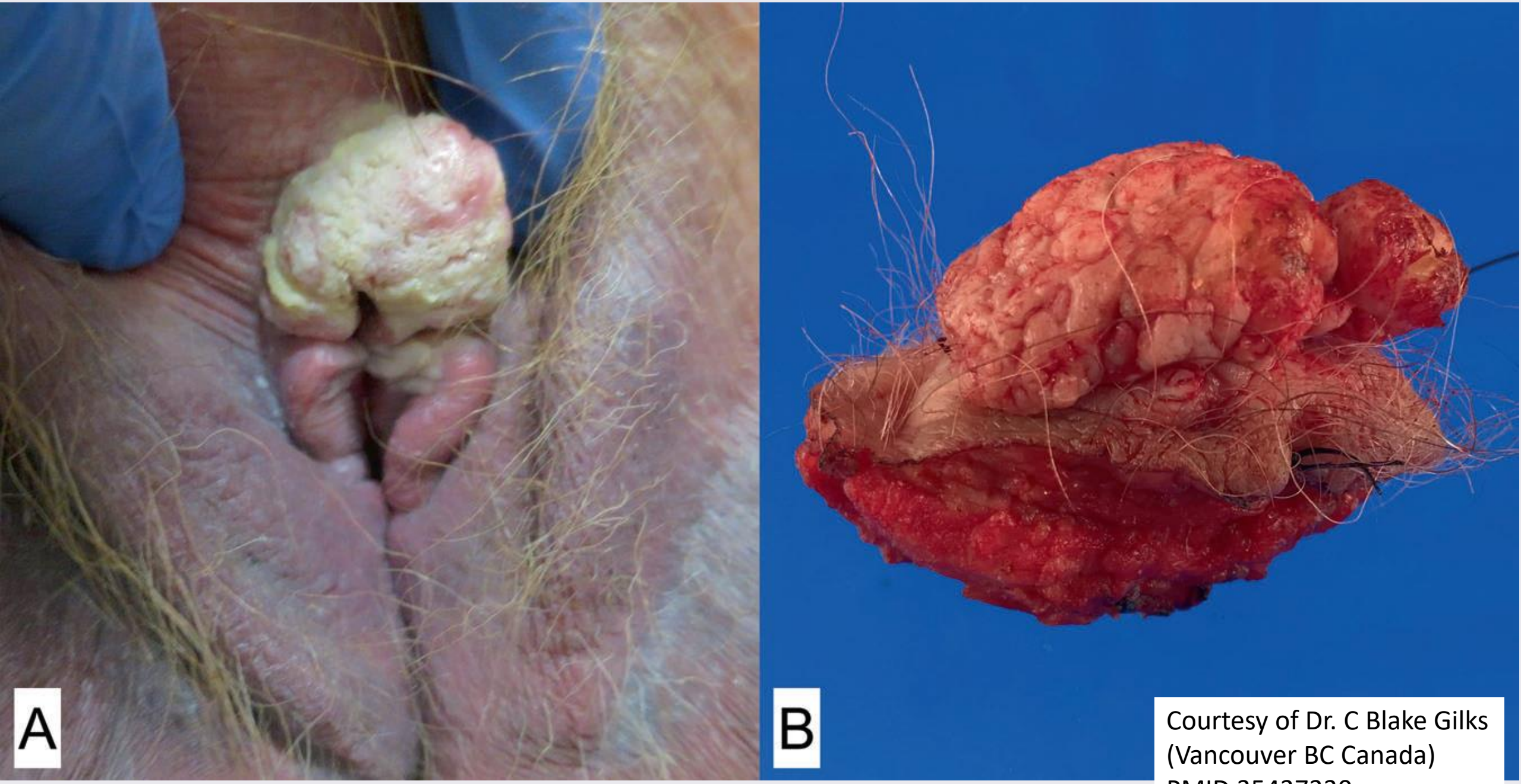
*** Log-Rank P-value.

vaVIN = DEFINITION

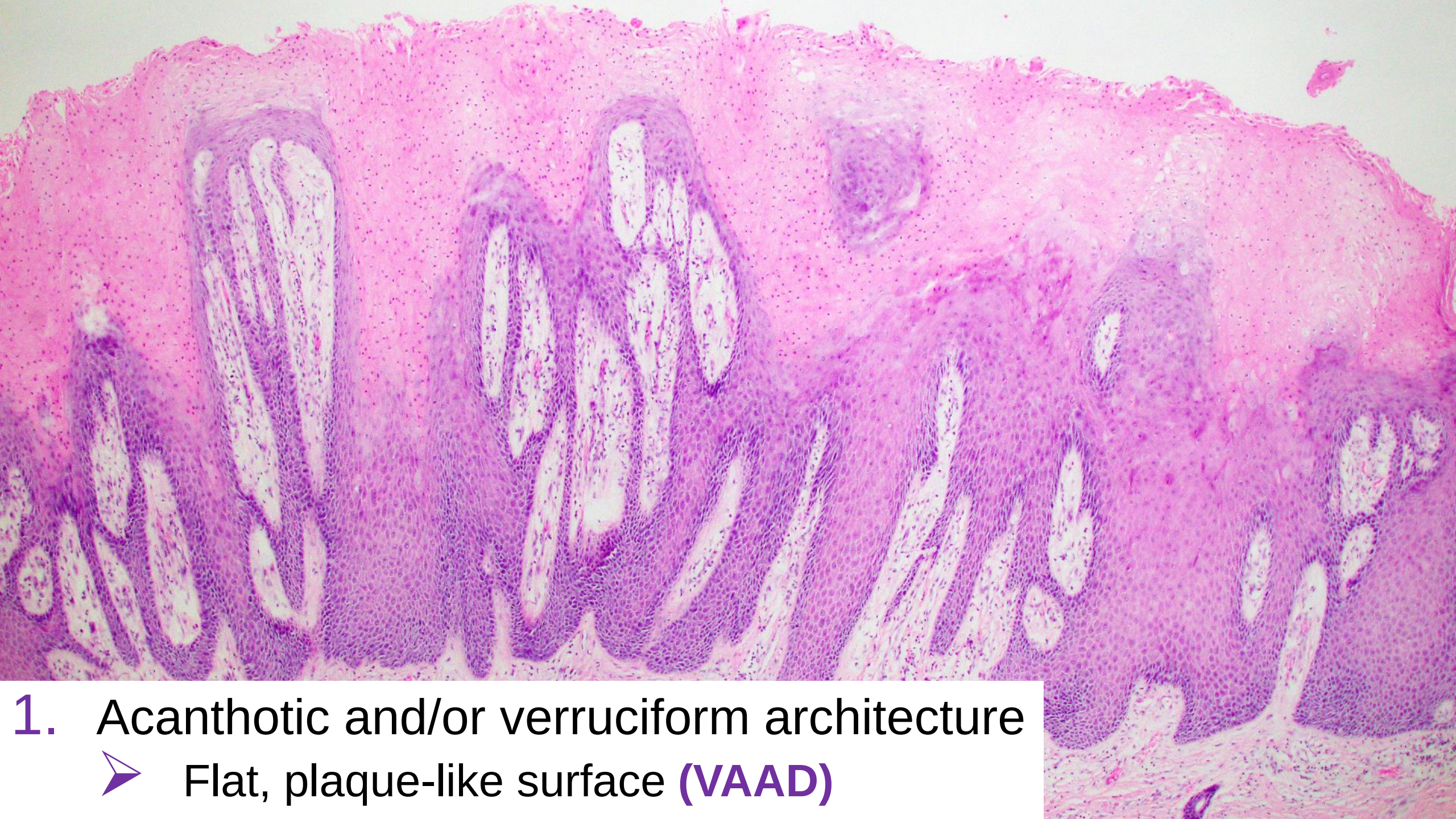
- Patient in their 6-9th decades of life
- Discrete (most often single) lesion
- Raised white or erythematous mass, with cauliflower-like or plaque-like appearance

*The clinical impression is a **TUMOR (cancer, condyloma)***

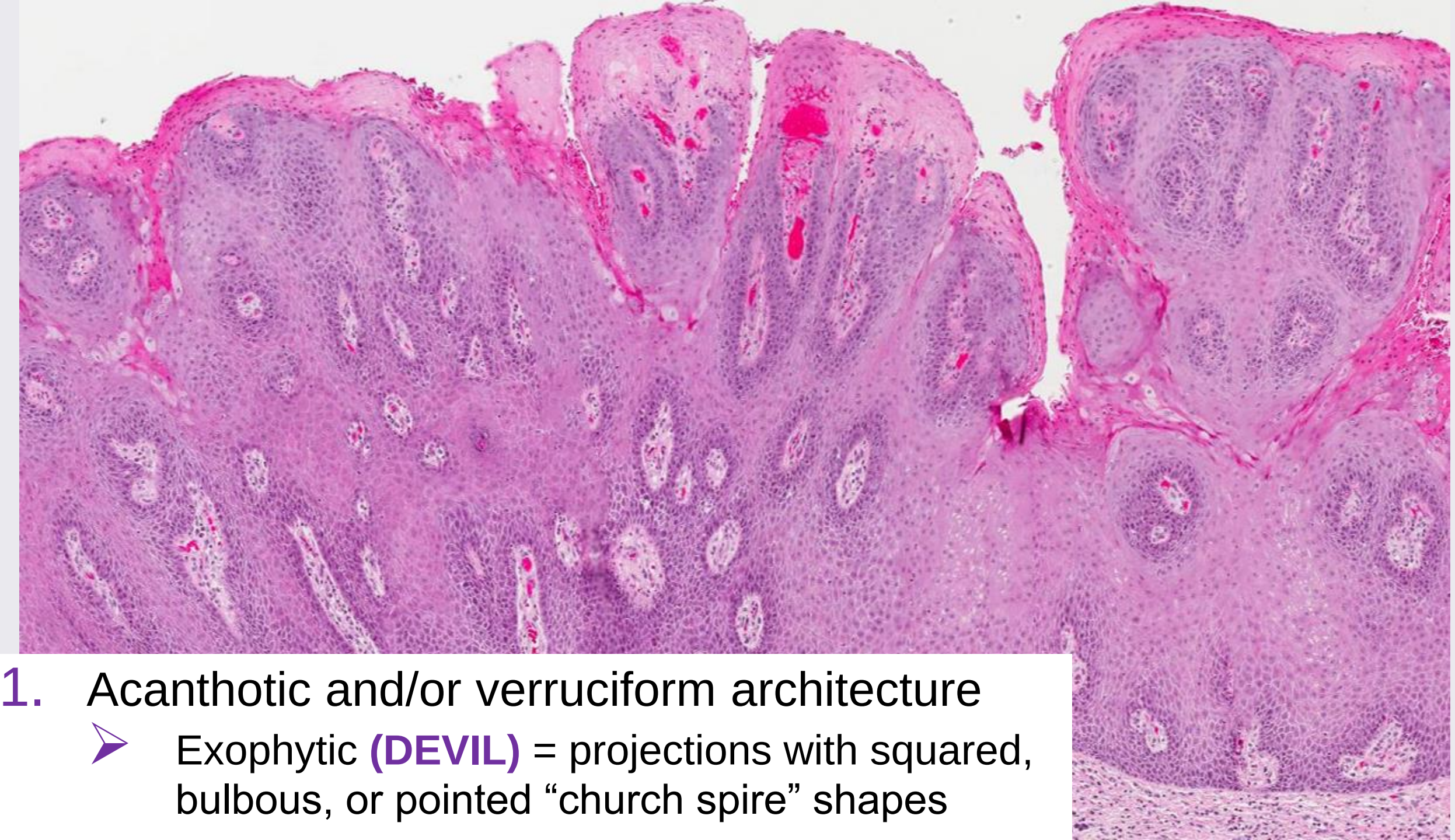
Less frequently LSC, psoriasis



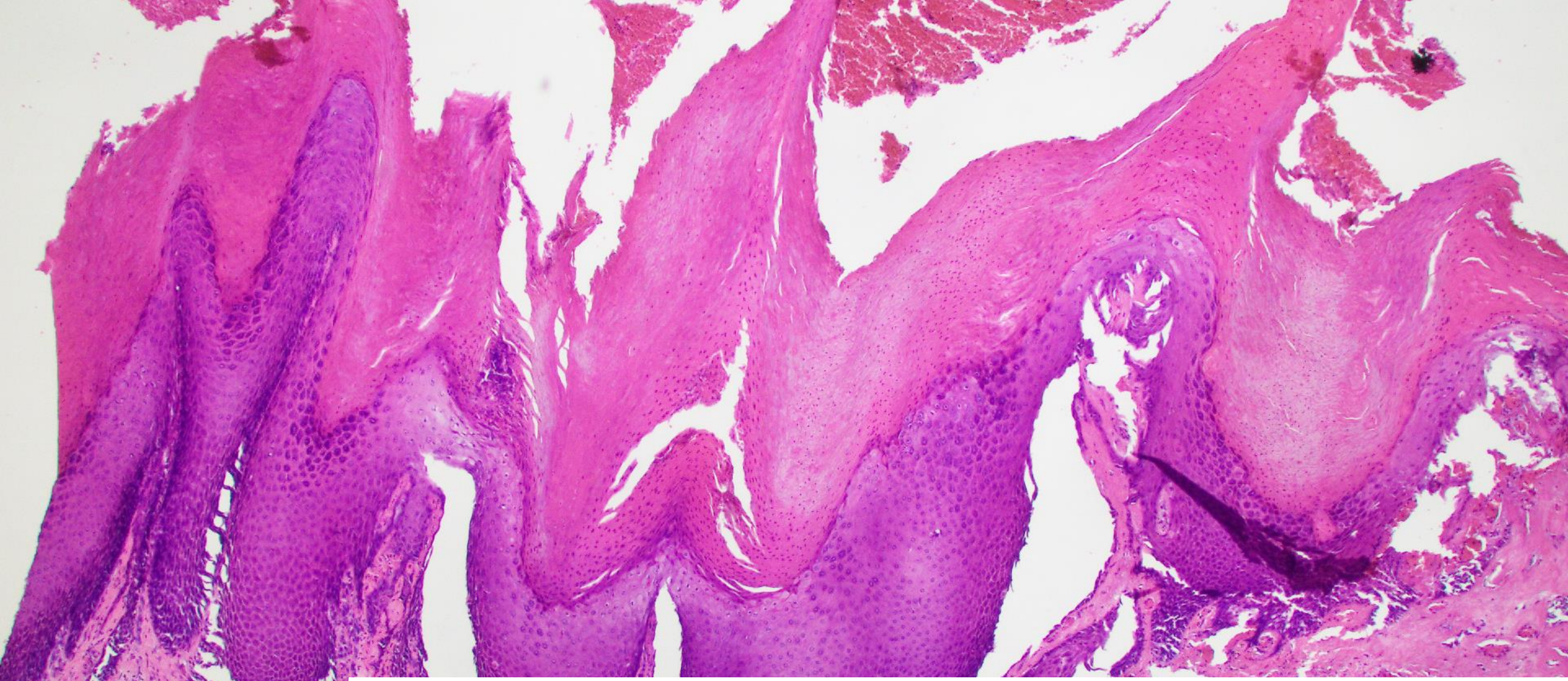
Courtesy of Dr. C Blake Gilks (Vancouver BC Canada)
PMID 35437330



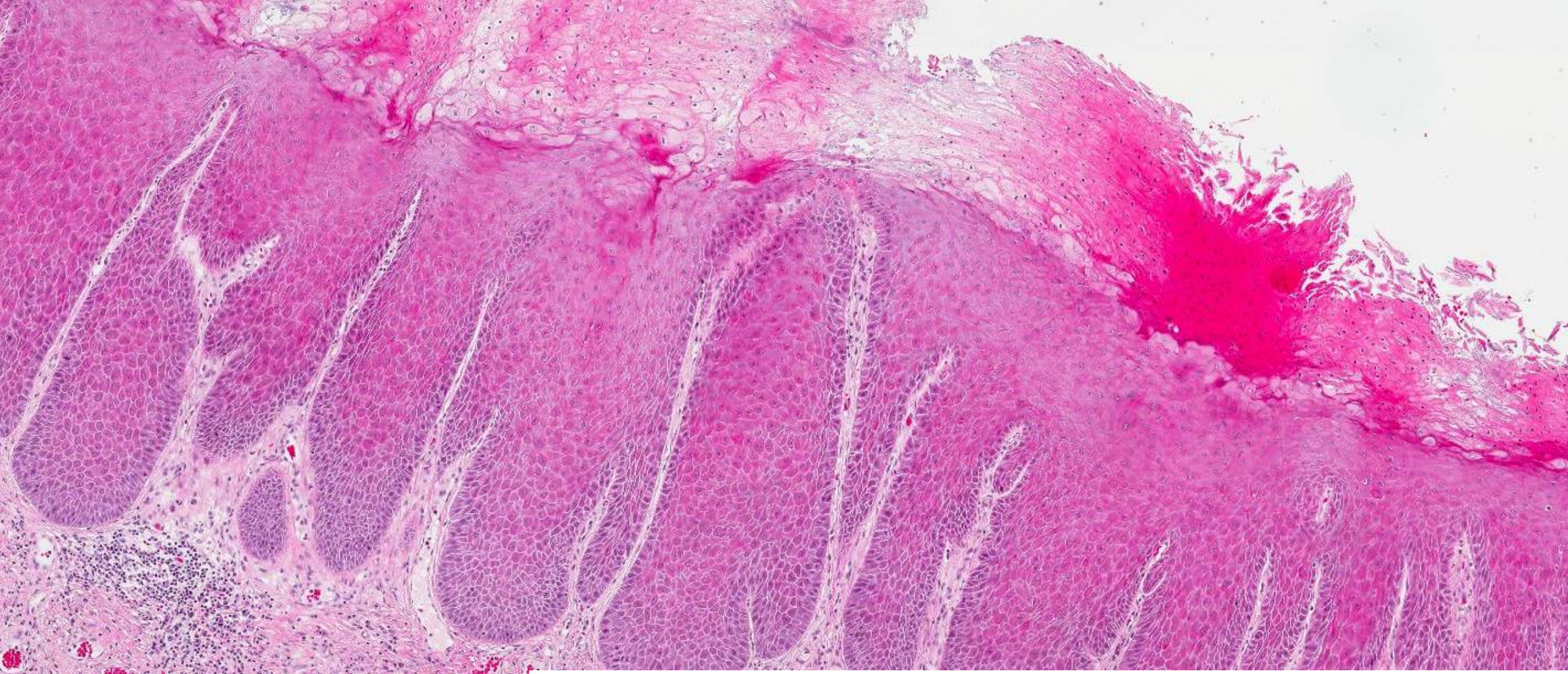
1. Acanthotic and/or verruciform architecture
   - Flat, plaque-like surface **(VAAD)**



1. Acanthotic and/or verruciform architecture
   - Exophytic **(DEVIL)** = projections with squared, bulbous, or pointed “church spire” shapes



1. Acanthotic and/or verruciform architecture
   - Exophytic **(DEVIL)** = projections with squared, bulbous, or pointed “church spire” shapes



2. Altered squamous differentiation
   - Partial or complete hypogranulosis **(VAAD)**
   - Cytoplasmic pallor

vaVIN = DEFINITION

- Absence of cytologic atypia
- Negative or patchy p16 staining / HPV testing
- Wild-type p53 expression

Vulvar Altered Maturation (VAM)

- International Society for the Study of Vulvovaginal Diseases (ISSVD) Difficult Pathologic Diagnoses Committee

Vulvar aberrant maturation is an umbrella term for HPV-independent lesions combining aberrant maturation with minimal nuclear atypia. Multiple names for this have been proposed: differentiated exophytic verruciform intraepithelial lesion, vulvar acanthosis with altered differentiation, atypical epithelial acanthosis, LS with acanthosis or hyperplasia, verruciform LSC, and squamous cell hyperplasia.[8,28,40,50,73,93] It is impossible to retroactively describe squamous cell hyperplasia beyond the ISSVD definition of "a hyperplastic process of unknown etiology."[8,10,27,28,78,93,94] The survey of pathologists could not identify a preferred nomenclature and one third of participants wrote in their own unique terms.[73] Several proposed names were too narrow to encompass the spectrum of VAM, which extends from lichenified LS and hypertrophic LP at one end to verrucous SCC and dVIN at the other.[19–21,53] Where one melds into the next, a clearer understanding of molecular events in the cancerization field should aid in diagnosis and prognosis.[10,14,19]

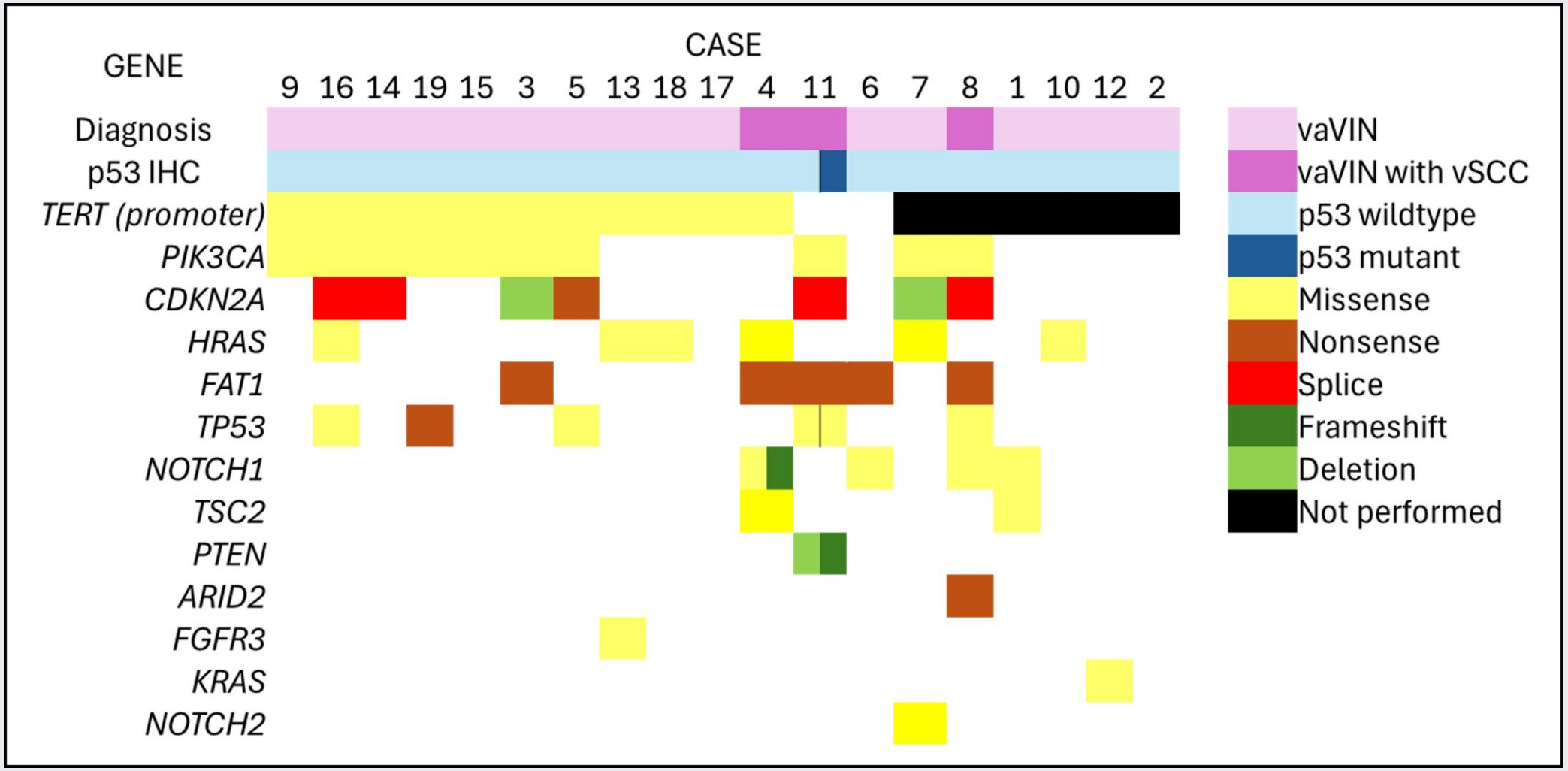
J Low Genit Tract Dis 2021;25: 57–70

Vulvar Altered Maturation (VAM)

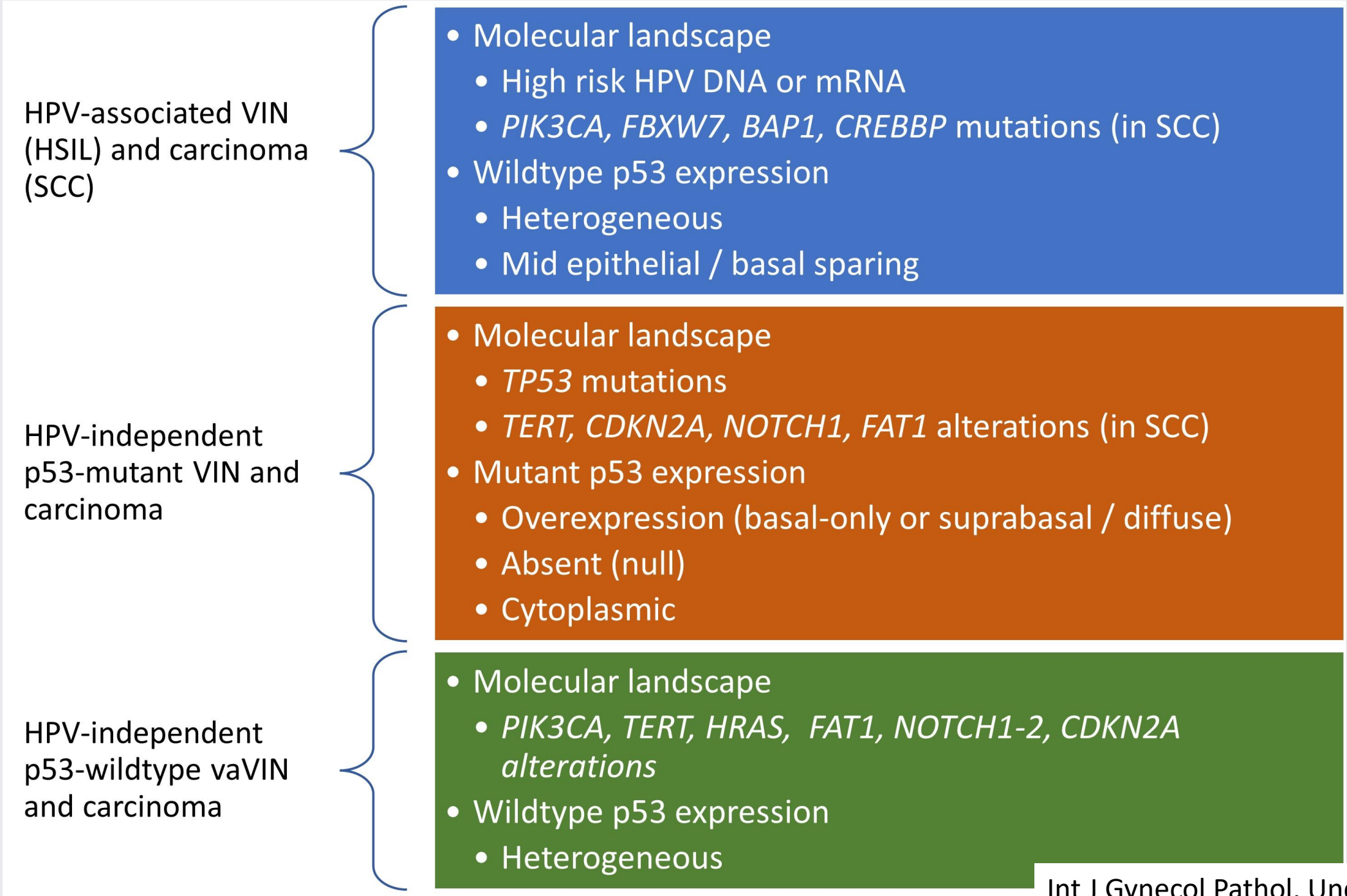
- Use in biopsy material or if Dx is inconclusive

- Verruciform acanthotic lesion. See note.

NOTE: The differential diagnosis includes a variety of hyperplasias as well as lesions associated with HPV-independent, p53 wild type squamous cell carcinoma, namely verruciform acanthotic VIN. Close observation and consideration for further sampling is recommended.



Int J Gynecol Pathol, Under Review



Int J Gynecol Pathol, Under Review

IHC

- CK17
- SOX2
- GATA3

Article

Evaluation of Immunohistochemical Markers, CK17 and SOX2, as Adjuncts to p53 for the Diagnosis of Differentiated Vulvar Intraepithelial Neoplasia (dVIN)

Shatavisha Dasgupta [1,*], Senada Koljenović [1], Thierry P. P. van den Bosch [1], Sigrid M. A. Swagemakers [1,2], Nick M. A. van der Hoeven [3,4], Ronald van Marion [1], Peter J. van der Spek [1,2], Helena C. van Doorn [4], Folkert J. van Kemenade [1,†] and Patricia C. Ewing-Graham [1,†]

Pharmaceuticals 2021;14;324

Differential expression patterns of GATA3 in usual and differentiated types of vulvar intraepithelial neoplasia: potential diagnostic implications

Abha Goyal[1] · Gloria Zhang[2] · Bin Yang[2]

Mod Pathol 2018;31(7):1131-1140

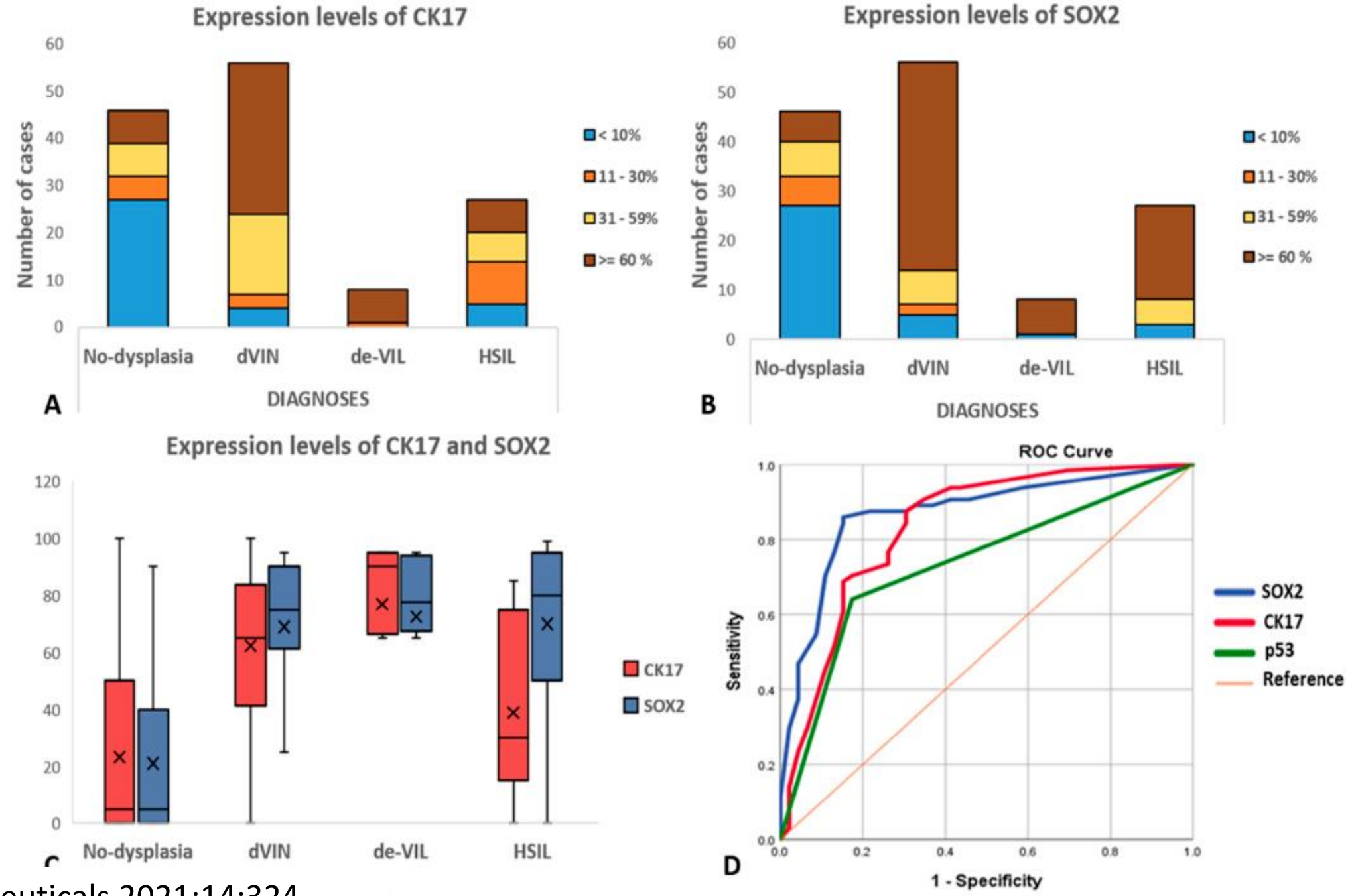
GATA3 immunohistochemistry as a diagnostic adjunct for differentiated vulvar intraepithelial neoplasia: utility and limitations☆,☆☆

Somaye Y. Zare MD, Elmira Vaziri Fard MD, MPH, Oluwole Fadare MD*

Hum Pathol 2023;139:55-64

Immunohistochemical Marker	Expression Patterns	Diagnoses			
		dVIN (n = 56)	de-VIL (n = 8)	HSIL (n = 27)	Non-Dysplastic Vulvar Tissue (n = 46)
		Number of Cases (Percentage)			
CK17	Diffuse, moderate-strong, full epithelial expression	27 (48)	5 (63)	6 (22)	1 (2)
	Diffuse, moderate-strong, suprabasal expression	18 (32)	2 (25)	11 (41)	3 (7)
	Patchy, moderate-strong, suprabasal expression	8 (14)	1 (12)	10 (37)	5 (11)
	Patchy, weak, suprabasal expression	2 (4)	0 (0)	0 (0)	19 (41)
	No expression	1 (2)	0 (0)	0 (0)	18 (39)
SOX2	Diffuse, moderate-strong, full epithelial expression	37 (66)	5 (63)	12 (44)	2 (4)
	Diffuse, moderate-strong, basal and suprabasal expression	11 (20)	2 (25)	12 (44)	7 (15)
	Scattered, weak, basal (predominant) and suprabasal expression	7 (13)	1 (12)	2 (8)	17 (37)
	No expression	1 (1)	0 (0)	1 (4)	20 (44)

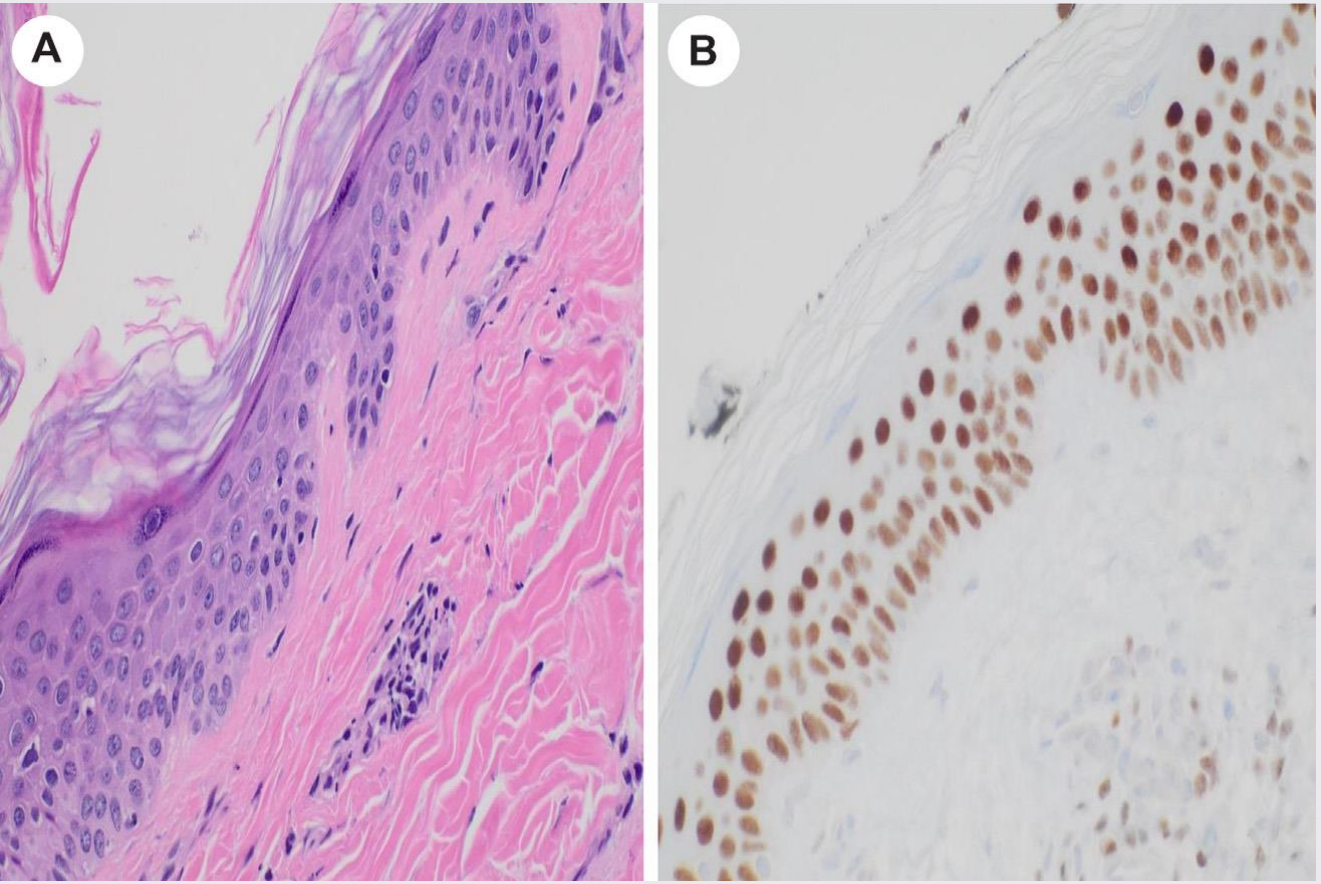
Pharmaceuticals 2021;14;324

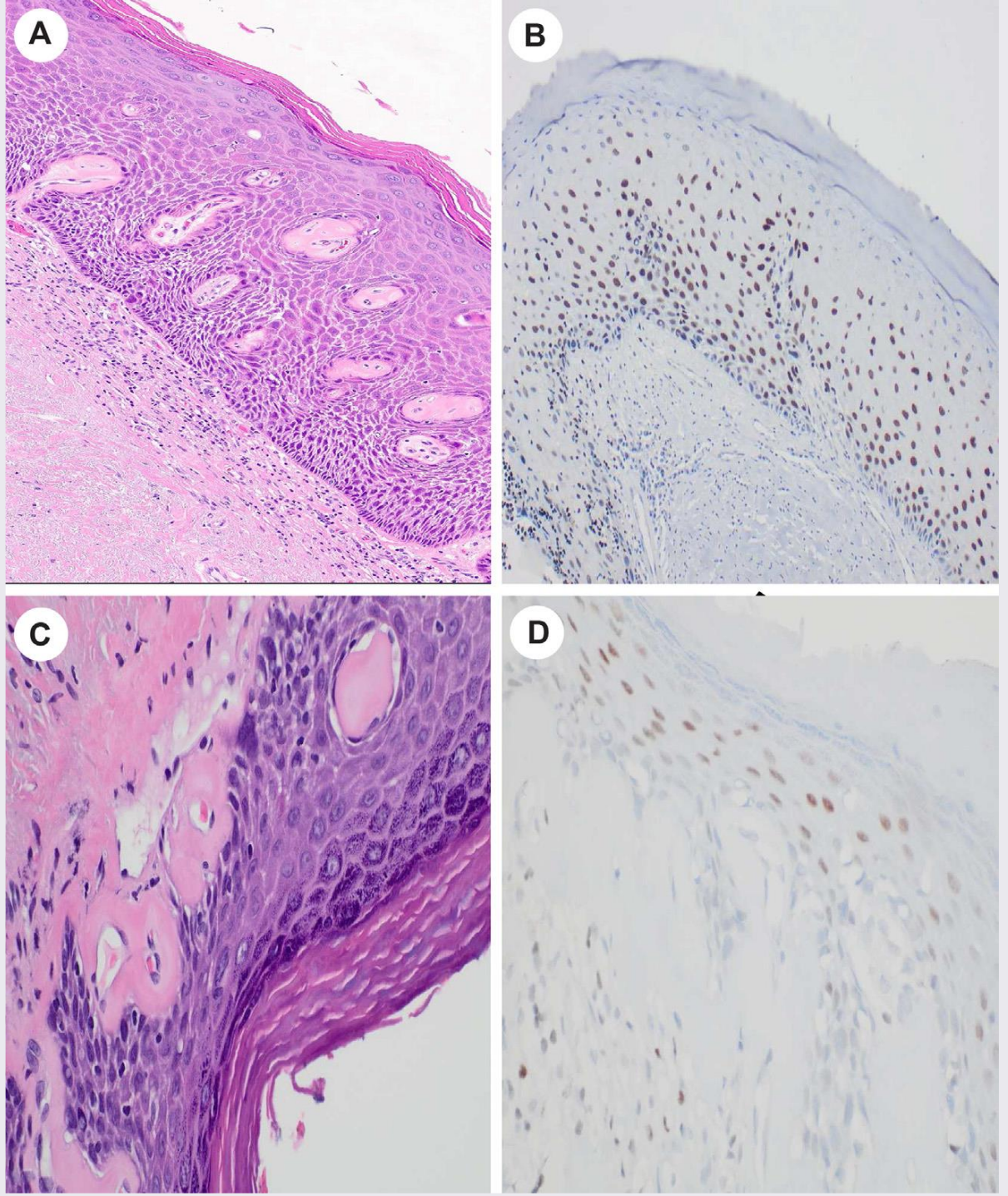


Pharmaceuticals 2021;14;324

GATA3 IMMUNOHISTOCHEMISTRY

- Pattern 0: Loss of nuclear expression in <25% basal cells
- Pattern 1: Loss of nuclear expression in 25-75% basal cells
- Pattern 2: Loss of nuclear expression in >75% basal cells





Hum Pathol 2023;139:55-64

	GATA3 staining patterns			p53 IHC results	
	Pattern 0	Pattern 1	Pattern 2	Wild type	Abnormal
VULVAR EPIDERMIS IN PATHOLOGIC STATES					
Dysplastic and precancerous lesions (number of cases)					
Differentiated VIN	2	3	16	1	20
Vulvar aberrant maturation	1	7	2	9	1 (strong basal)
VIN III	37	1	6	44	0
Non-neoplastic lesions (number of cases)					
Lichen sclerosus	23	1	1	23	2 (strong basal)
Lichen simplex chronicus	6	0	0	6	0
Spongiotic dermatitis	13	0	0	13	0
Lichen planus	2	0	0	2	0
Nonspecific interface dermatitis	3	0	0	3	0
NORMAL VULVAR EPIDERMIS	75	0	0	75	0

Hum Pathol 2023;139:55-64

Histopathology

Histopathology 2024 DOI: 10.1111/his.15156

Diagnosis of verruciform acanthotic vulvar intra-epithelial neoplasia (vaVIN) using CK17, SOX2 and GATA3 immunohistochemistry

Eleanor Cook,[1] Koen Van de Vijver[2,*] & Carlos Parra-Herran[1,*]

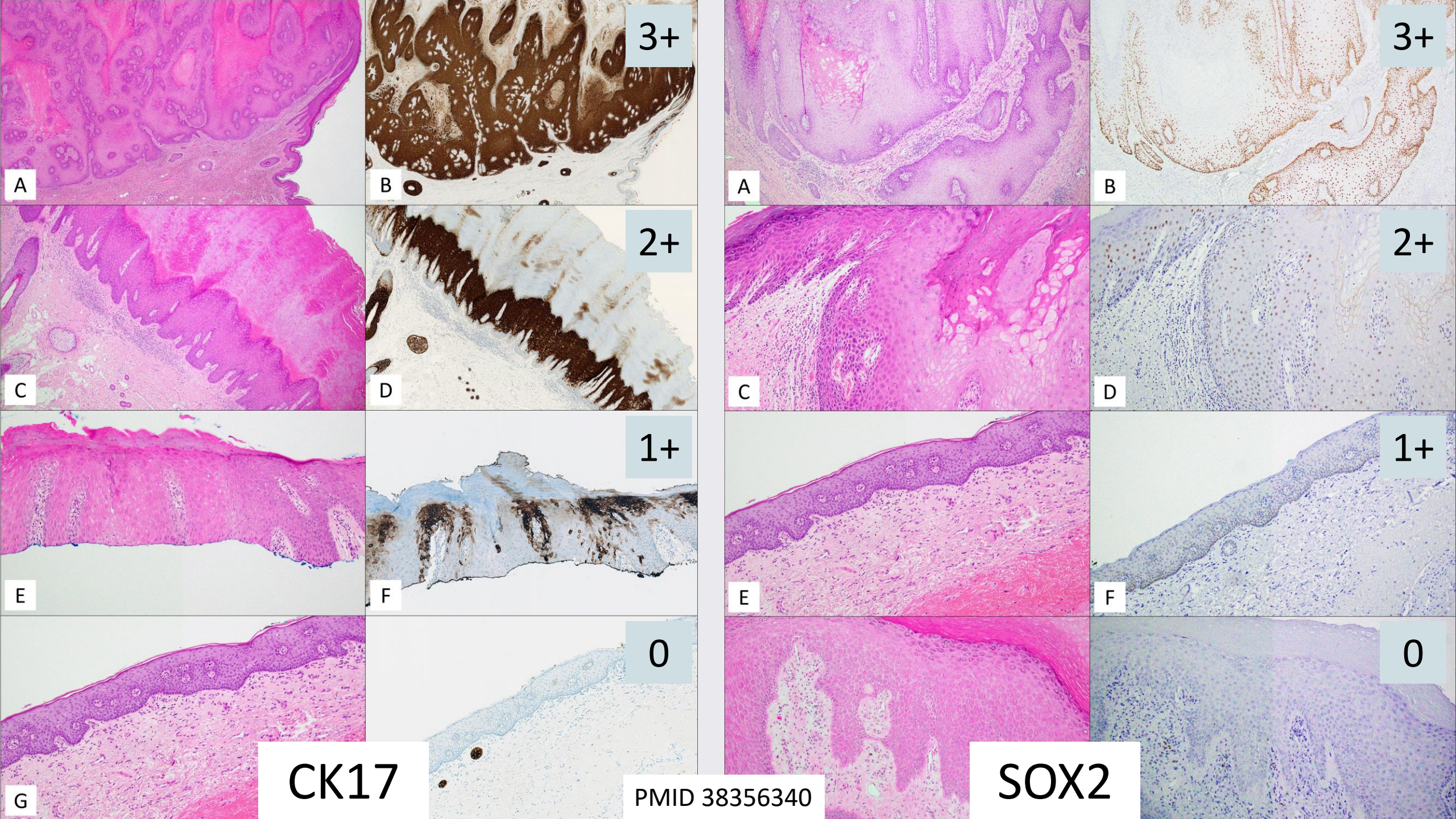
[1]*Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA and* [2]*University Hospital Ghent, Ghent, Belgium*

CK17 IMMUNOHISTOCHEMISTRY

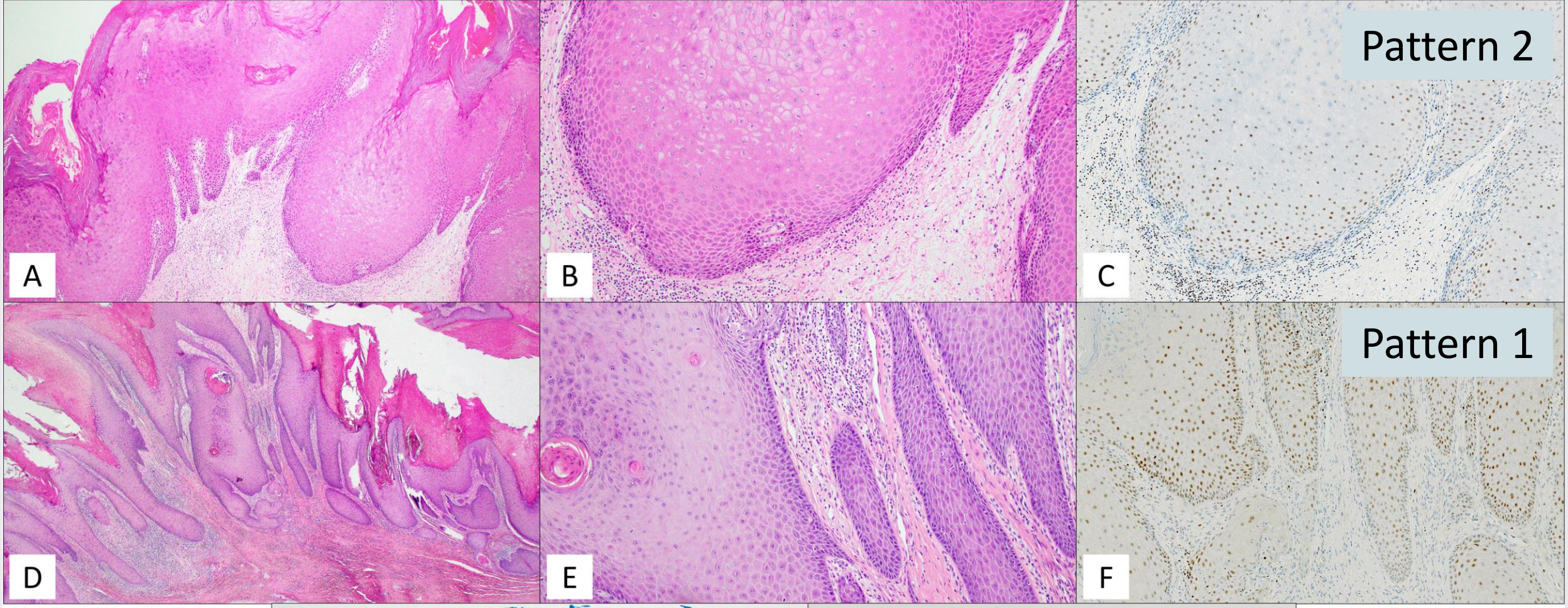
- 3+ = continuous, full-thickness
- 2+ = continuous, partial-thickness
- 1+ = discontinuous / patchy
- 0 = absent

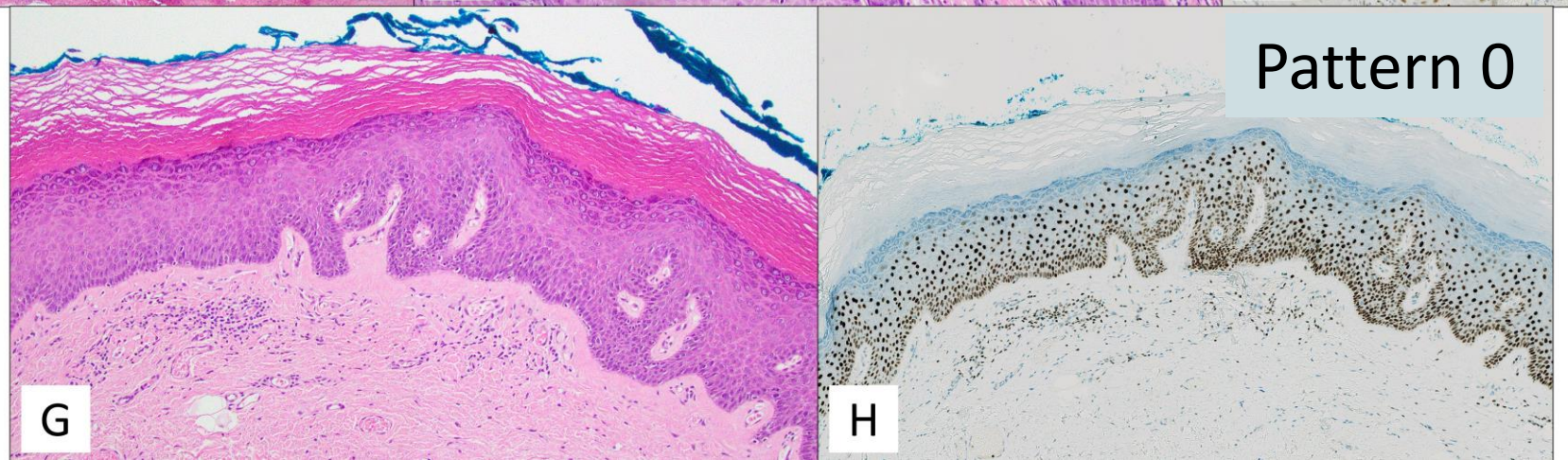
SOX2 IMMUNOHISTOCHEMISTRY

- 3+ = strong in ≥ 10% cells
- 2+ = moderate in ≥ 10% cells
- 1 + = weak in ≥ 10% cells
- 0 = staining in < 10% cells



PMID 38356340





GATA3

PMID 38356340

Table 5. Sensitivity, specificity and predictive values for CK17, SOX2 and GATA3 in the diagnosis of verruciform/acanthotic vulvar intra-epithelial neoplasia (vaVIN)

Differential	Statistic	CK17 positivity (3+ score) (%)	SOX2 positivity (3+ score) (%)	GATA3 positivity (pattern 1 or 2) (%)	2 or 3 positive markers (%)
vaVIN versus acanthotic/ verruciform mimicker	Sensitivity	81	75	58	83
	Specificity	68	83	78	88
	Pos predictive value[a]	54	64	50	71
	Neg predictive value[a]	88	89	83	93
	Accuracy	72	81	73	86
vaVIN versus normal mucosa	Sensitivity	81	69	58	83
	Specificity	100	50	75	86
	Pos predictive value[a]	100	69	78	91
	Neg predictive value[a]	79	50	55	75
	Accuracy	89	62	65	84

Positive: CK17 = 3+ SOX2 = 3+ GATA3 = patterns 1 & 2

Negative: CK17 = 2+/1+/0 SOX2 = 2+/1+/0 GATA3 = pattern 0

WHAT'S NEXT IN CLASSIFICATION

MORPHOLOGY BASED

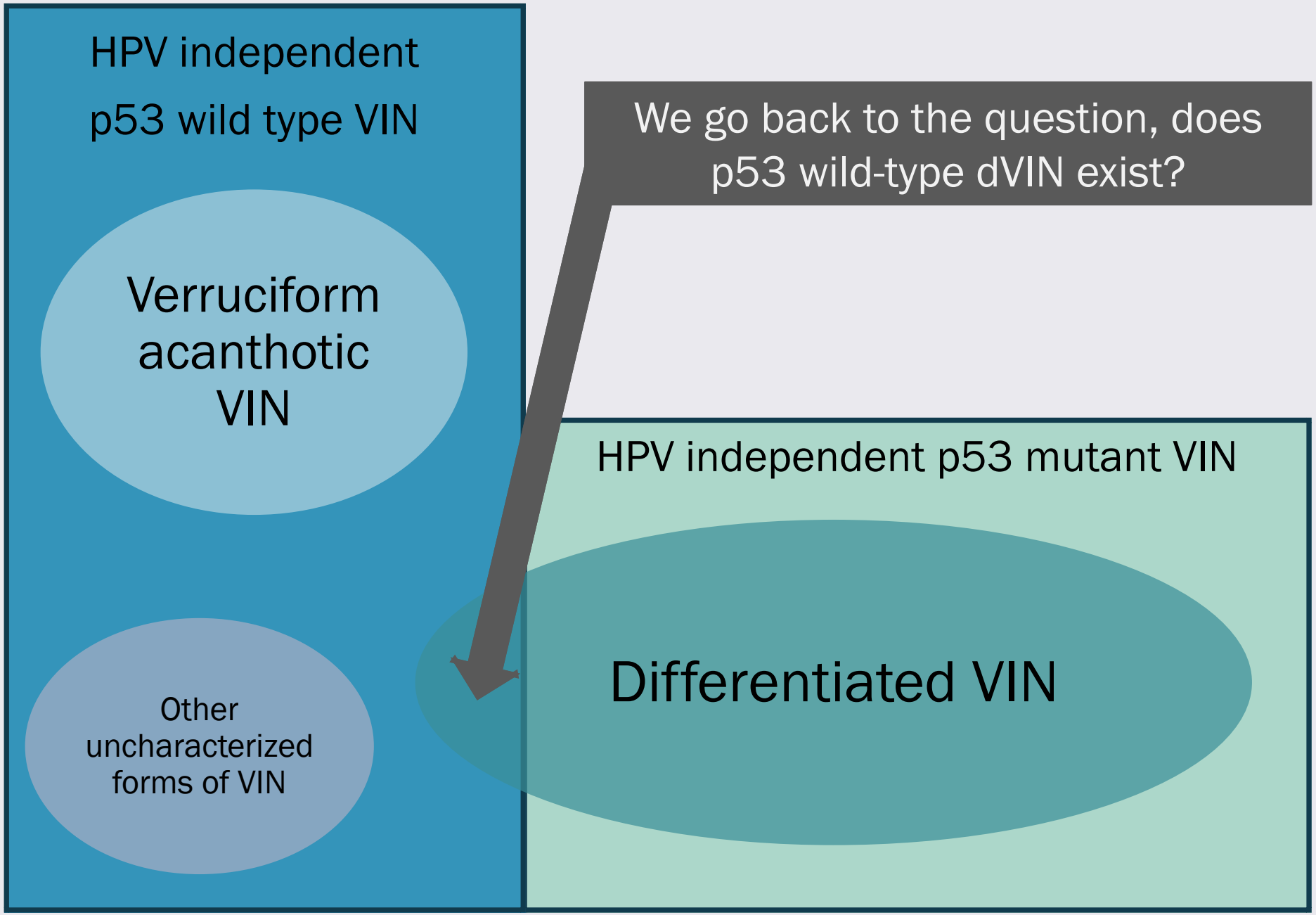
- Squamous intraepithelial lesion
- Differentiated VIN
- Verruciform acanthotic VIN

BIOMARKER BASED

- HPV-associated
- HPV-independent p53 mutant
- HPV-independent p53 wild type

WHO CLASSIFICATION

HPV associated = Squamous intraepithelial lesion


HPV independent
p53 wild type VIN
Verruciform acanthotic VIN
Other uncharacterized forms of VIN
We go back to the question, does p53 wild-type dVIN exist?
HPV independent p53 mutant VIN
Differentiated VIN

Histopathology

Histopathology 2024, **84**, 301–314. DOI: 10.1111/his.15050

High-grade vulvar intraepithelial neoplasia: comprehensive characterization and long-term vulvar carcinoma risk

Nikki B Thuijs,[1,2] Marc van Beurden,[3] Sylvia Duin,[1,2] Daniëlle A M Heideman,[1,2,4] Johannes Berkhof,[5] Renske D M Steenbergen[1,2] & Maaike C G Bleeker[1,2]

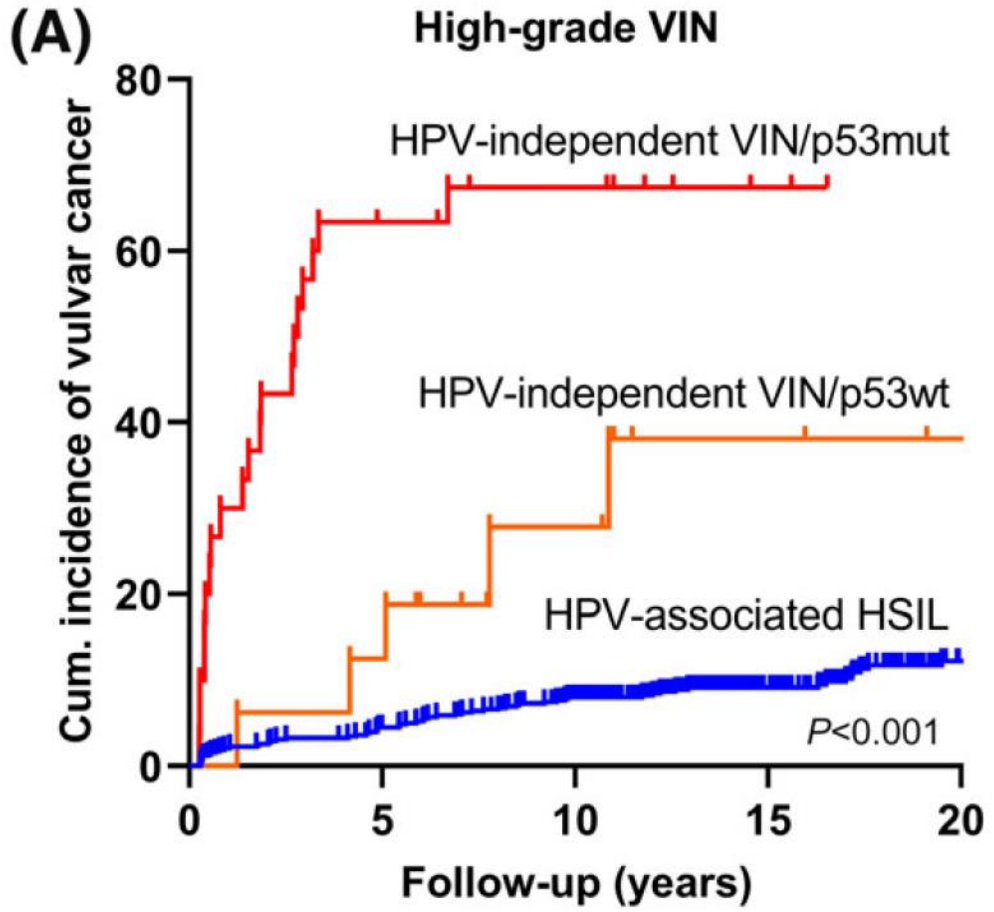
- 751 high-grade VINs
- Re-classified based on histopathology + immunohistochemistry (p16, p53, Ki-67) and HPV DNA
- 46 HPV-independent VIN
  - *30 (65%) p53mut* *16 (35%) p53 wt*
  - *59% differentiated*
  - *41% nondifferentiated ('HPV associated-like')*

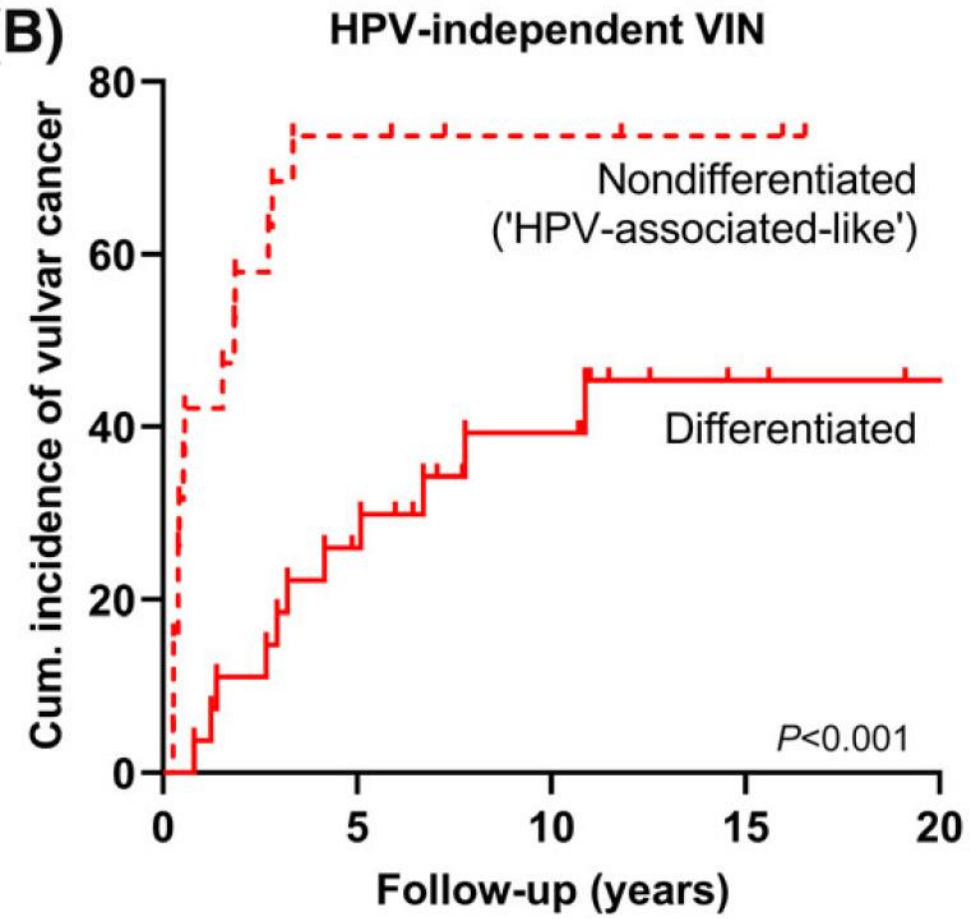
Histopathology 2024;84:301-14

Table 1. Categorization of vulvar lesions after reassessment in relation to the original diagnosis and age at baseline

	Original diagnosis			Age, years
	HSIL	DVIN	Total (%)	Median (range)
	743	8	751 (100)	45.0 (16–92)
Final categorization				
HPV-associated	663	1	664 (88.4)	44.0 (17–91)
HSIL	578	0	578 (77.0)	45.0 (17–90)
LSIL	81	1	82 (10.9)	39.0 (19–91)
VSCC	3	0	3 (0.4)	39.0 (37–48)
HPV-independent	75	7	82 (10.9)	67.0 (16–92)
HPV-independent VIN	39	7	46 (6.1)	72.0 (35–92)
Nondysplastic	35	0	35 (4.7)	58.0 (16–79)
VSCC	1	0	1 (0.1)	67.0 (NA)
Inconclusive	6	0	6 (1.1)	75.0 (46–88)

Histopathology 2023;84:301–314





HPV-ind/p53mut	30	10	7	2	0
HPV-ind/p53wt	16	14	8	4	2
HPV-ass HSIL	578	548	496	303	174

Nondiff.	19	5	3	2	0
Diff.	27	19	12	4	2

Histopathology 2024;84:301-14

Table 4. Risk of vulvar squamous cell carcinoma (VSCC), including time to VSCC, per disease category

	Absolute VSCC risk	Cumulative incidence of VSCC (95% CI)			Median time to VSCC,
	No. (%)	1 year	5 years	10 years	years (range)
HPV-associated HSIL	61/578 (10.6)	2.1 (0.9–3.3)	4.5 (2.7–6.3)	8.0 (5.8–10.2)	6.0 (0.3–24.2)
HPV-independent VIN	25/46 (54.3)	19.6 (8.2–31.0)	45.7 (31.4–60.0)	53.6 (38.7–68.5)	1.8 (0.3–10.9)
HPV-ind VIN/p53 mutant	20/30 (66.7)	30.0 (13.5–46.5)	63.3 (46.1–80.5)	67.4 (50.3–84.5)	1.5 (0.3–6.7)
HPV-ind VIN/p53 wildtype	5/16 (31.3)	0.0 (NA)	12.5 (0.0–28.8)	27.8 (3.9–51.7)	5.1 (1.2–10.9)
HPV-ind VIN/ differentiated	11/27 (40.7)	3.7 (0.0–10.8)	25.9 (9.4–42.4)	39.3 (19.9–58.7)	3.2 (0.8–23.3)
HPV-ind VIN/ nondifferentiated	14/19 (73.7)	42.1 (20.0–64.2)	73.7 (53.9–93.5)	73.7 (53.9–93.5)	0.5 (0.3–16.5)

HSIL, High-grade squamous intraepithelial lesion; HPV-independent VIN, Human papillomavirus-independent vulvar intraepithelial neoplasia; NA, Not applicable.

Histopathology 2024;84:301-14

Is p16/HPV and p53 available?

- Squamous intraepithelial lesion
- Differentiated VIN (with basal atypia)
- Verruciform acanthotic VIN
- HSIL (HPV-associated)
- HPV-independent p53-mut VIN
- HPV-independent p53-wt VIN
  - VIN (with basal atypia)
  - vaVIN

VIN, NOS
Suspicious for VIN

THANK YOU!

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