2017 WHO classification

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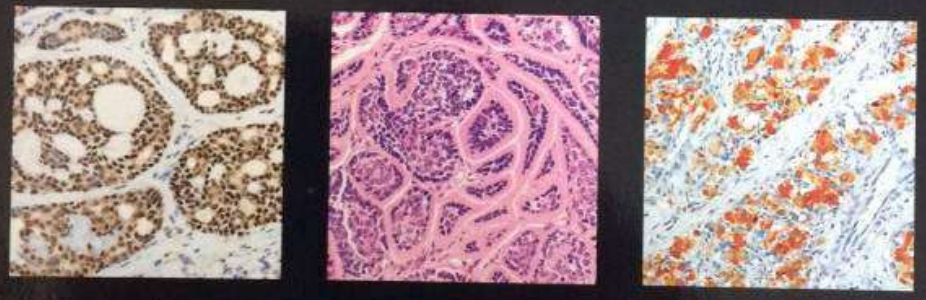
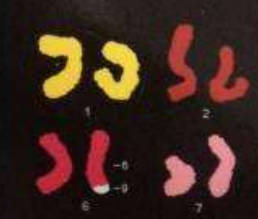
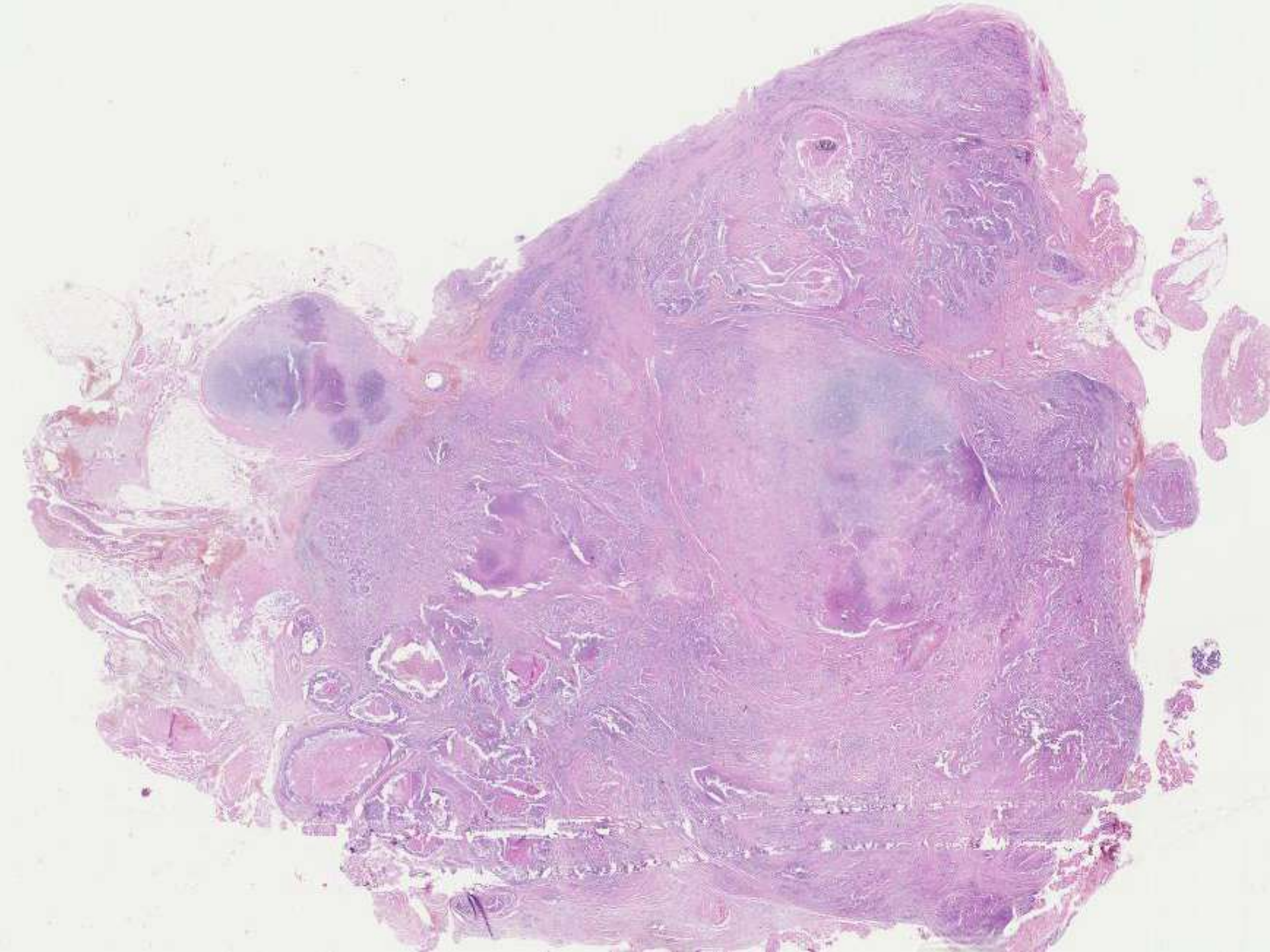
WHO Classification of Head and Neck Tumours

Edited by
Adel K. El-Naggar, John K.C. Chan, Jennifer R. Grandis, Takashi Takata, Pieter J. Slootweg





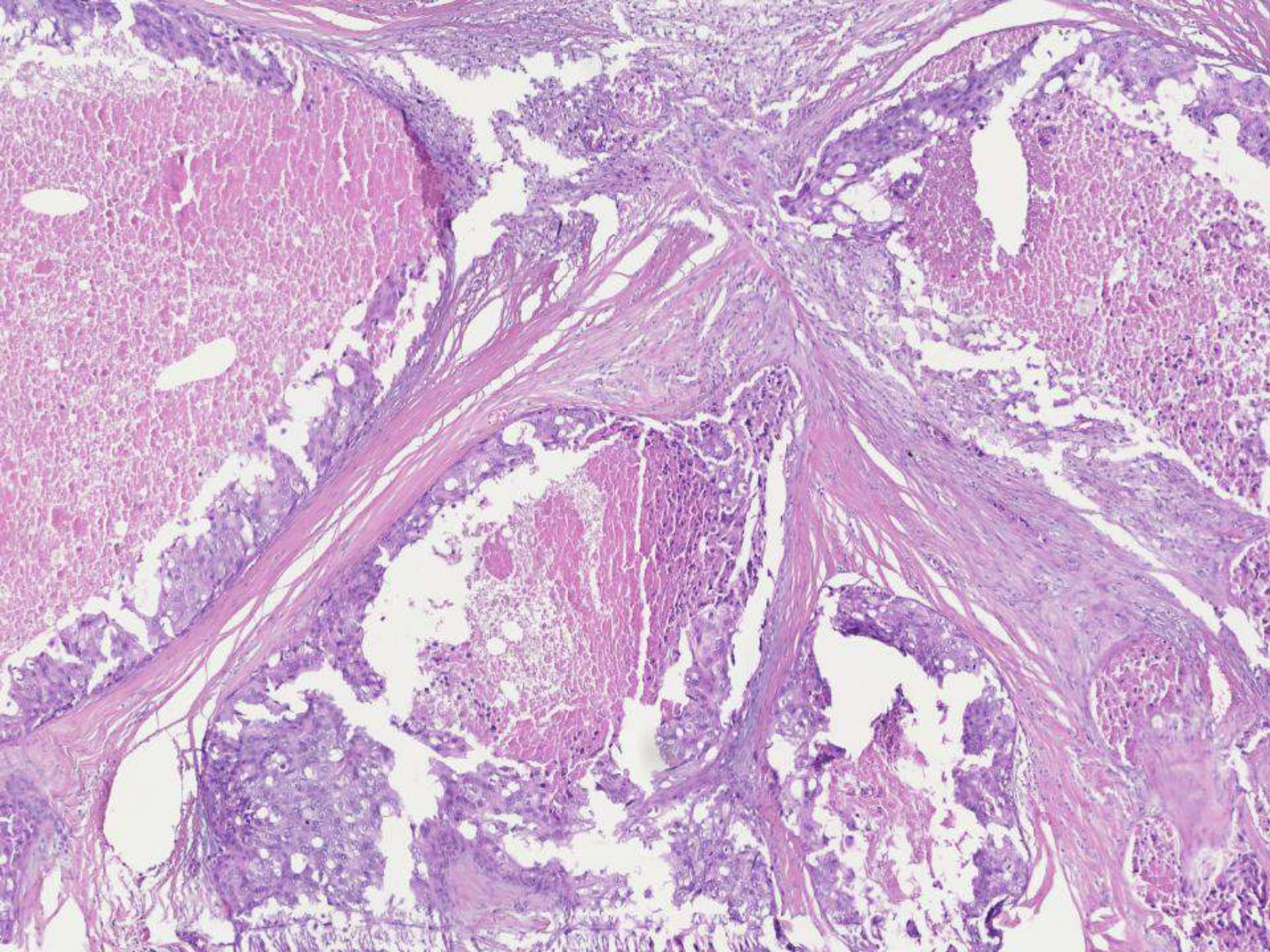
WHO



Pleomorphic adenoma

Evolution :

- Pleomorphous ex-adenoma carcinoma: pleomorphic adenoma with transformed tumor zones.
- Aggressiveness: infiltration of the capsule, of the glandular parenchyma, adipocytic tissue or peri-nervous sheaths + cytological criteria
- Most often high-grade (ductal) carcinoma but, all histological types of carcinomas described.
- The tumor type and grade of the carcinomatous contingent must be specified because they also participate in the evaluation of the prognosis.



Pleomorphic ex-adenoma carcinomas

Capsular invasion determinant for the prognosis

- Clearly proved that according to the extensions pleomorphic ex-adenoma carcinomas have a totally different prognosis: New 2017 WHO classification
- Strictly enclosed excellent prognosis almost comparable to the pleomorphic adenoma one.
- Capsular invasion,
  - minimal invasion (invasion outside the capsule <4-6 mm) more favorable prognosis,
  - Invasion out of the capsule> 4-6 mm, prognosis more reserved.
- Massively invasive> 8 mm prognosis consistently pejorative

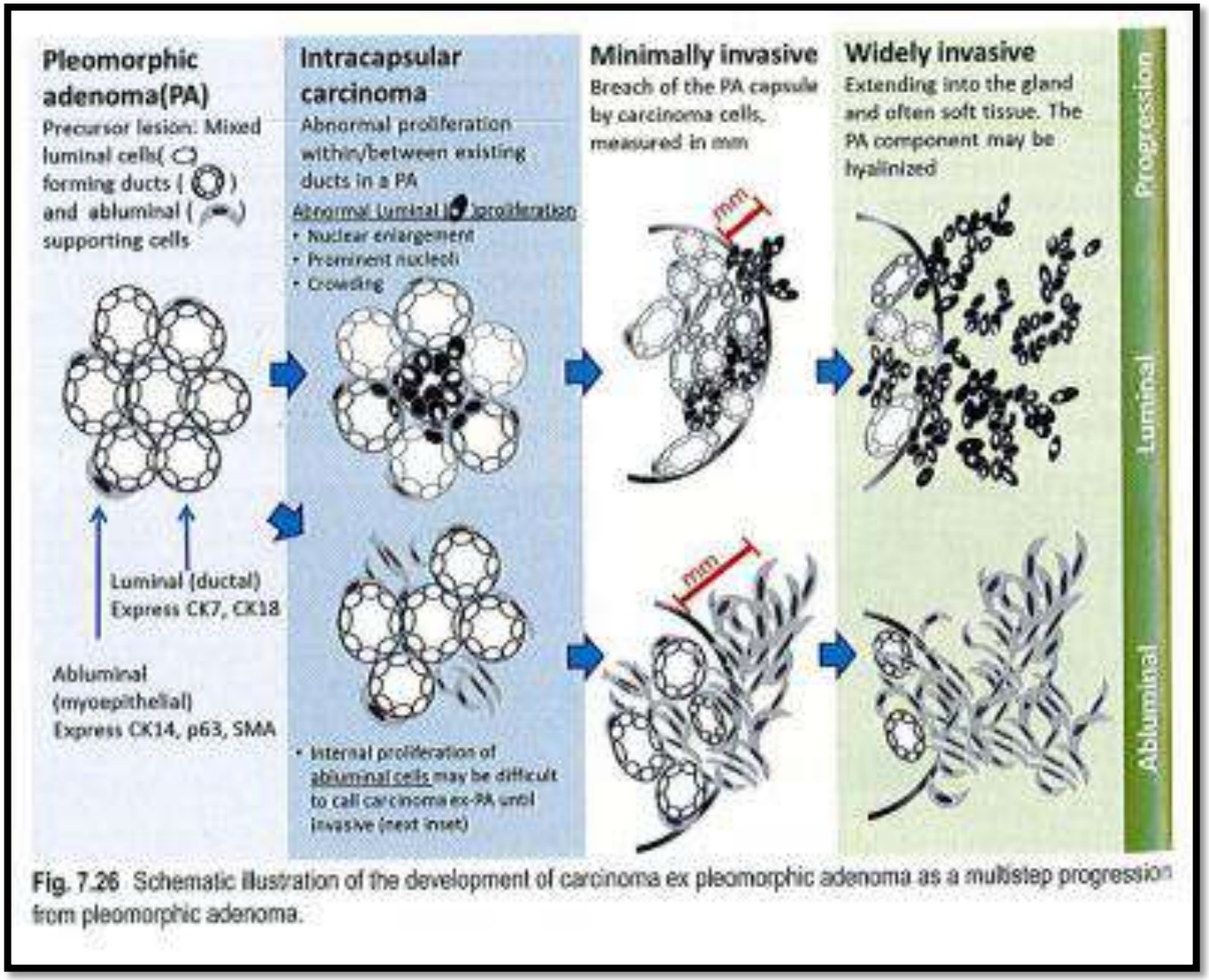
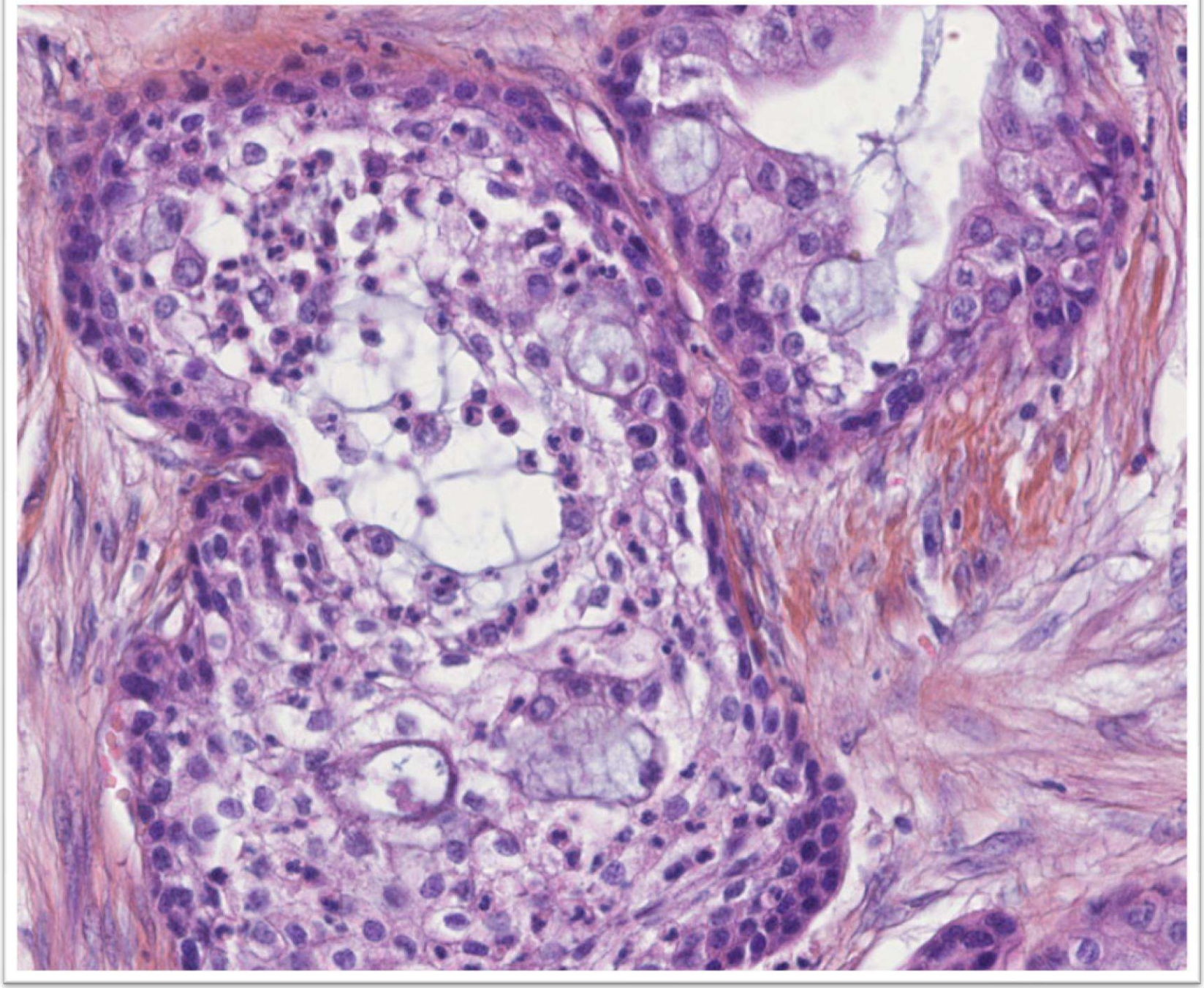


Fig. 7.26 Schematic illustration of the development of carcinoma ex pleomorphic adenoma as a multistep progression from pleomorphic adenoma.



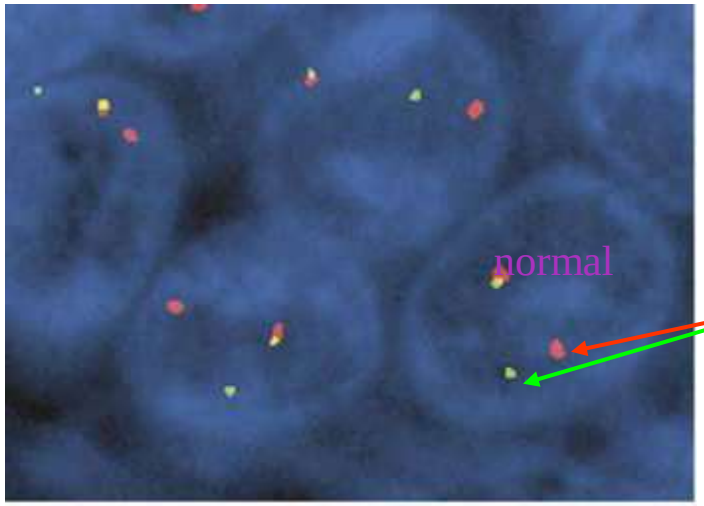
Mucopidermoid Carcinoma (CME) – Grading (OMS 2005)

Aspect histologique	Score
Cystic component < 20%	2
Neural invasion	2
Necrosis	3
4 mitoses or more /10 hpf	3
Anaplasia	4
Grade	
Low	0-4
Intermediate	5-6
High	>7

MECT1-MAML2 translocation associated with favorable prognosis

MECT1: CREB mediated transcription

MAML2:mastermind-like gene family: voie Notch



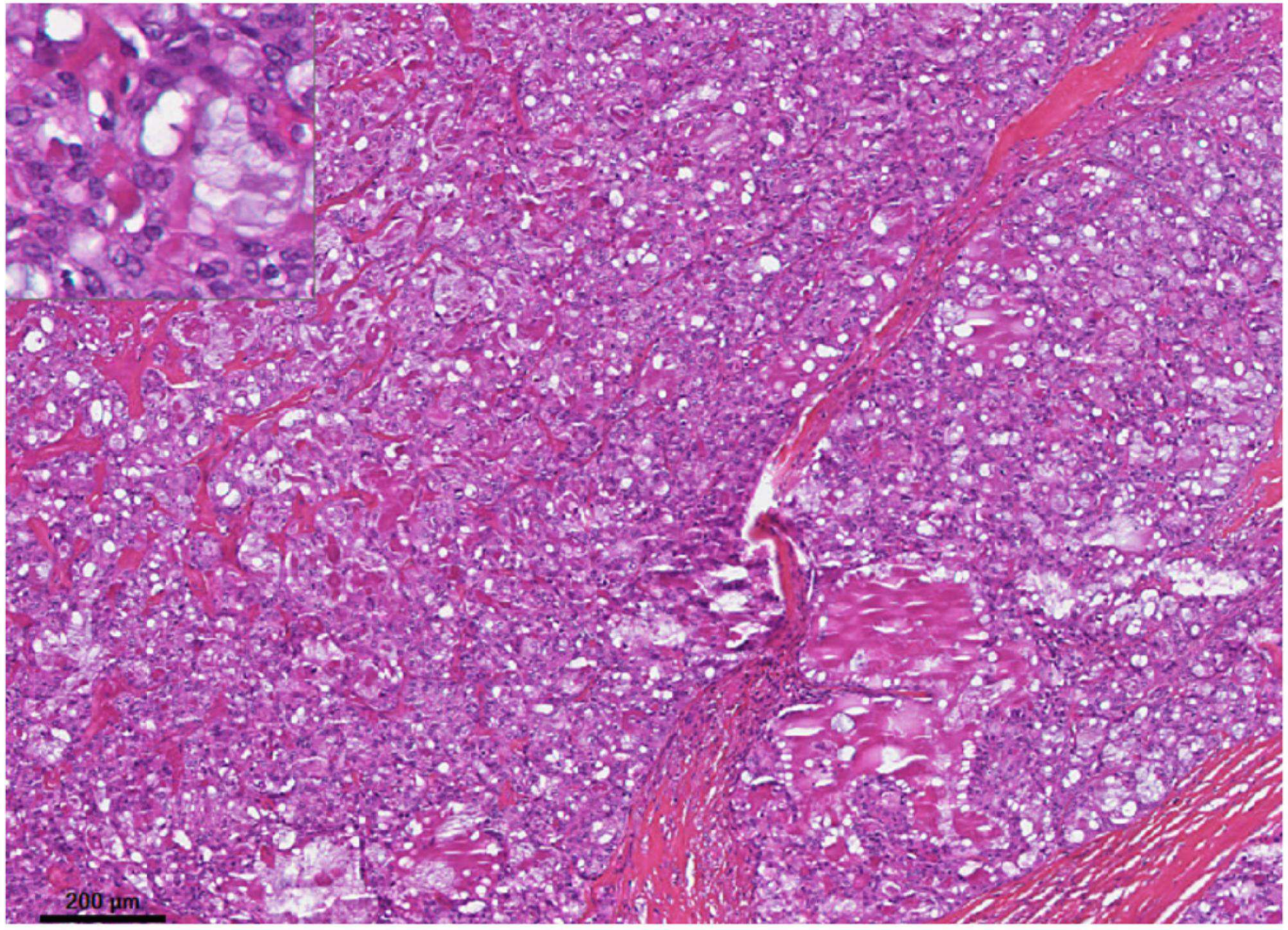
FISH MAML2

« split »

Behboudi and coll. (Cancer 2006)	Translocation MECT1-MAML2	No translocation
Survival mean	> 10 years	1,6 years
Mean age apparition	48 years	76 years
Tumor size	1	3
Tumor grade	low and intermediate grade	High and intermediate grade

High grade associated with low survival
CDKN2A methylation or deletion

Sethala Am J Surg Pathol 2010


200 µm

Mammary Analog Secretory Carcinoma of Salivary Gland Origin With the *ETV6* Gene Rearrangement by FISH: Expanded Morphologic and Immunohistochemical Spectrum of a Recently Described Entity

Ashton Connor, MD,† Bayardo Perez-Ordoñez, MD,*† Mary Shago, PhD,†‡ Alena Skálová, MD, PhD,§ and Ilan Weinreb, MD*†*

Abstract: Mammary analog secretory carcinoma (MASC) is a recently described tumor predominantly arising in the parotid gland. These tumors represent locally invasive malignancies with microcystic architecture, low-grade nuclei, and granular pink vacuolated cytoplasm. They display strong vimentin and S100 positivity and harbor an identical t(12;15)(p13;q25) to their breast counterpart, leading to a *ETV6-NTRK3* fusion oncogene. These features help exclude the most important differential diagnostic considerations, namely, acinic cell carcinoma (AciCC) and low-grade cystadenocarcinoma, not otherwise specified. Here we present a series of 7 recent examples of MASC, which showed features not previously described. These layer surrounding a minority of tumor cell nests and cysts, raised the possibility of a ductal epithelial origin for MASC. Alternatively, this could represent secondary ductal involvement by tumor. All cases showed rearrangement of the *ETV6* gene by fluorescence in situ hybridization, confirming the diagnosis of MASC. These findings reinforce MASC as a unique low-grade salivary gland tumor entity with morphologic overlap with AciCC, MEC, and cystadenocarcinoma.

Key Words: secretory carcinoma, mammary analog, acinic cell carcinoma, mucoepidermoid carcinoma, intraductal, ETV6

(*Am J Surg Pathol* 2012;36:27–34)

Secretory carcinoma (MASC)

• Recently described, rare salivary gland tumor that relates the morphology and genetics of an equally rare malignancy of the breast, secretory carcinoma (SC)

• Previously classified as acinic cell carcinoma ("zymogen poor", intercalated cell predominant variant), mucoepidermoid carcinoma and adenocarcinoma, NOS

•Mammaglobin +, PS100+, DOG1-

• Specific cytogenetic characteristic: t(12; 15)(q13;q25): *ETV6-NTRK3* translocation, demonstrated by either FISH or PCR

Secretory carcinoma (MASC)

- Typically it is a disease of young male patients but occurs in a wide age range (21 - 75), with a mean of 46 years
- Pediatric cases have been
- Sex ration :1

- Parotid gland (up to 70%); lips, hard palate, submandibular glands. More frequent in nonparotid sites compared to acinic cell carcinoma

Secretory carcinoma (MASC)

- Overall slowly growing, painless tumor, occasional extracapsular extension and perineural invasion
- Infrequent local recurrences
- Rare metastatic dissemination to cervical lymph nodes, pleura, pericardium and lungs
- Broad range of clinical behaviours, from indolent to aggressive
- Currently there is no way to predict which tumours will behave aggressively

Higher incidence of regional lymph node involvement than acinic cell carcinomas

Treatment

Local excision, radiation therapy in select cases

Molecular targeted gene therapy currently investigated

WHO Classification of Head and Neck Tumours

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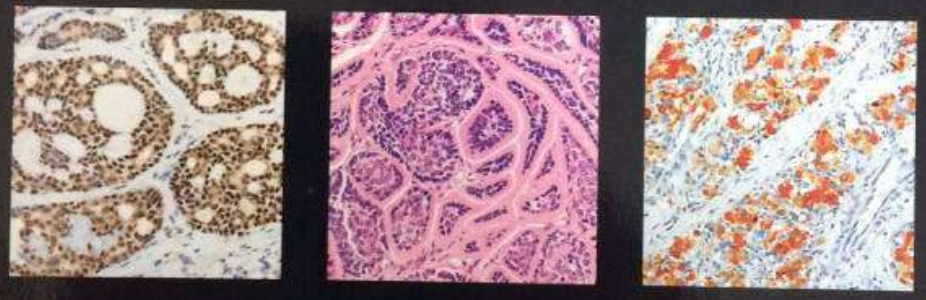
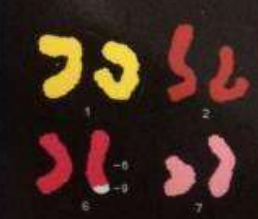
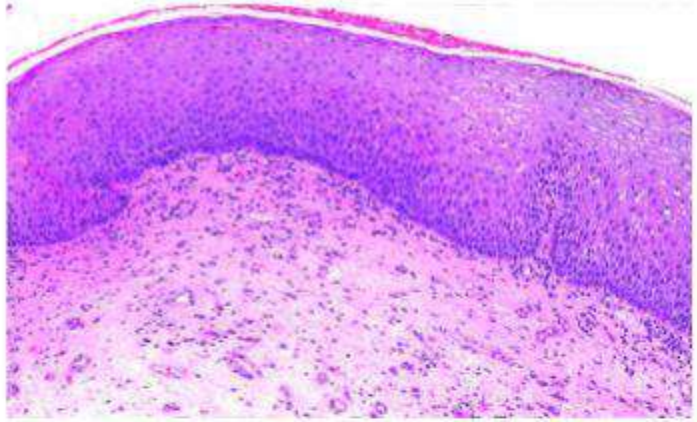




WHO



Figures 1. Low-grade squamous intraepithelial lesion. Hyperplastic squamous epithelium with augmented parabasal cells, oriented perpendicularly to the basement membrane, extends up to the middle of the epithelial thickness. The upper part of the epithelium is unchanged. There is no cytological atypia.

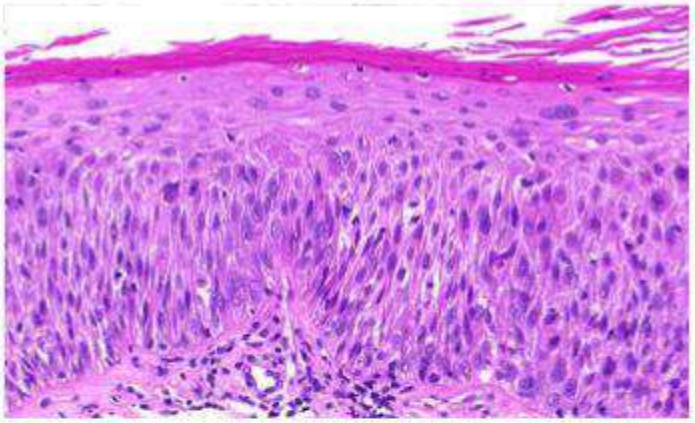


Figure 3. High-grade squamous intraepithelial lesion. Polymorphic epithelial cells occupy two-thirds of the epithelial thickness, and perpendicular orientation to the basement membrane is preserved.

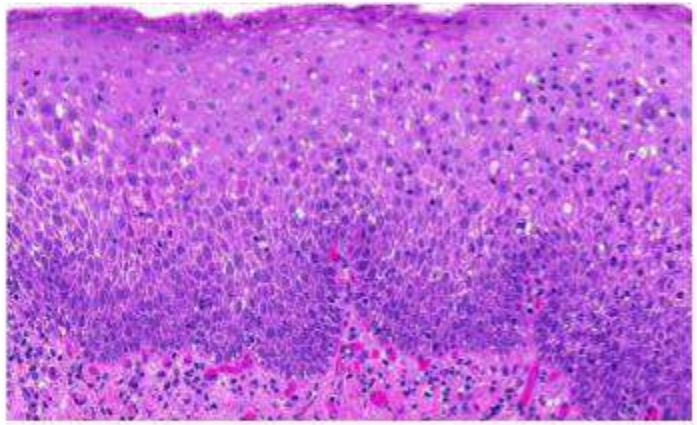
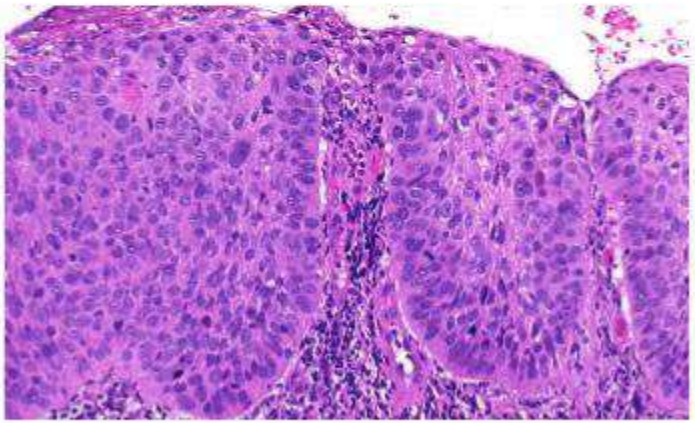


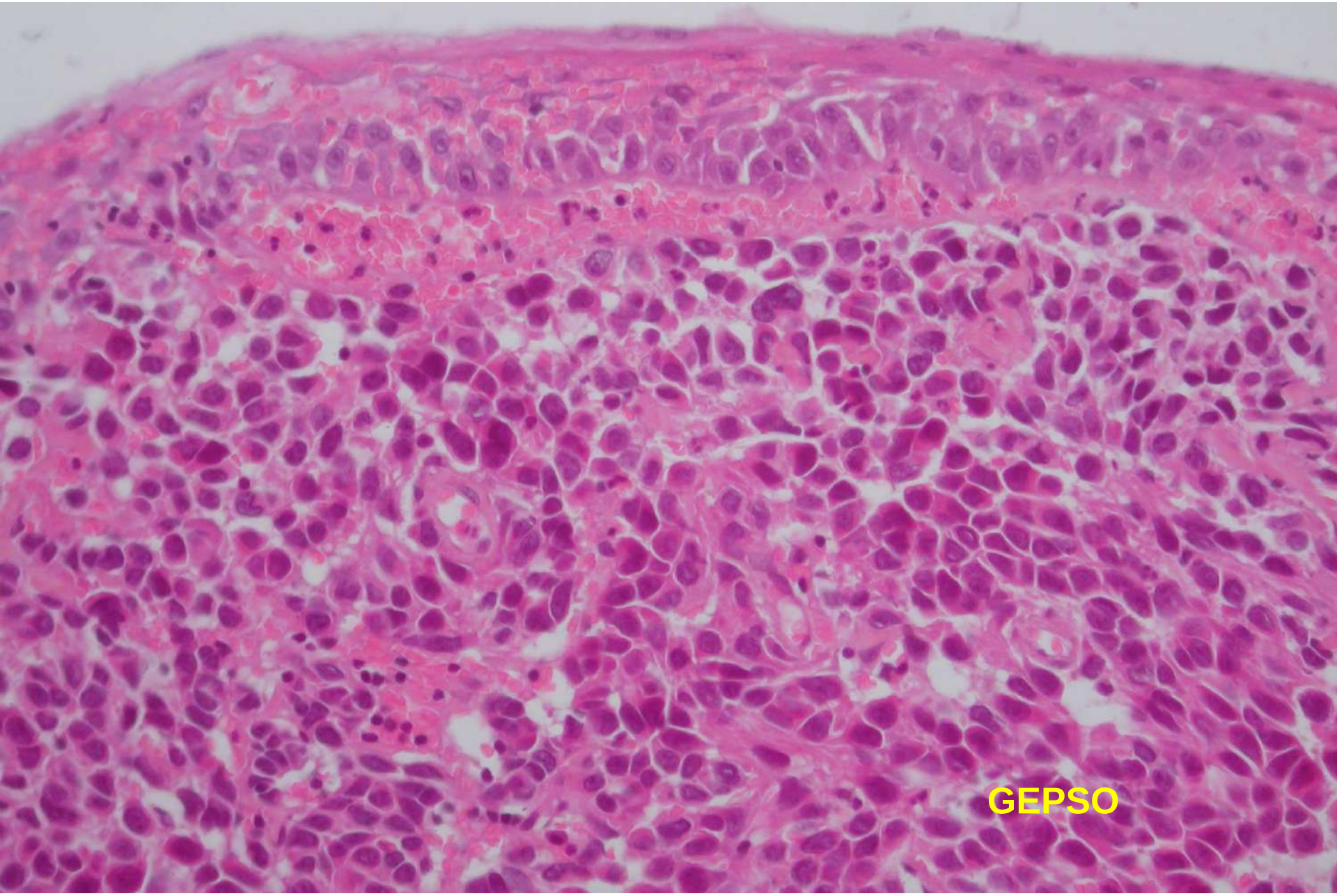
Figure 2. Low-grade squamous intraepithelial lesion. Augmented parabasal cells, oriented perpendicularly to the basement membrane, extends up to the one third of the epithelial thickness. The upper part of the epithelium is unchanged. There is no cytologic atypia.



Figures 4. High-grade squamous intraepithelial lesion. The thickened epithelium is almost entirely occupied by moderately polymorphic epithelial cells, which show preserved perpendicular orientation to the basement membrane. Increased mitotic activity is evident.

Level of abnormal maturation WHO 2005	WHO 2005 classification 92 832 2417 5 ISBN	SIN Classification 978 1 4160 2589 4 ISBN	Ljubljana classification 18752537	WHO **2017** classification 24689850
	Squamous hyperplasia	Squamous hyperplasia	Squamous hyperplasia	LG SIL
Lower 1/3	Mild dysplasia	SIN 1	Basal/parabasal hyperplasia	
1/3 to 1/2	Moderate	SIN 1? or SIN2	Atypical hyperplasia	HG-SIL
Upper 1/2-3/4	Moderate	SIN 2		
Full thickness	Severe dysplasia			
	CIS		CIS	CIS

SIN = squamous intraepithelial neoplasia
LG SIL= low-grade intraepithelial lesion
HG SIL = high-grade intraepithelial lesion


GEPSO

Neuroendocrine carcinomas

- Heterogeneous group of lesions, ranging just as in the lung, from benign tumors to high grade carcinomas
- The most common tumors are moderately differentiated carcinomas (atypical carcinoids) followed by poorly differentiated carcinomas (small cell carcinomas)
- Nests, cords, sheets, trabeculae +/- glands and / or rosettes.
- Tumors most often richly vascularisation. Cells have variable cytological aspects depending on the tumor subtype

(Modified) 2017 WHO Classification of Neuroendocrine carcinomas (NEC) of the Head and Neck

Classification		Criteria
Well-differentiated NEC		• Features of neuroendocrine differentiation • Minimal nuclear atypia • <2 mitoses/10HPFs
Moderately-differentiated NEC		• Necrosis and/or • 2-10 mitoses/10HPFs
Poorly-differentiated NEC	Small cell type	>10 mitoses/10 HPFs
	Large cell type	>10 mitoses/10 HPFs
Mixed neuroendocrine-non-neuroendocrine neoplasms		

Bayardo Perez-Ordoñez, USCAP 2018

ORIGINAL ARTICLE

(Am J Surg Pathol 2011;35:1679–1684)

Human Papillomavirus-Related Small Cell Carcinoma of the Oropharynx

Justin A. Bishop, MD and William H. Westra, MD*†*

ORIGINAL ARTICLE

(Am J Surg Pathol 2012;36:321–330)

HPV-associated Neuroendocrine Carcinoma of the Oropharynx: A Rare New Entity With Potentially Aggressive Clinical Behavior

Stefan Kraft, MD,† William C. Faquin, MD, PhD,* and Jeffrey F. Krane, MD, PhD†*

ORIGINAL ARTICLE

(Am J Surg Pathol 2016;40:471–478)

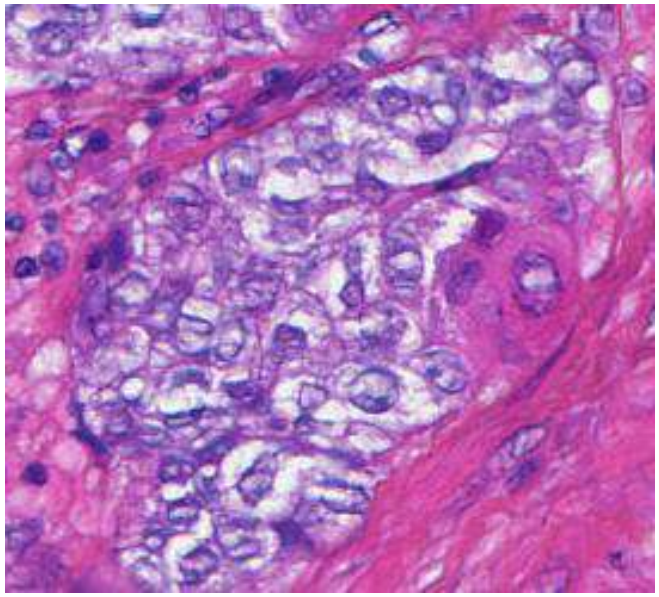
Large Cell Neuroendocrine Carcinoma of the Head and Neck

A Clinicopathologic Series of 10 Cases With an Emphasis on HPV Status

Elizabeth D. Thompson, MD, PhD, Edward B. Stelow, MD,† Stacey E. Mills, MD,† William H. Westra, MD,*‡§ and Justin A. Bishop, MD*‡§*

NUT Carcinoma

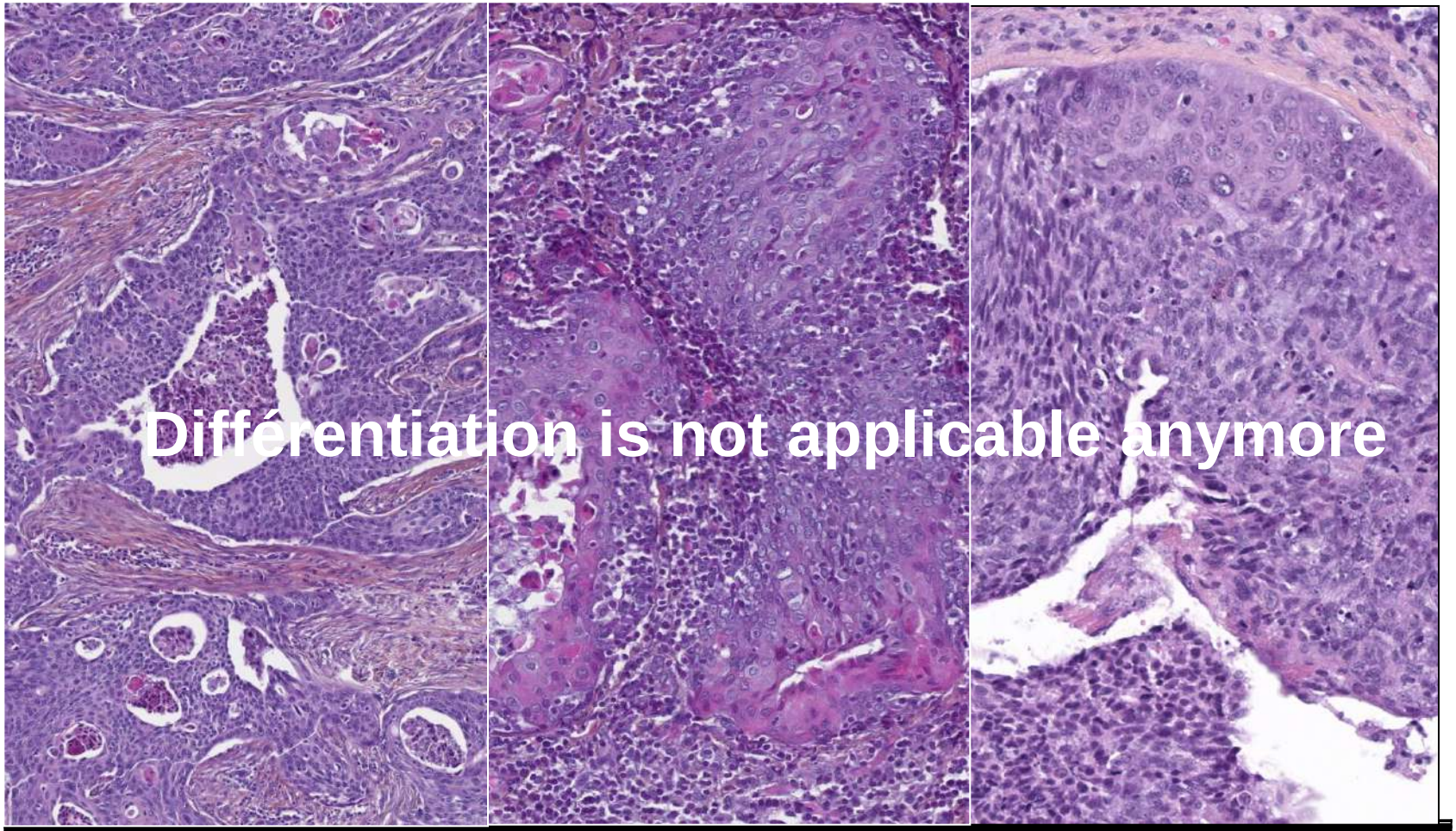
- New entity
- Rare but certainly under diagnosed
- Represents a rare subset of highly aggressive poorly differentiated carcinomas
- Characterized by rearrangement of the NUT (aka NUTM1, nuclear protein in testis) gene, most commonly fused to BRD4.
- Can be seen at any age but median age about 20 years old
- Think about it in front of a very monotonous AE1 / AE3 proliferation with abrupt keratinization (or large clear cells)
- Anti-NUT immunochemistry
- Targeted therapy
- Register patients in the database: www.nmcregistry.org



Am J Surg Pathol. 2017 April ; 41(4): 458–471. doi:10.1097/PAS.0000000000000797.

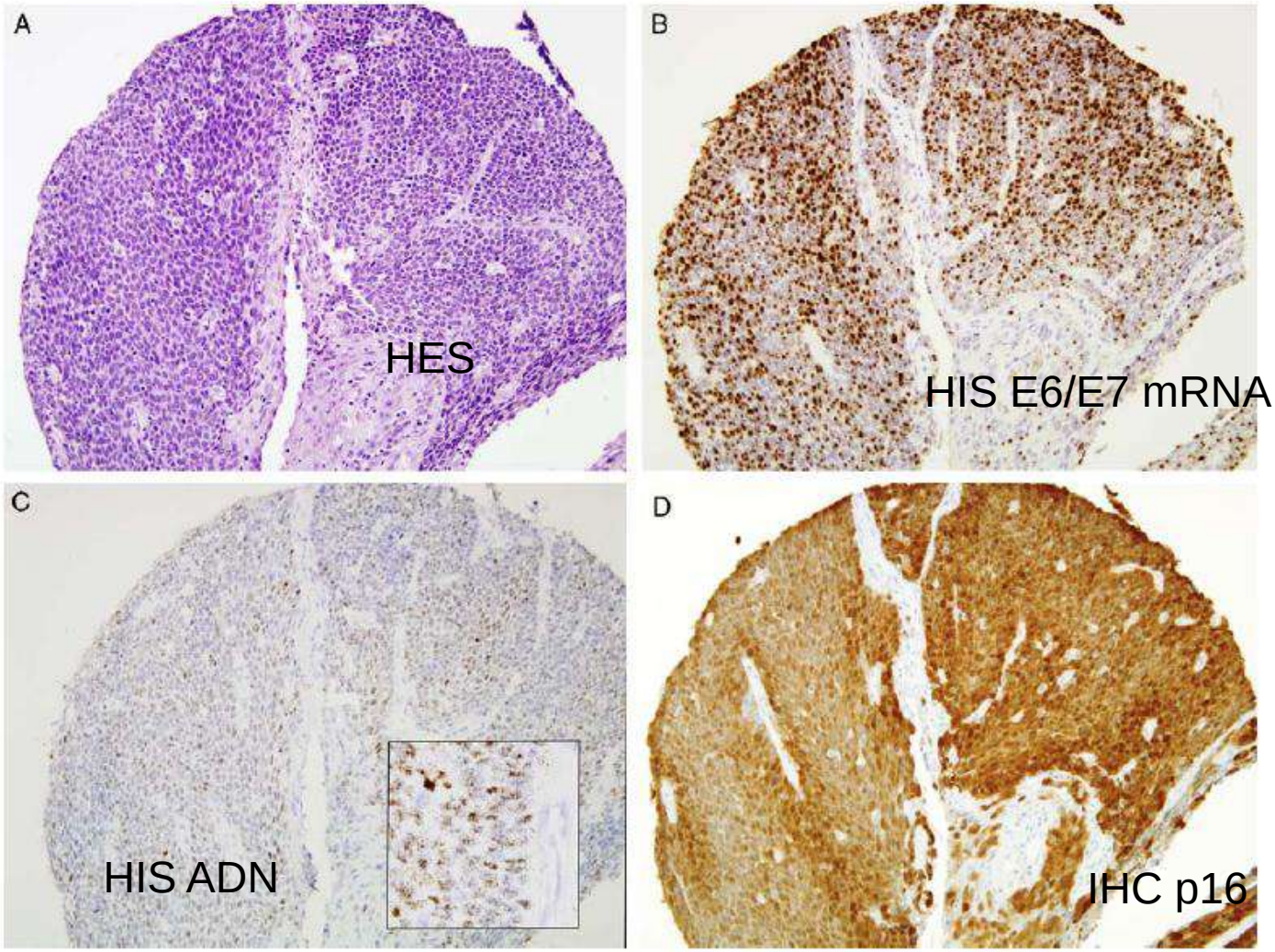
SMARCB1 (INI-1)-deficient Sinonasal Carcinoma: A Series of 39 Cases Expanding the Morphological and Clinicopathological Spectrum of a Recently Described Entity

Abbas Agaimy, MD[1], Arndt Hartmann, MD[1], Cristina R. Antonescu, MD[2], Simion I. Chiosea, MD[3], Samir K. El-Mofty, MD[4], Helene Geddert, MD[5], Heinrich Iro, MD[6], James S. Lewis Jr., MD[7], Bruno Märkl, MD[8], Stacey E. Mills, MD[9], Marc-Oliver Riener, MD[10], Thomas Robertson, MD[11], Ann Sandison, MB, ChB, FRCPath[12], Sabine Semrau, MD[13], Roderick H. W. Simpson, MB, ChB, FRCPath[14], Edward Stelow, MD[9], William H. Westra, MD[15], and Justin A. Bishop, MD[15]

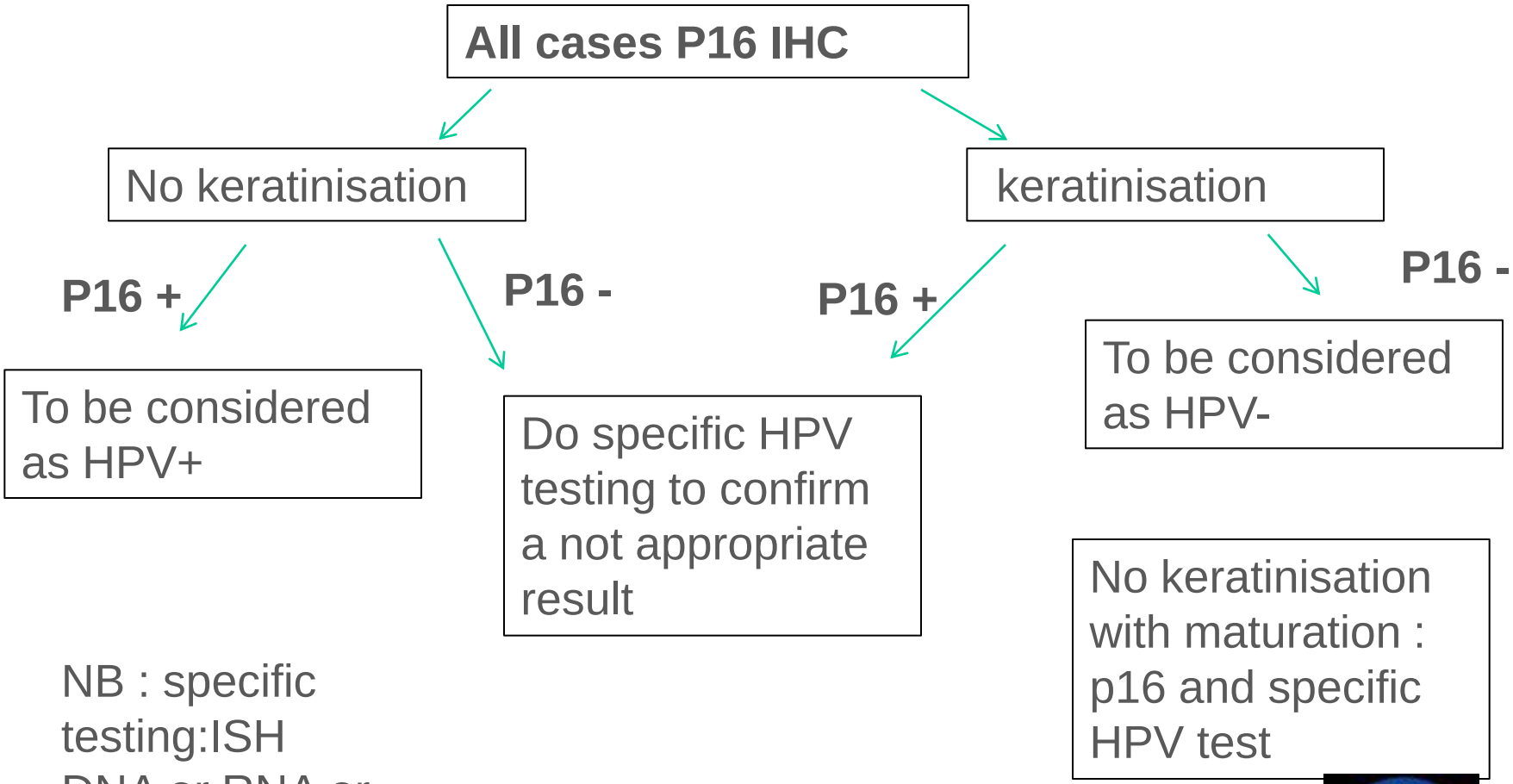


Keratinisation 100% mature cells with squamous cell differentiation	**No keratinisation, with maturation >10% but <100% of squamous cell differentiation**	**Non keratinisation <10% of differentiation**

Technics for *in situ* HPV detection

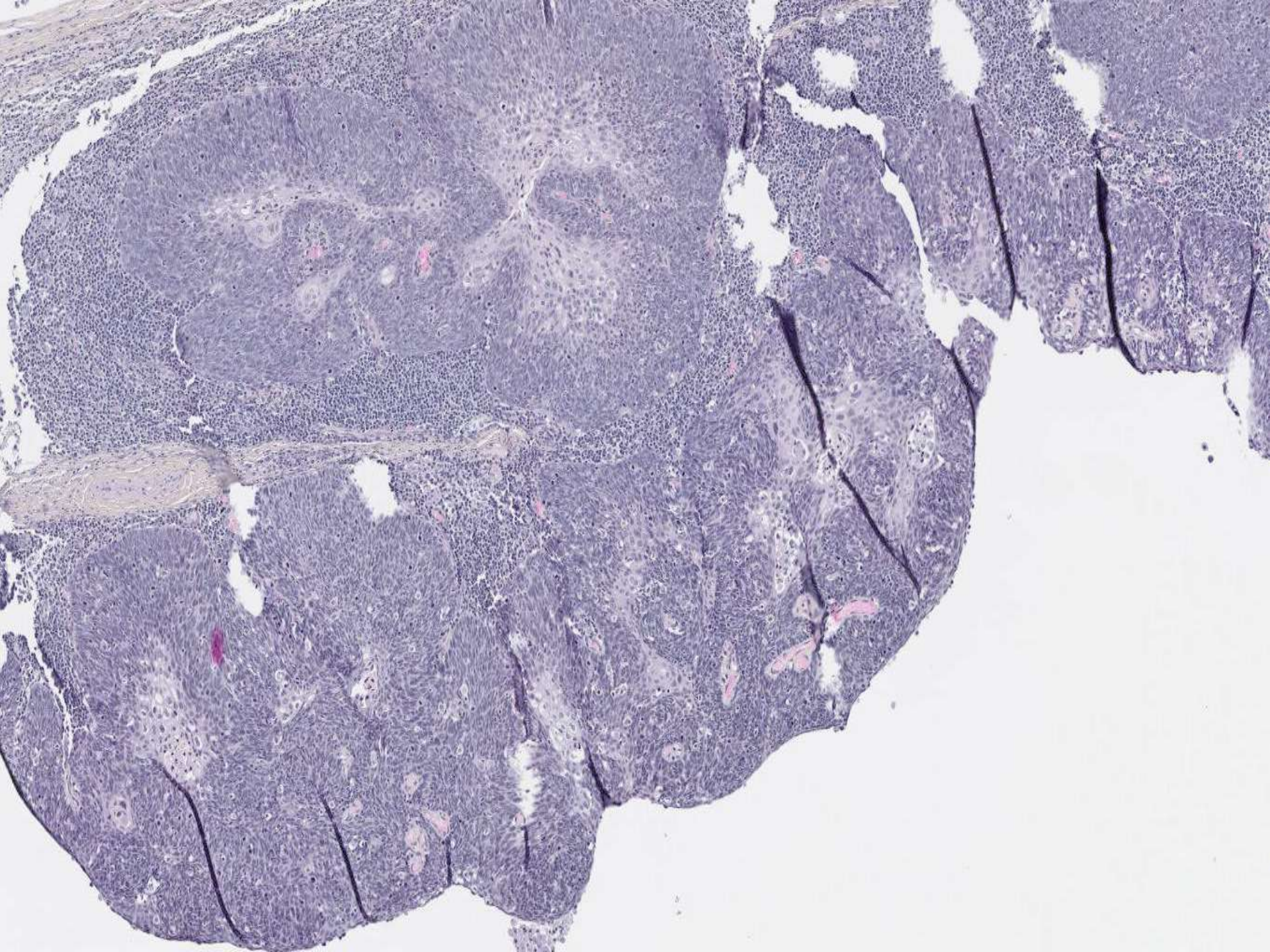


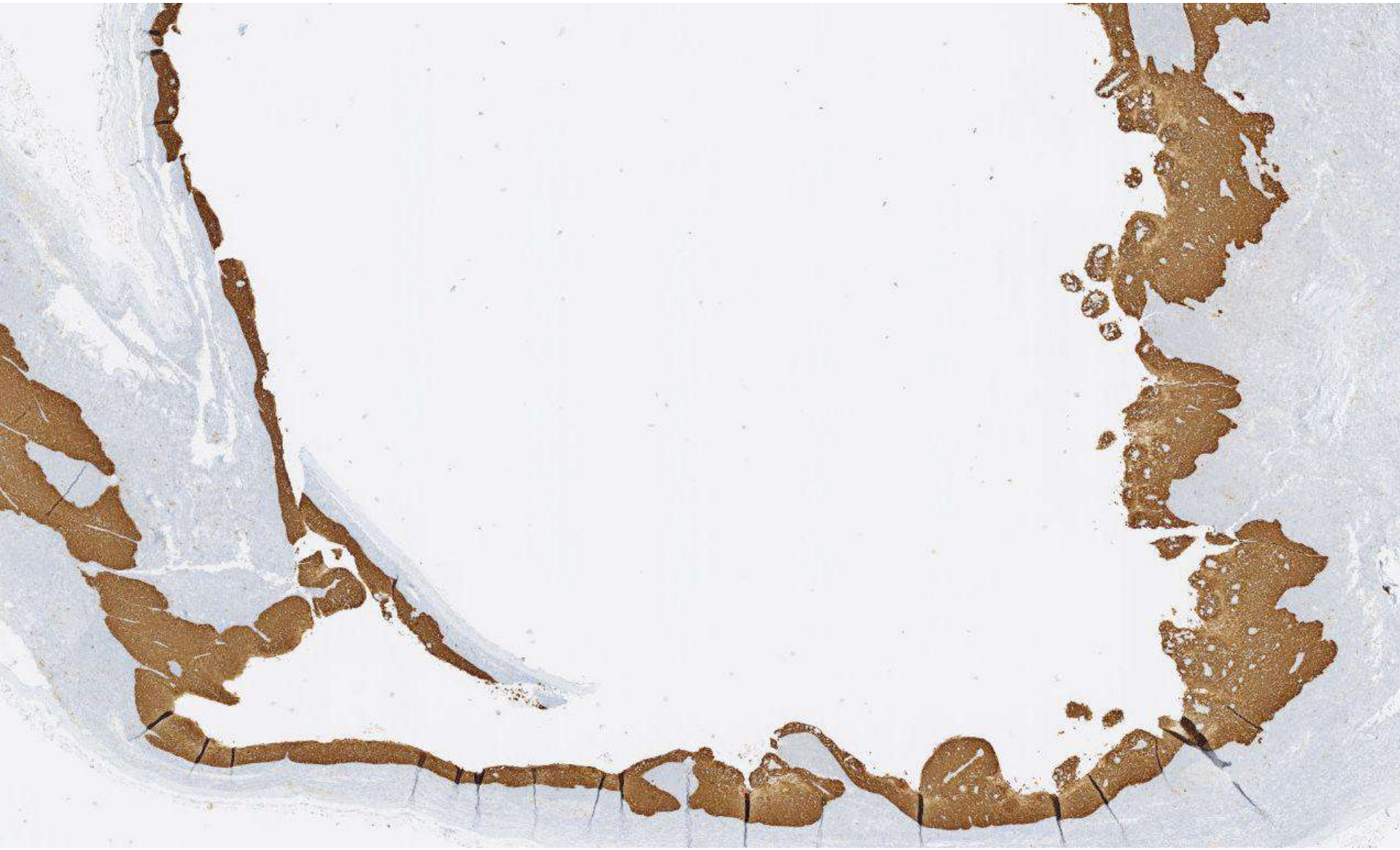
Proposition for routinely HPV testing for oropharyngeal SCC



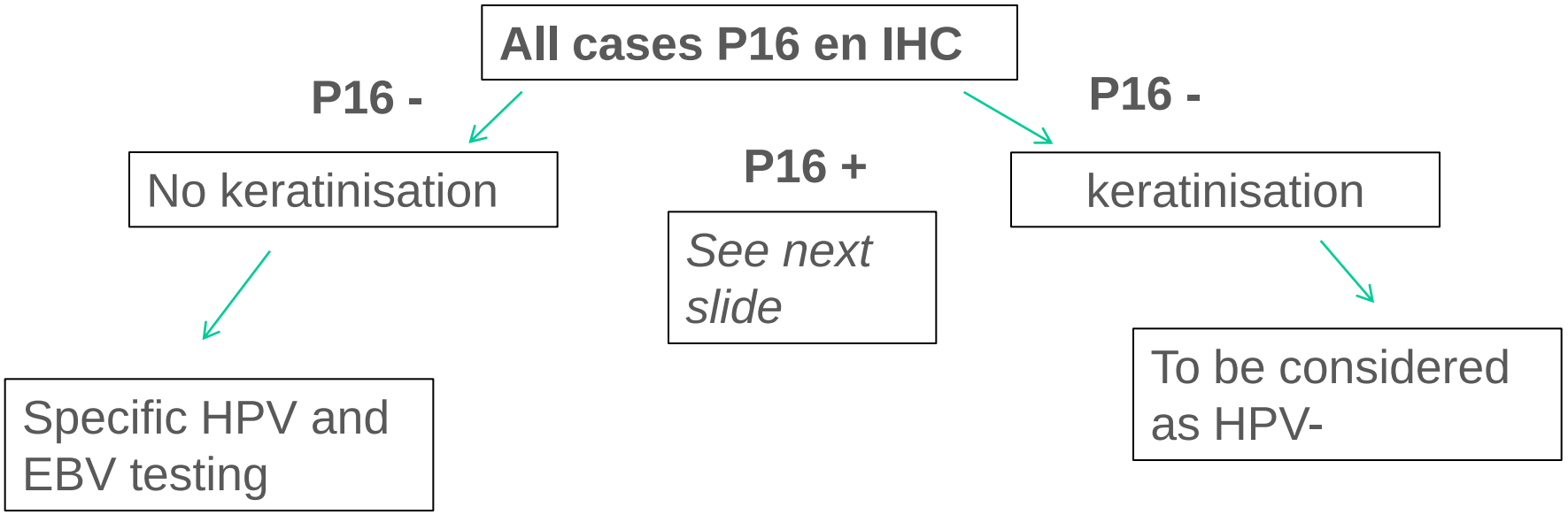
NB : specific testing:ISH DNA or RNA or PCR

Lewis, short course HPV ENT,USCAP 2016





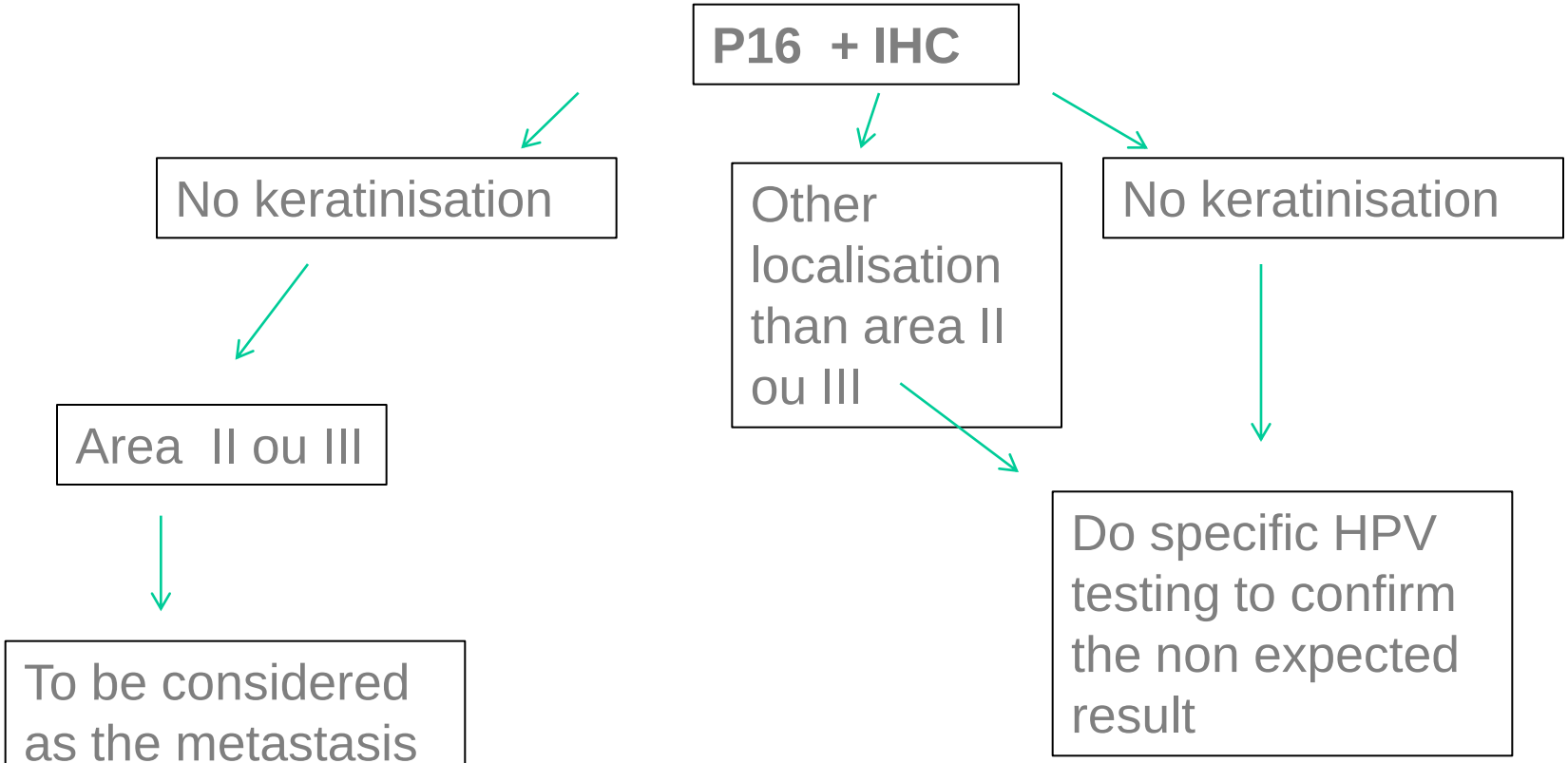
Proposition for HPV routinely testing for unknown primary metastasis in nodes



NB : specific testing:ISH DNA or RNA or PCR

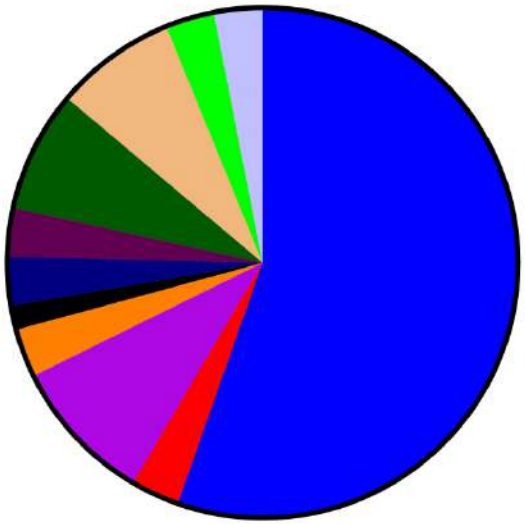
Présentation Lewis, USCAP 2016 short course HPV ENT

Proposition for HPV routinely testing for unknown primary metastasis in nodes



Presentation Lewis, USCAP short course HPV ENT

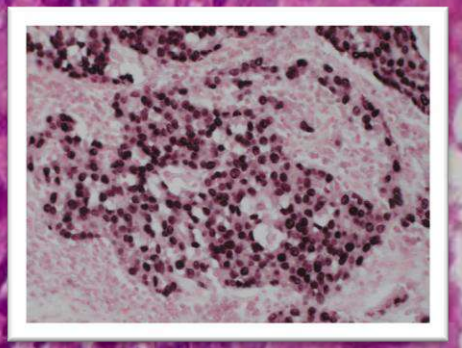
2. Combinations of positive HPV testings in oropharyngeal carcinomas (n=65)



Total=65

- P16(+), CISH(+), PCR(+), RNAscope (+) ; 55% (n=36)
- P16(+), CISH(+), PCR(+), RNAscope (-) ; 3% (n=2)
- P16(+), CISH(+), PCR(-), RNAscope (+) ; 0% (n=0)
- P16(+), CISH(-), PCR(+), RNAscope (+) ; 9% (n=6)
- P16(-), CISH(+), PCR(+), RNAscope (+) ; 3% (n=2)
- P16(-), CISH(+), PCR(+), RNAscope (-) ; 2% (n=1)
- P16(-), CISH(+), PCR(-), RNAscope (+) ; 0% (n=0)
- P16(+), CISH(+), PCR(-), RNAscope (-) ; 3% (n=2)
- P16(+), CISH(-), PCR(+), RNAscope (-) ; 3% (n=2)
- P16(+), CISH(-), PCR(-), RNAscope (+) ; 0% (n=0)
- P16(-), CISH(-), PCR(+), RNAscope (+) ; 8% (n=5)
- P16(+), CISH(-), PCR(-), RNAscope (-) ; 8% (n=5)
- P16(-), CISH(-), PCR(+), RNAscope (-) ; 3% (n=2)
- P16(-), CISH(+), PCR(-), RNAscope (-) ; 0% (n=0)
- P16(-), CISH(-), PCR(-), RNAscope (+) ; 3% (n=2)

J Augustin, Human Path 2018



EBER

Nasopharyngeal carcinoma

- Keratinizing squamous cell carcinoma (Well differentiated)
- Basaloid squamous cell carcinoma
- Non-keratinizing squamous cell carcinoma (eg UCNT)
- Node metastases ++ .
- Epidemiology Tabacco, salted and fermented food (nitrosamine), EBV (EBER +, less diffuse in keratinizers).