

**118ª REUNIÓN TERRITORIAL VALENCIANA  
DE LA SEAP  
15/XII/2023**

# **PATOLOGÍA DE CABEZA Y CUELLO – CASO 4**

Iván Rienda Martínez  
MIR-4

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Martínez LA, Zac Romero C, López Valdivia C.

**La Fe**  
Hospital  
Universitari  
i Politècnic

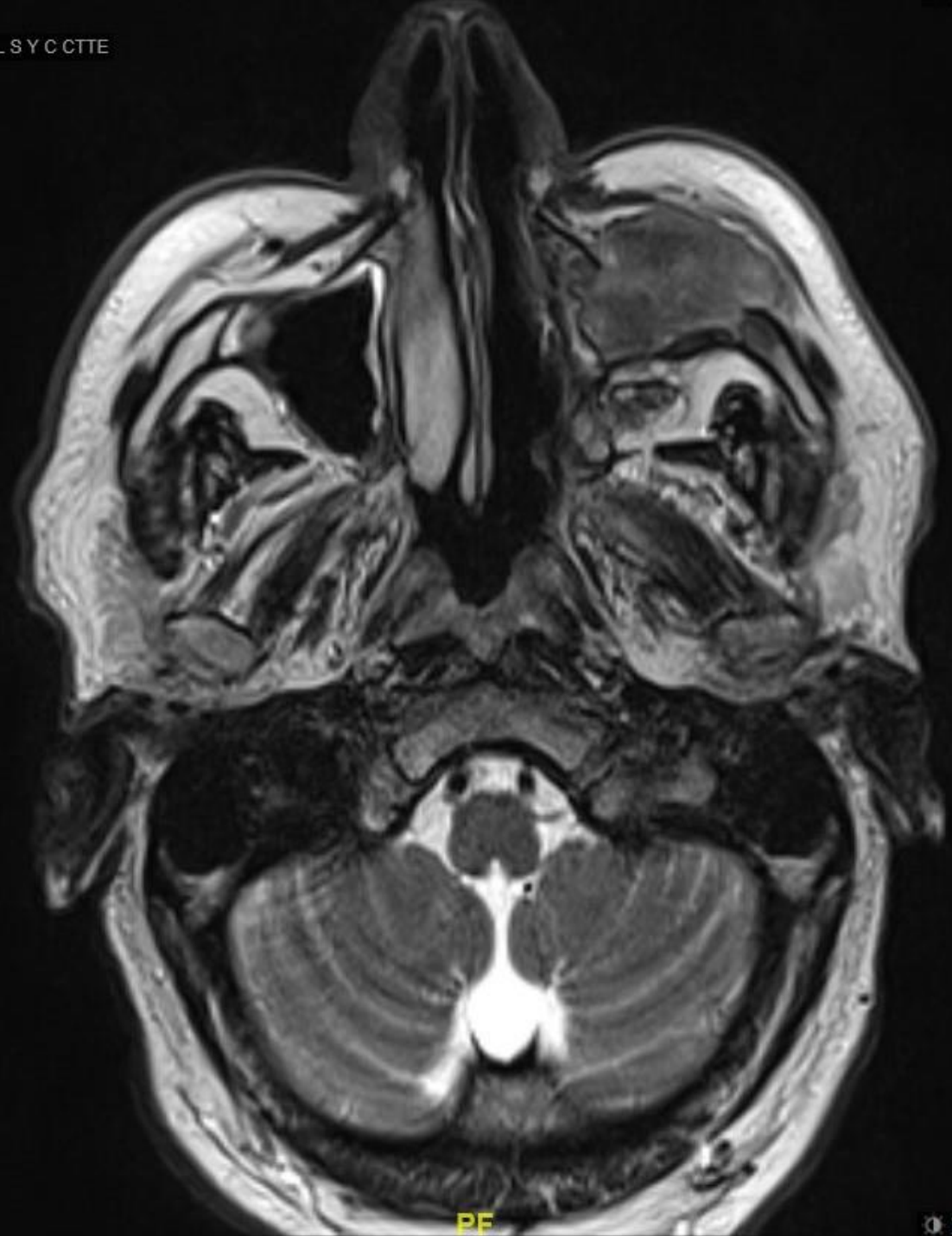
**SeAP-IAP**  
[Sociedad Española de Anatomía Patológica]  
[International Academy of Pathology]  
**ASOCIACIÓN TERRITORIAL DE LA  
COMUNIDAD VALENCIANA**

F.N. : 27-Mar-1961  
RM MAXILOFACIAL S Y C CTTE  
AX T2  
Se: 6  
Im: 18

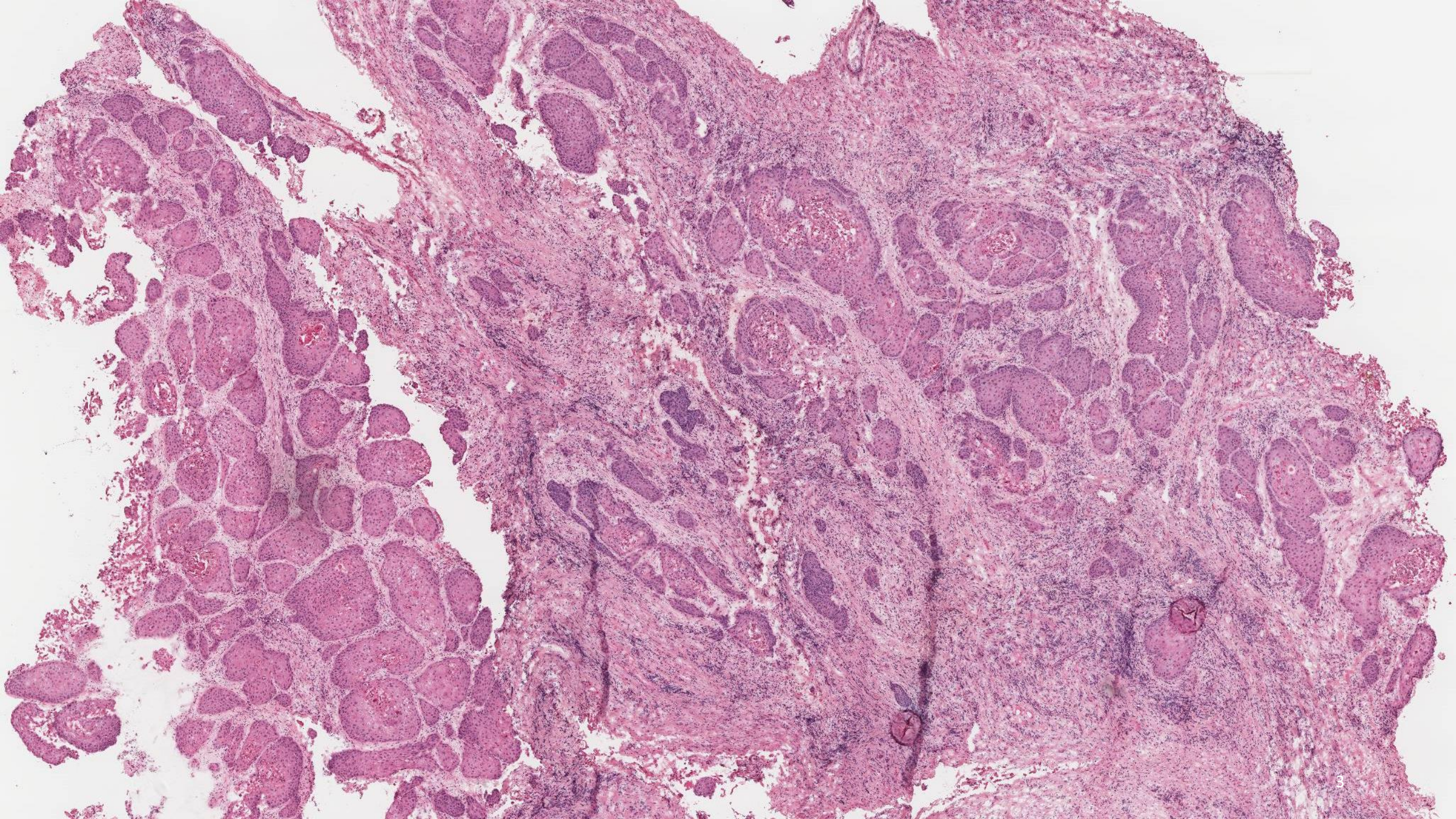
📍 Varón de 60 años  
Masa de 3,6 cm  
Ocupa seno maxilar y erosiona tejido óseo

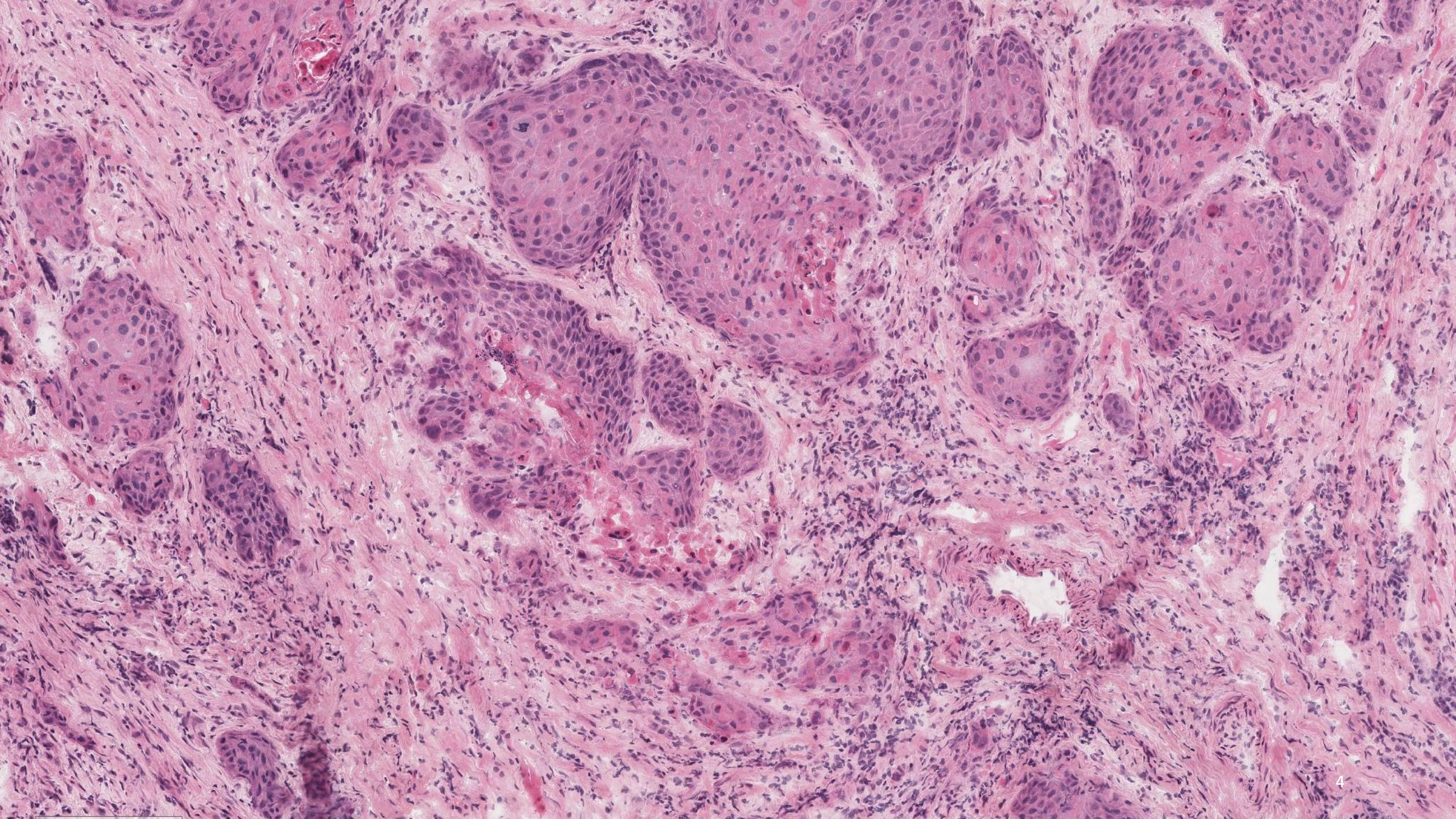
# 1. BIOPSIA INTRAOPERATORIA

RFA



LHP







## 1. DIAGNÓSTICO:

**Seno maxilar izquierdo; biopsia intraoperatoria:**

- **Carcinoma de células escamosas.**

F.N. : 27-Mar-1961  
RM MAXILOFACIAL S Y C CTTE  
AX T2  
Se:6  
Im:18

RFA

LHP

PF

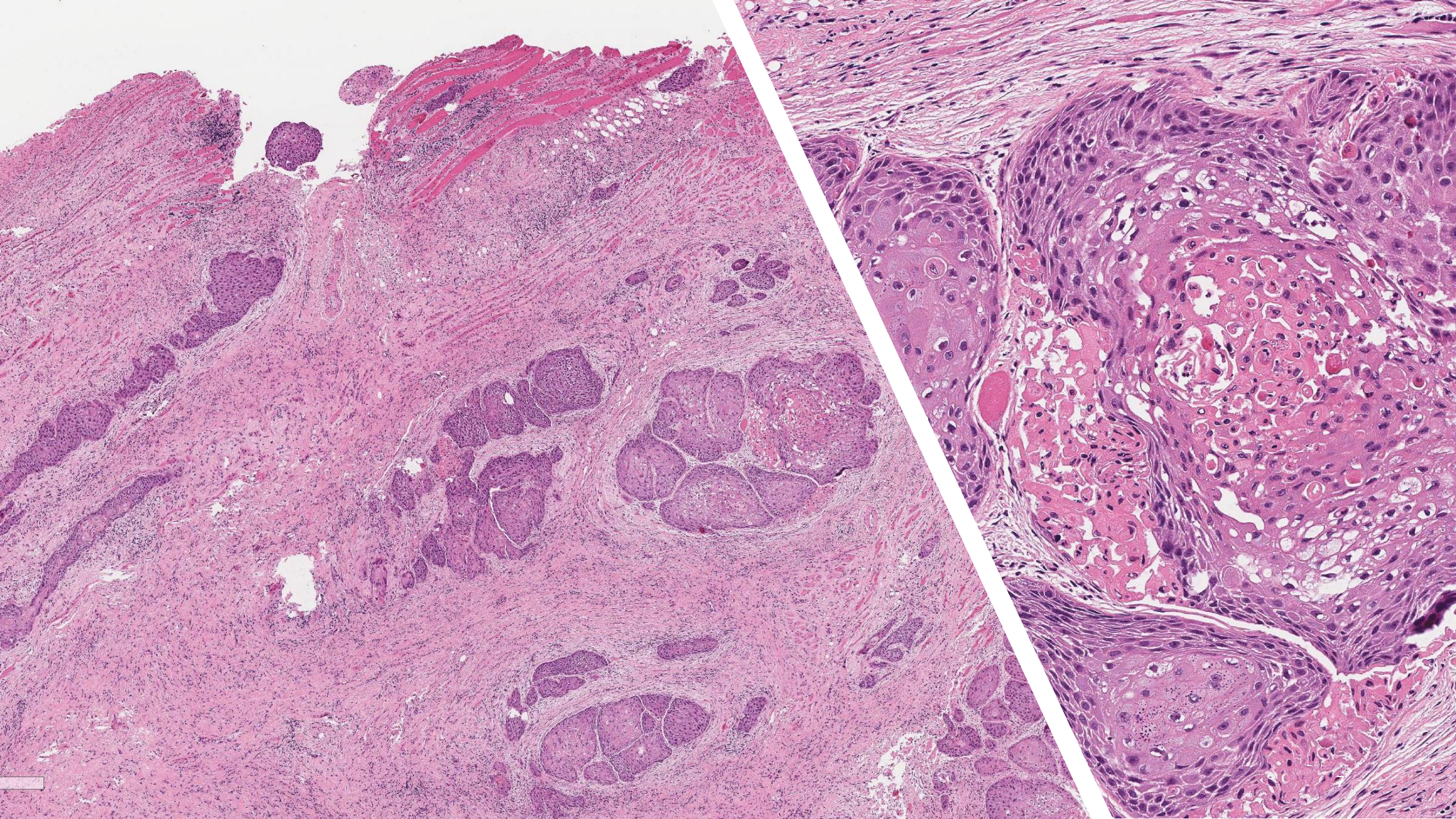
ST/SP:4/4.4

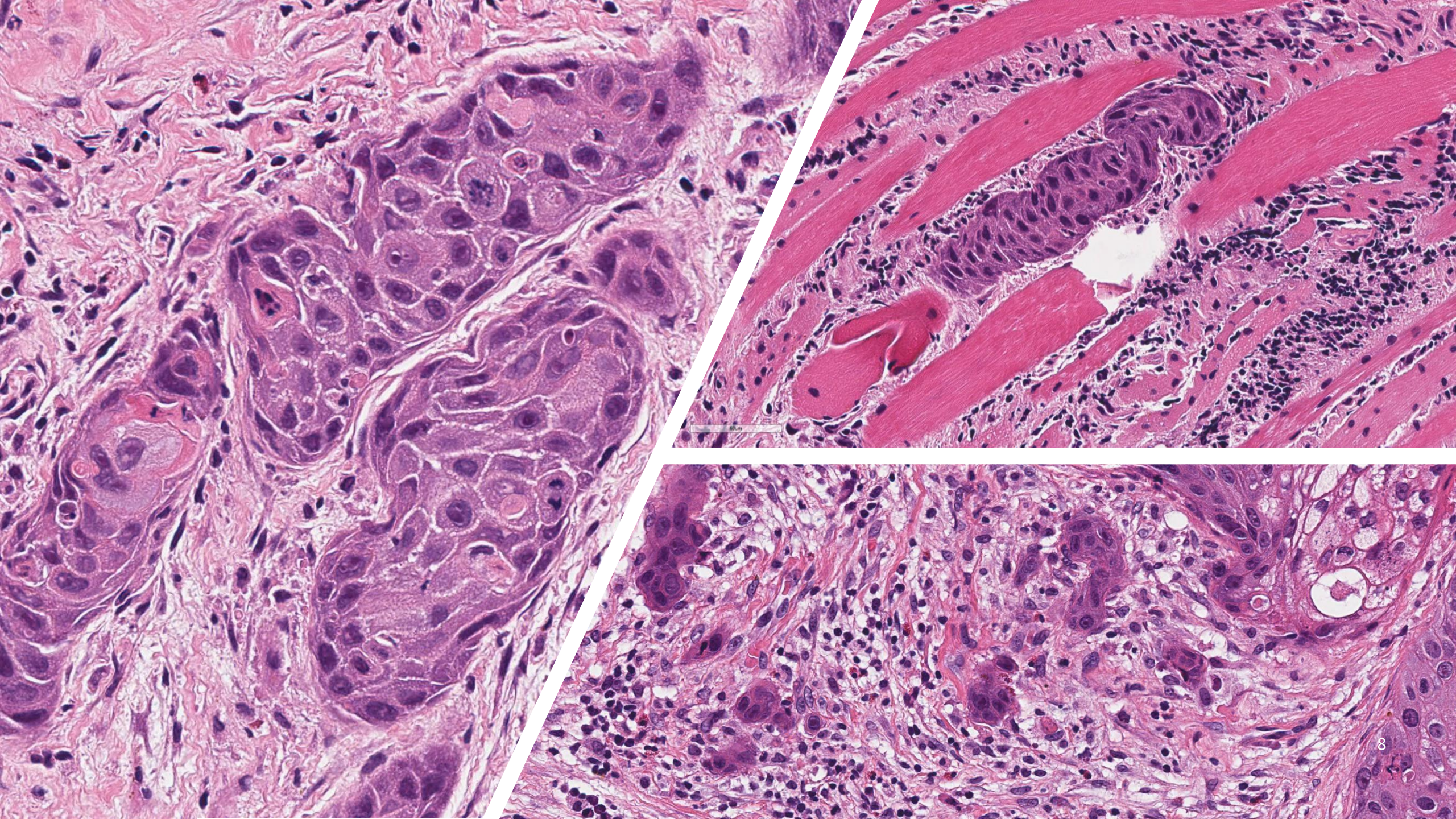
7.3  
WL-753 - WW:1610

## Exéresis de la lesión en fragmentos:

Contenido de seno maxilar, mucosa de seno maxilar, pared medial de seno maxilar, tumoración malar izquierda y suelo de órbita izquierda.

## 2. ESTUDIO DIFERIDO







## 2. DIAGNÓSTICO DEFINITIVO

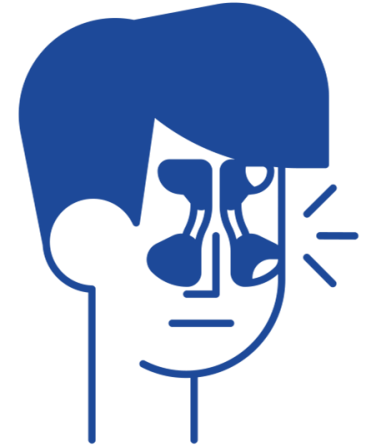
SEIS (6) FRASCOS:

BIOPSIA INTRAOPERATORIA:

A. Seno maxilar: **Carcinoma de células escamosas.**

BIOPSIA EN DIFERIDO:

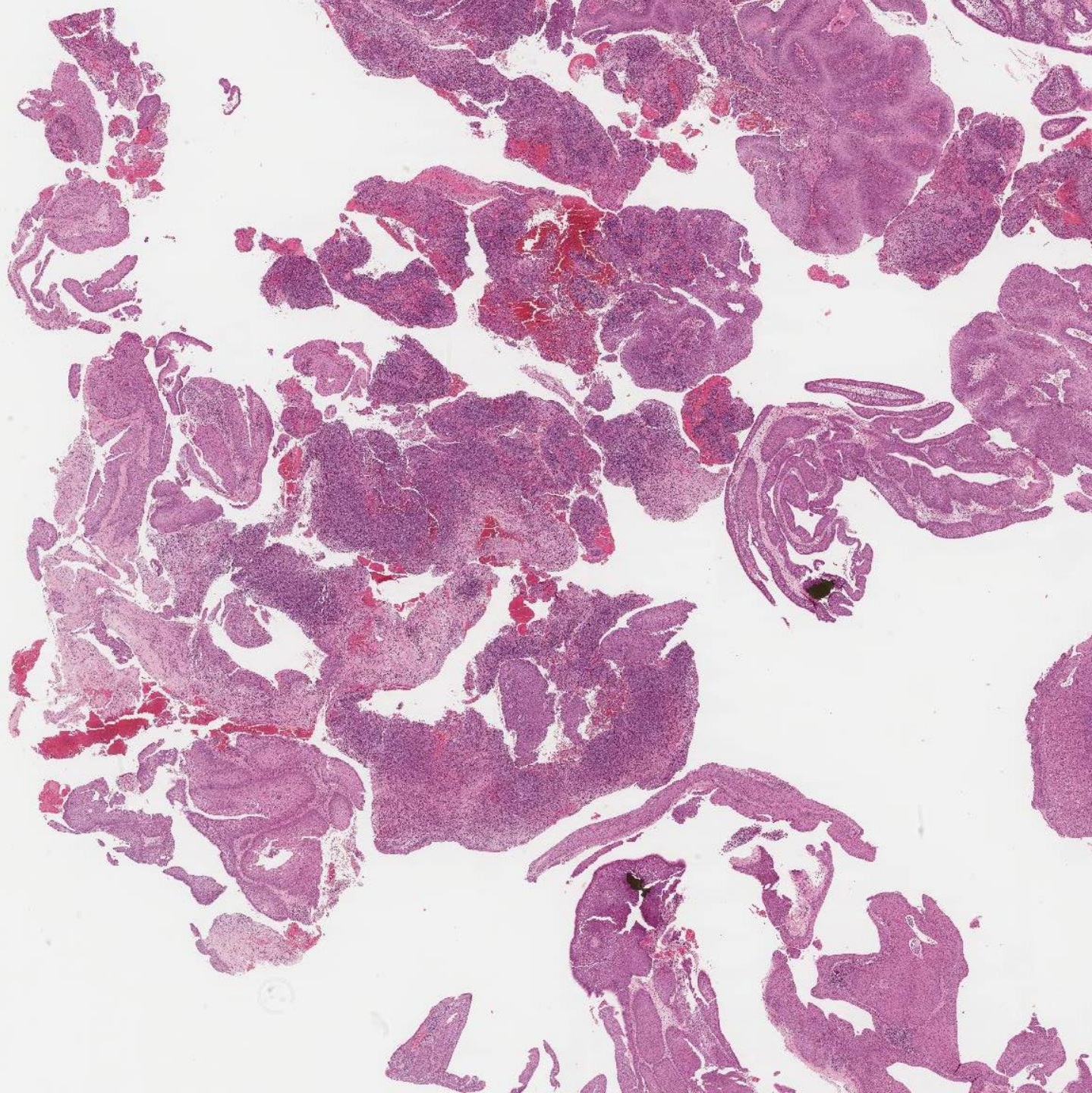
B. C. D. E. y F. Contenido de seno maxilar, mucosa de seno maxilar, pared medial de seno maxilar, tumoración malar izquierda y suelo de órbita izquierda: **Carcinoma de células escamosas.**

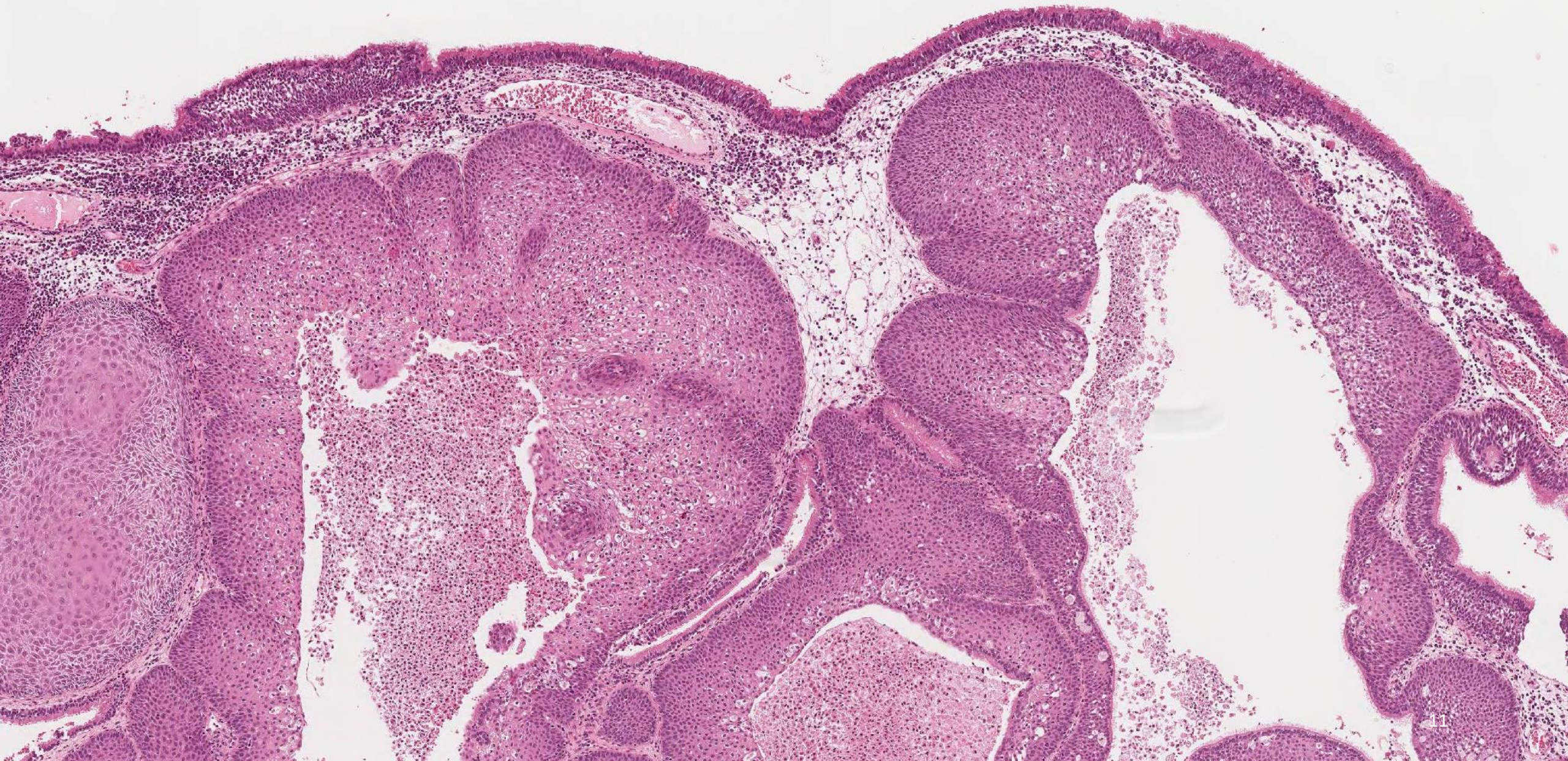


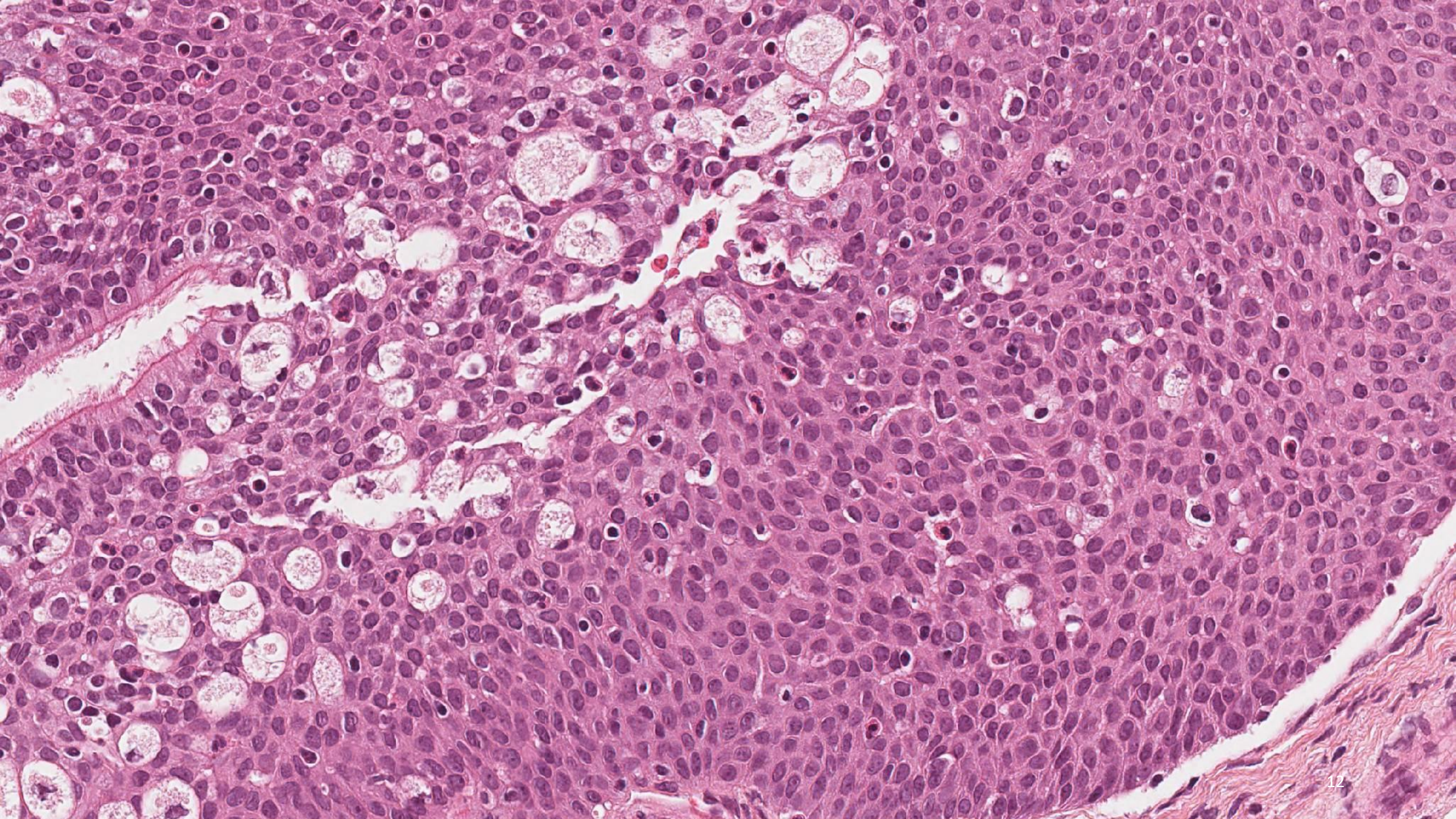


**Cuatro años atrás:  
Varón de 56 años.  
Tumoración en seno maxilar izquierdo.  
Cirugía endoscópica nasosinusal:  
resección en fragmentos.**

## **3. BIOPSIA PREVIA**









### 3. DIAGNÓSTICO PREVIO:

**Seno maxilar izquierdo; resección por CENS:**

- Papiloma sinonasal invertido.**

## 4. INCÓGNITA CLÍNICO-PATOLÓGICA

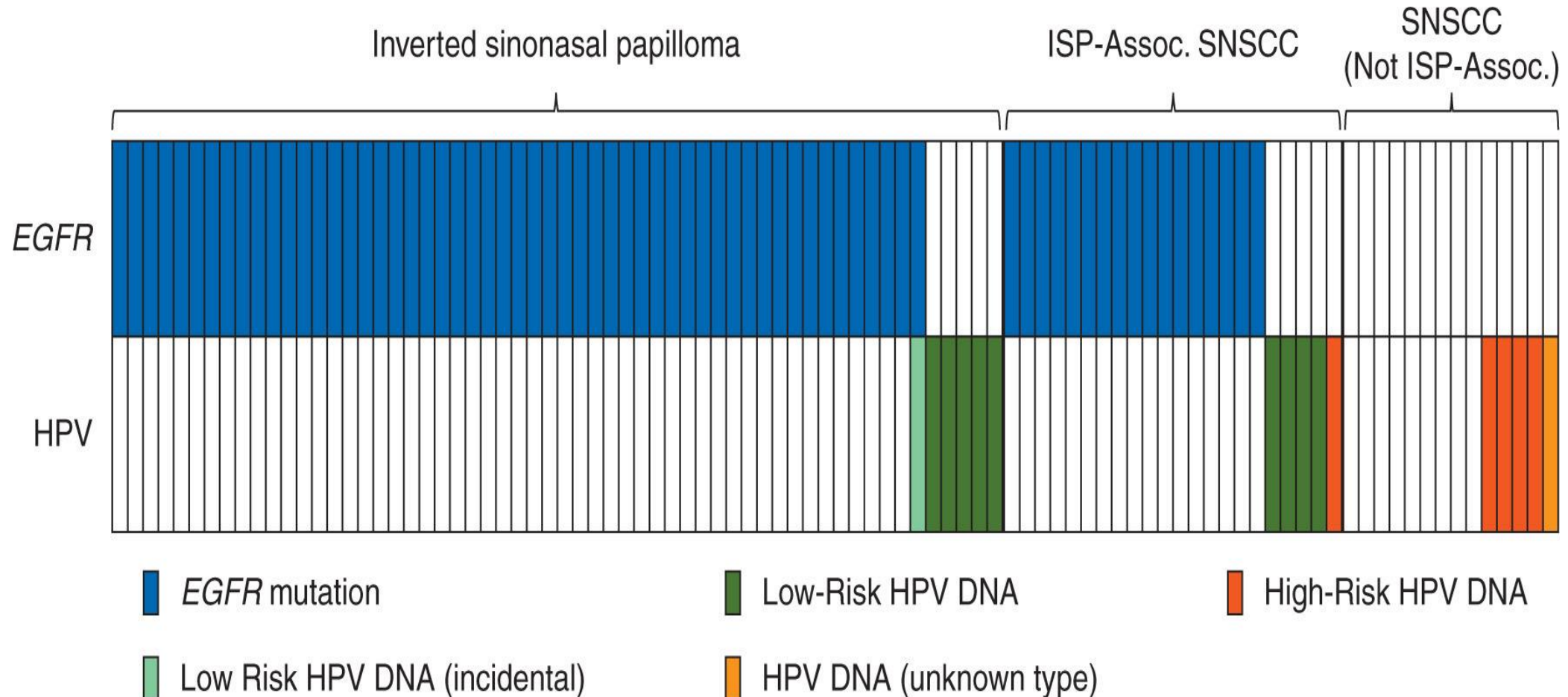
### PROCESO ETIOPATOGENICO



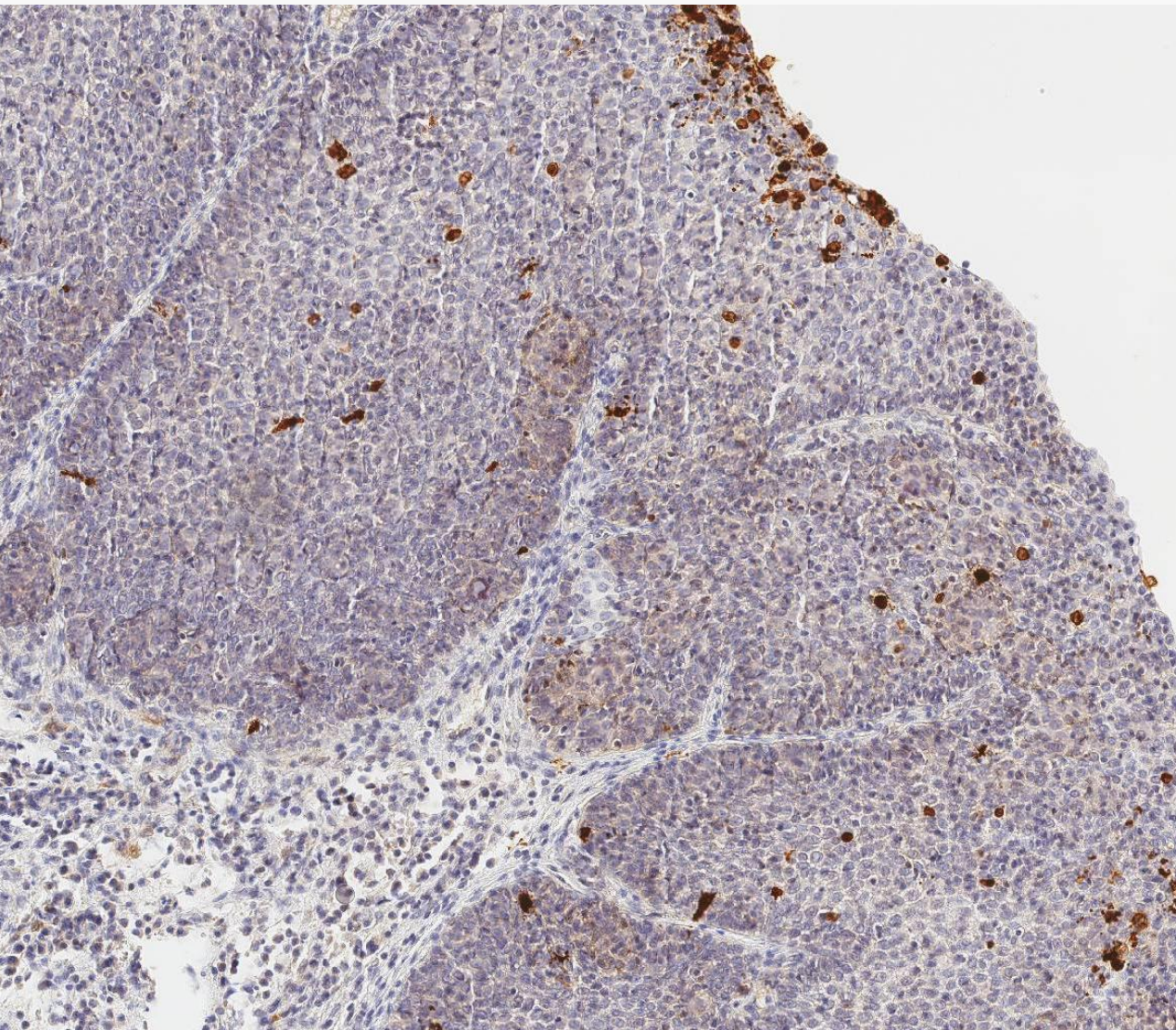
- En 2018: Papiloma sinonasal invertido en seno maxilar izquierdo, resecado.
- En 2023: Carcinoma de células escamosas en seno maxilar izquierdo

Carcinoma sinonasal asociado a papiloma sinonasal invertido.

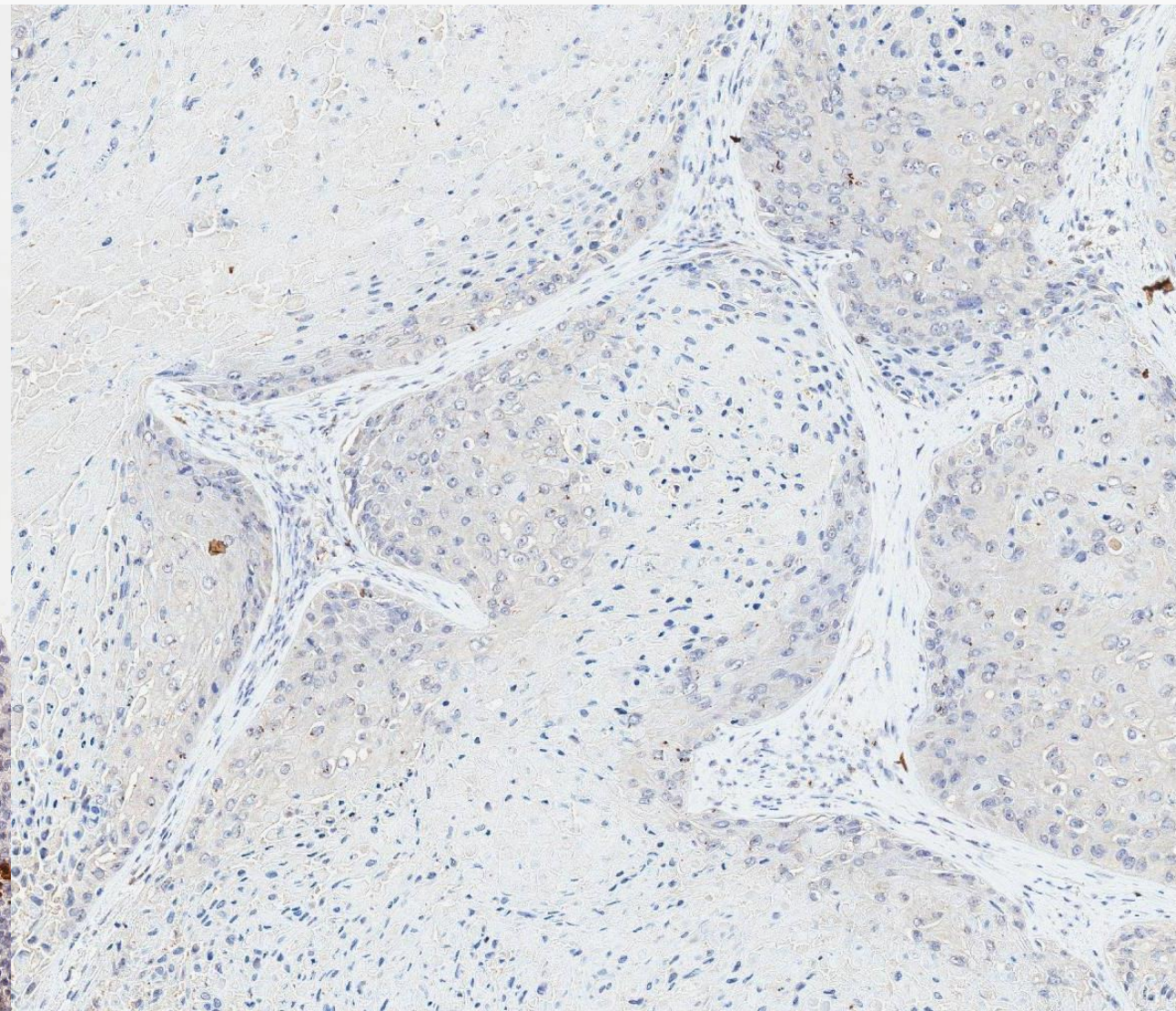
Human papillomavirus (HPV) and somatic *EGFR* mutations are essential, mutually exclusive oncogenic mechanisms for inverted sinonasal papillomas and associated sinonasal squamous cell carcinomas



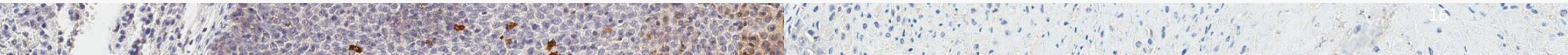
**PAPILOMA INVERTIDO**



**CARCINOMA**

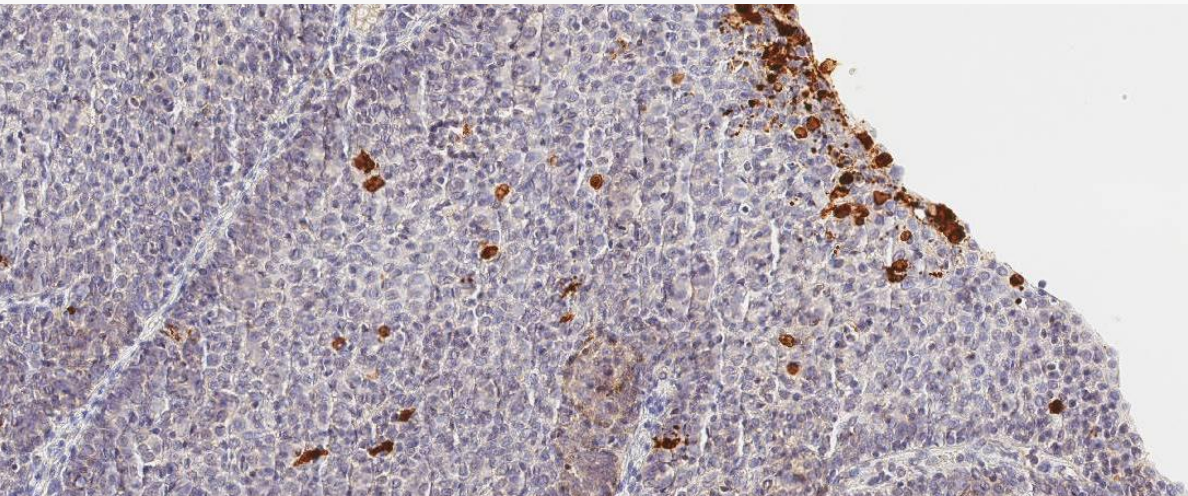


**INMUNOHISTOQUÍMICA: p16**

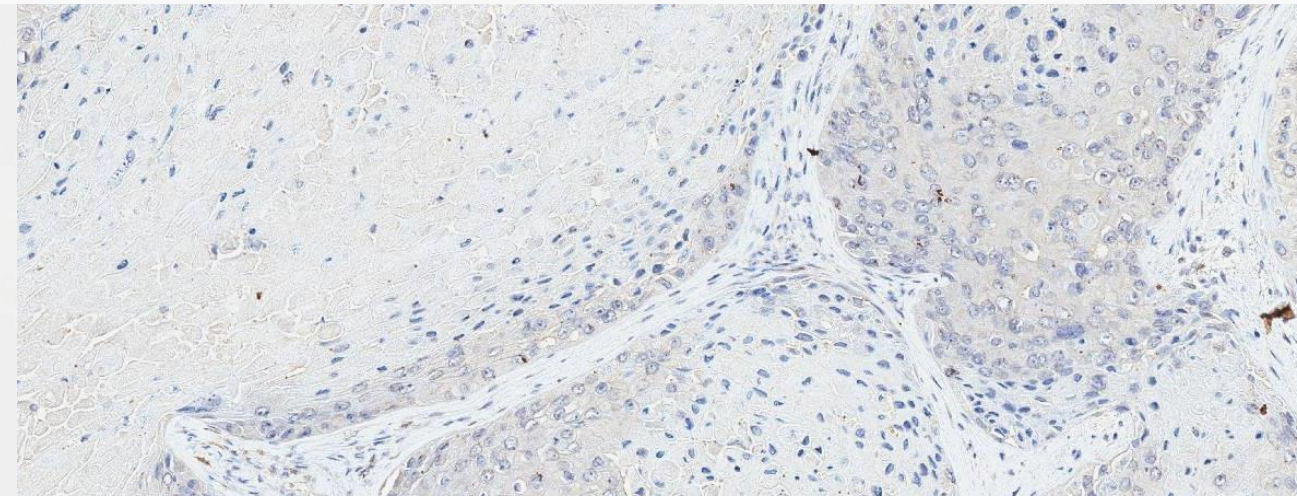




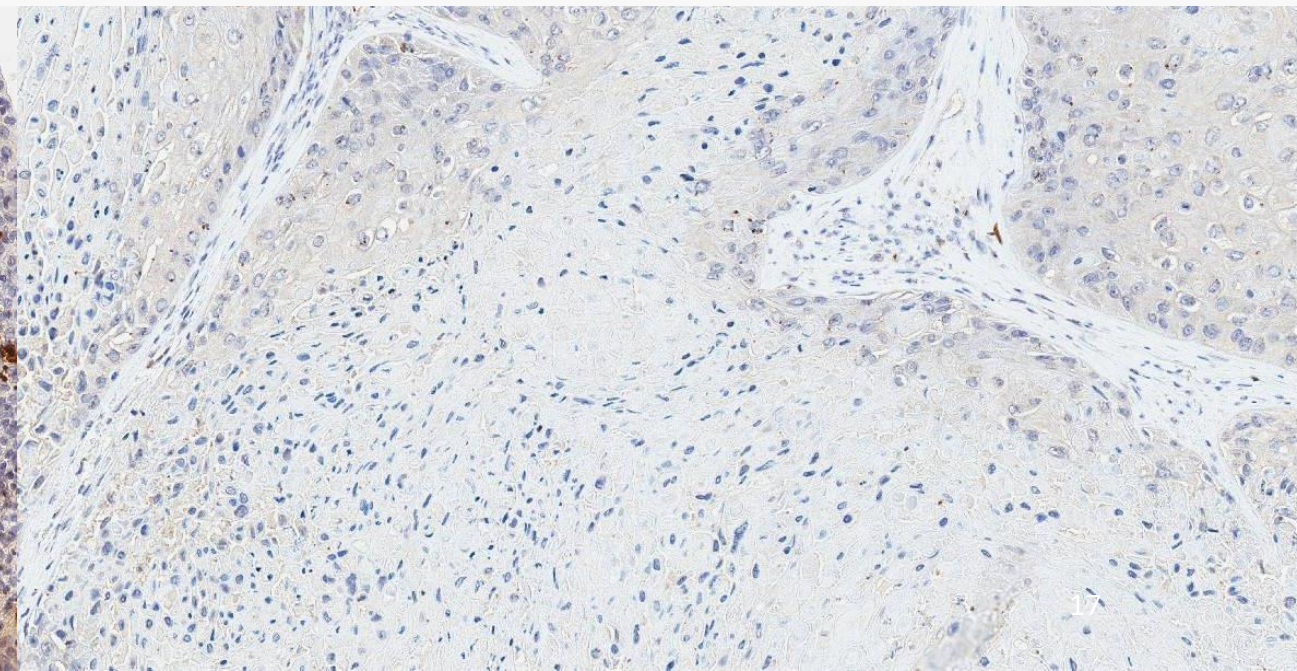
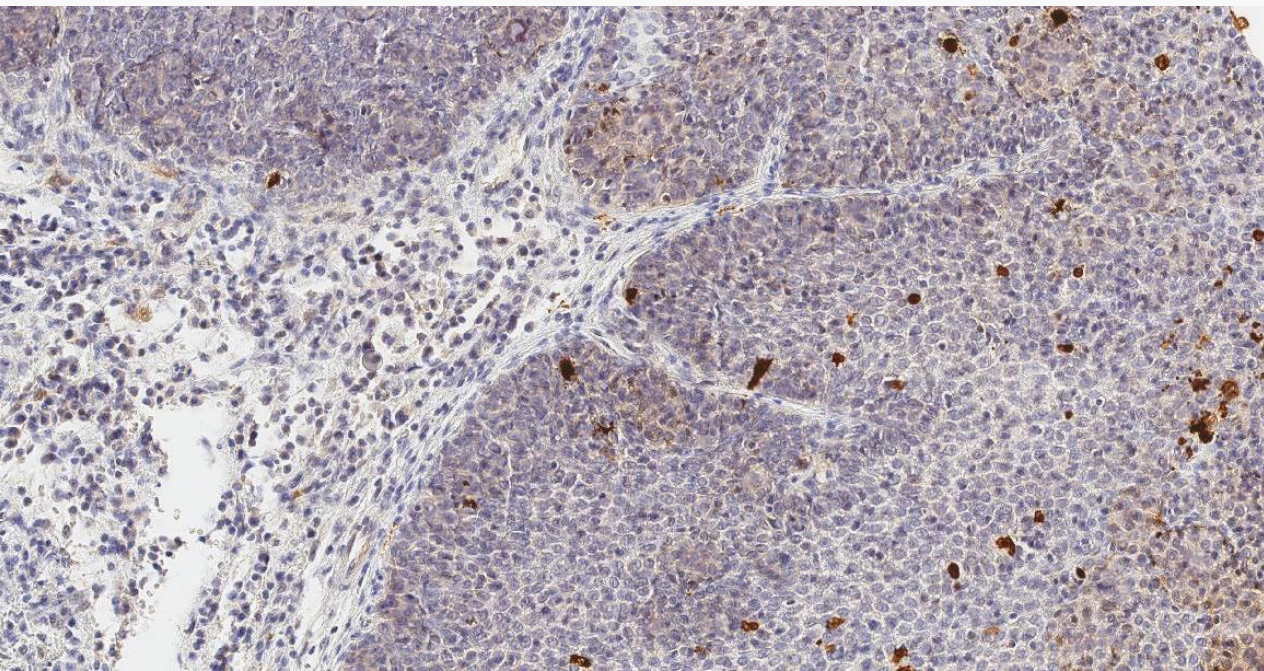
**PAPILOMA INVERTIDO**

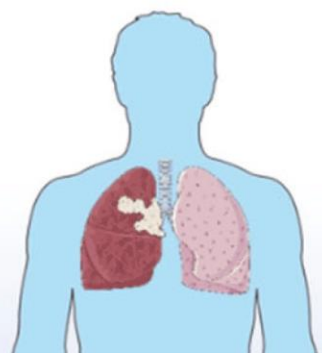


**CARCINOMA**



**PCR HPV: NEGATIVO**



**A**

Mutations in NSCLC

**EGFR**

Loop following C-helix

C-helix

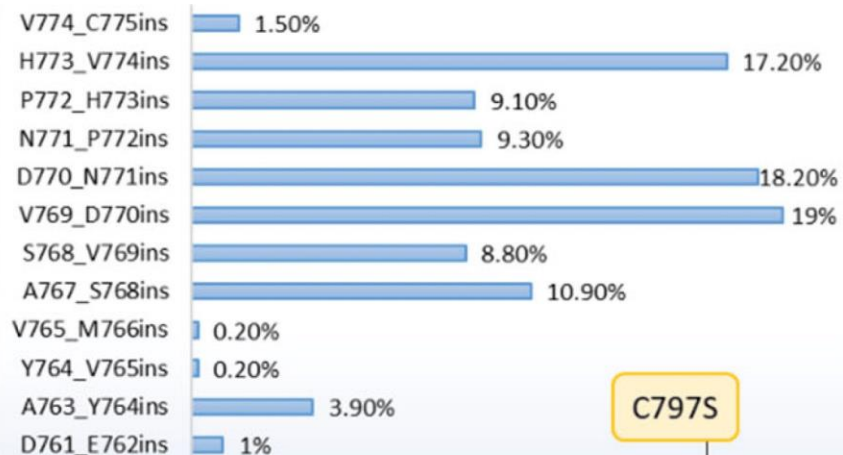
Exon 19 deletions

Exon 20 insertion

T790M

C797S

L858R

Classical *EGFR* mutations

Exon 20 insertions

Mutations associated with drug resistance

**B**

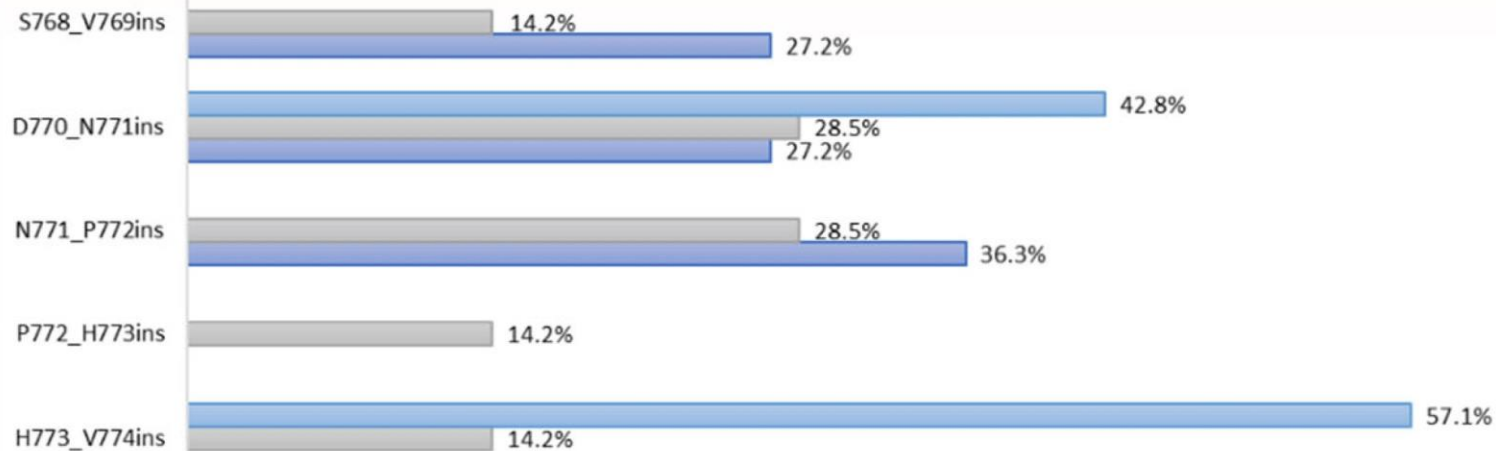
Mutations in ISP-associated SNSCC

Ex19delins 9.1%

■ Udager et al.

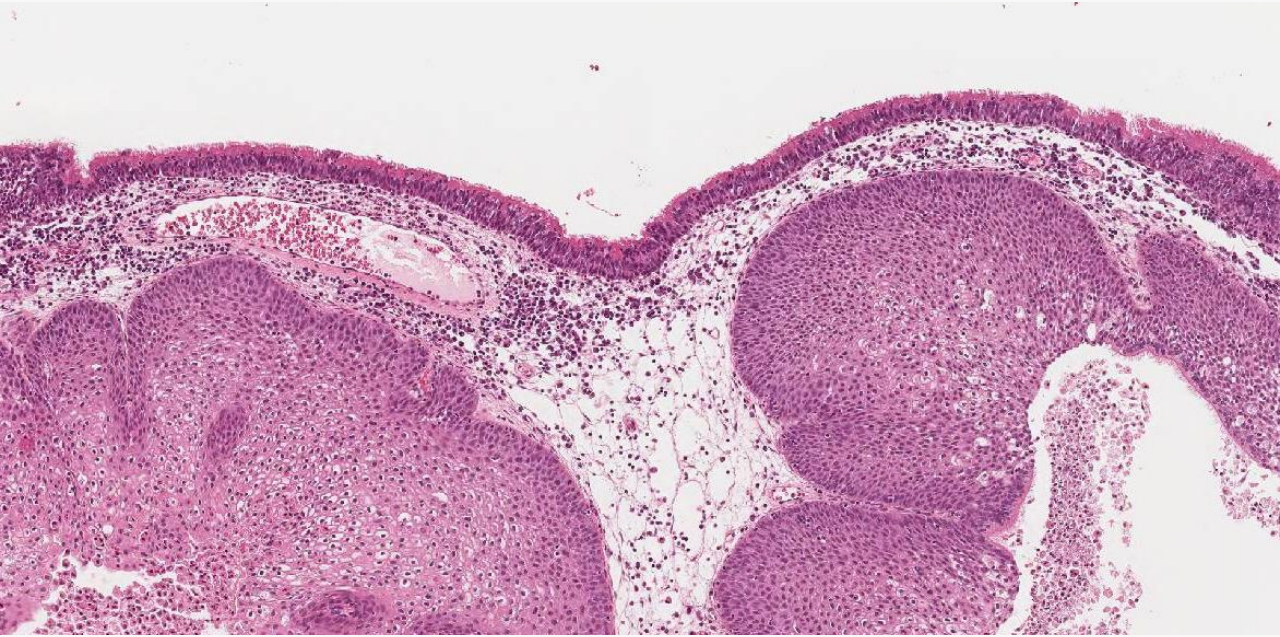
Loop following C-helix

Exon 20 insertion

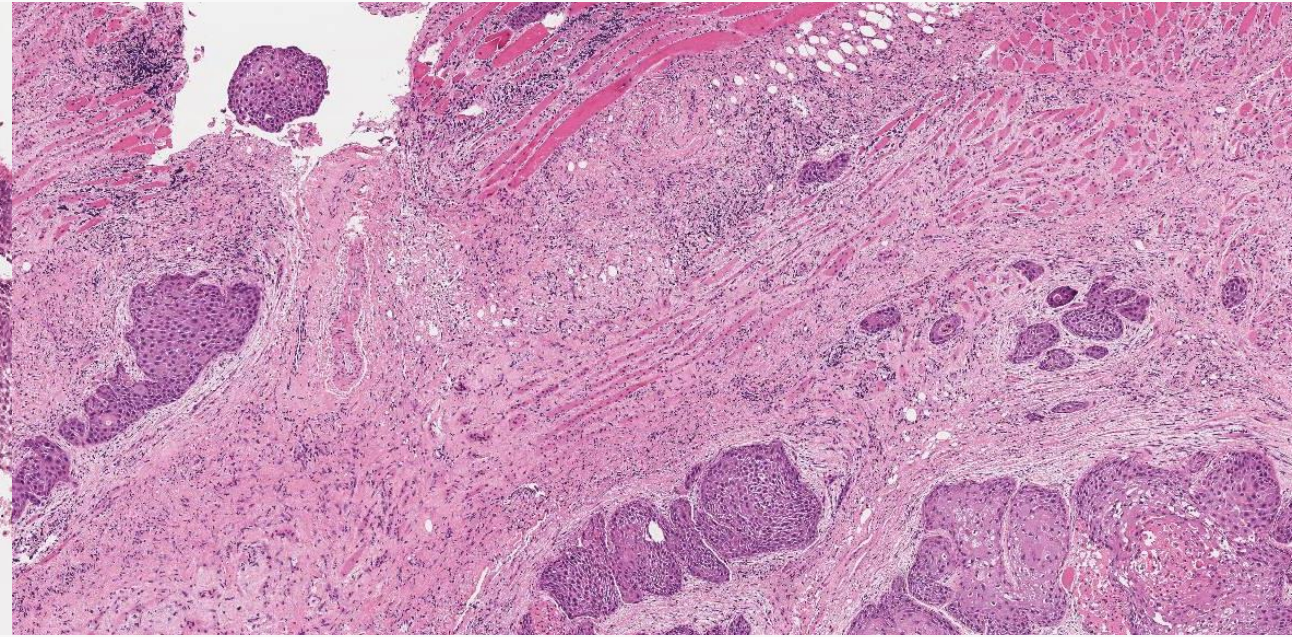


■ Sahnane et al. ■ Cabal et al. ■ Udager et al.

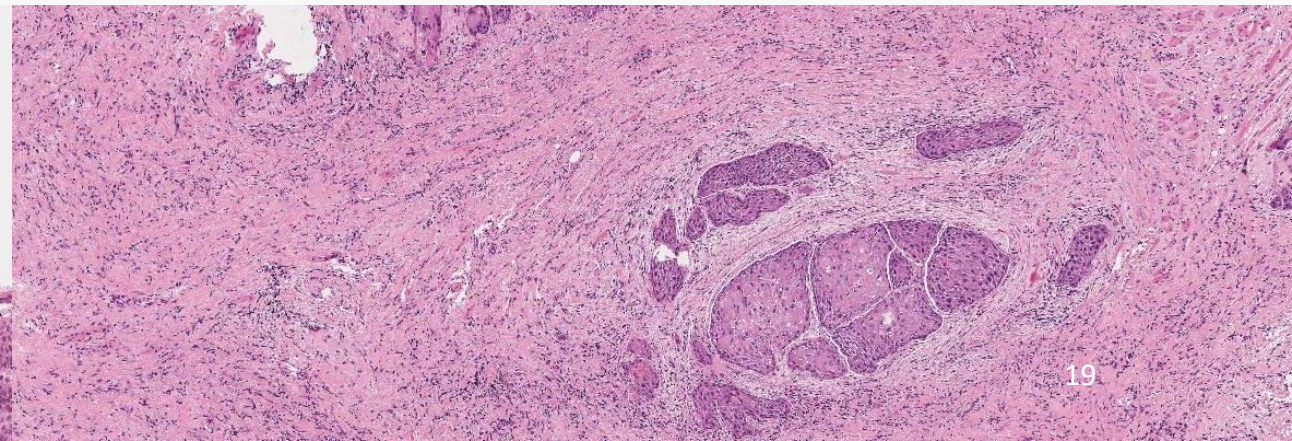
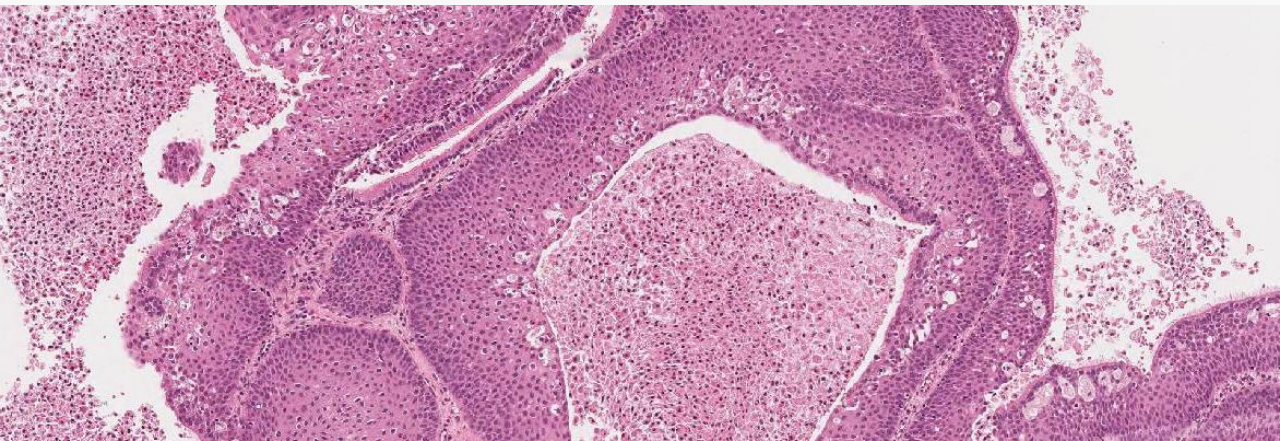
**PAPILOMA INVERTIDO**



**CARCINOMA**



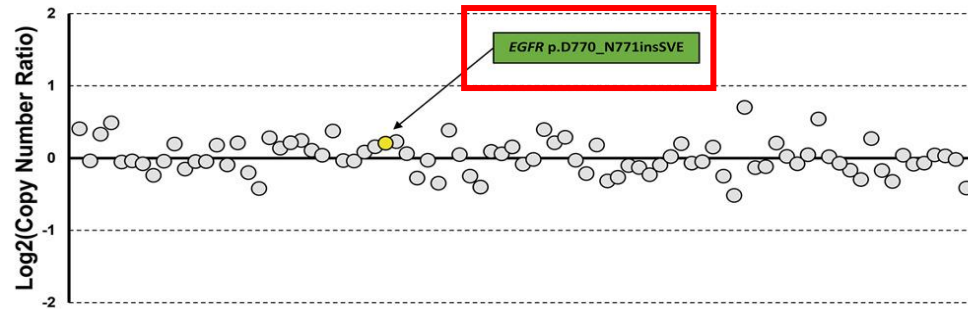
**Secuenciación *EGFR* exones 18-21: inserción exón 20  
(Ser768\_Asp770dup)**



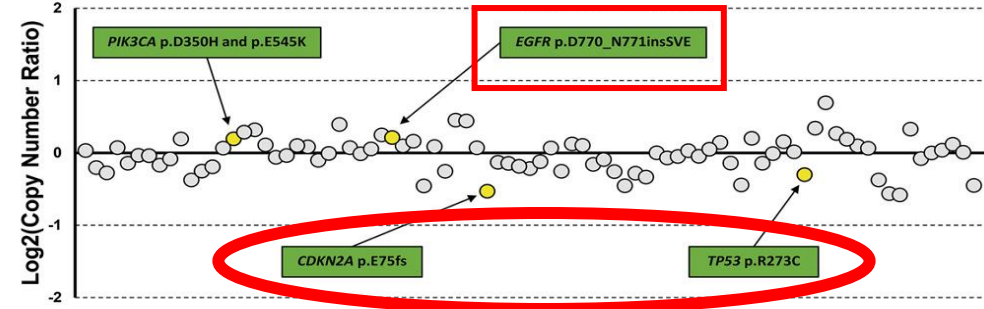
# MODERN PATHOLOGY

*TP53* mutations and *CDKN2A* mutations/deletions are highly recurrent molecular alterations in the malignant progression of sinonasal papillomas

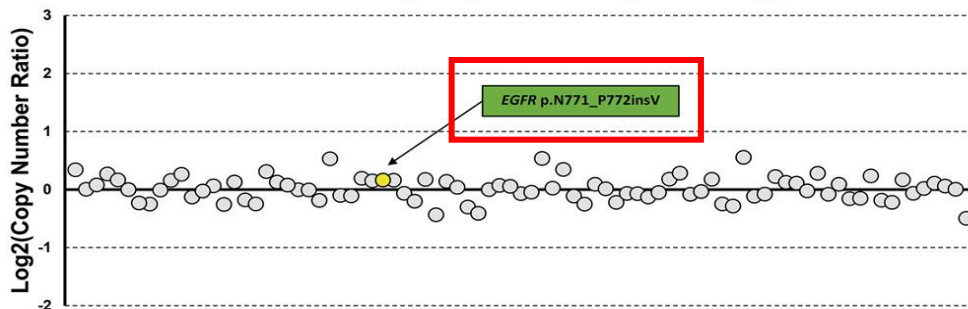
Patient #2 [Papilloma (HN-15)]



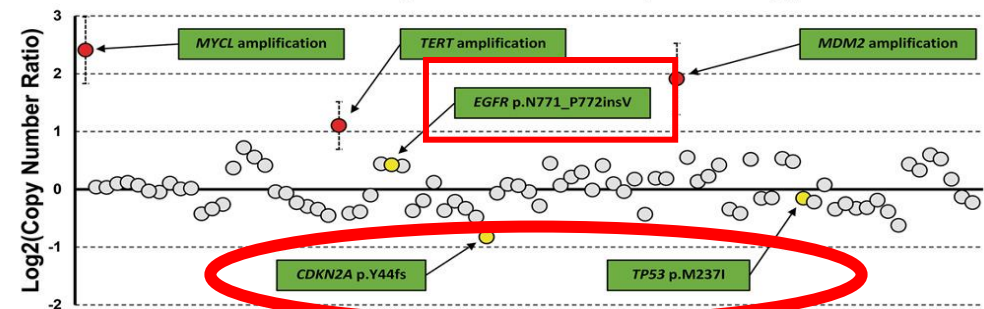
Patient #2 [Carcinoma (HN-14)]



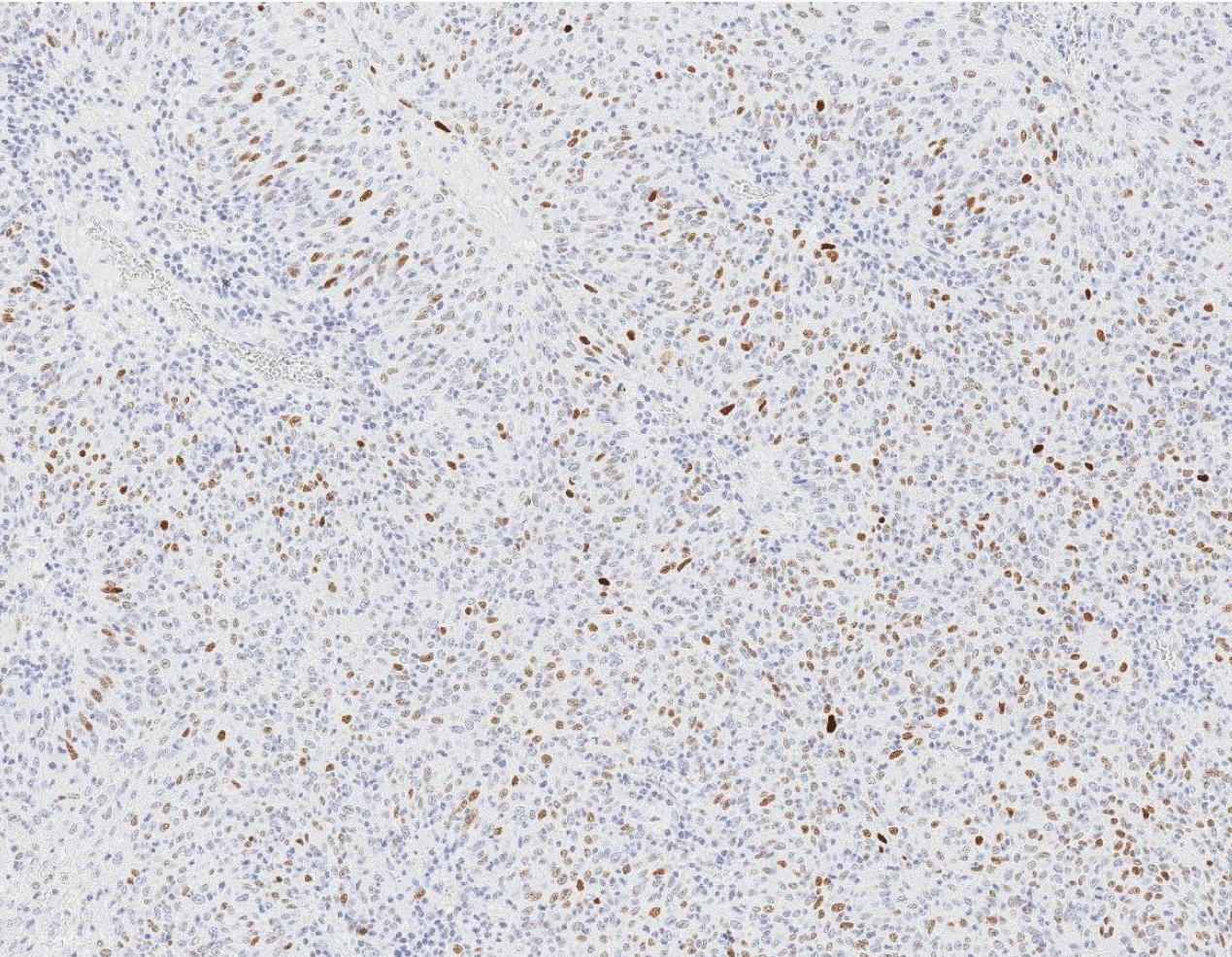
Patient #4 [Papilloma (HN-19)]



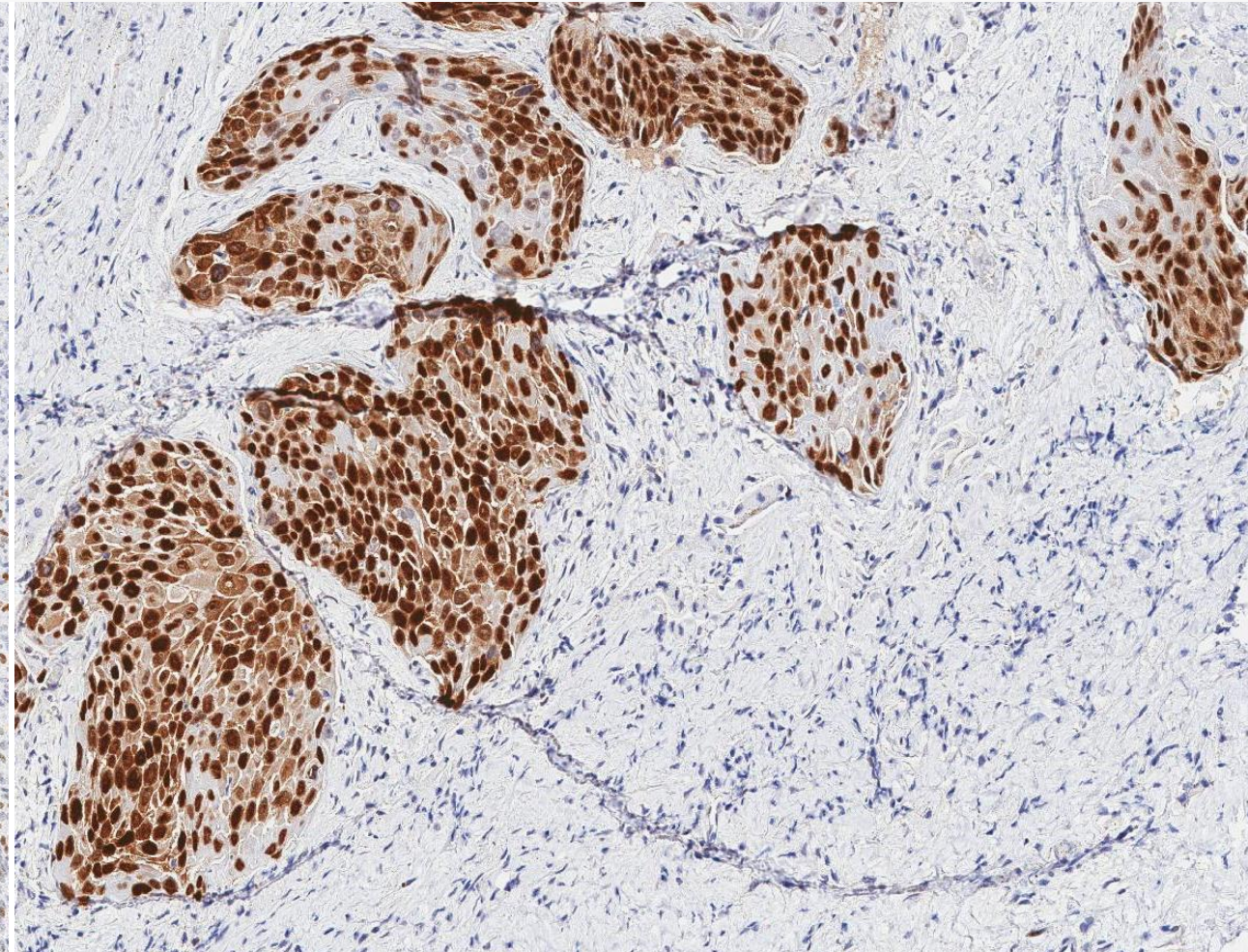
Patient #4 [Carcinoma (HN-18)]



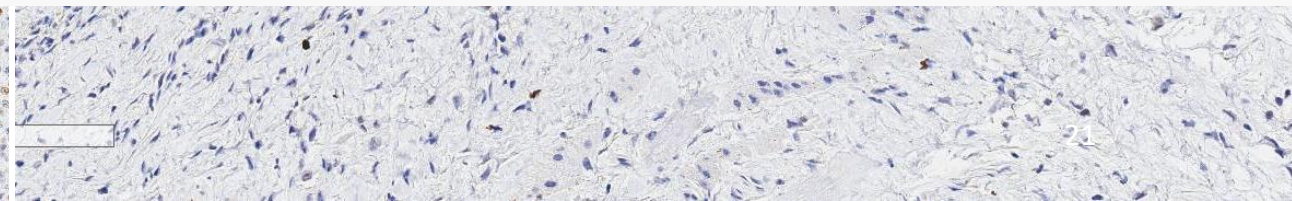
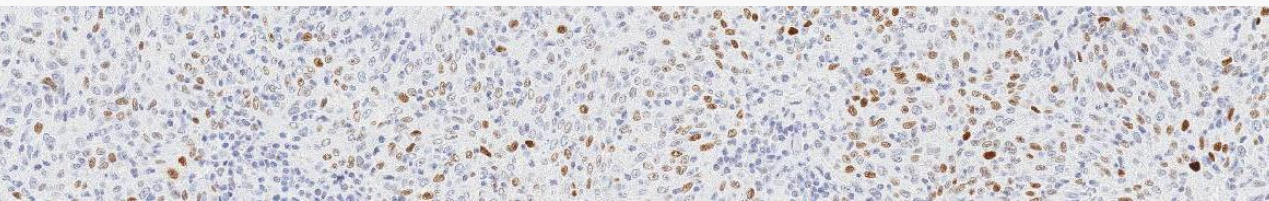
**PAPILOMA INVERTIDO**



**CARCINOMA**



**INMUNOHISTOQUÍMICA: p53**



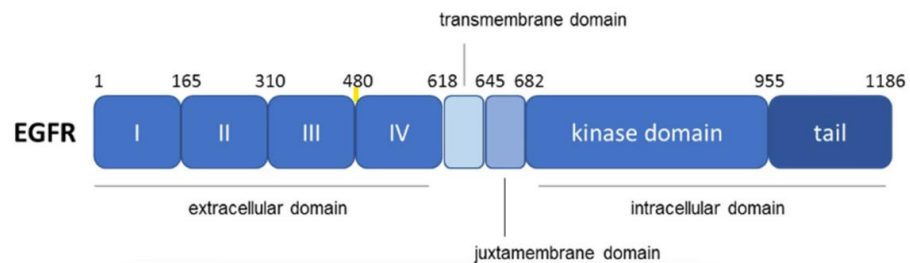
# 4. MUTACIÓN EXÓN 20 EGFR

## PROCESO ETIOPATOGÉNICO

Alteraciones moleculares:

- Inserción exón 20 *EGFR*, idéntica en muestra de 2023 (carcinoma) y de 2018 (papiloma).
- Patrón IHQ mutado p53 (mutación *TP53*): transformación a carcinoma.

**Carcinoma sinonasal asociado a papiloma sinonasal invertido, *EGFR* alterados.**

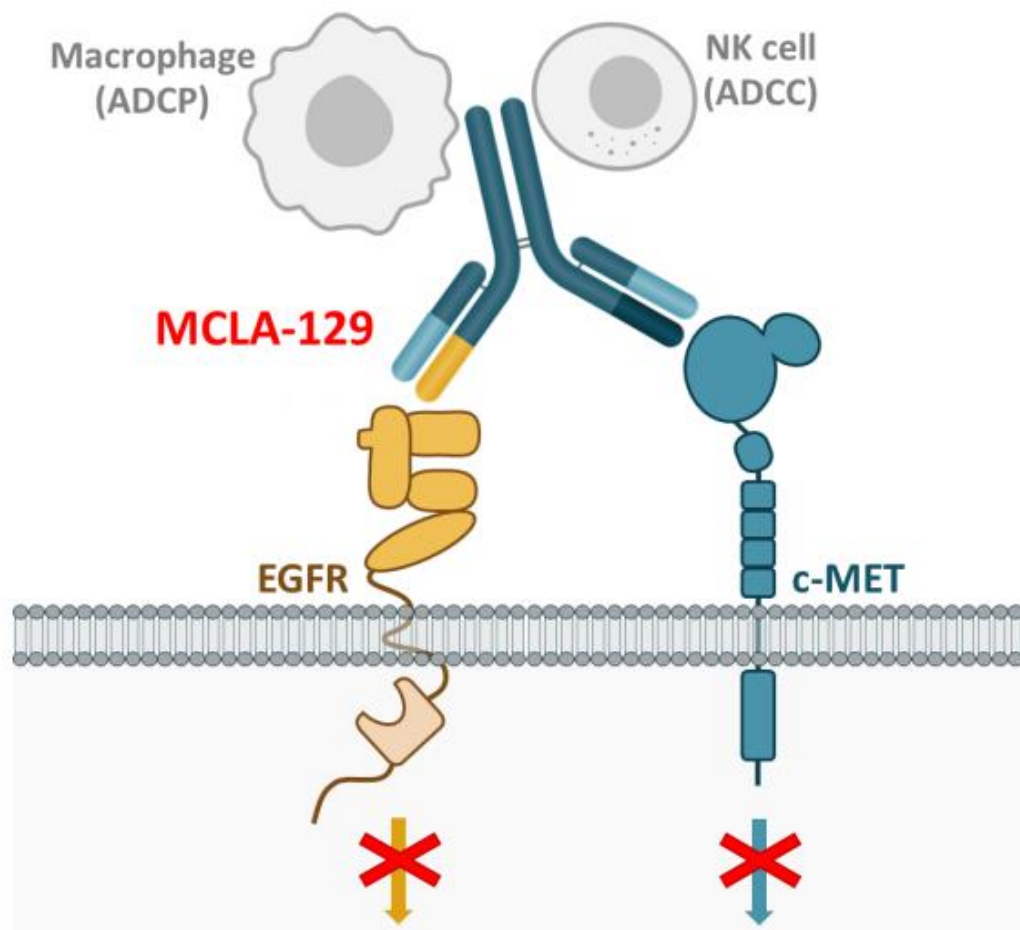


# 362P Efficacy and safety of MCLA-129, an anti-EGFR/c-MET bispecific antibody, in head and neck squamous cell cancer (HNSCC)

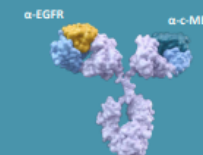
Presented at the European Society for Medical Oncology (ESMO) Asia Congress; December 1-3, 2023; Singapore.

ClinicalTrials.gov Identifier: NCT04868877

Contact information: Dr. Gianluca Laus (Merus N.V.), g.laus@merus.nl



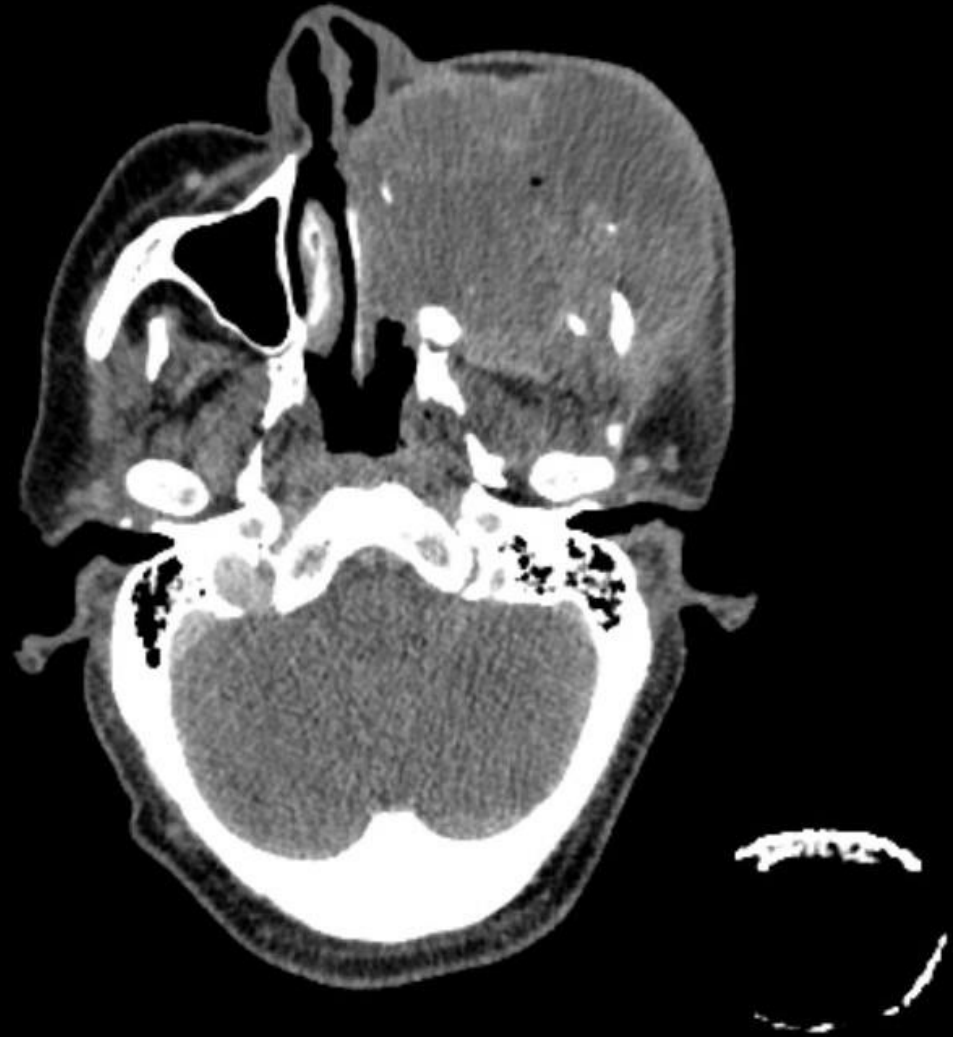
## Efficacy and safety of MCLA-129, an anti-EGFR/c-MET bispecific antibody, in head and neck squamous cell carcinoma (HNSCC)



📍 **Rápida progresión de la enfermedad.**

**Desestimado para tratamiento dirigido en ensayo clínico (fase 1/2).**

## **5. PROGRESIÓN DE LA ENFERMEDAD**





## 6. CONCLUSIONES

### LA BIOLOGÍA DE LA ENFERMEDAD: PARTE DE LA PATOLOGÍA

- La histología más habitual puede esconder características de importancia clínica: NO EXISTE ENEMIGO CONOCIDO
- Participación del patólogo/a en el Comité de Tumores.

**Ayudar a nuestros  
pacientes**

# 7. BIBLIOGRAFÍA

## 118ª REUNIÓN TERRITORIAL VALENCIANA DE LA SEAP · CASO 4

Udager AM, McHugh JB, Goudsmit CM, Weigelin HC, Lim MS, Elenitoba-Johnson KSJ, Betz BL, Carey TE, Brown NA. Human papillomavirus (HPV) and somatic EGFR mutations are essential, mutually exclusive oncogenic mechanisms for inverted sinonasal papillomas and associated sinonasal squamous cell carcinomas. *Ann Oncol*. 2018 Feb 1;29(2):466-471. doi: 10.1093/annonc/mdx736. PMID: 29145573; PMCID: PMC6248771.

Pacini L, Cabal VN, Hermsen MA, Huang PH. EGFR Exon 20 Insertion Mutations in Sinonasal Squamous Cell Carcinoma. *Cancers (Basel)*. 2022 Jan 13;14(2):394. doi: 10.3390/cancers14020394. PMID: 35053553; PMCID: PMC8774177

Brown NA, Plouffe KR, Yilmaz O, Weindorf SC, Betz BL, Carey TE, Seethala RR, McHugh JB, Tomlins SA, Udager AM. TP53 mutations and CDKN2A mutations/deletions are highly recurrent molecular alterations in the malignant progression of sinonasal papillomas. *Mod Pathol*. 2021 Jun;34(6):1133-1142. doi: 10.1038/s41379-020-00716-3. Epub 2020 Nov 17. PMID: 33203919; PMCID: PMC8126579.

Bossi P, Minuti G, Braña I, Moreno Garcia V, Boni V, Jamme P, Call JA, Yan C, Barasa B, Doze P, Joe AK, Laus G, Daste A. 362P Efficacy and safety of MCLA-129, an anti-EGFR/c-MET bispecific antibody, in head and neck squamous cell cancer (HNSCC). *Ann Onc*. 2023 Nov;34(Suppl4):S1610-S1611. doi: 10.1016/j.annonc.2023.10.470.

WHO Classification of Tumours Editorial Board. Head and neck tumours [Internet; beta version ahead of print]. Lyon (France): International Agency for Research on Cancer; 2022 [cited 2023 05 12]. (WHO classification of tumours series, 5th ed.; vol. 9). Available from: <https://tumourclassification.iarc.who.int/chapters/52>.

