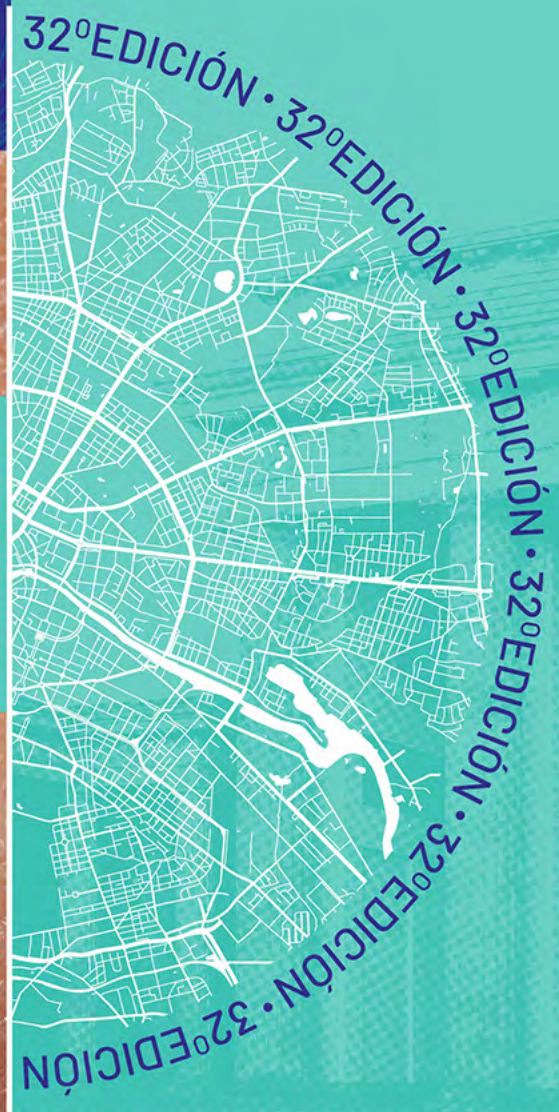
AEDV 2023 Highlights

Con el patrocinio de:

ucb



BERLÍN

11-14 OCTUBRE

Iniciativa científica de:

AEDV 1909

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

Highlights en Dermatoncología y Cirugía Cutánea

Melanoma. CBC. Cirugía de Mohs.

DR. DARÍO DE PEROSANZ LOBO

H. U. RAMÓN Y CAJAL (MADRID)

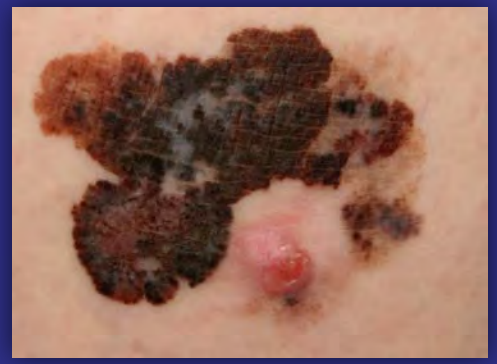
@dariodeperosanz

NO TENGO CONFLICTOS DE INTERÉS

BERLIN

11-14 OCTUBRE

NOVEDADES EN MELANOMA



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BERLIN

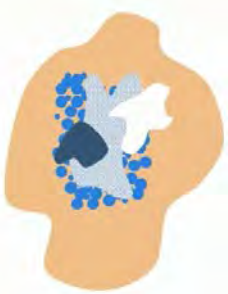
11-14 OCTUBRE

How dermoscopy can improve surgical management of melanoma

John Paoli, Professor
Dept. of Dermatology and Venereology
Sahlgrenska Academy, University of Gothenburg

GÖTEBORGS UNIVERSITET

Predictors for invasive melanoma



Atypical blue-white structures

Shiny white lines

Polymorphous vessels

Predictors for melanoma in situ

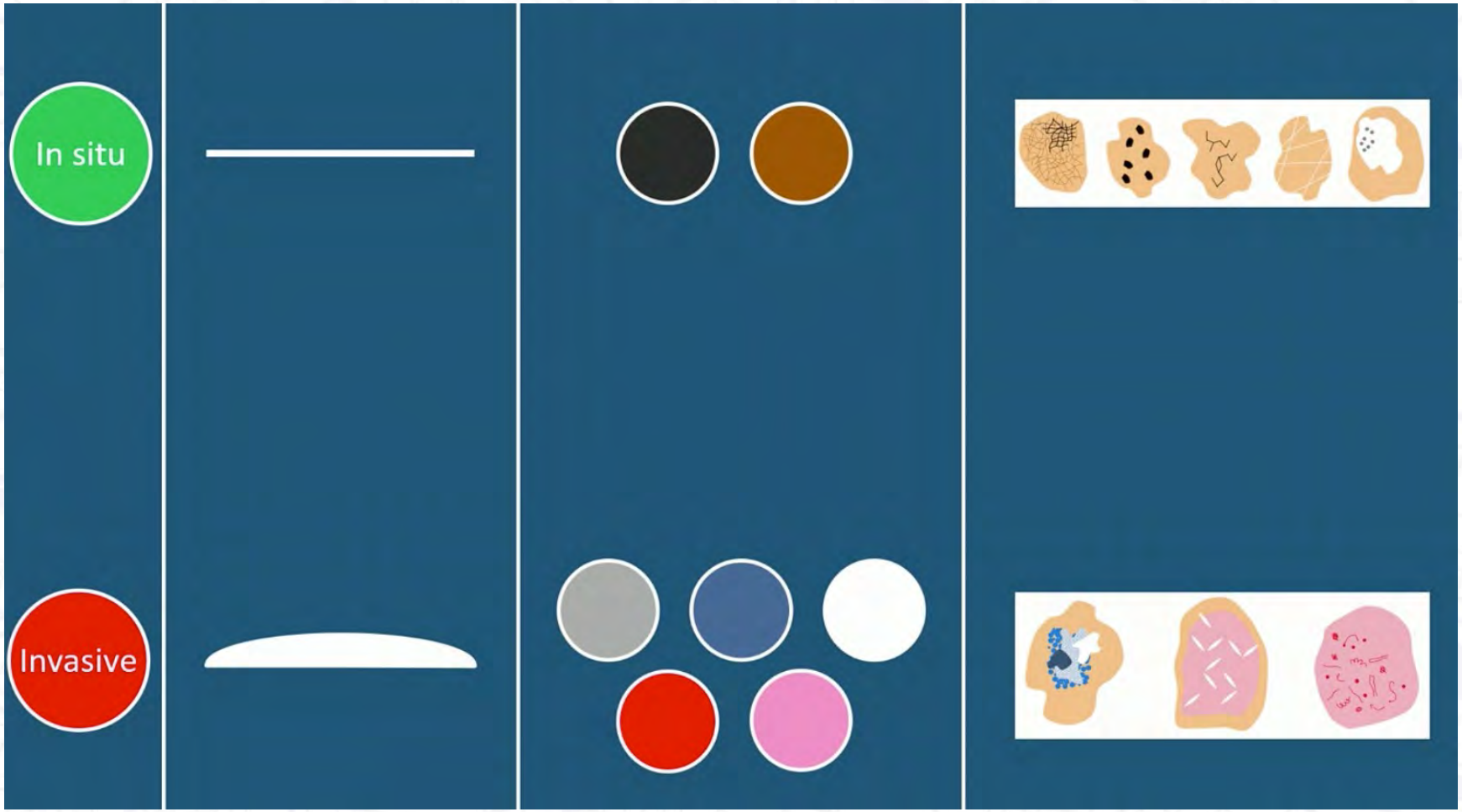
Atypical network

Multiple small hyperpigmented areas

Angulated lines

Prominent skin markings

Extensive regression


In situ
Invasive

#1

A lesion suspected to be melanoma should be excised with a 2-mm clinical margin

What are our goals?

90% de las lesiones melanocíticas atípicas NO se extirpan completamente con un margen de 2 mm

ActaDV

CLINICAL REPORT

Check for updates

1/5

Incomplete Excisions of Melanocytic Lesions: Rates and Risk Factors

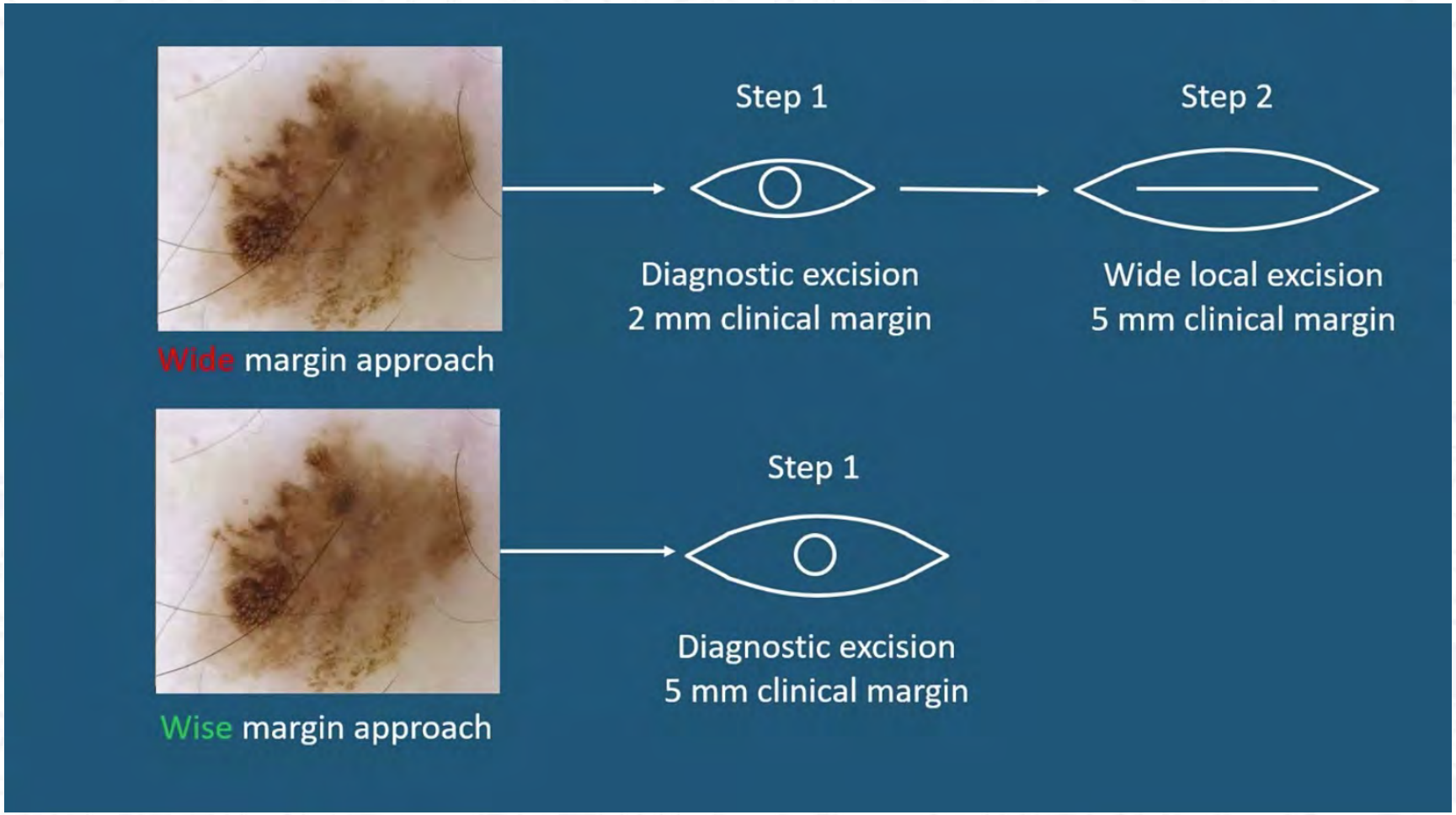
Sofia BERGLUND[1,2], Eva JOHANSSON BACKMAN[1,2], Zahra BALDAWI[1], Linda HORN[1], Rebecca ARBIN BORSIIN[1], Michelle MARJANOVIC[1], Thea CHRISTOFFERSSON[1], Martin GILLSTEDT[1,2] and John PAOLI[1,2]

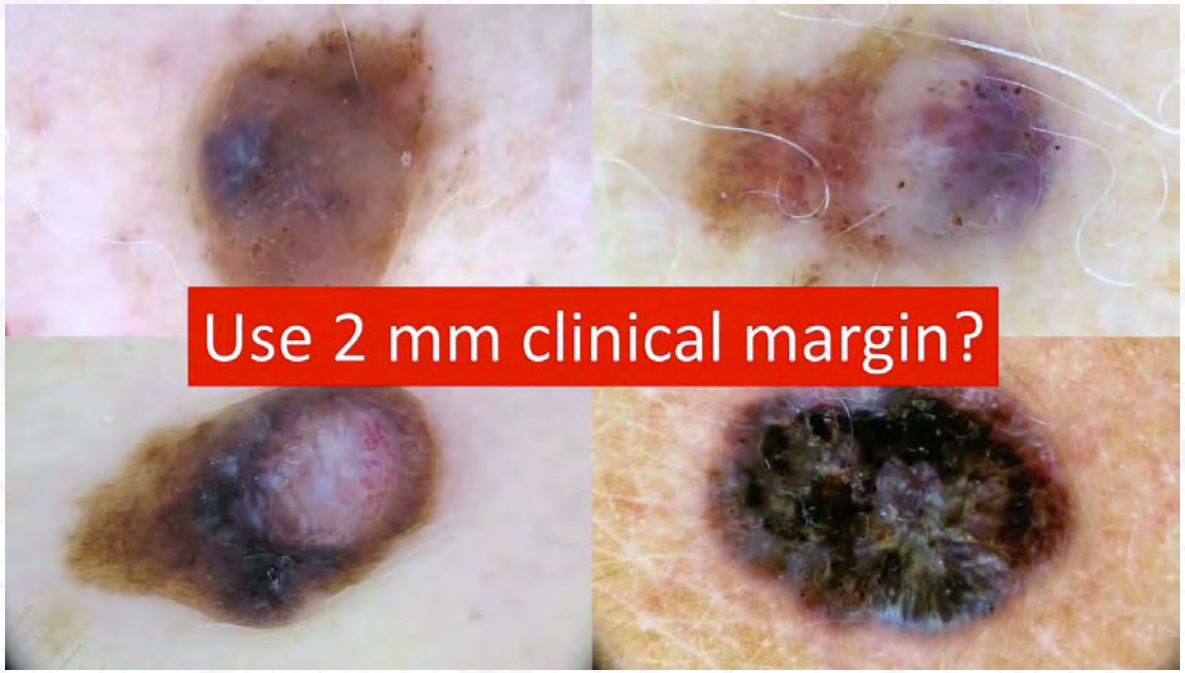
[1]Department of Dermatology and Venereology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and [2]Region Västra Götaland, Sahlgrenska University Hospital, Department of Dermatology and Venereology, Gothenburg, Sweden

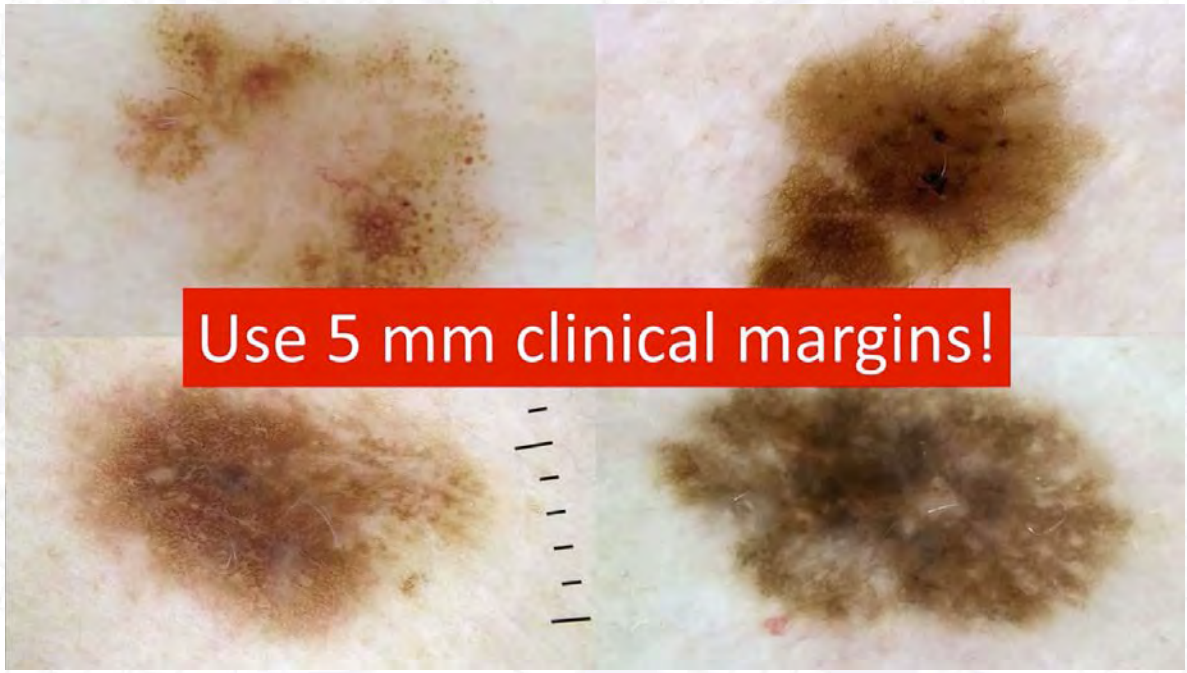
Acta Derm Venereol 2021; 101: adv00421.

2,782 consecutive excisions of atypical melanocytic lesions (non-lentiginous subtypes)

Complete excision rate:


Step 1
Step 2
Diagnostic excision
2 mm clinical margin
Wide local excision
5 mm clinical margin
Wide margin approach
Step 1
Diagnostic excision
5 mm clinical margin
Wise margin approach


Use 2 mm clinical margin?


Use 5 mm clinical margins!

EA DV CONGRESS

Role of tissue biomarkers in clinical decision making

Session: Melanoma

Thursday 12, October 2023

Marlies Wakkee

Dermatologist/Associate professor

m.wakkee@erasmusmc.nl

Mitotic rate

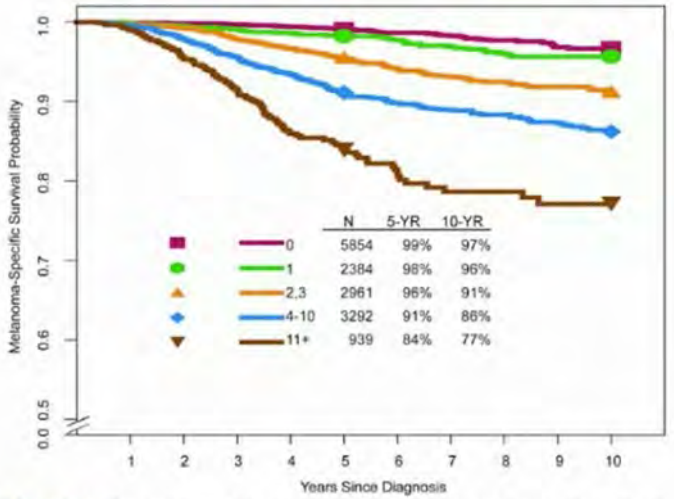


FIGURE 2. Kaplan-Meier Melanoma-Specific Survival Curves According to Mitotic Rate (Mitoses per mm^2) in Patients With Stage I and II Melanoma From the Eighth Edition International Melanoma Database.

Gershenwald JE, et al. CA Cancer J Clin. 2017 Nov;67(6):472-492.

CA CANCER J CLIN 2017;67:472-492

Melanoma Staging: Evidence-Based Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

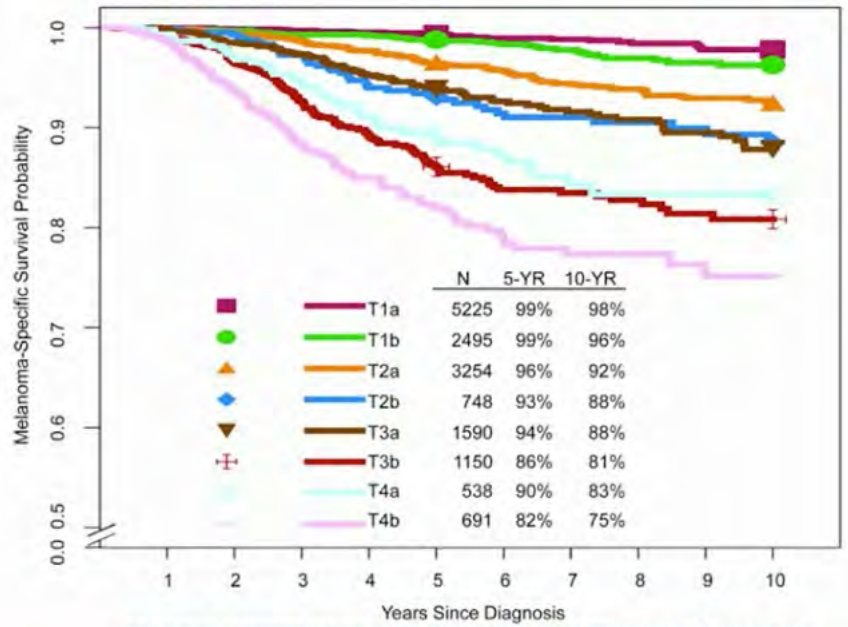
Jeffrey E. Gershenwald, MD [1†]; Richard A. Scolyer, MD [2,3†]; Kenneth R. Hess, PhD [4†]; Vernon K. Sondak, MD [5];

CHANGE	DETAILS OF CHANGE/HIGHLIGHT
Definition of primary tumor (T)	All principal T-category tumor thickness ranges are maintained, but T1 is now subcategorized by tumor thickness strata at 0.8-mm threshold Tumor mitotic rate is removed as a staging criterion for T1 tumors: T1a melanomas are now defined as nonulcerated and <0.8 mm in thickness; T1b is now defined as melanomas 0.8-1.0 mm in thickness regardless of ulceration status OR ulcerated melanomas <0.8 mm in thickness

- Stronger role for tumor thickness and ulceration to predict melanoma specific survival within T1 melanoma
- Contradicting findings on the predictive role of mitotic rate for MSS
- AJCC Melanoma Expert Panel strongly recommends that mitotic rate be assessed and recorded for all primary melanomas

A pesar de eliminarlo para la estadificación, **la AJCC recomienda medir el índice mitótico y tenerlo en cuenta** para las decisiones clínicas

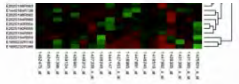
Need for new biomarkers



CA A Cancer J Clinicians, Volume: 67, Issue: 6, Pages: 472-492, First published: 13 October 2017.

60% de todos los melanomas estadio IV fueron diagnosticados inicialmente como E. I-II

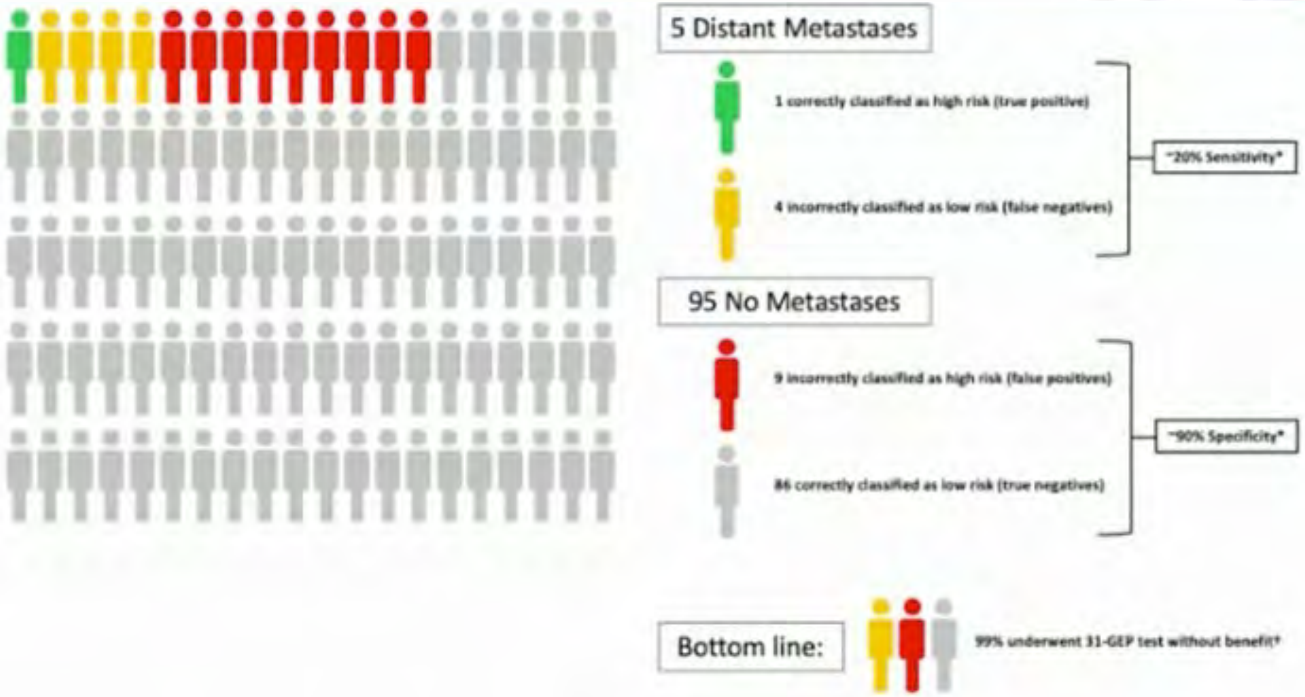
41% de pacientes fallecidos por melanoma fueron diagnosticados inicialmente como E. I-II



J Am Acad Dermatol
January 2019

Identification of patients at risk of metastasis using a prognostic 31-gene expression profile in subpopulations of melanoma patients with favorable outcomes by standard criteria

Brian R. Gastman, MD,[a] Pedram Gerami, MD,[b,c,d] Sarah J. Kurley, PhD,[c] Robert W. Cook, PhD,[c] Sancy Leachman, MD, PhD,[f] and John T. Vetto, MD[g]



2019: panel de 31 genes de riesgo

- **20% sensibilidad**: 4/5 FN
- **90% especificidad**: 9/95 FP

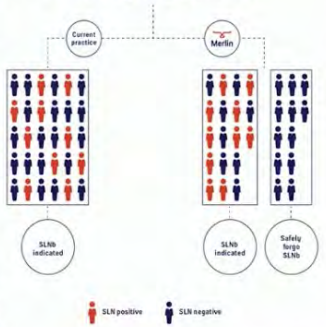
Primary cutaneous melanoma risk stratification using a clinicopathologic and gene expression model: a pilot study

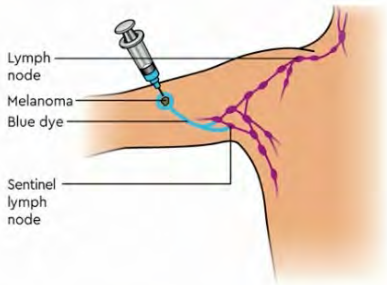
Suzette M. Arias-Mejias, MD, MS, [1,†] Enrica Quattrocchi, MD, [1,†] Dennie Tempel, PhD, [2] Mark Luna-Vargas, PhD, [2]

(a)

Gene (Protein)	Gene Function
MLANA (melanoma antigen recognized by T cells 1)	Melanosome biogenesis
GDF15 (growth/differentiation factor 15)	EMT, angiogenesis, metabolism/cachexia
CXCL8 (interleukin 8)	EMT, angiogenesis
LOXL4 (lysyl oxidase homolog 4)	EMT, angiogenesis
TGFBR1 (TGFβ receptor type 1)	EMT, angiogenesis
ITGB3 (integrin β3)	EMT, angiogenesis, cell adhesion & migration, blood coagulation
PLAT (tissue-type plasminogen activator)	EMT, blood coagulation
SERPINE2 (glia derived nexin)	EMT, blood coagulation

(b) SLNb eligible population





Int J Dermatology, Volume: 59, Issue: 11, Pages: e431-e433, First published: 09 June 2020, DOI: (10.1111/ijd.14987)

Table 2 Performance of the CP-GEP model

	T1–T3 n = 175	T1 n = 11	T2 n = 94	T3 n = 70	T4 n = 35
CP-GEP high risk	133	1	66	66	35
True positive	43	0	14	29	9
False positive	90	1	52	37	26
CP-GEP low risk	42	10	28	4	0
True negative	38	10	25	3	0
False negative	4	0	3	1	0
Sensitivity	91·5%	0	82·4%	96·7%	100%
95% CI	(80·1–96·6)		(59·0–93·8)	(83·3–99·4)	(70·1–100)
Specificity	29·7%	90·9%	32·5%	7·5%	0
95% CI	(22·5–38·1)	(62·3–98·4)	(23·1–43·5)	(2·6–19·9)	
PPV	32·3%	0	21·2%	43·9%	25·7%
95% CI	(25·0–40·7)		(13·1–32·5)	(32·6–55·9)	(14·2–42·1)
NPV	90·5%	100%	89·3%	75·0%	0
95% CI	(77·9–96·2)	(72·2–100)	(72·8–96·3)	(30·1–95·4)	

CP-GEP, Clinicopathological Gene Expression Profile; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Mulder EEAP, et al. Br J Dermatol. 2021 May;184(5):944-951.

European Journal of Cancer 182 (2023) 77–86

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

ELSEVIER

EJC

Original Research

Identification of high-risk patients with a seven-biomarker prognostic signature for adjuvant treatment trial recruitment in American Joint Committee on Cancer v8 stage I–IIA cutaneous melanoma

Immunohistochemistry based, 7-biomarker signature

S-100 staining is performed to confirm melanoma presence → Staining is performed for each of the signature's 7 markers → Based on staining percentage/intensity, each marker is scored on a 0–3 scale

Score for each marker is multiplied x co-efficient; totals are summed, normalized by 7 to generate overall **risk score** → Based on overall score, patients dichotomized into high-risk or low-risk 7-marker signature **risk categories**

Ziemer, M.; et al. Analytical Validation of an Immunohistochemical 7-Biomarker Prognostic Assay (immunoprint®) for Early-Stage Cutaneous Melanoma in Archival Tissue of Patients with AJCC v8 T2–T3 Disease. *Diagnostics* **2023**, *13*, 3096.

Cada vez más **modelos de expresión genética / inmunohistoquímica** para identificar pacientes de alto riesgo (mejor VPN y VPP)

AEDV2023 Highlights BERLIN

TRATAMIENTOS PARA MELANOMA AVANZADO

(Neo)adjuvant therapies in melanoma

2022-2023 UPDATE

Yannick Elshot MD, Dermatologist

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

Targeted Therapy for metastatic melanoma

Simone Ribero, MD, MSc, PhD
Associate Professor
Dermatology Clinic
University of Turin
Turin, Italy

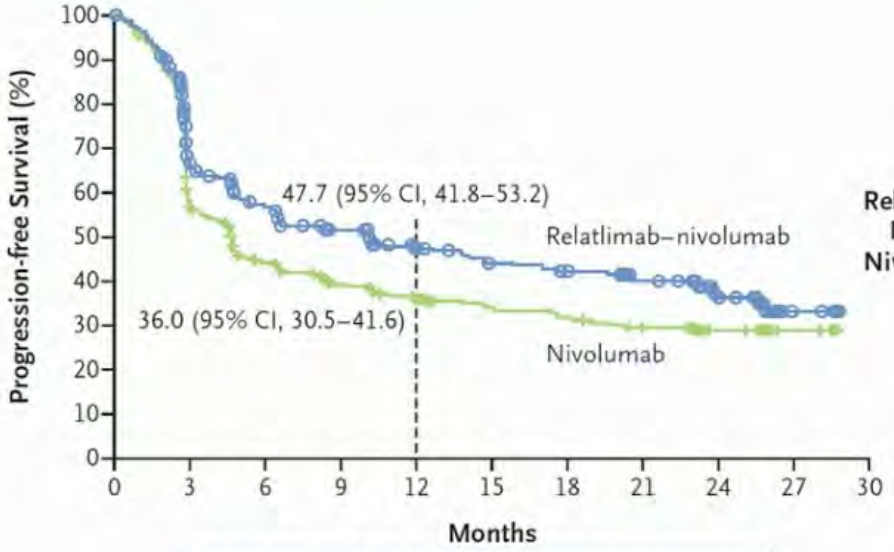
UNIVERSITAS STUDII TAURINENSIS 1404

Immunotherapy for metastatic melanoma

Prim.Priv.Doz.Dr.med.PhD
Christian Posch

The "3rd checkpoint inhibitor": anti-LAG-3 (Lymphocyte activation gene 3)

- Induces T-cell exhaustion / ↓ effector function in microenvironment
- Favorable safety profile



	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Relatlimab–Nivolumab	355	10.12 (6.37–15.74)
Nivolumab	359	4.63 (3.38–5.62)

Hazard ratio for progression or death, 0.75 (95% CI, 0.62–0.92)
P=0.006

↑ Efficacy ≥ 1% LAG-3 expression

Nueva inmunoterapia: **RELATLIMAB (anti-LAG-3)**

Ensayos clínicos prometedores en combinación con Nivolumab

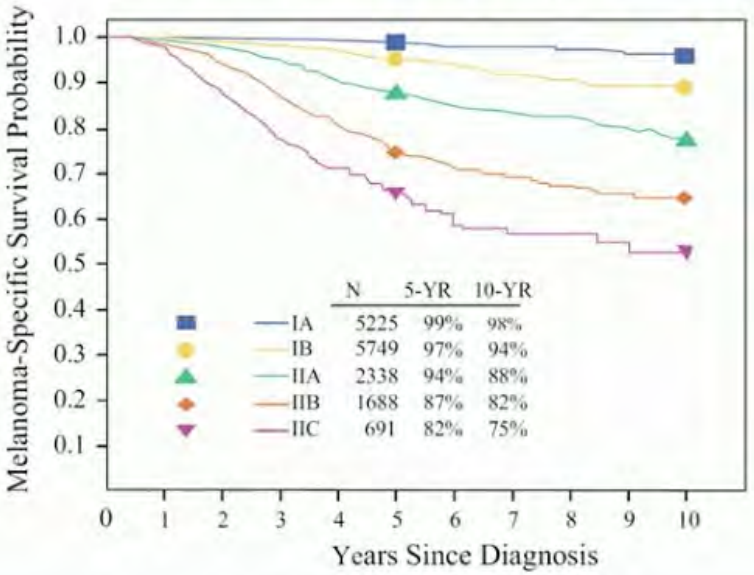
RELATIVITY-047

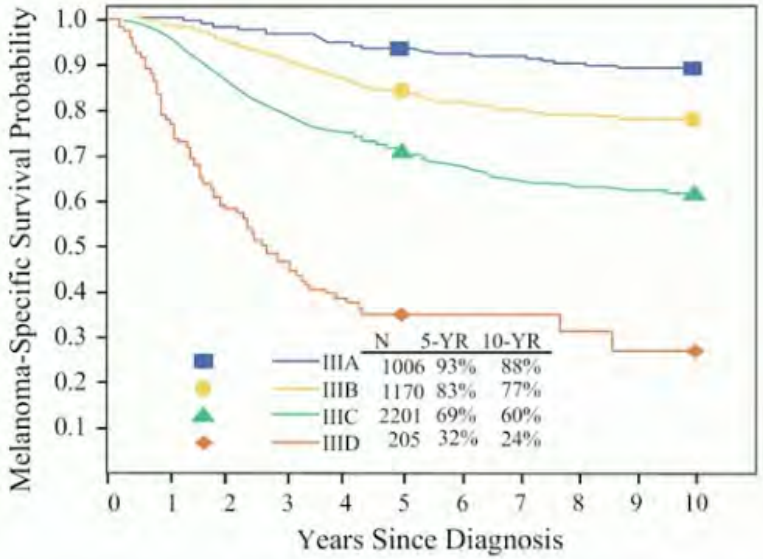
Mullick, et al. J Am Acad Derm. 2023
Tawbi, et al. N Enlg J Med. 2022

Adjuvant in stage ≤II

- Stage I/II SLNB-negative melanoma
- Low(er) individual risk; but significant absolute numbers
- Heterogenous group → 40% recurrent melanoma/mortality

¿Adyuvancia en estadios I-II?
Grupo heterogéneo: necesidad de encontrar nuevas formas de estratificar el riesgo

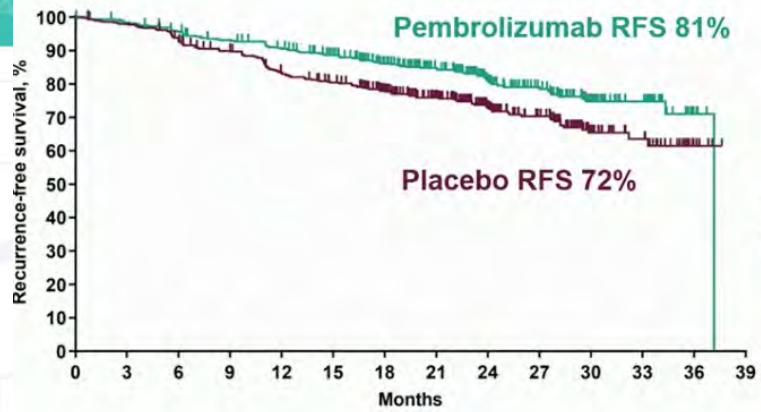


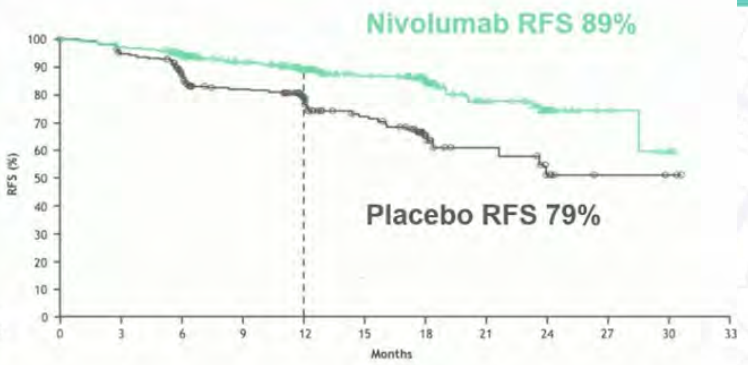


Stage	10-year survival
IIA / IIIA	88
IIB	82
IIIB	77
IIC	75
IIIC	60
IIID	24

Gershenwald, et al. CA. 2017
Lee, et al. Eur J Cancer, 2023
Gershenwald, et al. Ann Surg Oncol. 2018

Stage II – Adjuvant anti-PD-1





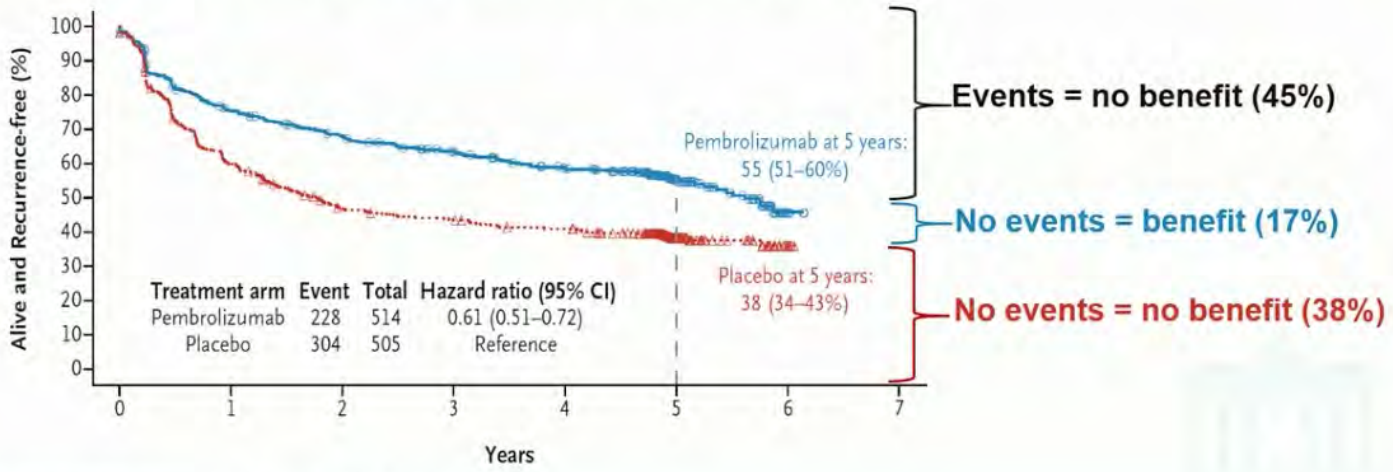
2-year survival
- RFS: HR 0.64
- DMFS: 6% absolute reduction

1-year survival
- RFS: HR 0.42
- DMFS: 5% absolute reduction

Luke, et al. Lancet. 2022
Long, et al. Lancet Oncol. 2022
Khattak, et al. Eur J Cancer. 2022
Long, et al. WCH23 Dermatology Conference - Poster

Resected IIB-C [AJCC-8]

KEYNOTE-716/ CheckMate 76K

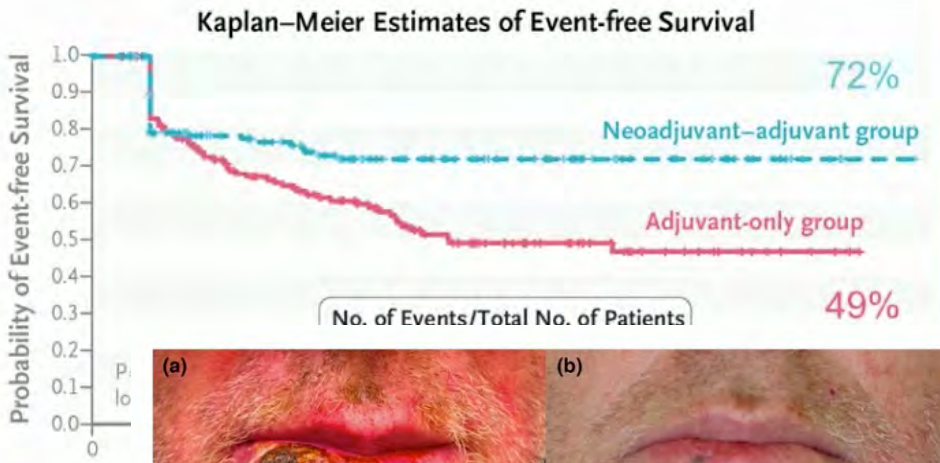


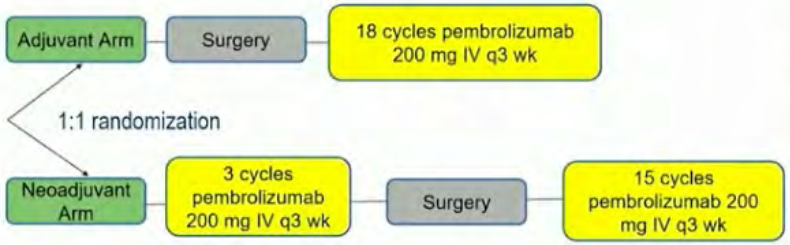
Reducción de las recaídas en estadios II tratados con anti-PD1 adyuvante

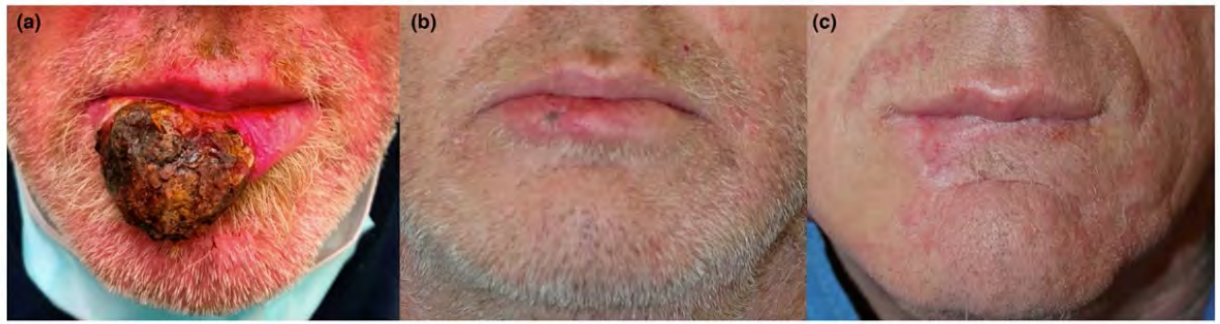
Sin embargo, solo es beneficioso en un 17% de los pacientes

Neo+adjuvant vs. adjuvant

¿NEO Adyuvancia mejor que sólo adyuvancia?
Mayor supervivencia libre de enfermedad
Igual efectos adversos





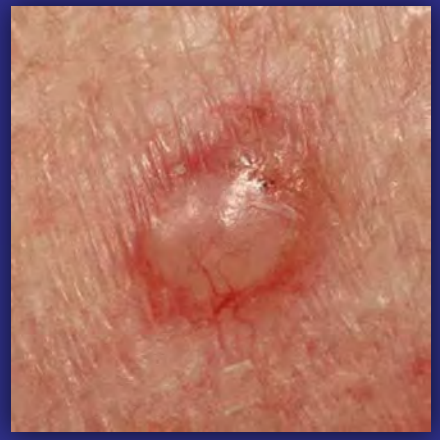


Patel, et al. N Engl J Med. 2023
Garbe, et al. Nat Med. 2023

Resectable stage IIIB-D & oligo

Desmoplastic melanoma – Stage IIC (pT4N0M0)

NOVEDADES EN CARCINOMA BASOCELULAR



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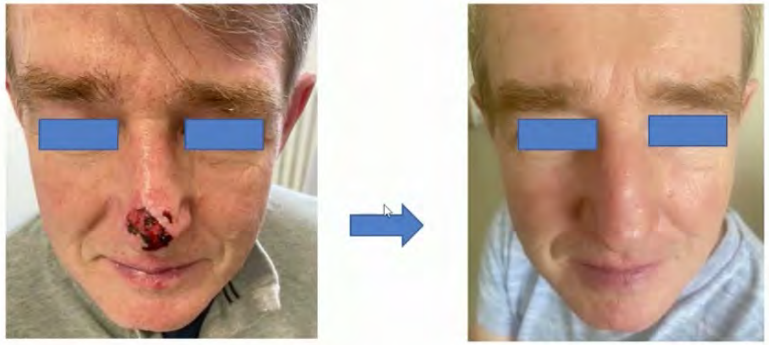
TRATAMIENTOS PARA CBC AVANZADO

Non-Surgical Treatment of BCC



Pr Boussemart Lise, MD, PhD
Department of Dermatology, CHU de Nantes, France
INCIT research lab, INSERM 1302

EMERGING TREATMENTS OF ADVANCED BCC

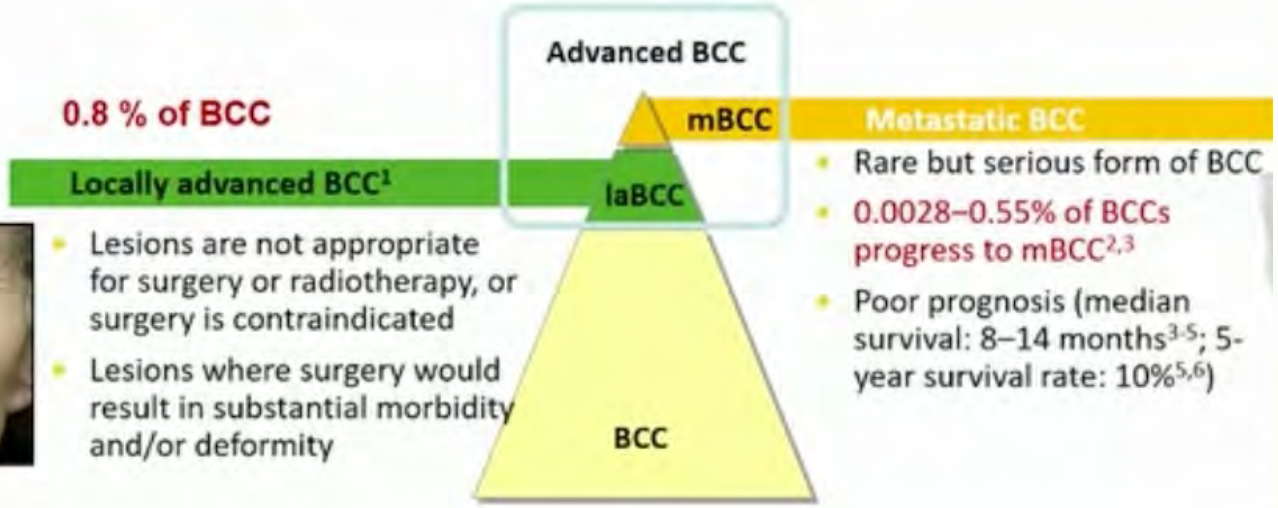
Alexander J. Stratigos, MD
Professor and Chair
1st Dept of Dermatology-Venereology
Andreas Sygros Hospital
University of Athens
Athens, Greece

NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS
SCHOOL OF MEDICINE

Melanoma and Skin Cancer Unit

Advanced BCC

- Advanced (locally advanced or metastatic) BCC occurs in a small proportion of patients who have lesions that are not appropriate for surgery or radiotherapy, or for whom surgery would result in substantial deformity[1]

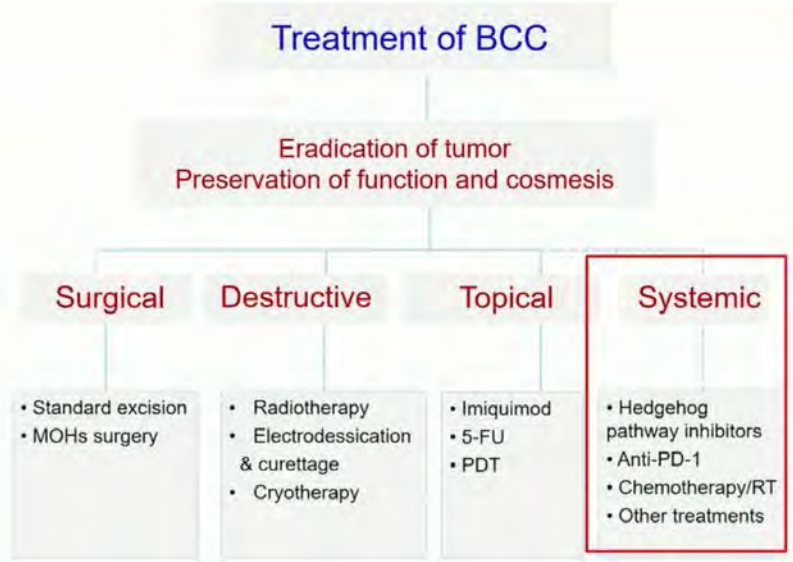


- Lesions are not appropriate for surgery or radiotherapy, or surgery is contraindicated
- Lesions where surgery would result in substantial morbidity and/or deformity

- Rare but serious form of BCC
- 0.0028–0.55% of BCCs progress to mBCC[2,3]
- Poor prognosis (median survival: 8–14 months[3-5]; 5-year survival rate: 10%[5,6])

0,8% DE CBC SON LOCALMENTE AVANZADOS

Tratamientos: inhibidores de Hedgehog, inmunoterapia, quimio/radio, otros



Efficacy of HH inhibitors

Outcome	Vismodegib (150 mg/day)			Sonidegib (200 mg/day)	
	ERIVANCE study (39-month update)[29]	STEVIE study (median follow-up: 17.9 m)[28]		BOLT study (30- month and 42-month update)[30,34]	
	n =63 laBCC	n =1119 laBCC	n =1215 total	n =66 laBCC	n =79 total
Investigator-assessed ORR, n (%)	38 (60.3)	738 (68.5)	769 (66.2)	47 (71.2%)[34]	NR
CR	20	360 (33.4)	364 (31.4)	6 (9.1)	
PR	18	378 (35.1)	405 (34.9)	41 (62.1)	
SD	15	270 (25.1)	309 (26.6)	13 (19.7)	
PD	6	21 (1.9)	30 (2.6)	1 (1.5)	
Median duration of response in responders, m (95% CI)	26.2 (9.0-37.6)	23 (20.4-26.7)	22.7 (20.3-24.8)	26.1 (central review) [30,34]	NR
Median treatment duration, m (range)	12.7 (1.1-47.8)	NR	8.6 (0-44)	NR	11.0 [30]

* Half of patients will discontinue HHI after approximately 8 to 12 months

Desinioti, Stratigos. Dermatology Practical & Conceptual 2023

Eficacia inhibidores de HH:

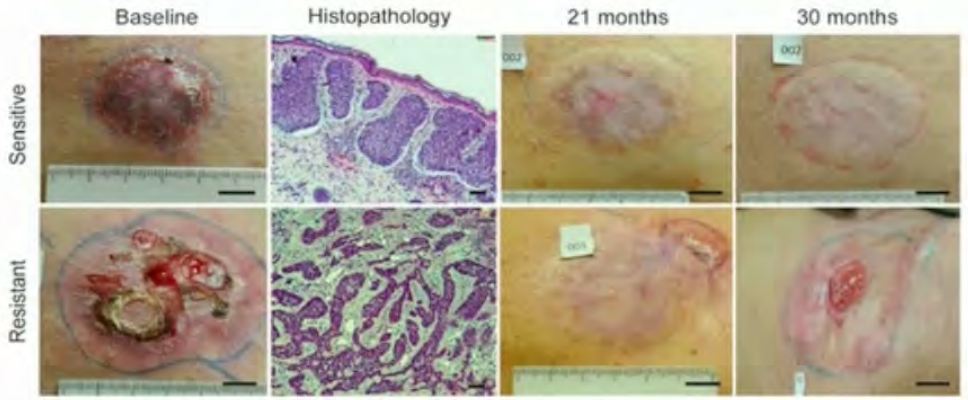
- Vismodegib: **60-68%** respuesta (completa o parcial)
- Sonidegib: **71%** respuesta (completa o parcial)

PROBLEMAS:

- **Efectos adversos** (muy frecuentes, casi nunca graves): alopecia, disgeusia, calambres, pérdida de peso
- **Pérdida de respuesta**

BCC: resistance to HHIs

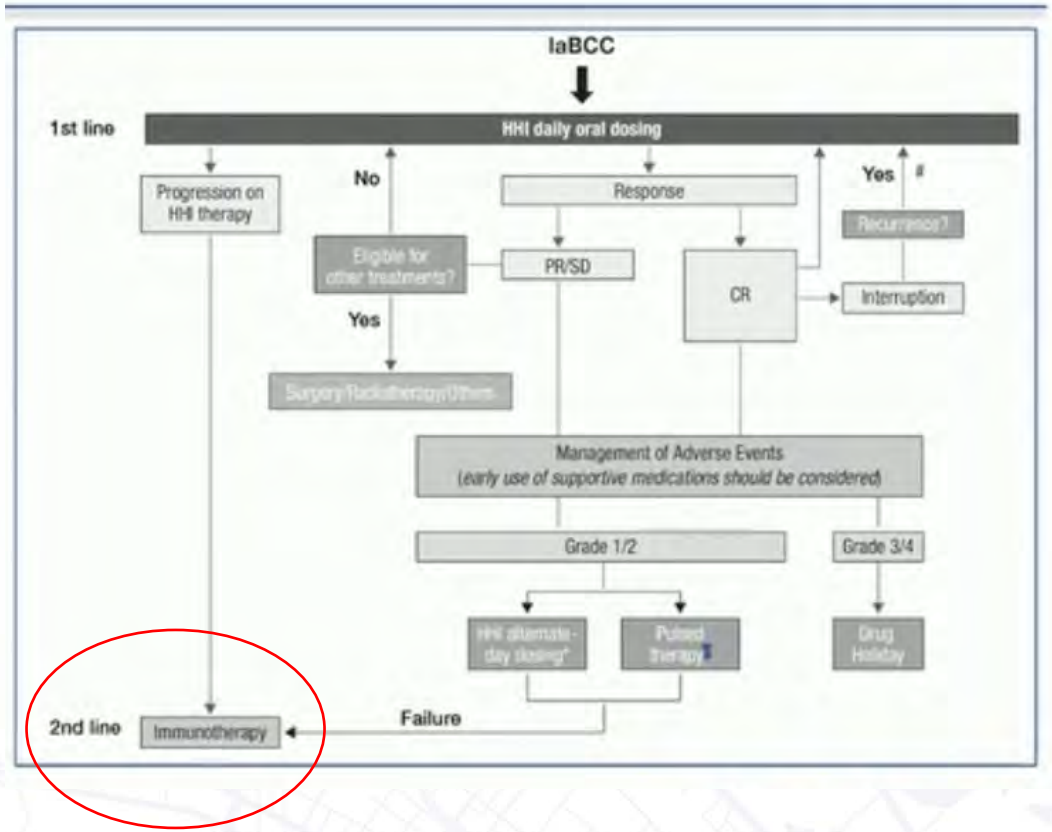
- **Primary resistance:** tumor never responds to HHI
- ✓ ~ 50% of patients with aBCC
- **Secondary (acquired) resistance:** tumor regrowth during HHI treatment after initial response
- ✓ In 20% of patients with aBCC during the first year of HHI
- ✓ Caused mainly by acquired *SMO* mutations



Atwood et al. Cancer Cell 2015;27:342-53

Resistencia:

- **Primaria** (hasta 50%)
- **Secundaria** (20% durante el primer año de tratamiento, por mutaciones en SMO)



Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy: an open-label, multi-centre, single-arm, phase 2 trial

Clinical response in laBCC

Cemiplimab: peores respuestas que en CEC

- Respuesta completa o parcial: **31%**
- Control de la enfermedad (ORR + enfermedad estable): **80%**

Trials with anti-PD-1 immunotherapy for aBCC

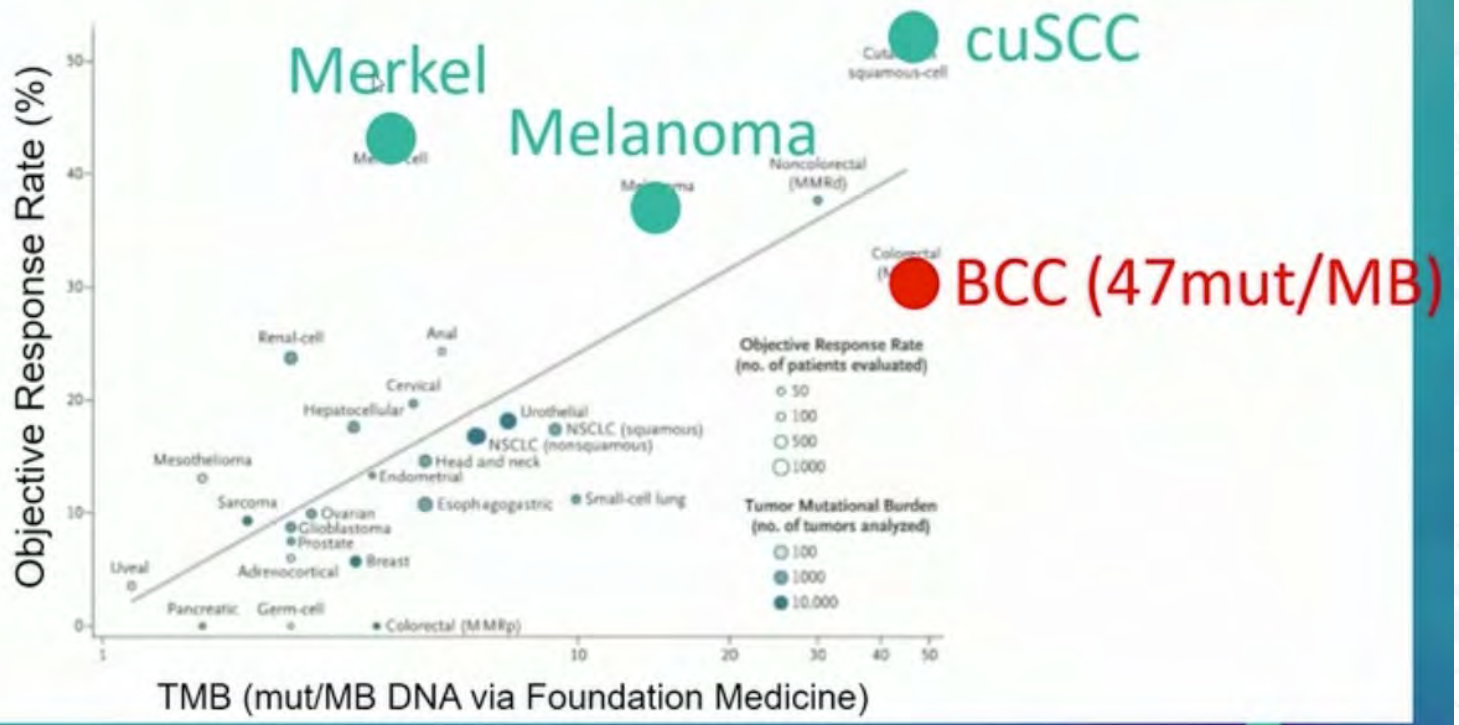
	Stratigos, 2021[64]	Veron, 2022[66]
Anti-PD-1 agent	Cemiplimab	Nivolumab
N	84 laBCC	29 laBCC and 3 mBCC
Prior systemic treatment		
HHI (vismodegib or sonidegib)	All	All
Chemotherapy	NR	17 (53%)
Median FU, m	15	17
ORR (ICR), n (%)	26 (31%)	**At 12 weeks** 21.9%
Complete Response	5 (6%)	1 (3.1%)
Partial Response	21 (25%)	6 (18.8%)
Stable Disease	41 (49%)	14 (43.8%)
Progressive Disease	9 (11%)	11 (34.3%)
Not evaluable	8 (10%)	
Median time to response (IQR), m	4.3 (4.2, 7.2)	5.3
Disease control rate, n (%)	67 (80%)	21 (65.7%)
Duration of response in responders		
Median	Not reached	13.8 m
≥ 12 months	11 (46%)	
Estimated duration of response at 12 months (95% CI)	85% (61-95)	
Estimated 1-year PFS (95%C CI)	57% (44-67)	
Estimated 2-year OS (95%C CI)	80% (63-90)	
OS, median	Not reached	
Discontinued	52 (62%)	
Median treatment duration, w (IQR)	47 (27-80)	32

Veron et al. Eur J Cancer 2022;177:103-111

Nivolumab: peores respuestas que cemiplimab

- Respuesta completa o parcial: **21.9%**
- Control de la enfermedad (ORR + enfermedad estable): **65.7%**

Pan-cancers correlation between TMB and response to anti PD-1 (Yarchoan et al., NEJM 2019)

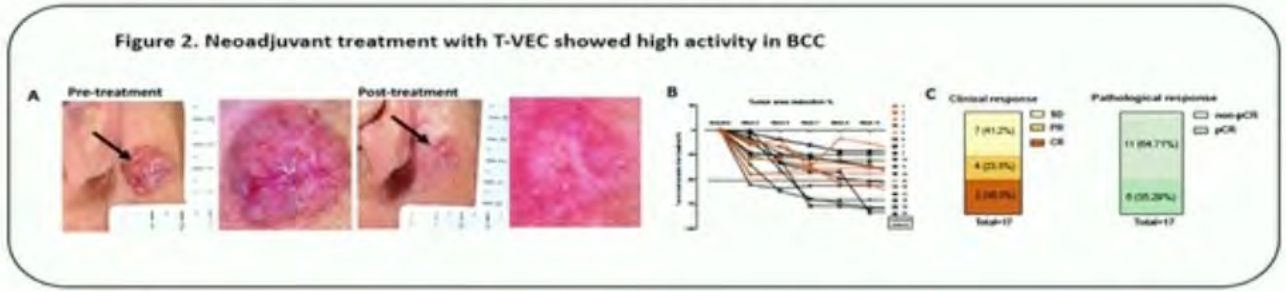


En general, a más número de mutaciones, mayor respuesta a inmunoterapia. **No se cumple en el CBC**

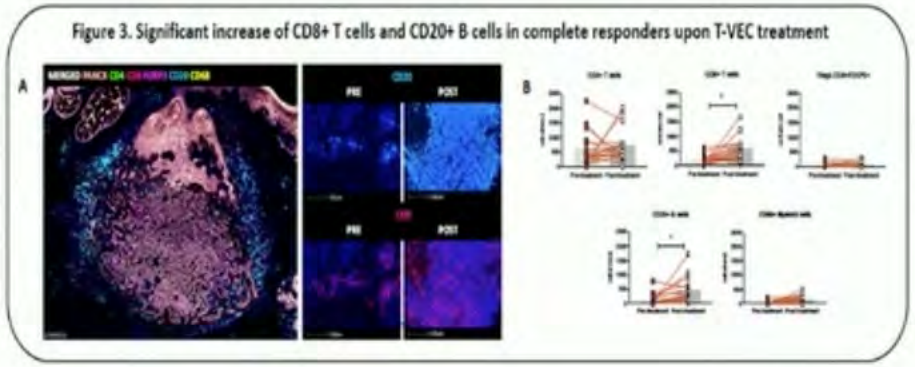
Causa: expresión disminuida de MHC-1, que llevan a un ”escape inmunitario”

MEDICAL UNIVERSITY OF VIENNA

Efficacy and tolerability of neoadjuvant treatment with T-VEC in difficult to resect primary basal cell carcinoma: a phase II clinical trial (NeoBCC)



Avoid flap or graft: 52.9% ORR 59% Pathologic complete response 35.3%



Increase of CD8⁺ T-Cells and CD20+ B-Cells in patients with a complete pathological response

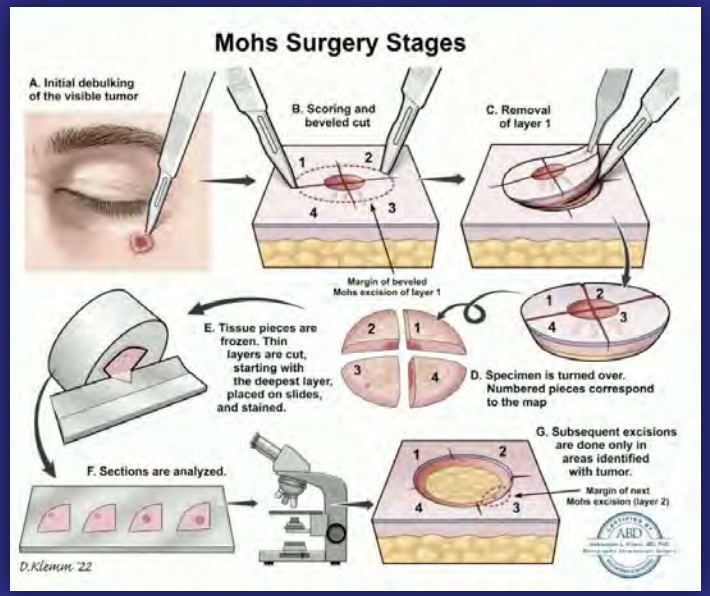
Ressler et al, 2022

T-VEC: Talimogene Laherparepvec

Virus herpes modificado que se inyecta de forma intratumoral

Respuesta **59%** (completa 35.3%)
Evitan cirugías complejas en 52.9%

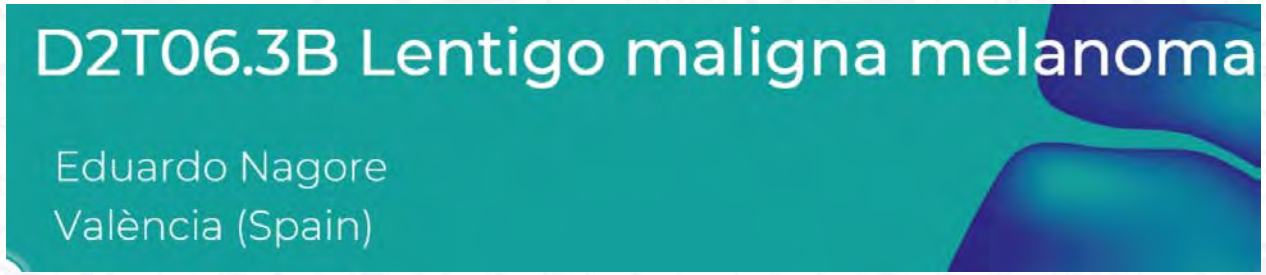
NOVEDADES EN CIRUGÍA DE MOHS



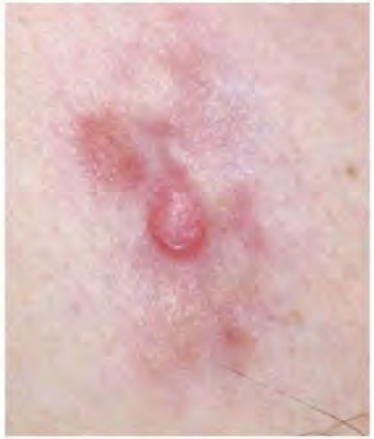
BERLIN

11-14 OCTUBRE

REVISIÓN DE LAS INDICACIONES



DERMATOFIBROSARCOMA PROTUBERANS



DFSP typically has subclinical spread

Table 2. Recurrences and surgical treatments of DFSP during follow-up between 2000 and 2022

DFSP patients 2000-2022 *n* = 394	
Follow-up, in years, mean (95% CI)	
After all primary treatments	9.1 (8.4-9.7)
After WLE	10.8 (9.9-11.6)
After (slow) MMS	6.5 (5.9-7.2)
Recurrences, *n* (%)	
0	355 (90)
1	32 (8)
≥2	7 (2)
Recurrences	
After WLE	50
Negative resection margins	9
Positive resection margins	33
Unknown resection margins	8
After (slow) MMS	0
Time until recurrence, in years, mean (95% CI)	
Total recurrence group	5.4 (3.5-7.3)
After negative resection margins	5.3 (1.1-9.6)
After positive resection margins	5.3 (2.7-8.0)
After unknown resection margins	5.6 (1.6-9.6)
Surgical treatments during follow-up[a], *n* (%)	
1	152 (39)
2	193 (49)
3	34 (9)
≥4	15 (4)

394 pacientes
Recurrencias:
- Tras escisión amplia: **18%** (el 10% tras márgenes libres)
- Tras Mohs: **0%**

El **60%** de pacientes con escisión amplia requirieron más de 1 intervención

Recomienda realizar ***slow-mohs*** **= mohs en diferido** (tamaño)

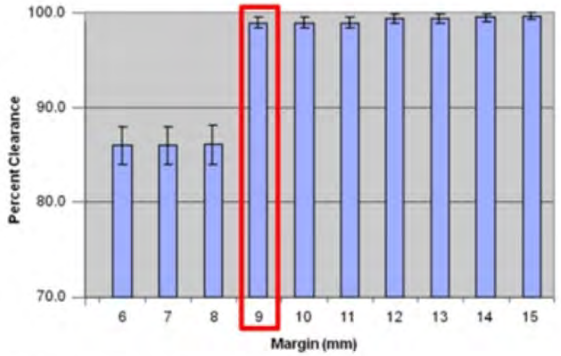
LENTIGO MALIGNO

Surgical margins for melanoma in situ

Joy H. Kunishige, MD,[a] David G. Brodland, MD,[b] and John A. Zitelli, MD[b]

MMis
1072 patients with 1120 tumor
Mohs surgery, frozen sections
-H&E
-HMB-45 (1990-2002)
-MART-1 (2002-)

Recurrence rate:
0.3% at 5 years
0.8% at 10 years



J Am Acad Dermatol 2012;66:438-44.

Cutaneous head and neck melanoma treated with Mohs micrographic surgery

Gregory M. Bricca, MD,[a] David G. Brodland, MD,[b] Dianxu Ren, MS,[c] and John A. Zitelli, MD[c]

N = 412
(261 cases additionally immunostained with HMB-45)

Local reccurrence rates:

Mohs surgery (N=331) = 0.3%

Conventional surgery/0.5 cm (N=81) = 20%

Cumulative margins required for complete excision

	MIS (%)
6 mm	295 (89.1)
9 mm	326 (98.5)
12 mm	327 (98.8)
24 mm	331 (100.0)

J Am Acad Dermatol 2005;52:92-100.

Recurrence rate of lentigo maligna after micrographically controlled staged surgical excision*

K. de Vries,[1,2] K. Greveling,[2] L.M. Prens,[2] K. Munte,[3] S. Koljenović,[4] M.B.A. van Doorn[2] and E.P. Prens[2]

N = 100 cases

Table 2 Number of stages and cumulative margin needed to achieve free margins

Number of stages	Cumulative margin (mm)	Free margins (%)
1	3	49
2	8	88
3	13	97
4	18	100

5% invasive component

4% recurred at 5 yrs

British Journal of Dermatology (2016) **174**, pp588–593

Mohs micrographic surgery for melanoma: A prospective multicenter study

Patrick M. Ellison, MD,[a] John A. Zitelli, MD,[b] and David G. Brodland, MD[b]

JAAD

J Am Acad Dermatol 2019;81:767-74

Prospective, multicenter
April 2013 – August 2014
MMS for melanoma
- 562 melanomas (518 patients)
Mohs: H&E + MART-1

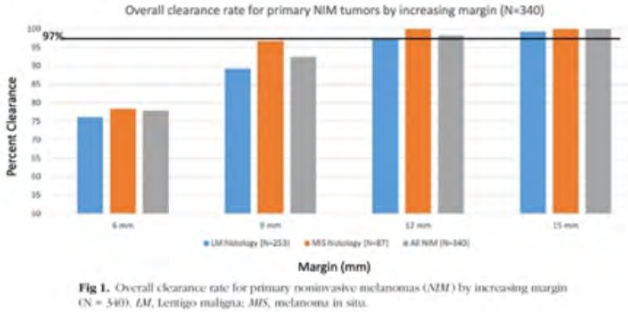


Fig 1. Overall clearance rate for primary noninvasive melanomas (*NIM*) by increasing margin (N = 340). *LM*, Lentigo maligna; *MIS*, melanoma in situ.

Dificultad de alcanzar márgenes libres con la extirpación amplia recomendada (5 mm)

Mohs en melanomas no invasivos de CyC (Zitelli)

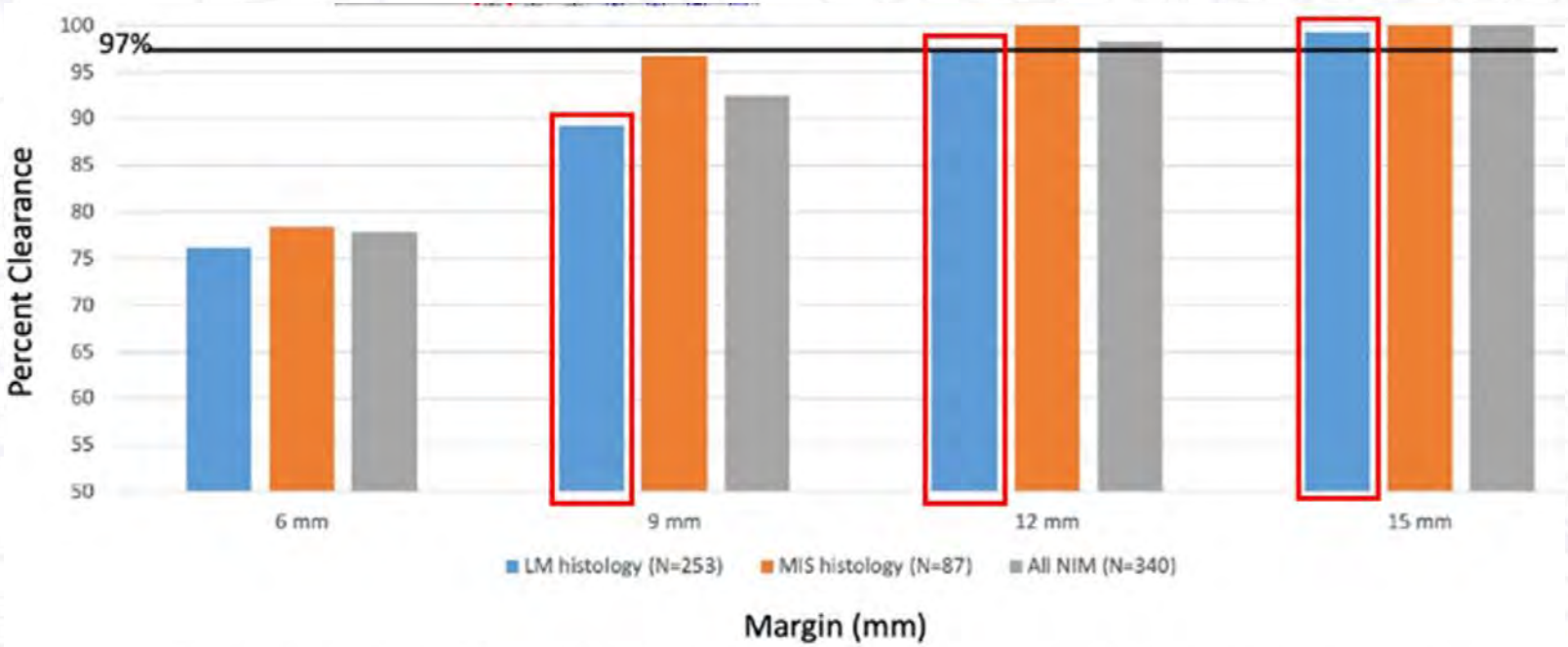


Fig 1. Overall clearance rate for primary noninvasive melanomas (*NIM*) by increasing margin

Margen necesario para alcanzar curación en LM:

- 6 mm: cura < 80%
- 9 mm: cura < 90%
- **12 mm: cura 97%**

nsive **NCCN Guidelines Version 2.2023**
Melanoma: Cutaneous

NC

PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

Tumor Thickness	Recommended Clinical Margins[b]
In situ[a]	0.5–1.0 cm
≤1.0 mm	1.0 cm (category 1)
>1.0–2 mm	1–2 cm (category 1)
>2.0–4 mm	2.0 cm (category 1)
>4 mm	2.0 cm (category 1)

- Margins may be modified to accommodate individual anatomic or functional considerations.
- Consider histologic margin assessment prior to reconstruction and closure.

European consensus-based interdisciplinary guideline for melanoma. Part 2: Treatment - Update 2022

Claus Garbe [a,*], Teresa Amaral [a], Ketty Peris [b,c], Axel Hauschild [d], et al.

Recommendation 16

Microscopically controlled surgery	Consensus-based recommendation
GCP	In some melanoma subtypes, such as lentigo maligna melanoma, genital and acral melanomas, and microscopically controlled surgery can be used to spare tissue and ensure complete resection.
	Consensus rate: 90%; 2 abstentions

Benefit of Mohs Micrographic Surgery Over Wide Local Excision for Melanoma of the Head and Neck: A Rational Approach to Treatment

Addison M. Demer, MD, Karl K. Vance, MD, Nikoo Cheraghi, MD, Hilary C. Reich, MD, and Peter K. Lee, MD, PhD*

10-year retrospective study
388 patients (389 tumors):
- LM: 229
- LMM: 160

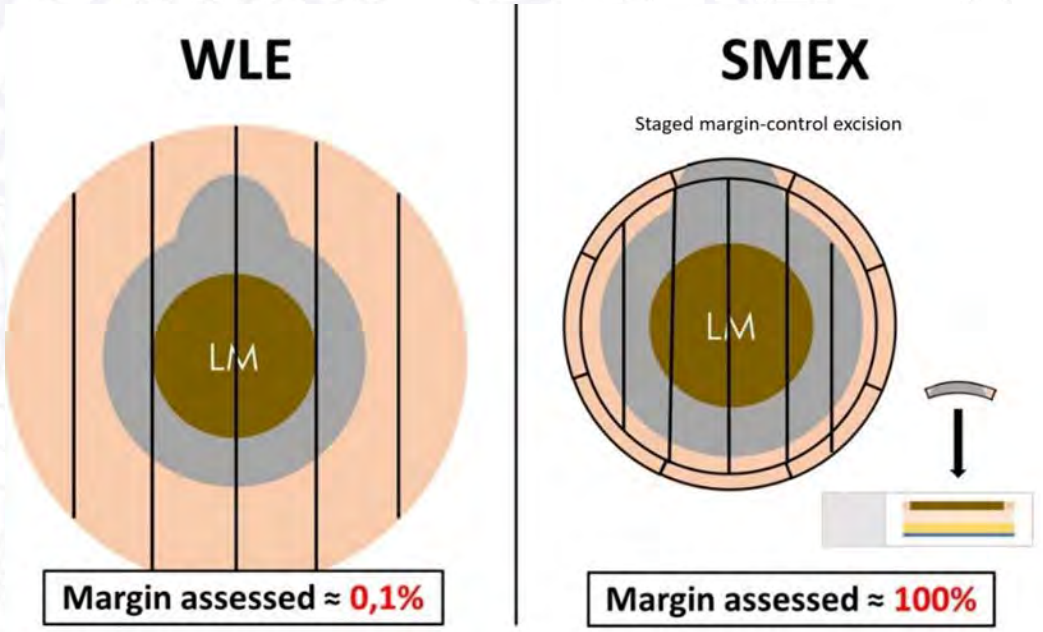
MMS (292) vs. WLE (97):
WLE was more frequently used in thick tumors or with histologic risk factors (TMR, ulceration, satellitosis, desmoplasia).
Average #stages: 1.4

TABLE 2. Local Recurrence Outcomes by Tumor Subgroup

Stage/Subgroup	Outcome Measure	Wide Local Excision (N = 97)	Mohs Micrographic Surgery (N = 292)	p (HR)
All tumors (*N* = 389)	Local recurrence, *n* (%)	7 (7%)	2 (0.7%)	0.0012*
	Median time to recurrence, mo.	12.6	16.5	0.0102 (12.4)*
In situ (*N* = 228)	Number treated (%)	8 (8%)	221 (76%)	—
	Local recurr	WLE	MMS	0.1020
	Median tim recurrence	6-13%	0-0.9%	0.0148 (31.8)
Invasive (≤0.8 mm) (*N* = 66)	Number tre			—
	Local recurr			0.0634
	Median tim recurrence, mo			0.0634
Group B (>0.8 mm) (*N* = 94)*	Number treated (%)	72 (74%)	22 (8%)	—
	Local recurrence, *n* (%)	4 (6%)	0	0.5697
Group A (MIS + ≤0.8 mm) (*N* = 294)†	Number treated (%)	25 (26%)	269 (92%)	—
	Local recurrence, *n* (%)	3 (12%)	2 (0.7%)	0.0049*

*Group B defined as invasive tumors with depth >0.8 mm.
†Group A defined as in situ tumors and tumors with depth ≤0.8 mm.
MIS, melanoma in situ.

Dermatol Surg 2019;45:381–389



Mohs sugery (frozen)

- Rapid section
- Limited by poor cytological definition
- Depends heavily on observer experience.
- Can be improved with MART-1 (16' protocol) or MITF (32' protocol), but false negative rate could increase.

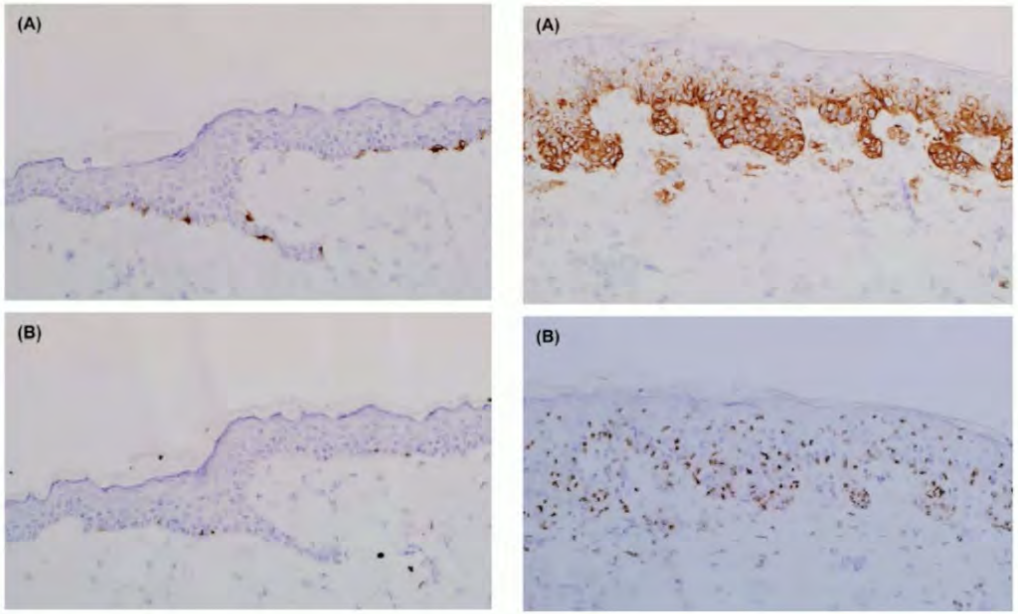
Staged surgical excision

- Variant of slow Mohs
- 90° incision (adequate as the lateral margin is what really matters)
- Paraffin: H&E ± immunohistochemistry
- Time between stages varies (2-7 days)

Mohs clásico (congelación)
VS
Mohs diferido y variantes (Spaguetti)

Comparison of MITF and Melan-A Immunohistochemistry During Mohs Surgery for Lentigo Maligna-Type Melanoma In Situ and Lentigo Maligna Melanoma

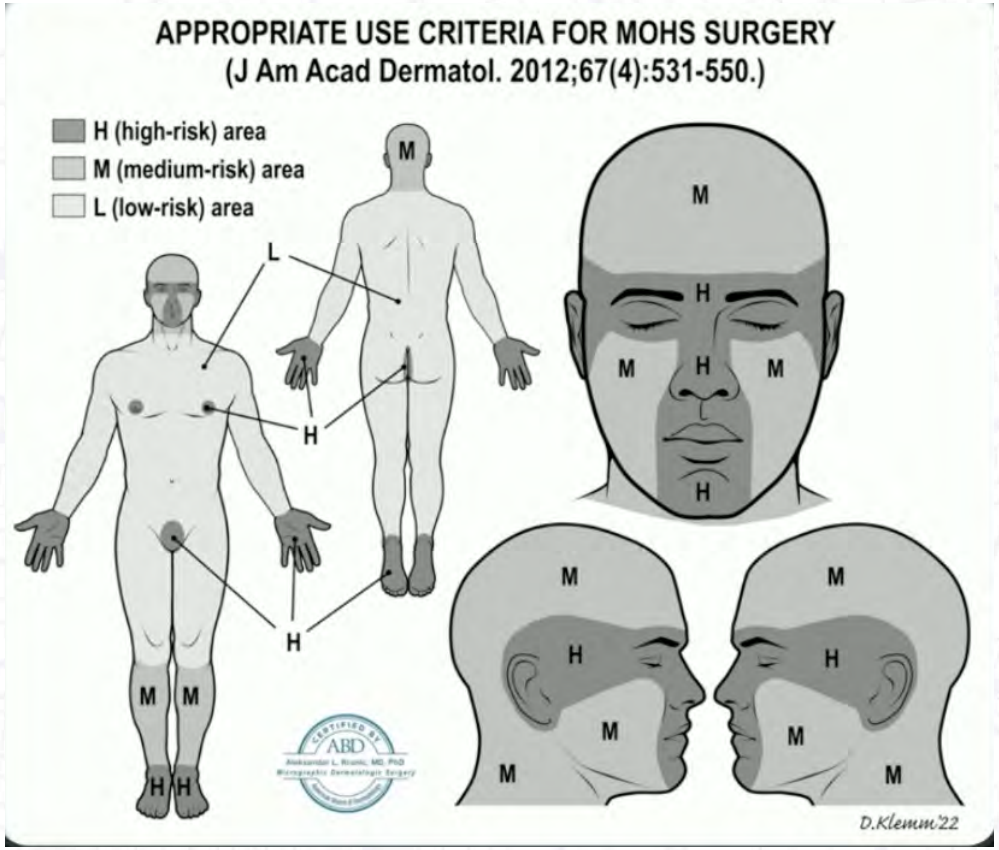
Kevin N. Christensen, MD, Phillip C. Hochwalt, MD, Thomas L. Hocker, MD, Randall K. Roenigk, MD, Jerry D. Brewer, MD, Christian L. Baum, MD, Clark C. Otley, MD, and Christopher J. Arpey, MD



- MART-1/Melan-A:
  - stains melanosomes
  - can be found in keratinocytes
  - A high number of MART-1 positive melanocytes are normally present in chronically sun-exposed skin
- MITF or SOX10:
  - Nuclear staining
  - Very helpful when quantifying the number of intraepidermal melanocytes

Dermatol Surg 2016;42:167–175

CARCINOMA BASOCELULAR



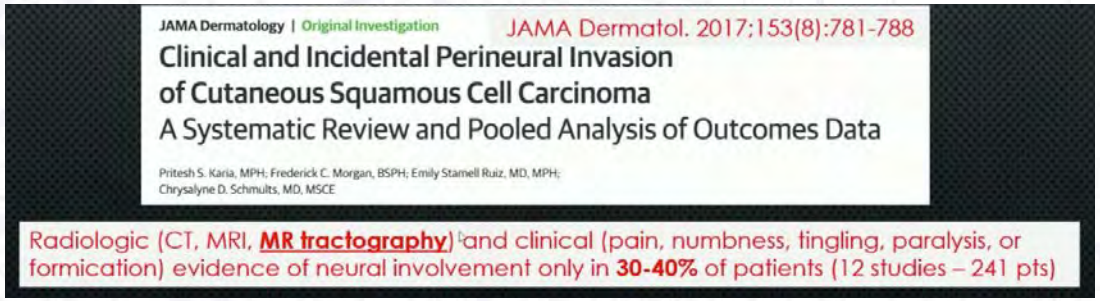
FEATURES	LOW RISK	HIGH RISK
LOCATION/SIZE	Area L< 20 mm Area M<10 mm	Area L>20 mm Area M>10 mm **Area H – any size**
BORDERS	Well defined	Ill defined
PRIMARY VS. RECURRENT	Primary	Recurrent
IMMUNOSUPPRESSION	No	Yes
SITE OF PRIOR RADIATION OR CHRONIC INFLAMMATION	No	Yes

FEATURES	LOW RISK	HIGH RISK
GROWTH PATHERN	SUPERFICIAL	MIXED INFILTRATIVE
	NODULAR	MICRONODULAR
	KERATOTIC	SCLEROSING (MORPHEAFORM)
	INFUNDIBULOCYSTIC	METATYPICAL (BASOSQUAMOUS)
	FIBROEPITHELIOMA PINKUS	PLEOMORPHIC
PERINEURAL INVASION	NO	YES

CARCINOMA ESPINOCELULAR

FEATURES	LOW RISK	HIGH RISK
Rapidly growing tumor	NO	YES
Neurologic symptoms	NO	YES

FEATURES	LOW RISK	HIGH RISK
DIFFERENTIATION	WELL-DIFFERENTIATED	POORLY - DIFFERENTIATED
DEPTH	CLARK I-III, < 2 mm	CLARK IV-V, > 2 mm
AGGRESSIVE HISTOLOGIC SUBTYPE	NO	YES
PERINEURAL INVASION, INTRAVASCULAR, INTRALYMPHATIC SPREAD	NO	YES



Invasión perineural: evidencia clínica o radiológica solo en el 30-40% de los pacientes con IPN > 0.1 mm

Squamous cell carcinoma of the nail and Mohs

Dermatol Surg 2020;46:725–732

Mohs Micrographic Surgery as the Standard of Care for Nail Unit Squamous Cell Carcinoma

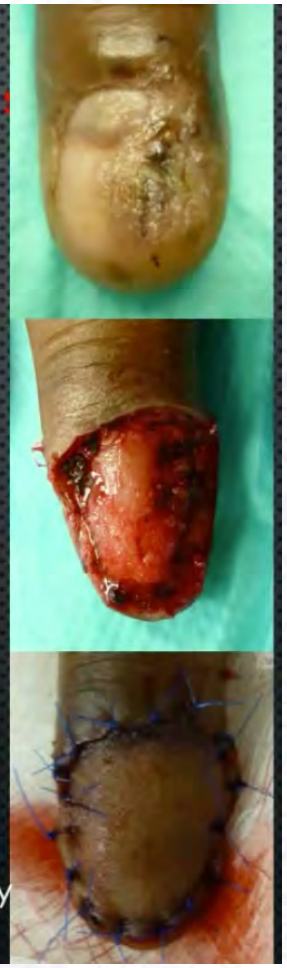
Darlene Gou, MD, Rajiv I. Nijhawan, MD, and Divya Srivastava, MD*

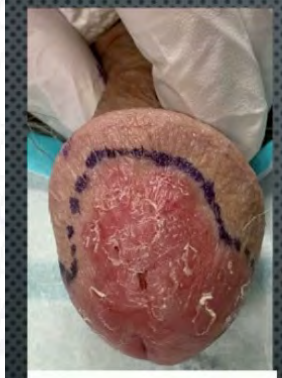
Forty-two cases of nail unit SCC w Mohs
Recurrences in 3 patients **(7.1%).**
Recurrent cases were treated with MMS.
No cases of distant metastases, subsequent recurrence, or death.
Two of 3 recurrences occurred in patients with histologic features of verruca vulgaris

31. Dika E, Fanti PA, Patrizi A, Misciali C, Vaccari S, Piraccini BM. Mohs Surgery for Squamous Cell Carcinoma of the Nail Unit: 10 Years of Experience. Dermatol Surg. 2015;41(9):1015–1019

MMS
3,5-4%

Conventional surgery
28.5-52.6%





• With Squamous cell carcinoma of the penis (Figure 1), without Mohs surgery, there would be unnecessary sacrifice of the penile tissue, often resulting in hemi-amputation, or partial resection (removal) of the penis.

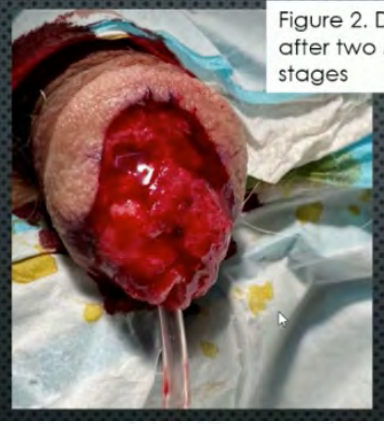
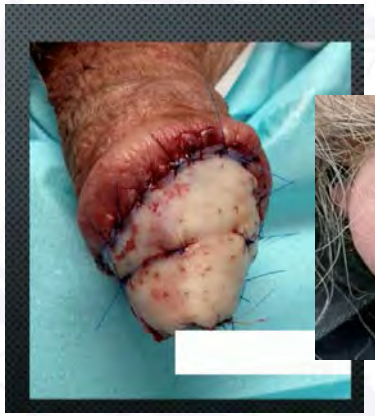
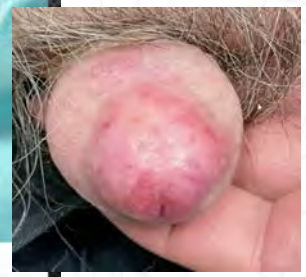
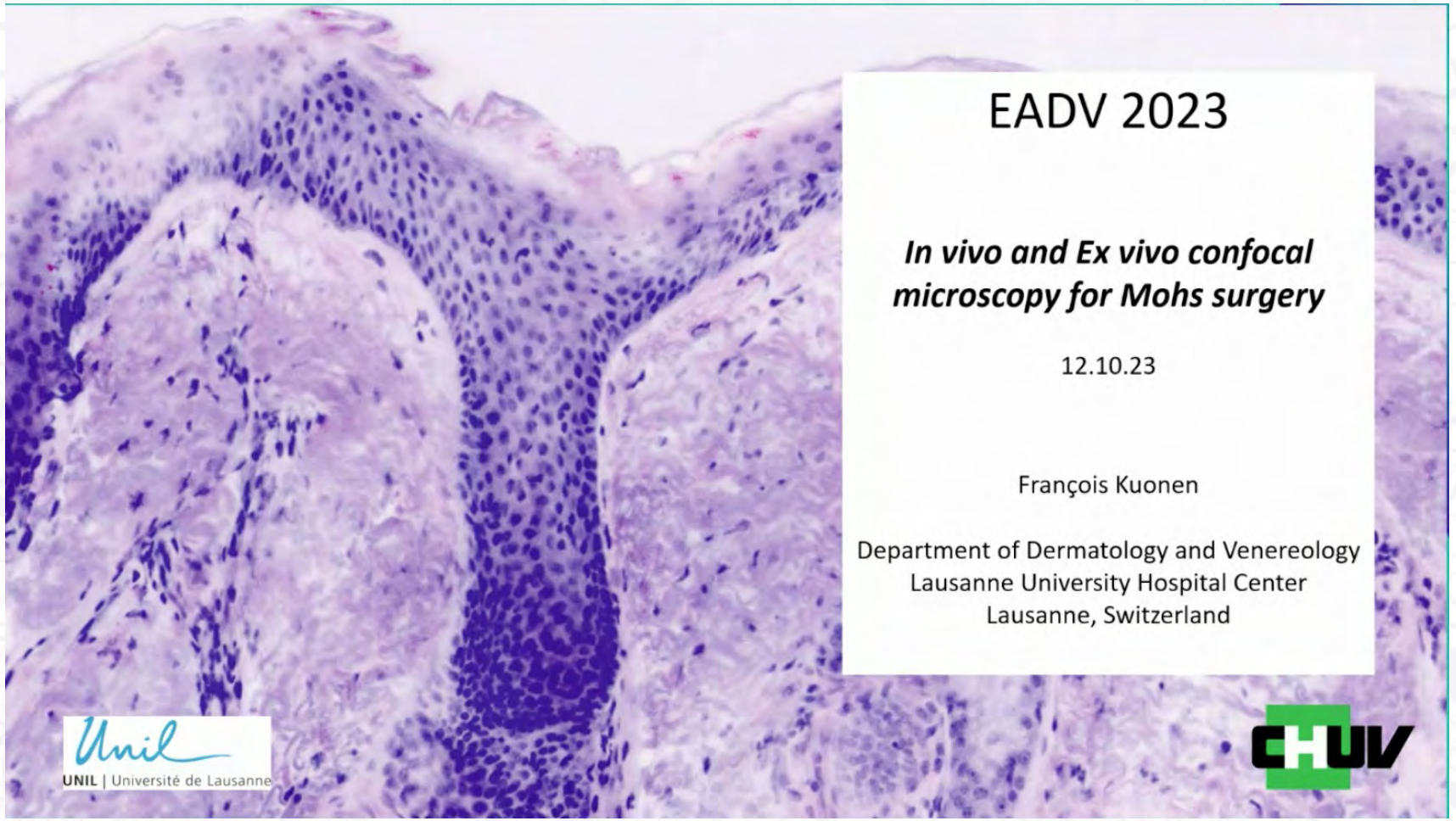


Figure 2. Defect after two Mohs stages





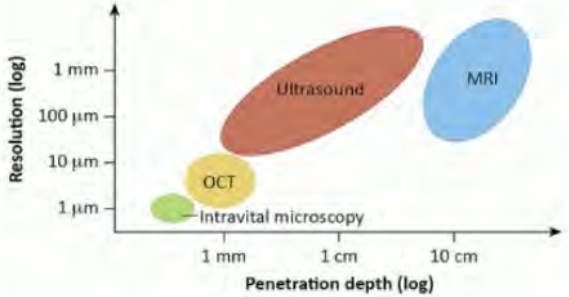
1ª elección en localizaciones especiales: UÑA, GENITALES (evita amputación)


EADV 2023
In vivo and Ex vivo confocal microscopy for Mohs surgery
12.10.23
François Kuonen
Department of Dermatology and Venereology
Lausanne University Hospital Center
Lausanne, Switzerland
UNIL | Université de Lausanne
CHUV

Confocal microscopy for Mohs – different settings

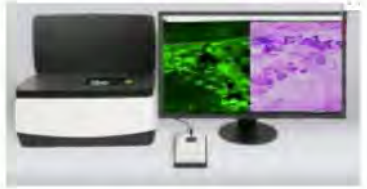
IN VIVO

- Pre-operative
- Lateral margins
- Lentigo maligna, (basal cell carcinoma)



EX VIVO

- Pre-operative & intra-operative
- Lateral and deep margins
- Basal cell carcinoma, squamous cell carcinoma

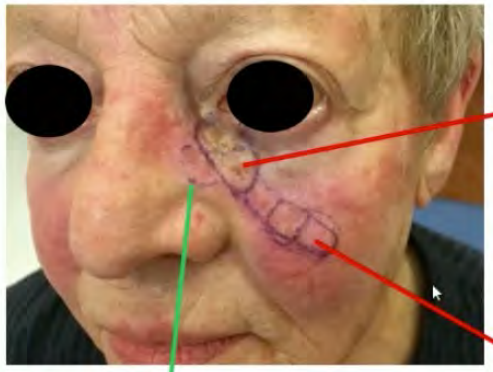


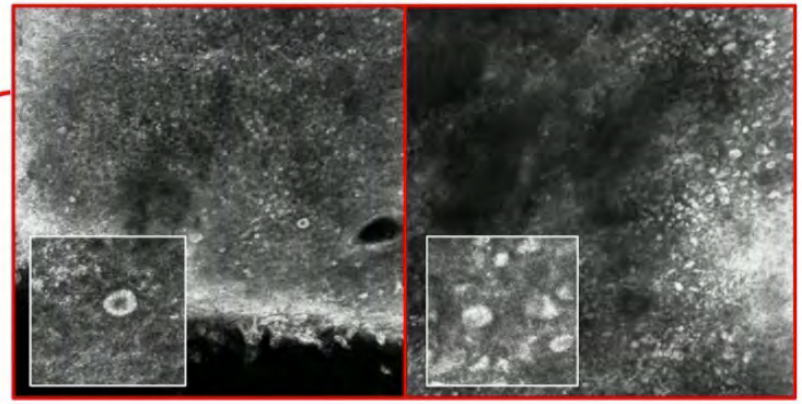
Muy elevada **resolución** (celular) pero muy poca **penetración** (dermis papilar)

Confocal in vivo para mapeo de LM previo a Cirugía de Mohs

In vivo confocal microscopy for Mohs – mapping of Lentigo maligna

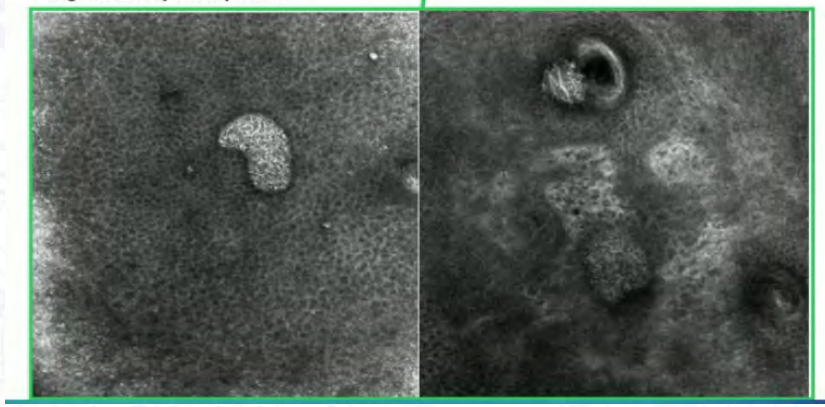
- Pleomorphism of size/shape of large, bright cells
- Pagetoid melanocytes
- NO normal honeycomb pattern ->"disarranged pattern"

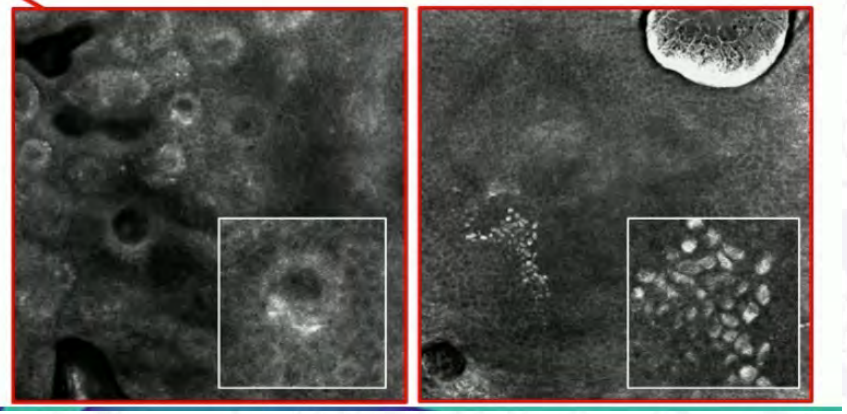




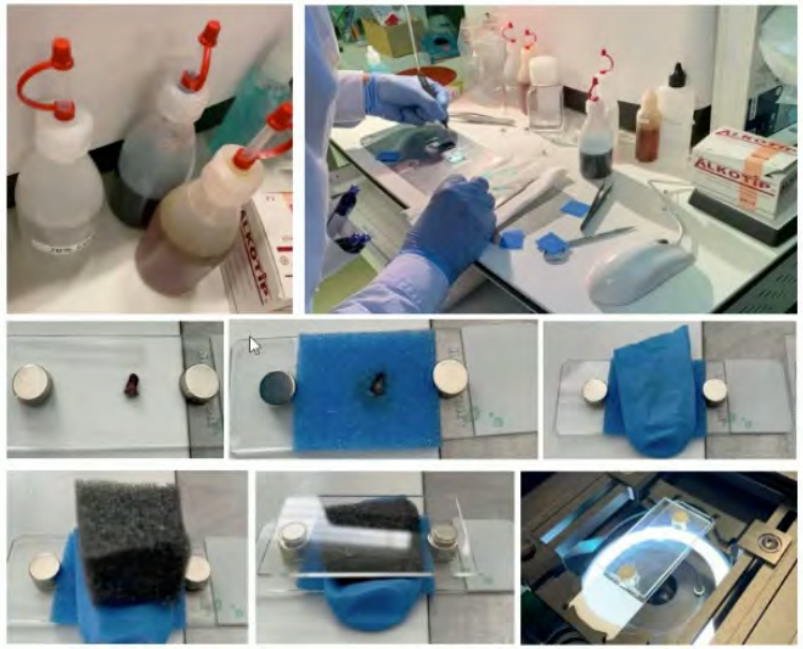
Granular Layer (normal skin)

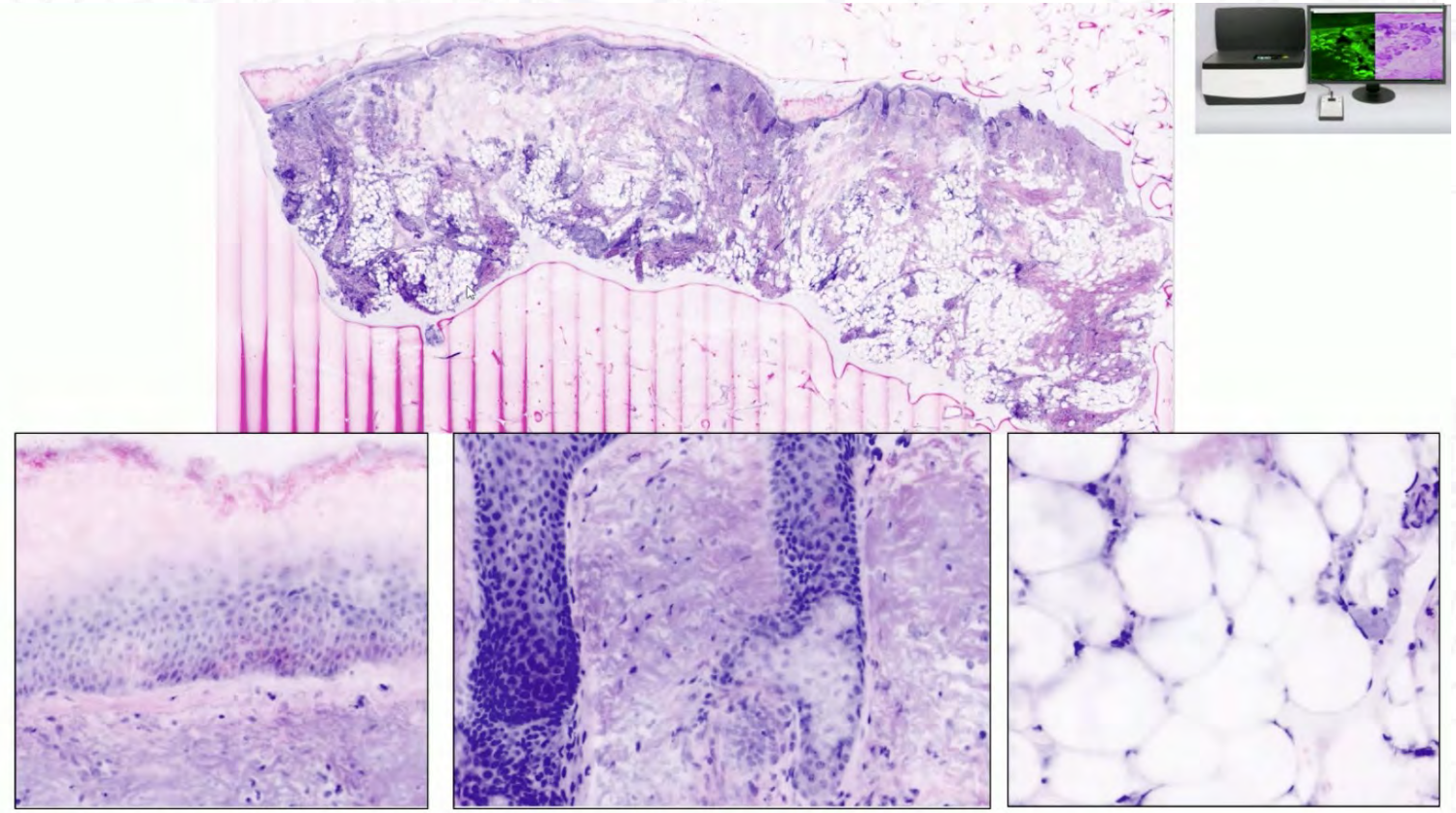
Regular **honeycomb pattern**





Confocal ex vivo para Cirugía de Mohs de CBC





REVIEW ARTICLE
BJD British Journal of Dermatology

Ex vivo confocal microscopy: revolution in fast pathology in dermatology

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Table 6 Diagnostic accuracy of *ex vivo* confocal microscopy in skin cancer compared with traditional histopathology in different studies

Study	Device	Mode	Stain	Number, sections	Detection rates
Karen[24]	V2000	FCM	AO	149 BCC Mohs submosaics	Se 96·6%, Sp 89·2%, PPV 92·3%, NPV 94·7%
Larson[43]	V2000	FCM	AO	17 BCCs, 34 Mohs submosaics	Se 97%, Sp 89%, PPV 92%, NPV 95%
Bennàssar[44]	V2500	FCM	AO	80 BCCs, 480 Mohs submosaics	Se 89%, Sp 99%, PPV 98%, NPV 97%
Mu[45]	V2500	FCM	AO	64 BCCs/SCCs, 133 Mohs mosaics	Se 99%, Sp 93%
Espinasse[46]	V2500	FCM	AO	42 BCCs of the eyelid	Se 100%, Sp 100%
Longo[47]	V2500	FCM	AO	127 BCCs, 753 Mohs sections	Se 79·8%, Sp 95·8%, PPV 80·5%, NPV 95·7%
Peters[34]	Histolog scanner	FCM	0·01% proflavine	148 suspected BCCs, 525 images (punch, shave/excision)	Se 73%, Sp 96%, 100% in Se and Sp in punch biopsies
Horn[48]	V2500	FCM	AO	120 images, 10 SCCs	Se 95%, Sp 96%, PPV 96·3%, NPV 95·2%

AO, acridine orange; BCC, basal cell carcinoma; FCM, fluorescence confocal microscopy; NPV, negative predictive value; PPV, positive predictive value; SCC, squamous cell carcinoma; Se, sensitivity; Sp, specificity. V2000 and V2500, VivaScope 2000 and VivaScope 2500. These older versions of the VivaScope device do not have the capability to produce digital staining or fusion images.

Revisión: S y E variables
S 80-100%
E 89-100%

SKIN HEALTH AND DISEASE Open Access

ORIGINAL ARTICLE Open Access

Ex vivo confocal microscopy for surgical margin assessment: A histology-compared study on 109 specimens

L. Grizzetti, F. Kuonen

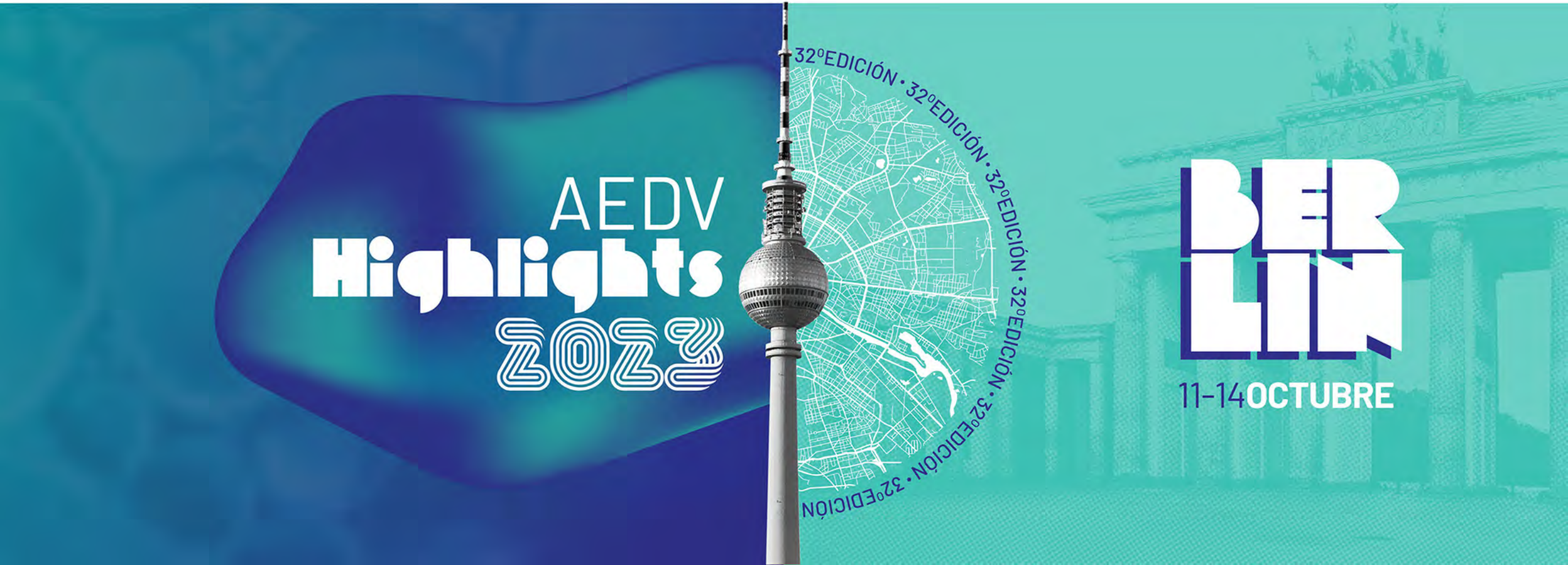
TABLE 3 Sensitivity and specificity of ex vivo CM using Histolog Scanner compared to histologic analysis on paraffin-embedded or frozen (Mohs) H&E sections

	n	True positive	False positive	True negative	False negative	Sensitivity (%)	Specificity (%)
Biopsies	16	13	0	2	1	93 (CI: 66.1%–99.8%)	100 (CI: 15.8%–100%)
Tumour type							
BCC	10	9	0	1	0	100 (CI: 66.4%–100%)	100 (CI: 2.5%–100%)
SCC	6	4	0	1	1	80 (CI: 28.4%–99.4%)	100 (CI: 2.5%–100%)
Surgical margins	93	8	4	76	5	61.5 (CI: 31.6–86.1)	95 (CI: 87.7–98.6)
Tumour type							
BCC	42	4	0	37	1	80 (CI: 28.4–99.4)	100 (CI: 90.6–100)
SCC (including BSC)	51	4	4	39	4	50 (CI: 15.7–84.3)	91 (CI: 77.9–97.4)
Mohs	24	5	0	17	2	71 (CI: 29–96.3)	100 (CI: 80.5–100)

Abbreviation: CI, 95% confidence intervals.

FALSOS NEGATIVOS: reservar para CBC nodulares

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2023.



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