HIGHLIGHTS

SINGAPORE

3-8 / july / 2023

Con el patrocinio de:

ucb

Iniciativa científica de:

AEDV 1909

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

Oncología y cirugía

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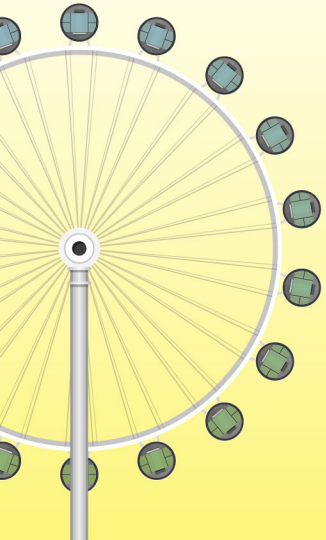
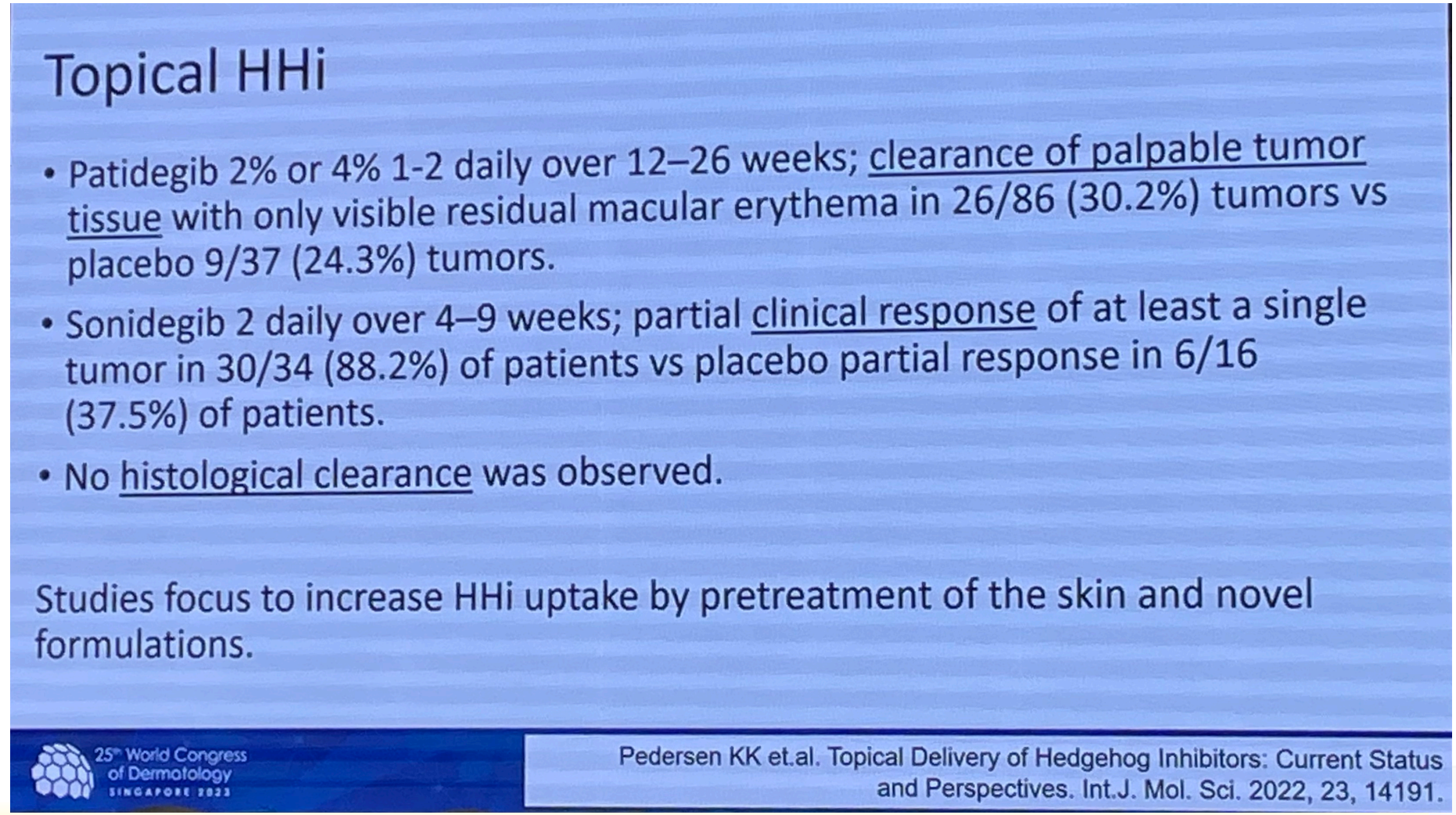


NO TENGO CONFLICTOS DE INTERÉS

CBC Inhibidores de Hedgehog tópicos no han presentado respuesta patológica



Topical Therapies
Barrier penetration dependent efficacy!

- In practice, difficult to achieve
  - Barrier limits penetration
  - Formulation effects on target uptake

Michael R. Migden (USA)

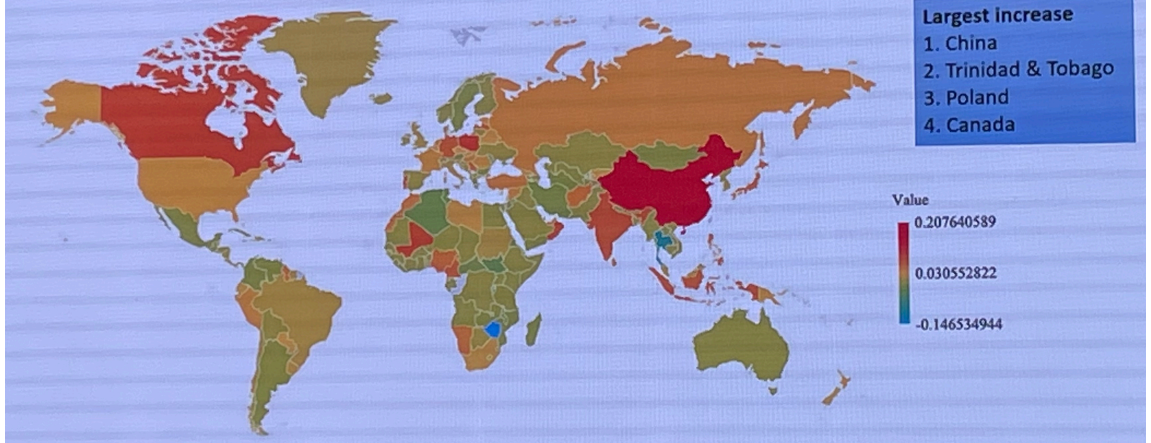
Nicole Kelleners- Smeets (Netherlands)

CBC “Desintensificación” del tratamiento del CBC de bajo riesgo en ancianos

De-intensification of treatment

Christopher Bichakjian (USA)

Percent Changes in Prevalence Rate of Keratinocyte Carcinoma from 1990 to 2017



Urban K, et al. J Amer Acad Dermatol. 2021;2:98-108

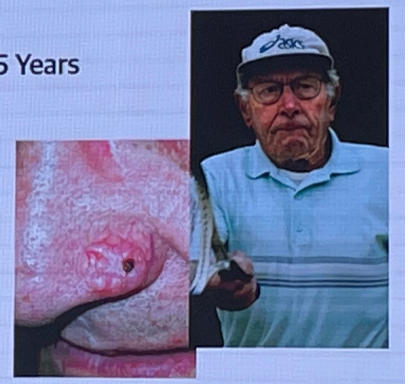
Global Incidence of Neoplasms in 2017

2017 Incidence rank	Cause	Number of new cases (2017)	Percent change (1990-2017)
1	Benign/in situ neoplasms	9,714,953	42.8%
2	Basal cell carcinoma	5,884,759	77.4%
3	Lung cancer	2,163,132	100.4%
4	Breast cancer	1,960,682	123.1%
5	Colorectal cancer	1,833,451	121.9%
6	Cutaneous squamous cell carcinoma	1,778,829	309.7%
7	Prostate cancer	1,334,315	179.1%
8	Stomach cancer	1,220,662	41.2%
21	Melanoma	308,684	161.3%

Urban K, et al. J Amer Acad Dermatol. 2021;2:98-108

JAMA Dermatology | Original Investigation

Nonmelanoma Skin Cancer in Patients Older Than Age 85 Years Presenting for Mohs Surgery
A Prospective, Multicenter Cohort Study



Amanda Maisel-Campbell, MD; Katherine A. Lin, BS; Sarah A. Ibrahim, BA; Bianca Y. Kang, BS; Noor Anvery, BA; McKenzie A. Dirr, BA, BS; Rachel E. Christensen, BS; Juliet L. Aylward, MD; Omar Bari, MD; Hamza Bhatti, DO; Diana Bolotin, MD, PhD; Basil S. Cherpelis, MD; Joel L. Cohen, MD; Sean Condon, MD; Sheila Farhang, MD; Bahar Firoz, MD; Algin B. Garrett, MD; Roy G. Geronemus, MD; Nicholas J. Golda, MD; Tatyana R. Humphreys, MD; Eva A. Hurst, MD; Oren H. Jacobson, BS; S. Brian Jiang, MD; Pritesh S. Karia, PhD, MPH; Arash Kimyai-Asadi, MD; David J. Kouba, MD; James G. Lahti, MD; Martha Laurin Council, MD; Marilyn Le, BA; Deborah F. MacFarlane, MD; Ian A. Maher, MD; Stanley J. Miller, MD; Eduardo K. Moioli, MD, PhD; Meghan Morrow, MD; Julia Neckman, MD; Timothy Pearson, MD; Samuel R. Peterson, MD; Christine Poblete-Lopez, MD; Chad L. Prather, MD; Jennifer S. Ranario, MD; Ashley G. Rubin, MD; Chrysalyne D. Schmults, MD; Andrew M. Swanson, MD; Christopher Urban, MD; Y. Gloria Xu, MD; Murad Alam, MD; and the Dermbase Research Group

JAMA Dermatol. 2022;158(7):770-778.

CONCLUSIONS AND RELEVANCE This study found that older patients who received Mohs surgery often had high functional status, high-risk tumors, and tumors located on the face. These findings suggest that timely surgical treatment may be appropriate in older patients given that their tumors may be aggressive, painful, disfiguring, and anxiety provoking.

VIEWPOINT

Active Surveillance as a Management Option for Low-risk Basal Cell Carcinoma

Eleni Linos, MD, DrPH
Department of Dermatology, Stanford University, Stanford, California.

Mary-Margaret Chren, MD
Department of Dermatology, Vanderbilt University Medical Center, Nashville, Tennessee.

JAMA Internal Medicine August 2021 Volume 181, Number 8

BJD Improving patient outcomes in skin disease worldwide

Basal cell carcinoma in older adults: how to decide when active surveillance or watchful waiting is appropriate? Get access

Laura Van Coile, Evelien Verhaeghe, Katia Ongenae, Lieve Brochez, Isabelle Hoorens

British Journal of Dermatology, Volume 187, Issue 2, 1 August 2022, Pages 244–245,

The perspectives of 606 US dermatologists on active surveillance for low-risk basal cell carcinoma

Get access

Sven van Egmond, Isabella de Vere Hunt, Zhuo Ran Cai, Nada Rizk, Marlies Wakkee, Mary-Margaret Chren, Noah Goldfarb, Julia F Simard, Eleni Linos

British Journal of Dermatology, Volume 188, Issue 1, January 2023, Pages 136–137,

Observación en el CBC

Evaluation of Watchful Waiting and Tumor Behavior in BCC Pts

- 280 BCCs in 89 patients in the Netherlands (median age 83)
- Estimated tumor diameter increase was 4.46 mm in 1 year for BCCs containing at least an infiltrative/micronodular component
- 1.06 mm increase in diameter for the remaining BCCs (only nodular/superficial component/clinical diagnosis).
- *Conclusion:*
  - *Watchful waiting could be an appropriate approach in patients with BCC with a limited life expectancy and asymptomatic nodular or superficial BCCs*

Van Winden et al, JAMA Derm, 2021

“Desintensificación” del tratamiento del CBC de bajo riesgo en ancianos

Open access Protocol

BMJ Open Study protocol of the BASINEL Study: a pragmatic randomised controlled trial investigating treatment versus no treatment of low-risk basal cell carcinomas in older persons

Van Coile L, *et al*. *BMJ Open* 2022;**12**:e063526.

ClinicalTrials.gov Identifier: NCT05110924

Recruitment Status : Recruiting

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	280 participants
Allocation:	Randomized
Actual Study Start Date :	November 1, 2021
Estimated Primary Completion Date :	October 31, 2025
Estimated Study Completion Date :	October 31, 2025

Michigan University

- Evaluate active surveillance vs standard of care for low risk BCC
  - <1 cm diameter
  - Trunk and proximal extremities
  - Patients > 65 years
- Aim 1 – pilot & feasibility trial
- Aim 2 – patient acceptability
- Aim 3 – dermatologist acceptability

De-intensification of treatment

Christopher Bichakjian (USA)

Queratosis actínicas

"encompassing patient priorities and goals to set realistic treatment expectations and improve care outcomes".

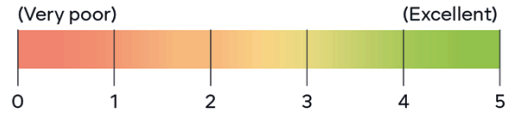
- **PHOTOPROTECTION**
- Destructive therapies – 'clinician controlled'
  - Cryotherapy
  - Curettage
  - Photodynamic therapy
  - Radiotherapy
  - Ablative laser
- Topical therapies therapies
  - 5-fluorouracil
  - Imiquimod
  - Diclofenac
  - Ingenol mebutate
  - Tirbanibulin

Actinic keratosis: Treatment options and how to choose the best one

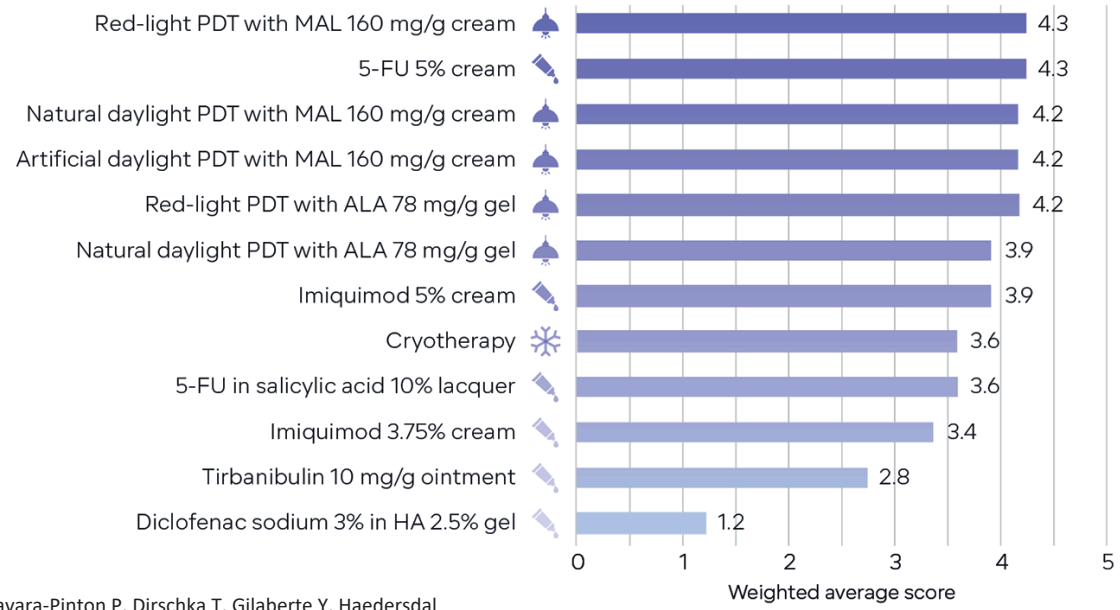
Peter Foley (Australia)

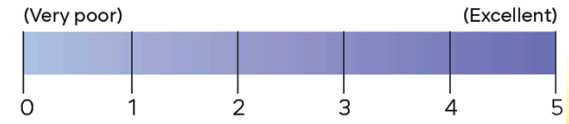
A

	Good efficacy	High tolerability	Good convenience	Short treatment duration	Good cosmesis	Field-cancerisation management
Red-light PDT with MAL 160 mg/g cream	4.3	2.5	3.3	4.3	4.3	3.8
5-FU 5% cream	4.3	2.5	2.8	2.3	3.2	4.3
Natural daylight PDT with MAL 160 mg/g cream	4.2	4.4	3.9	4.3	4.7	4.3
Artificial daylight PDT with MAL 160 mg/g cream	4.2	4.2	3.3	3.7	4.3	4.2
Red-light PDT with ALA 78 mg/g gel	4.2	2.3	2.9	4.5	4.4	4.3
Natural daylight PDT with ALA 78 mg/g gel	3.9	4.1	3.9	4.6	4.4	4.1
Imiquimod 5% cream	3.9	2.1	2.5	2.5	3.3	3.4
Cryotherapy	3.6	2.7	3.4	4.2	2.1	0.6
5-FU in salicylic acid 10% lacquer	3.6	2.9	3.0	2.7	3.1	1.1
Imiquimod 3.75% cream	3.4	2.4	2.5	2.5	3.2	3.4
Tirbanibulin 10 mg/g ointment	2.8	4.0	3.5	4.3	3.8	2.5
Diclofenac sodium 3% in HA 2.5% gel	1.2	4.6	3.0	0.7	3.4	2.1



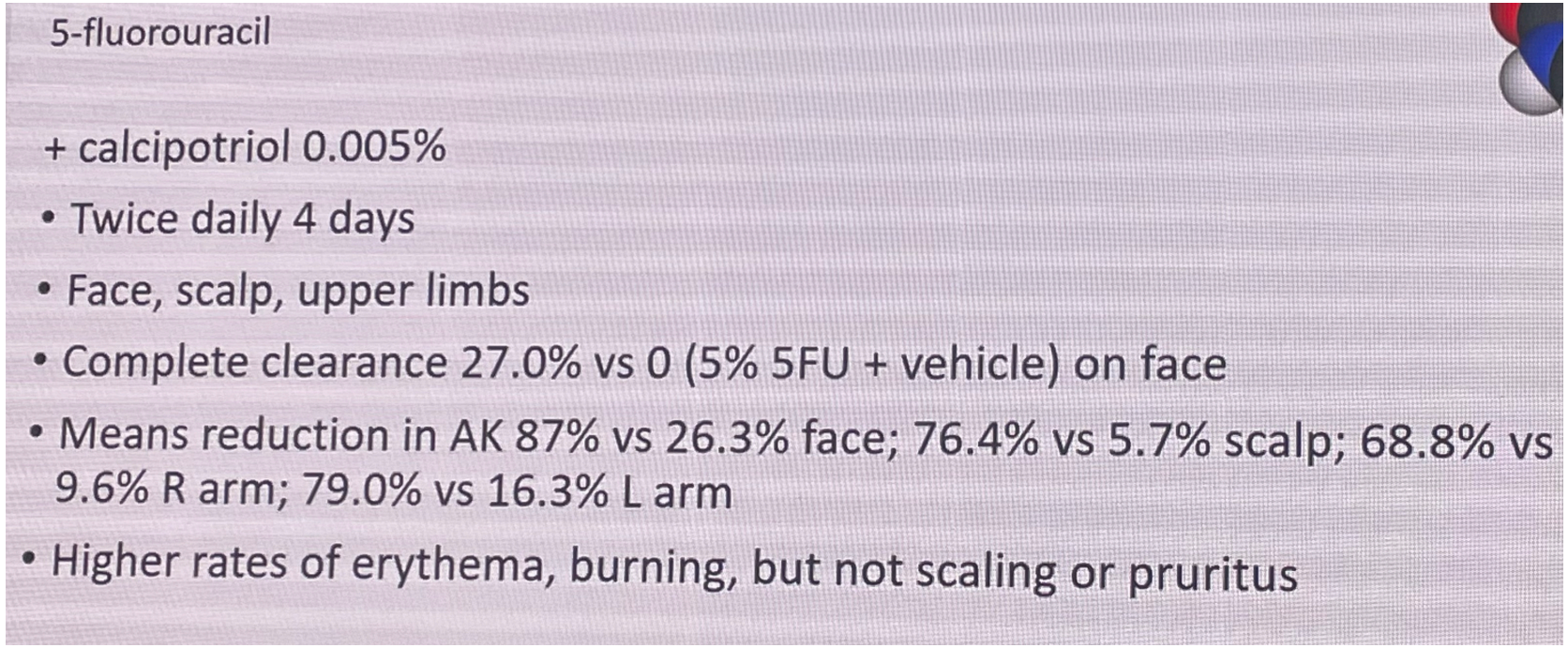
B **Efficacy**





Morton C, Baharlou S, Basset-Seguin N, Calzavara-Pinton P, Dirschka T, Gilaberte Y, Haedersdal M, Hofbauer G, Sapra S, Waalboer-Spuij R, Yip L, Szeimies RM. Expert Recommendations on Facilitating Personalized Approaches to Long-term Management of Actinic Keratosis: The Personalizing Actinic Keratosis Treatment (PAKT) Project. Acta Derm Venereol. 2023 Jun 8;103:adv6229.

5-FU + calcipotriol



Mohney L, Singh R, Grada A, Feldman S. Use of Topical Calcipotriol Plus 5-Fluorouracil in the Treatment of Actinic Keratosis: A Systematic Review. J Drugs Dermatol. 2022 Jan 1;21(1):60-65.

Tirbanibulina

Tirbanibulin

- 1% ointment once daily for 5 consecutive days
  - Microtubule inhibitor (tubulin polymerization and Src kinase signaling inhibitor)
  - Two Phase III clinical studies, 702 participants, tirbanibulin 1% ointment was superior to vehicle ointment as a topical treatment for AK of the face and scalp at 2 months
  - Complete clearance rates were 44% compared to 5% in trial 1 and 54% compared to 13% in trial 2, respectively
  - Among participants with a complete response to tirbanibulin, the estimated percentage of patients with recurrent lesions at 1 year was 47%
  - Mild to moderate local reactions
    - no participants were reported to have been withdrawn from the trials due to adverse event

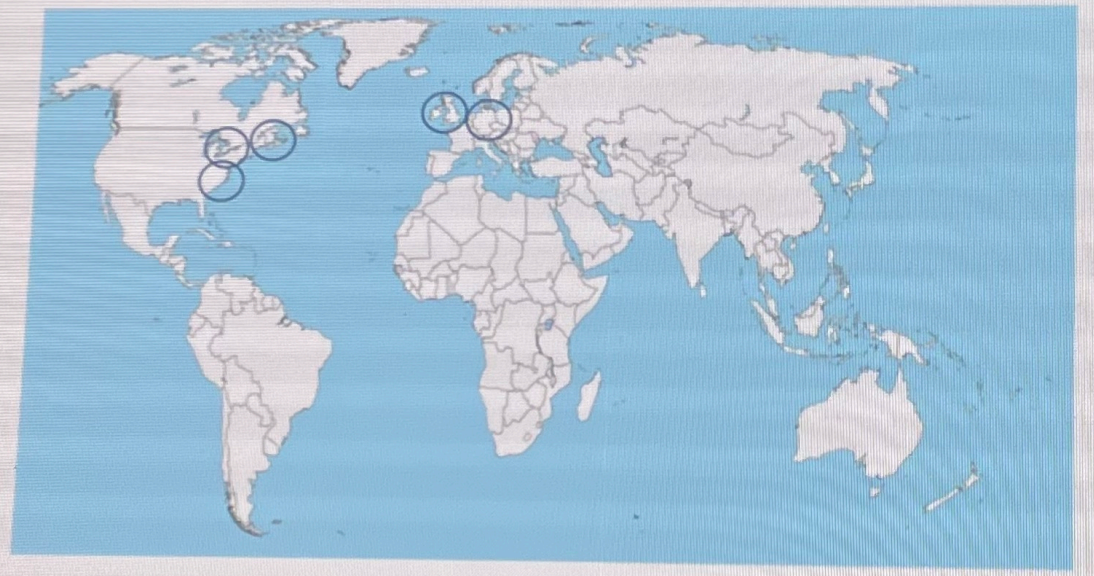
Blauvelt A et al. Phase 3 Tirbanibulin for Actinic Keratosis Group. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis. N Engl J Med. 2021 Feb 11;384(6):512-520.

Actinic keratosis: Treatment options and how to choose the best one

Peter Foley (Australia)

CEC Mortalidad por CEC

How many die from cutaneous SCC?



- 1-2% metastasize
- 1% die from the disease
- Probably more than melanoma
  - Melanoma 7,300 U.S. deaths
  - CSCC 15,000 if 1% of 1.5 million
- Those who die
  - 1/3 distant organ mets
  - 1/3 nodal/regional
  - 1/3 local extension

T Eigentler, H Breuninger, et al, EJC 2022

RF Rose, JA Newton-Bishop, Br J Derm, 2013
C Schmults, A Qureshi, et al, JAMA Derm 2013
T Eigentler, H Breuninger, et al, JID 2017
L sun, BV Manyam, JAMA Derm 2019
Tschetter, Brodland et al, JAAD 2020

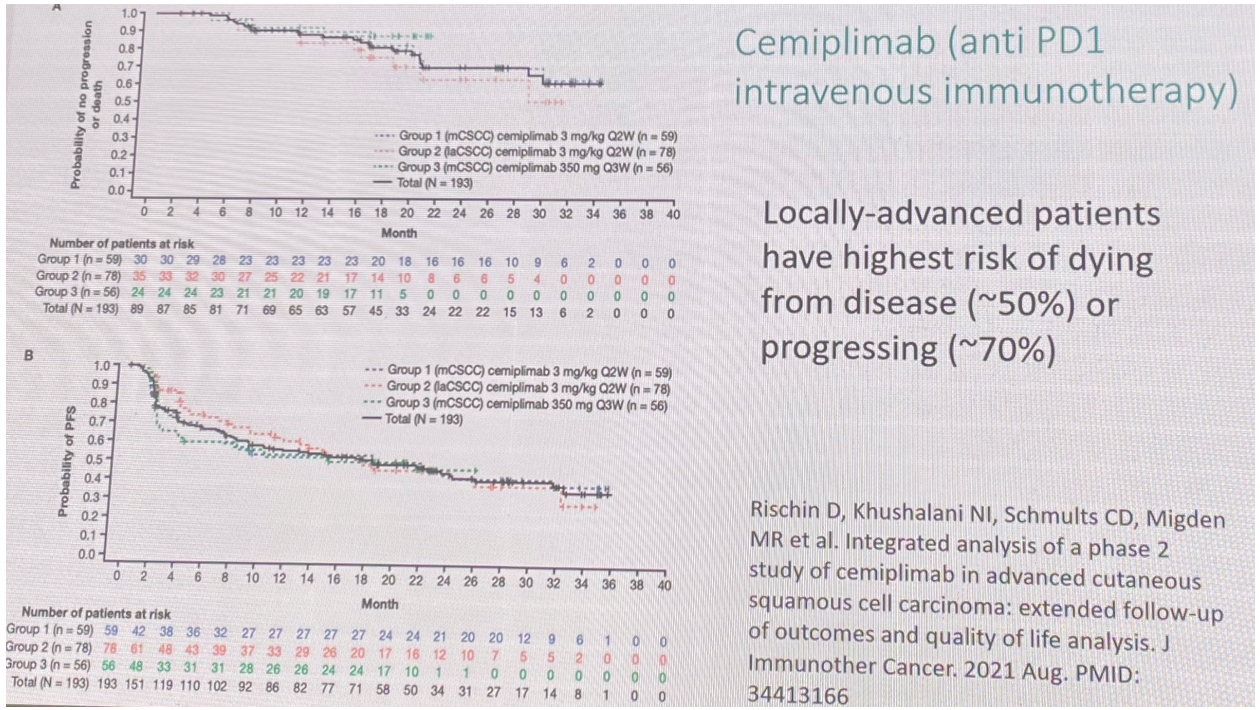
Chrysalyne D. Schmults (USA)

Squamous cell carcinomas: Advances in systemic therapy

ANTI PD-1 IMMUNOTHERAPY IS THE STANDARD FOR CSCC NOT AMENABLE TO SURGERY

HIGHLIGHTS SINGAPORE
3-8 / july / 2023
25th World Congress of Dermatology

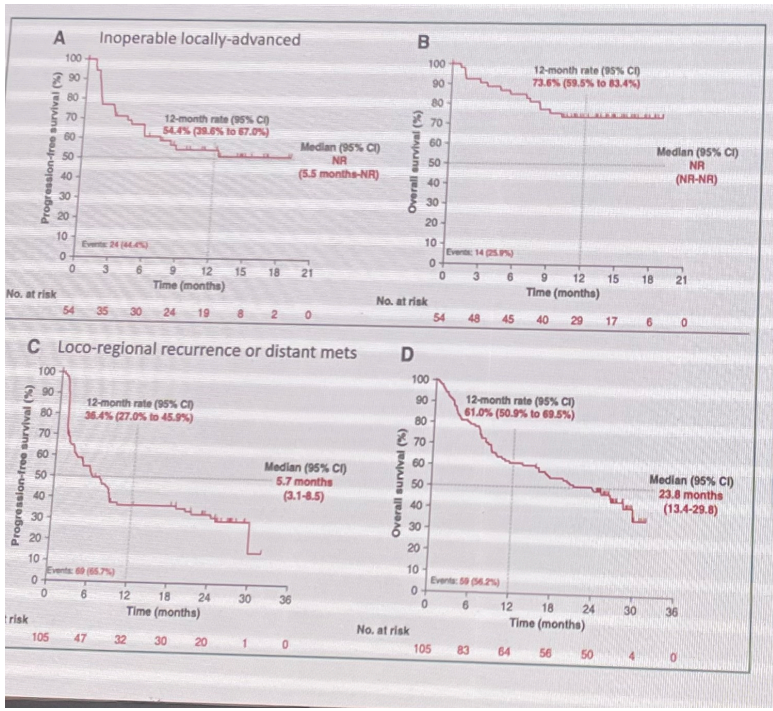
Anti PD1 infusion therapy (cemiplimab and pembrolizumab) is the only approved treatment for unresectable cSCC
-Response rate up to 50%, disease stabilization >70%, complete response <20%
-Transplant patients have a 50% chance of organ rejection so meeting their therapeutic needs remains challenging



Cemiplimab (anti PD1 intravenous immunotherapy)

Locally-advanced patients have highest risk of dying from disease (~50%) or progressing (~70%)

Rischin D, Khushalani NI, Schmults CD, Migden MR et al. Integrated analysis of a phase 2 study of cemiplimab in advanced cutaneous squamous cell carcinoma: extended follow-up of outcomes and quality of life analysis. J Immunother Cancer. 2021 Aug. PMID: 34413166



Pembrolizumab (anti PD1 intravenous immunotherapy)

- Shorter follow-up (1 vs 3 years) for locally-advanced in pembro trial
- Nodal/distant mets: ~85% progression vs ~60% for cemiplimab at 3 years
- Pembrolizumab trial had higher fraction of previously-treated, second-line patients
  - 87% pembro trial
  - 50% cemiplimab trials

Hughes BGM, Grob JJ et al. Corrigendum to 'Pembrolizumab for locally advanced and recurrent/metastatic cutaneous squamous cell carcinoma: an open-label, nonrandomized, multicenter, phase II trial. Annals of Oncology October 2021, PMID: 35690517

DO AL METASTATIC CASES NEED ANTI-PD1?

Many nodal metastases do NOT need systemic therapy

- N1 disease has 92% 5-year cure rate with surgery +/- radiation
  - N1: single node, ≤3 cm, no extracapsular spread
- So N1 does not need systemic therapy in general

Ebrahimi A, Clark JR, Lorincz BB, Milross CG, Veness MJ. Metastatic head and neck cutaneous squamous cell carcinoma: defining a low-risk patient. Head Neck. 2012 Mar;34(3):365-70.

WHAT IF WE GAVE IMMUNOTHERAPY EARLIER IN THE COURSE OF DISEASE, BEFORE IT WAS UNRESECTABLE? BEFORE SURGERY (NEOADJUVANT)?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Neoadjuvant Cemiplimab for Stage II to IV Cutaneous Squamous-Cell Carcinoma

N.D. Gross, D.M. Miller, N.I. Khushalani, V. Divi, E.S. Ruiz, E.J. Lipson, F. Meier, Y.B. Su, P.L. Swiecicki, J. Atlas, J.L. Geiger, A. Hauschild, J.H. Choe, B.G.M. Hughes, D. Schadendorf, V.A. Patel, J. Homsi, J.M. Taube, A.M. Lim, R. Ferrarotto, H.L. Kaufman, F. Seebach, I. Lowy, S.-Y. Yoo, M. Mathias, K. Fenech, H. Han, M.G. Fury, and D. Rischin

- 79 patients: all but 5 were stage III/IV (M0); 60% had nodal mets
- 4 doses cemiplimab q3 weeks, then surgery
- 51% complete histologic response when the tumors were removed
- Grade 3/4 adverse events: 18%

WHO SOULD GET OFF-LABEL NEOADJUVANT CEMIPLIMAB?

- BORDERLINE RESECTABLE
- HIGH RISK FOR RECURRENCE DESPITE SURGERY
- HIGHLY MORBID SURGERY

NCCN Guidelines Version 1.2023: Updated CSCC Recommendations for Neoadjuvant Therapy[a]

- For patients with operable disease, neoadjuvant cemiplimab may be considered in patients:
  - Who are borderline resectable
  - Who are unresectable
  - For whom surgery may carry a high morbidity
- Category 2B recommendation

ANYONE ELSE FOR OFF-LABEL NEOADJUVANT CEMIPLIMAB?

*"**In-transit metastases** and **high-stage SCC with LVI** may merit off-label consideration of neoadjuvant or postoperative immunotherapy as we await FDA indication"*

Chrysalyne D. Schmults (USA)

Squamous cell carcinomas: Advances in systemic therapy

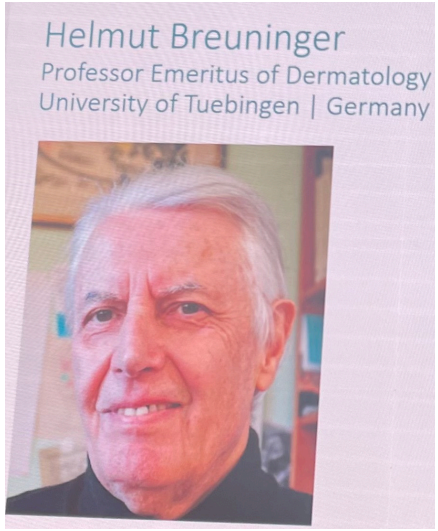
WHEN TO USE ADJUVANT IMMUNOTHERAPY AFTER SURGERY?

Esperando resultados de ensayos clínicos

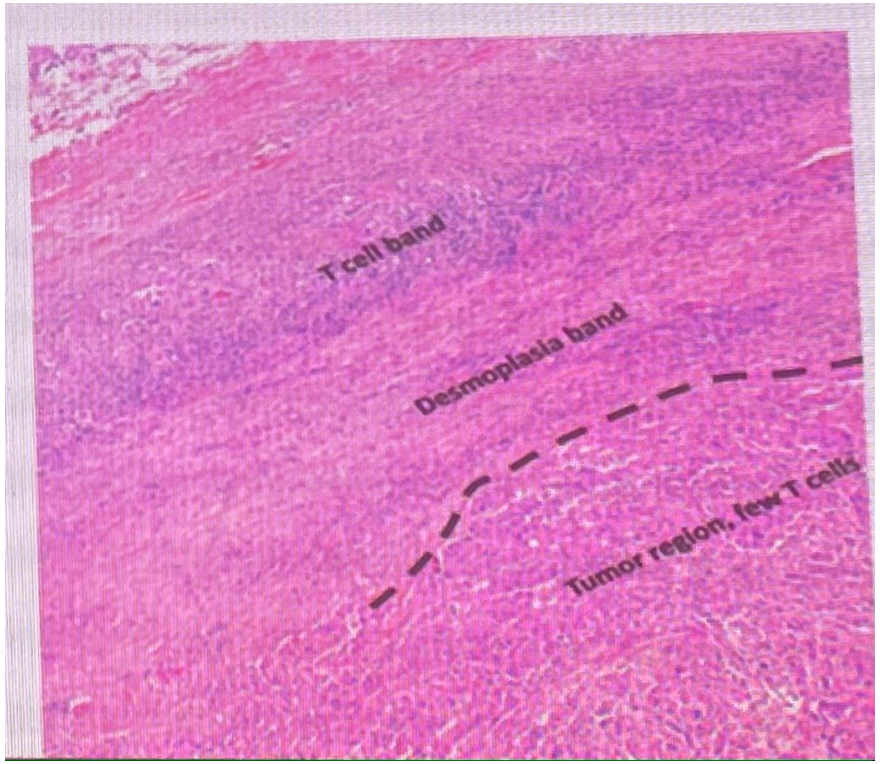
Q + RT +- inmunoterapia adyuvante (cemiplimab, pembrolizumab)

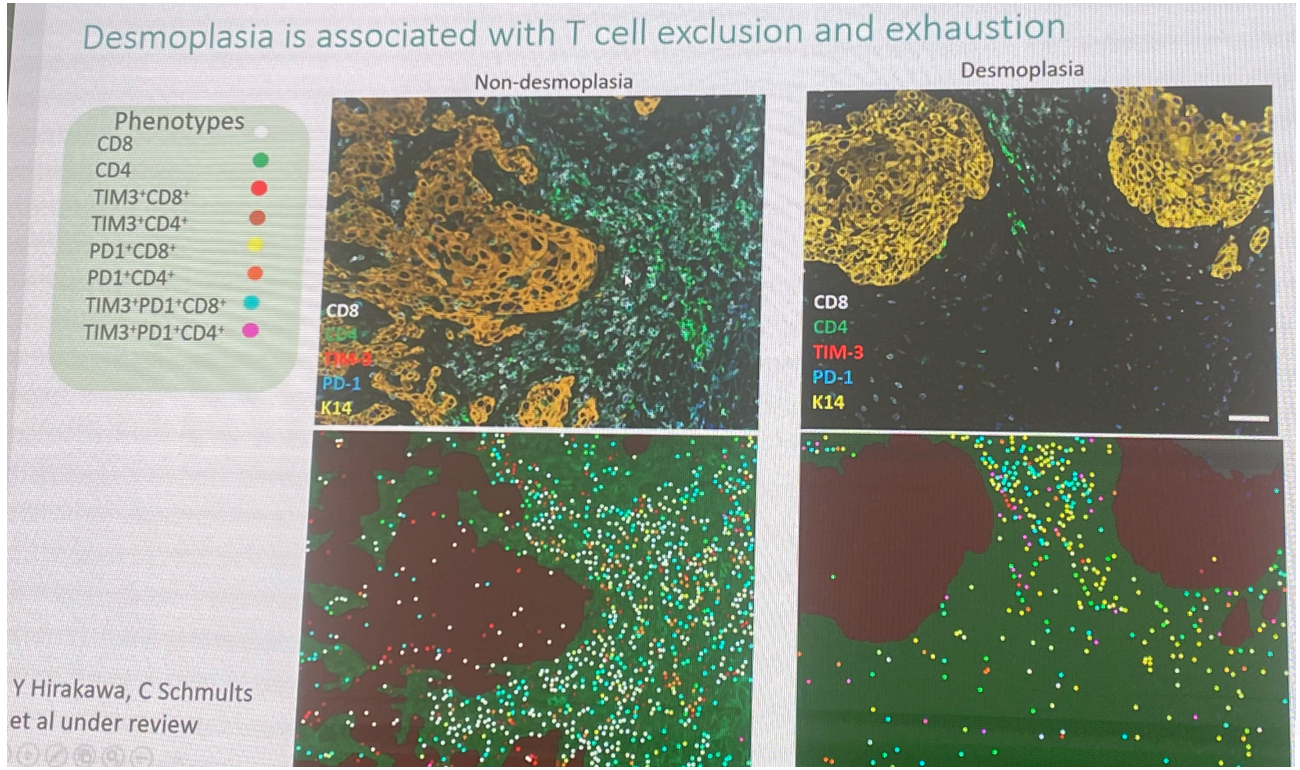
Se necesitan ensayos:
-Adjuvant anti PD1 vs radiation for high-risk local disease
-Adjuvant vs neoadjuvant

WHY DOES IMMUNOTHERAPY FAIL OVER HALF THE TIME ?



FIBRAS DE COLÁGENO **DESMOPLÁSICAS** SE SITUAN PARALELAS AL TUMOR HACIENDO UNA “PARED” QUE MANTIENE ”APARTADAS” A LAS CÉLULAS DEL SISTEMA INMUNE





Chrysalyne D. Schmults (USA)

WHY DOES IMMUNOTHERAPY FAIL OVER HALF THE TIME ?

Statistical summery

- In desmoplastic stroma, all 3 cell major immune types are reduced
  - Especially B and T cells
- In desmoplastic tumors, T-cells are low
  - Dendritic and B cells are few at baseline

Density (cell/mm2) in stroma	Non-desmoplasia N=38	Desmoplasia N=25	p-value
T cell	1459	525	0.0002
B cell	177	30	0.0044
DC	385	304	N.S

Density (cell/mm2) in tumor	Non-desmoplasia N=38	Desmoplasia N=25	p-value
T cell	180	68	0.0048
B cell	<5	<5	
LC	43	28	N.S
DC	29	34	N.S

/ Hirakawa, C Schmults et al under review

PORQUE LAS ALTERACIONES DEL ESTROMA CONOCIDAS COMO DESMOPLASIA MANTIENEN "ALEJADAS" DEL TUMOR A LAS CÉLULAS T ACTIVADAS (Y LAS B)

GUÍA EUROPEA SCC

Guidelines on cSCC

National Comprehensive Cancer Network

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Squamous Cell Skin Cancer

Version 1.2023 — March 10, 2023

GUIDELINES

BJD British Journal of Dermatology

British Association of Dermatologists guidelines for the management of people with cutaneous squamous cell carcinoma 2020*

S.G. Keohane, J Botting, P.G. Budny, O.M. Dolan, K. Fife, C.A. Harwood, R. Mallipeddi, J.R. Marsden, R.J. Motley, C. Newlands, C. Proby, A. Rambiklak, D.N. Slater, J.A. Smithson, P. Buddley, P. Fairbrother, M. Hashme, M.F. Mohd Mustapa, L.S. Exton and the British Association of Dermatologists' Clinical Standards Unit

Brief S2k Guidelines – Cutaneous squamous cell carcinoma

JDDG

Cutaneous squamous cell carcinoma

Brief S2k guidelines – Cutaneous squamous cell carcinoma

On behalf of EADO-EDF-ESTRO-UEMS-EADV-EORTC

EJC

European Interdisciplinary Guidelines on Invasive Squamous Cell Carcinoma of the Skin

2023 update in preparation

Ketty Peris (Italy)

What is new in the squamous cell carcinoma guidelines

cSCC with highest risk for poor prognosis

European Guideline 2023	NCCN 2023	BAD Guideline 2020
High-risk for local recurrence or metastasis	**Very high-risk for local recurrence, metastasis, or disease-specific death**	**Very high-risk for local recurrence, nodal metastasis, or disease-specific death**
Diameter >20 mm	Diameter >40 mm	Diameter >40 mm
Localization on lip/ear/temple	-	-
Thickness >6 mm	Thickness >6 mm	Thickness >6 mm
Invasion beyond subcutaneous fat	Invasion beyond subcutaneous fat	Invasion beyond subcutaneous fat
Bone erosion	-	Bone invasion
Histological type: desmoplastic	Desmoplastic Lymphatic or vascular involvement	Histological subtype: desmoplastic, adenosquamous, spindle/sarcomatoid/metaplastic
Poor differentiation	Poor differentiation	In-transit metastasis
Immunosuppression	_	Immunosuppression
PNI (microscopic, symptomatic or radiological)	Histological PNI of a nerve deeper than the dermis or ≥ 0.1 mm	Histological PNI in named nerve, nerve ≥ 0.1 mm or beyond dermis
Positive histological margins	-	One or more involved or close (<1 mm) histological margin in a high-risk tumour

Staging work/up of cSCC

Imaging for staging of cSCC	Evidence-based recommendation
GPP	- Patients with **low-risk cSCC** should undergo **physical examination only** with no need for imaging studies unless indicated by physical examination - Patients with primary common **cSCC with high-risk factors*** should be staged for non-palpable lymph node involvement, preferably by **US** or by **CT scan**. - For suspected **underlying tissue involvement (bone or soft tissue)**, **CT or MRI** should be done to determine extent of local infiltration. LacSCC should undergo imaging to rule out metastasis. - cSCC with nodal involvement should undergo a full skin examination and imaging studies to rule out distant metastatic disease.
Level of evidence: 3	There are no precise clinical guidelines for radiologic evaluation for cSCC Retrospective studies Review of studies on nodal staging of high-risk cSCC
	Strength of consensus: 100%

*Specification of high-risk factors for imaging for non-palpable regional nodal metastasis cannot be given, as the independent effect of high-risk factors has not been consistently reported. cSCC at higher risk for nodal metastasis according to staging systems include (but are not restricted to) AJCC8 T3/T4 and BWH T2b/T3 stages.

European cSCC Guidelines 2023, in preparation

Surgical management of primary cSCC

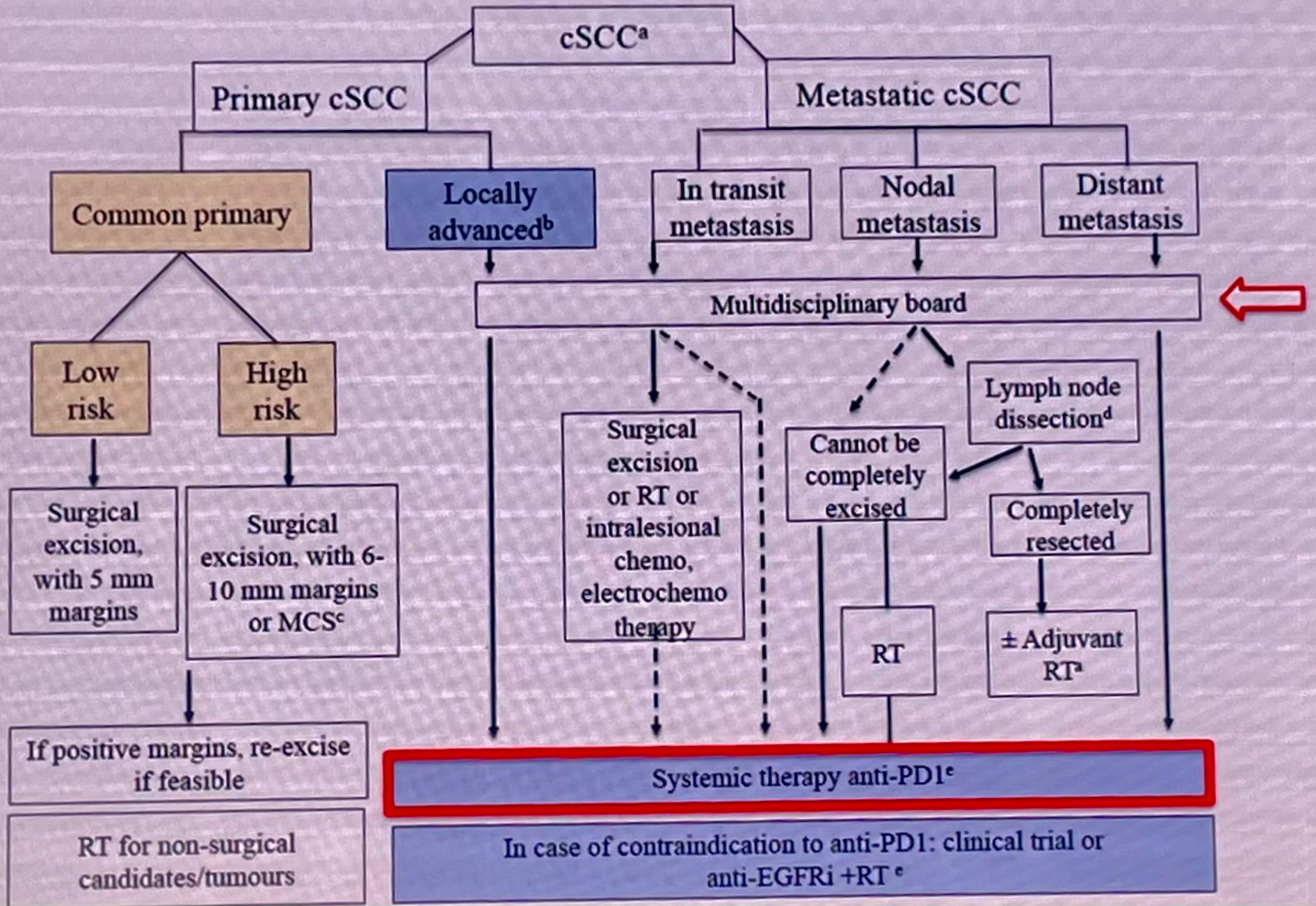
Surgical excision with histological control shall be performed as standard treatment. The aim of cSCC surgery shall be a complete excision (R0) with histological confirmation of peripheral and deep excision margins

	EADO 2020 (update 2023)	BAD 2020	NCCN 2023
Low risk cSCC	Clinical safety margins of 5 mm	≥ 4 mm for a low-risk cSCC ≥ 6 mm for a high-risk cSCC ≥ 10 mm for a very high-risk cSCC	Low risk: 4-6 mm
High risk cSCC	Clinical safety margins of 6-10 mm or MCS/MMS	Ensure at least a 1 mm histological clearance (peripheral and deep tissues)	High risk/very high risk cSCC: wider margins or MMS or CCPDMA technique

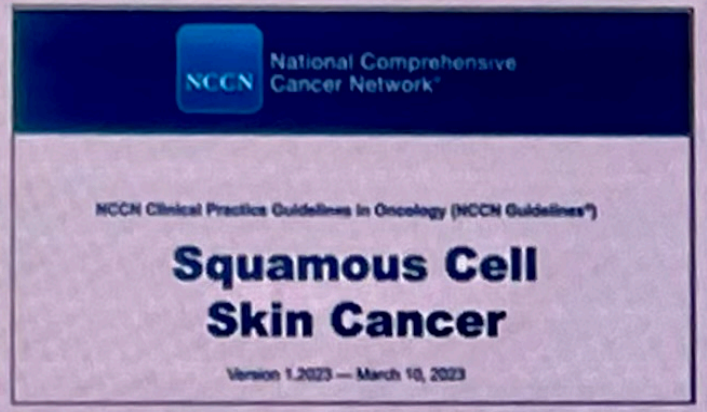
MCS: micrographically controlled surgery; MMS: Mohs Micrographic Surgery; CCPDMA: complete circumferential peripheral and deep margin assessment

Therapeutic recommendations for cSCC

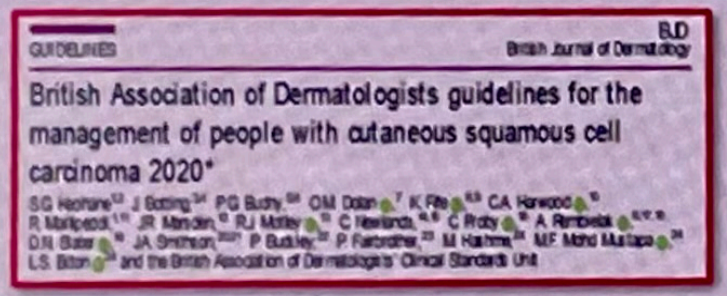
European Guidelines. Part 2. 2023; in preparation



SYSTEMIC THERAPY FOR ADVANCED CSCC



- The recommended systemic therapy options for use alone without RT are *cemiplimab-rwlc and pembrolizumab* (preferred if curative RT or surgery is not feasible for locally advanced, recurrent, or metastatic disease)



- R. 37 (↑) Consider ***immune checkpoint inhibitors (ICI)*** in people with laSCC where curative surgery or RT is not reasonable, or those with mSCC, **except OTR or patients who have significant autoimmune conditions**

- Patients with metastatic cSCC or locally advanced cSCC, who are not candidates for curative surgery or curative radiation, should receive **first-line treatment with a PD-1 antibody** (cemiplimab or pembrolizumab)

COMBINACIONES E INMUNOTERAPIA INTRALESIONAL

HIGHLIGHTS SINGAPORE 3-8 / july / 2023

Combined therapies under investigations

www.clinicaltrial.gov

Type of combination	Drug
ICIs	IPI + nivolumab IPI + nivolumab+ tacrolimus
ICI + Radiotherapy	Pembrolizumab + RT Pembrolizumab + quad-shot RT Avelumab + radical RT
ICI + Targeted Therapy	Pembrolizumab + cetuximab Avelumab + cetuximab Pembrolizumab/cemiplimab + ASP-1929 (EGRF antibody-dye coniugated) Atezolizumab + cobimetinib
ICI + Oncolytic viruses	Nivolumab + talimogene laherparepvec Cemiplimab + RP1 Nivolumab + RP1 Pembrolizumab + ONCR-177
ICI + Cancer vaccines	Nivolumab or pembrolizumab + CIMAvax vaccine Pembrolizumab + Ad/MG1-MAGEA3
Others	Pembrolizumab + abexinostat (HDAC inhibitor) Pembrolizumab or cemiplimab + cavrotolimod (TLR agonist) Pembrolizumab + IFX-1 (C5a antibody)

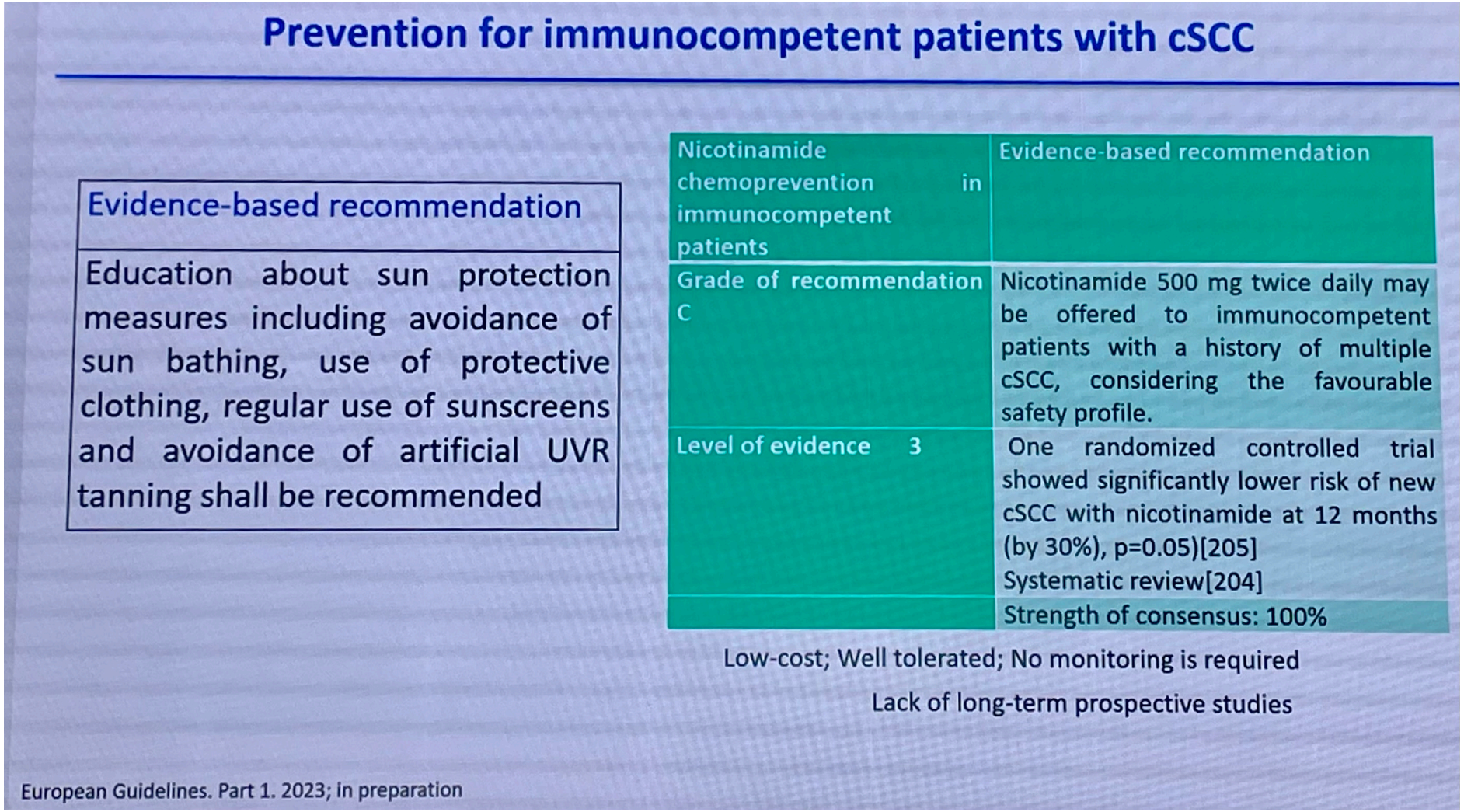
Why intralesional immunotherapy?

- As an **alternative to iv in NMSC**?
  - Increase **local tissue concentration**, **minimize systemic exposure**,
  - **Neoadjuvant** use to reduce disfigurement/dysfunction **prior to surgery**
- **As an alternative to surgery in some cases;** would you offer patients an effective, nonsurgical option?
  - **Surgical fatigue**
  - **Surgical aversion**
  - **BCNS** TNTC/ field **cancerization**

Neoadjuvant, Intralesional and Combination Immunotherapy of Cutaneous Squamous Cell Carcinoma

Michael R. Migden (USA)

Nueva guías europeas CEC, nicotinamida 500mg 2/día inmunocompetentes



Nicotinamida reduce NMSC?

HIGHLIGHTS SINGAPORE 3-8 / july / 2023 — 25th World Congress of Dermatology

ORIGINAL ARTICLE

A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention

Subgroup	Placebo (mean no. of lesions/person)	Nicotinamide (mean no. of lesions/person)	Rate Ratio (95% CI)	Relative Difference, % (95% CI)	P Value
12-mo intervention period					
NMSCs	2.4	1.8		23 (4 to 38)	0.02
BCCs	1.7	1.3		20 (−6 to 39)	0.12
SCCs	0.7	0.5		30 (0 to 51)	0.05
6-mo postintervention period					
NMSCs	0.8	0.8		−17 (−59 to 14)	0.33
BCCs	0.6	0.5		−6 (−53 to 26)	0.73
SCCs	0.3	0.3		−59 (−163 to 4)	0.07

0.4 0.6 0.8 1.0 2.0 3.0

Nicotinamide Better — Placebo Better

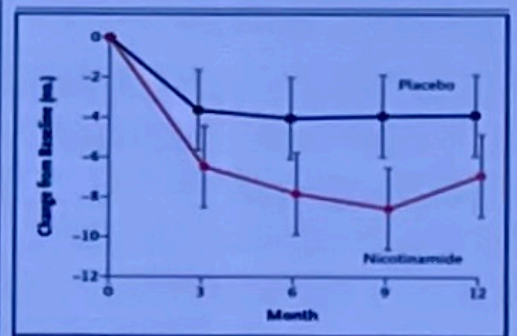


Figure 3. Change from Baseline to Month 12 in Number of Actinic Keratoses.

At 12 months: rate of NMSC was **23% lower** in the nicotinamide group vs. the placebo group (P=0.02)

No of AKs: 11% ⇩ in the nicotinamide group vs. placebo group (3 months), 14% ⇩ (6 months), 20% ⇩ (9 months) and 13% ⇩ (12 months)

⇨No maintenance of benefit after discontinuation

⇨No serious AEs

STUDY PARTICIPANTS

Eligible participants were 18 years of age or older and had had at least two histologically confirmed nonmelanoma skin cancers in the previous 5 years. Participants were ineligible if they were immunosuppressed; were pregnant or breast-feeding; had notably impaired liver or kidney function; had active peptic ulcer disease, a recent myocardial infarction, hypotension, a genetic skin-cancer syndrome, or large areas of confluent skin cancer (i.e., individual lesions that could not be counted); or had used nicotinamide supplements, oral retinoids, or field treatments for actinic keratosis, such as topical fluorouracil, in

Chen AC, Martin AJ et al. A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention. **N Engl J Med. 2015** Oct 22;373(17):1618-26.

RESEARCH SUMMARY

Nicotinamide for Skin-Cancer Chemoprevention in Transplant Recipients

Allen NC et al. DOI: 10.1056/NEJMoa2203086

CLINICAL TRIAL

Design: A randomized trial compared the incidence of skin cancer among solid-organ transplant recipients after receipt of oral nicotinamide or placebo.

Intervention: 158 adult solid-organ transplant recipients who had had ≥2 keratinocyte cancers within the past 5 years were assigned to receive either 500 mg of nicotinamide or placebo orally twice daily for 12 months; 157 participants were included in the analyses. The primary end point was the number of new keratinocyte cancers at 12 months.

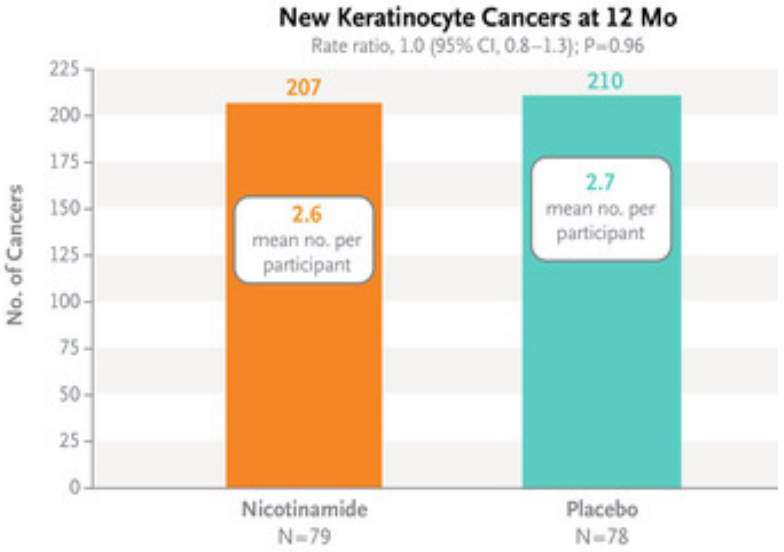
RESULTS

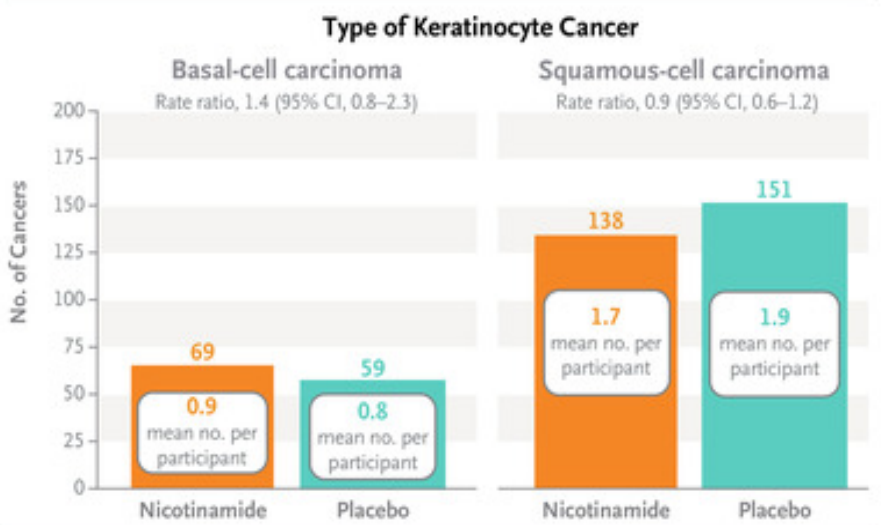
Efficacy: The mean number of keratinocyte cancers per participant did not differ significantly between the nicotinamide group and the placebo group.

Safety: The trial groups had similar numbers and types of adverse events, the most frequent of which were infections and infestations. Three systemic cancers occurred in the placebo group and one in the nicotinamide group.

LIMITATIONS AND REMAINING QUESTIONS

- The sample size was smaller than the target because of slow recruitment.
- The number of keratinocyte cancers detected during the trial was lower than the expected mean of 7 per participant.
- The authors hypothesize that some transplant recipients with a high skin-cancer burden were already using nicotinamide, which may have resulted in a lower-risk participant pool and affected participant recruitment.





CONCLUSIONS

In solid-organ transplant recipients taking immunosuppressive drugs, daily nicotinamide supplementation for 12 months did not lead to a lower incidence of keratinocyte cancers than placebo.

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.

HIGHLIGHTS

SINGAPORE

3-8 / july / 2023

Con el patrocinio de:

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