AAD **ANNUAL** MEETING

AEDV highlights

SAN DIEGO
8-12 MARZO

#AEDVENAAD2024

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

DERMATOLOGÍA ONCOLOGICA Y CIRUGÍA

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

ROMAN MIÑANO MEDRANO

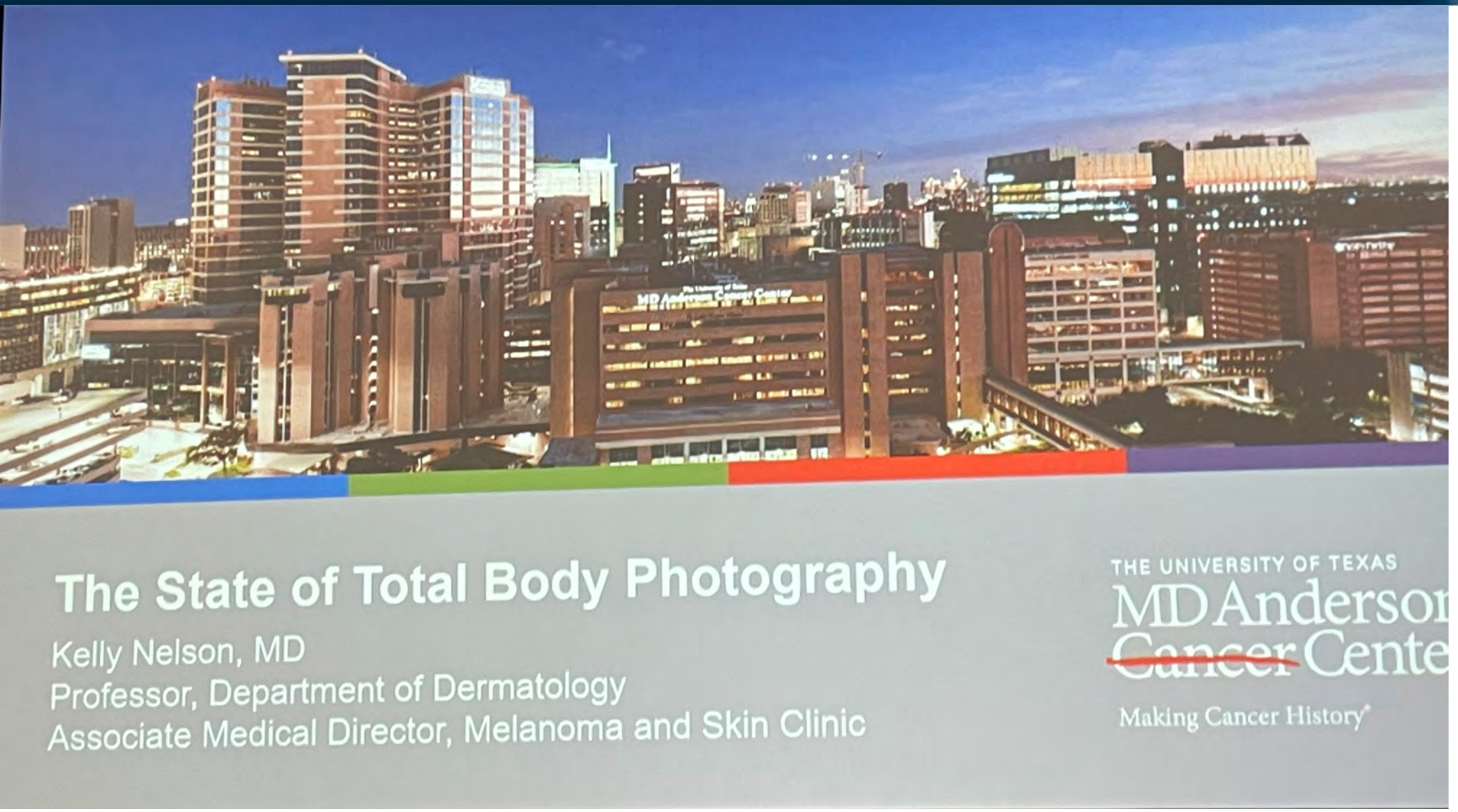
HOSPITAL UNIVERSITARIO FUNDACION ALCORCON

NO TENGO CONFLICTOS DE INTERÉS

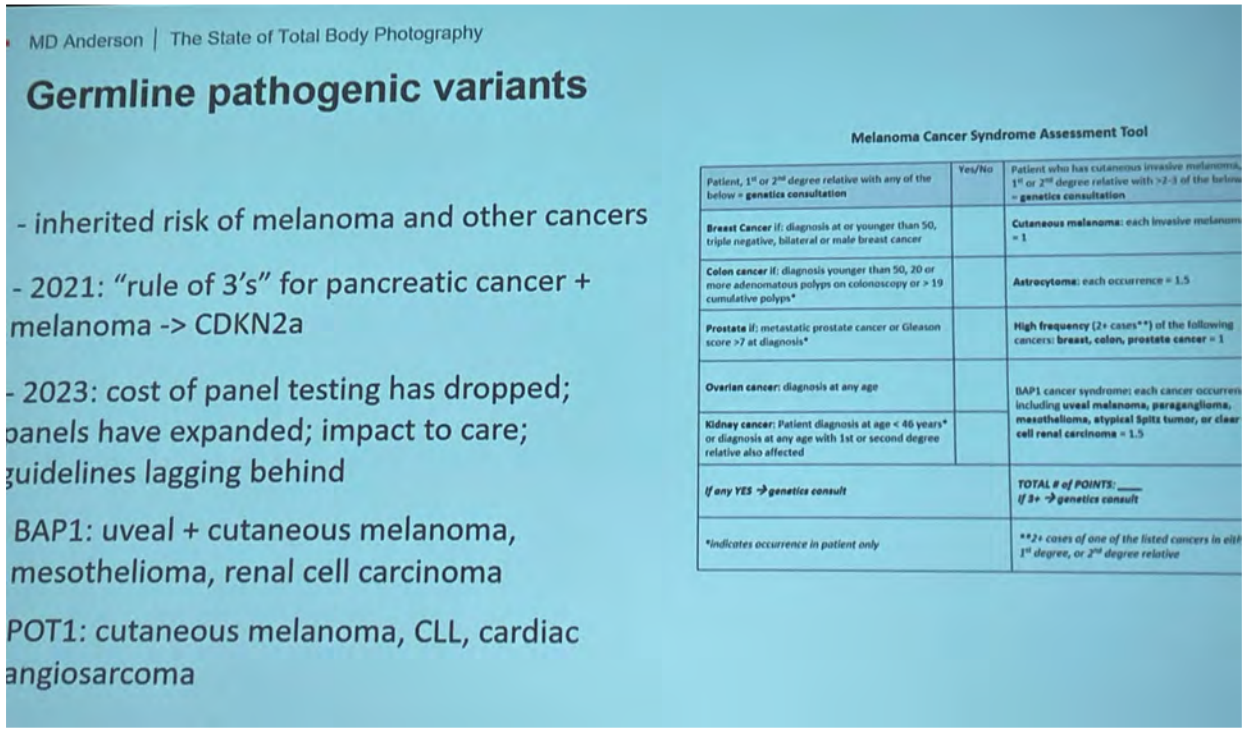
THE CHANGING LANDSCAPE OF EARLY-STAGE MELANOMA MANAGEMENT Room 8 9:00

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO



The State of Total Body Imaging Dra Kelly C Nelson



Objetivos

Detección temprana de melanoma

Manejo de la ansiedad del paciente

Reducir número de biopsia de lesiones benignas

Pacientes benefician de TBP

Germline pathogenic variantes

Fenotipos desafiantes

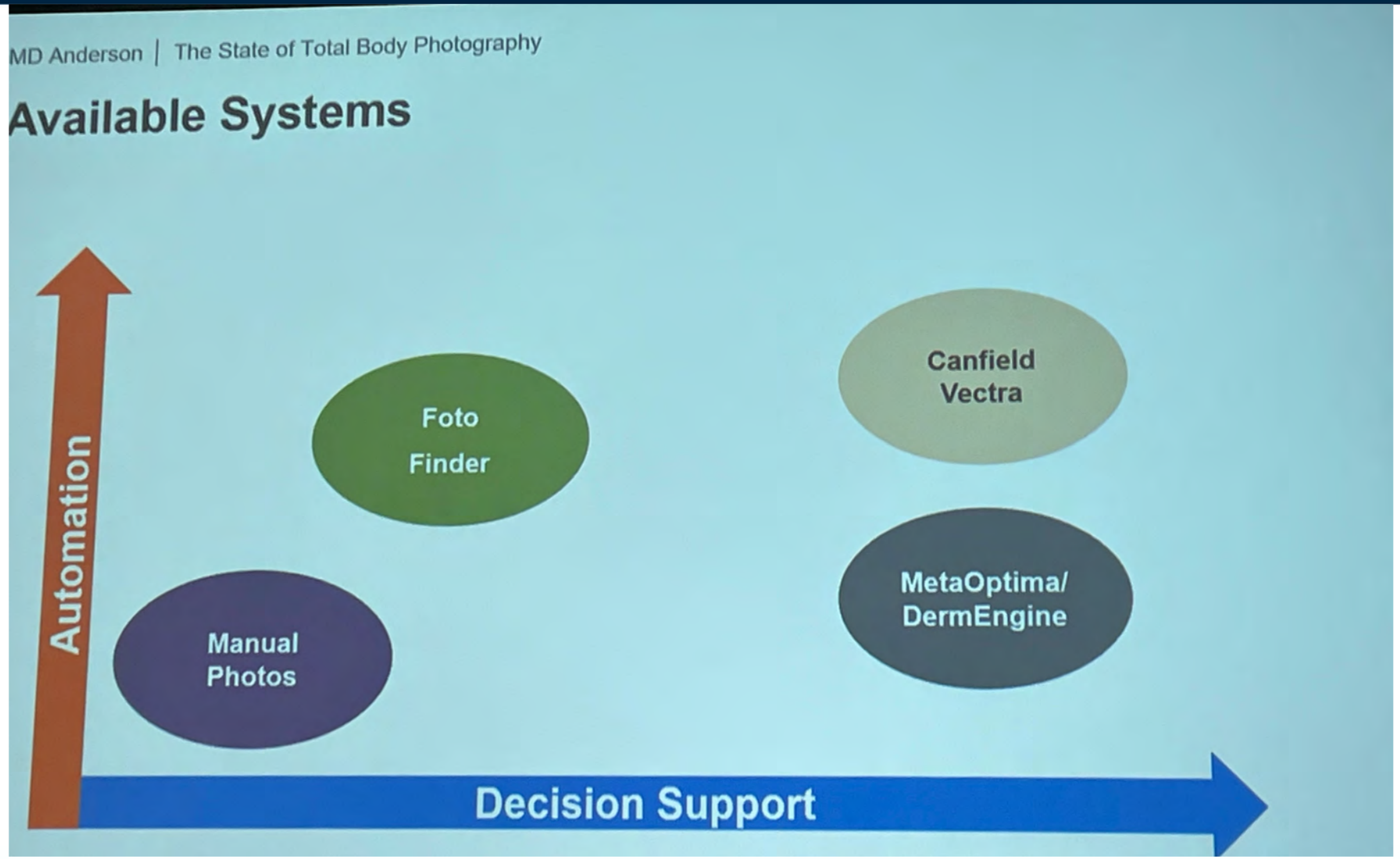
Ansiedad.

The State of Total Body Imaging Dra Kelly C Nelson

Melanoma Cancer Syndrome Assessment Tool

Patient, 1st or 2nd degree relative with any of the below = **genetics consultation**	Yes/No	Patient who has cutaneous invasive melanoma, 1st or 2nd degree relative with >2-3 of the below = **genetics consultation**	No. of points
Breast Cancer if: diagnosis at or younger than 50, triple negative, bilateral or male breast cancer		**Cutaneous melanoma**: each invasive melanoma = 1	
Colon cancer if: diagnosis younger than 50, 20 or more adenomatous polyps on colonoscopy or > 19 cumulative polyps*		**Astrocytoma**: each occurrence = 1.5	
Prostate if: metastatic prostate cancer or Gleason score >7 at diagnosis*		**High frequency** (2+ cases**) of the following cancers: **breast, colon, prostate cancer** = 1	
Ovarian cancer: diagnosis at any age		BAP1 cancer syndrome: each cancer occurrence including **uveal melanoma, paraganglioma, mesothelioma, atypical Spitz tumor, or clear cell renal carcinoma** = 1.5	
Kidney cancer: Patient diagnosis at age < 46 years* or diagnosis at any age with 1st or second degree relative also affected			
If any YES → genetics consult		***TOTAL # of POINTS: ____ If 3+ → genetics consult***	
**Indicates occurrence in patient only*		***2+ cases of one of the listed cancers in either the patient, 1st degree, or 2nd degree relative*	

The State of Total Body Imaging Dra Kelly C Nelson

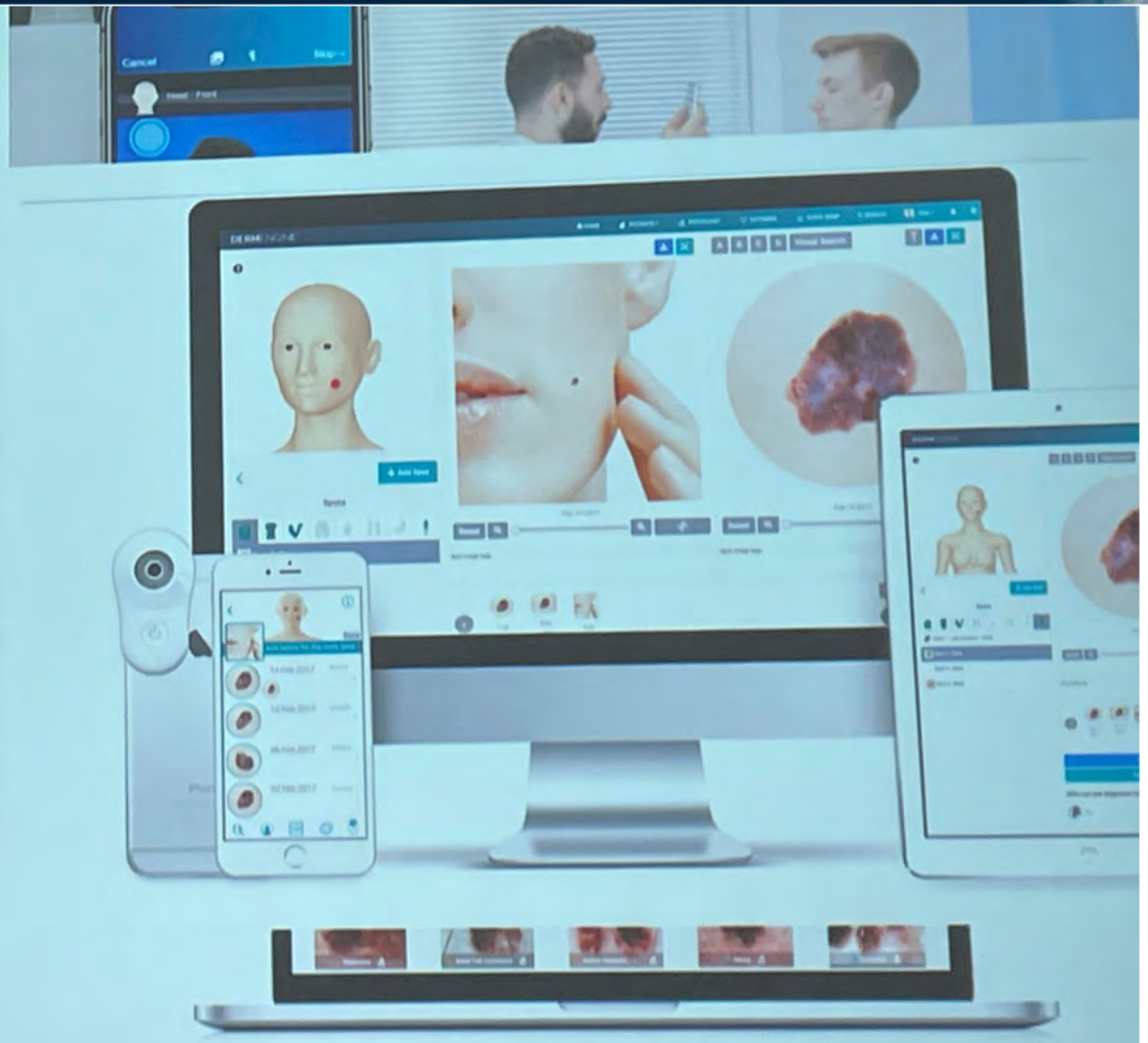


The State of Total Body Imaging Dra Kelly C Nelson

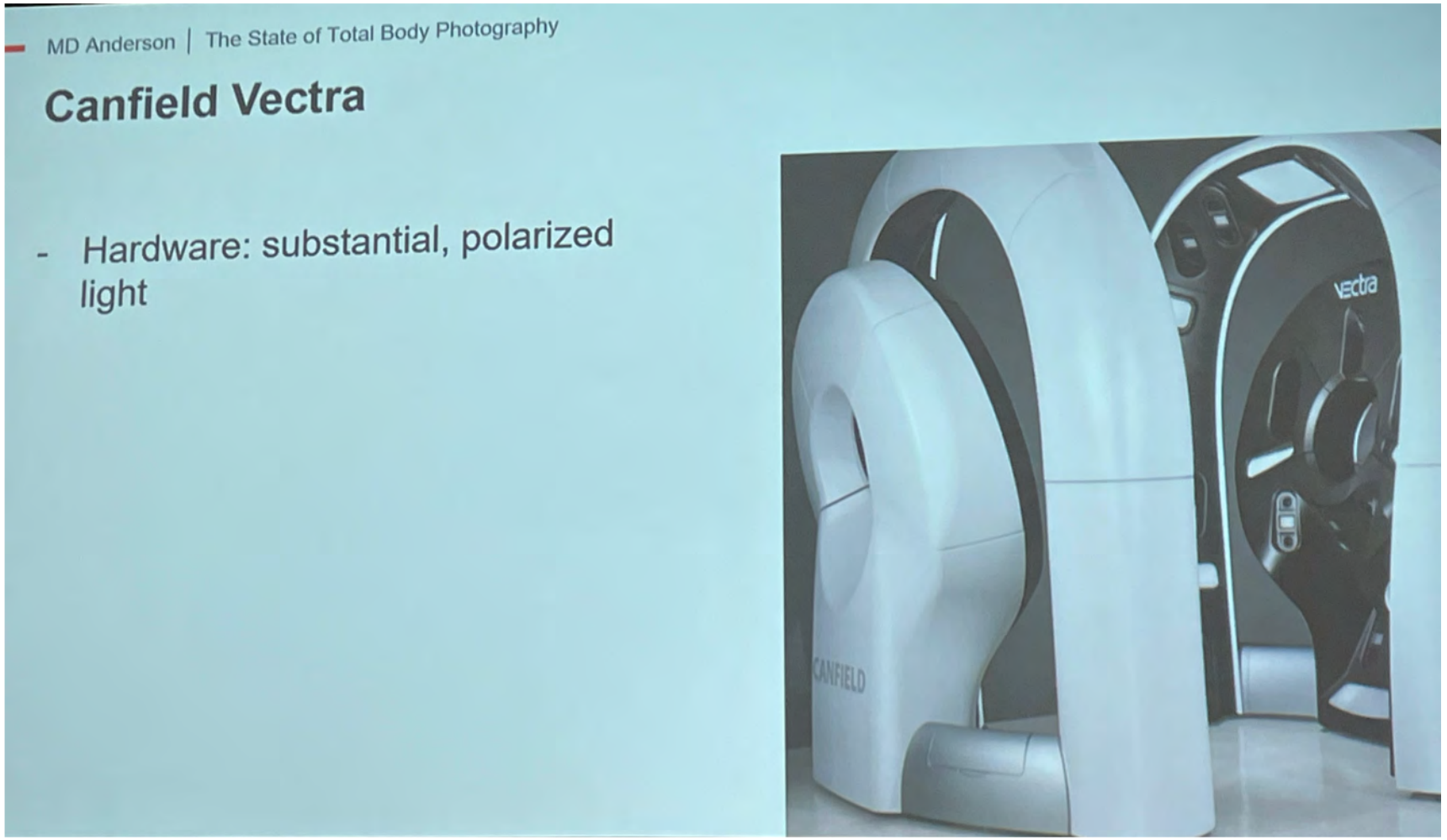
MD Anderson | The State of Total Body Photography

MetaOptima/DermEngine

- Hardware: variable
- Image capture: variable = ghosting
- Comparison: automated + change, any computer
- Decision support: Visual Search
- Dermoscopic image tagging: yes



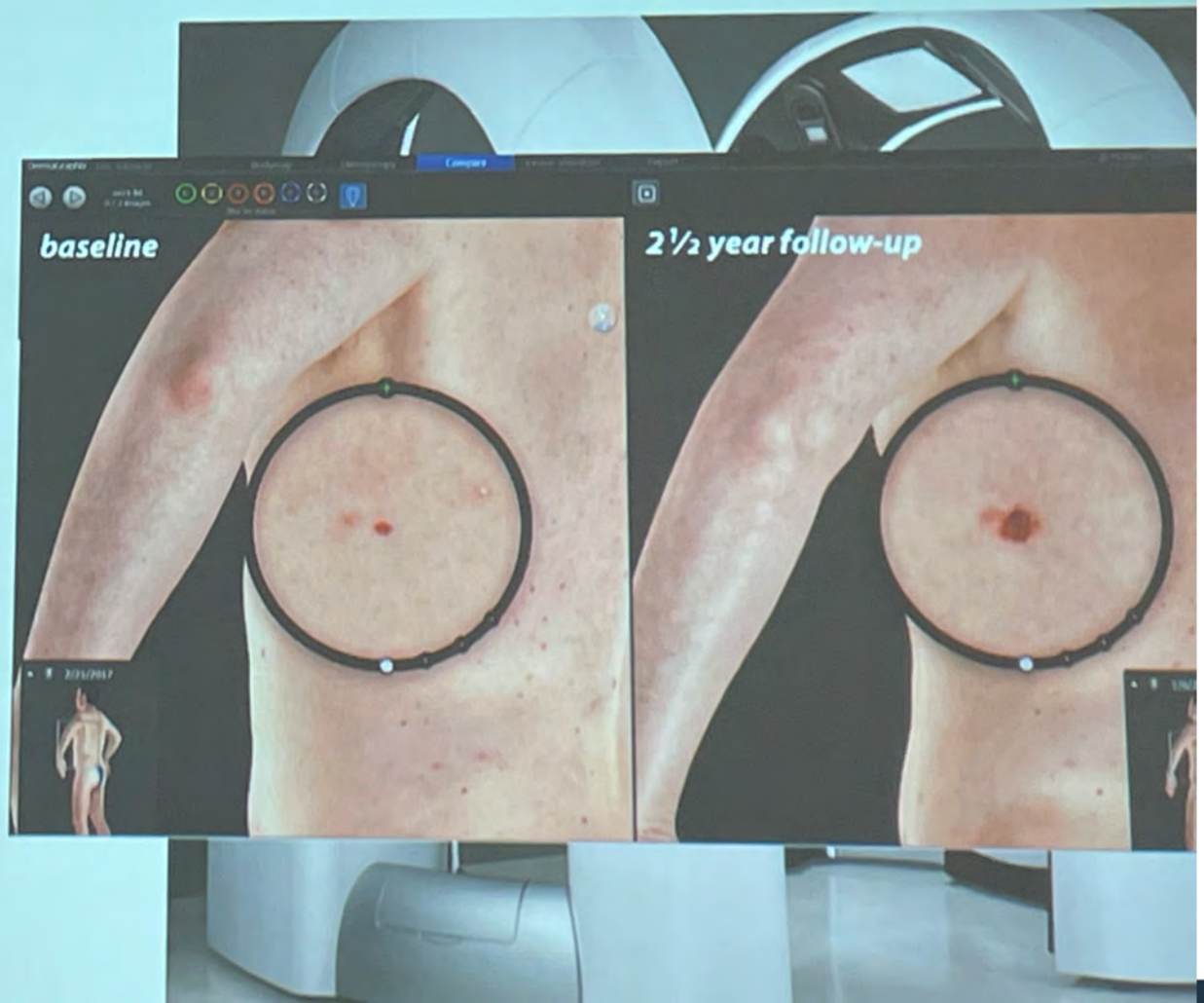
The State of Total Body Imaging Dra Kelly C Nelson



The State of Total Body Imaging Dra Kelly C Nelson

Canfield Vectra

- Hardware: substantial, polarized light
- Image capture: instantaneous
- Comparison: automated + change, touch screen computer *single lesion registration



Take Home Messages

- Variety of systems, more coming to market
- More patients are being identified with high –risk pathogenic variants

Benefit of out-of-the-exam-room comparison

Melanoma Literature Update

Michael E Ming, MD, MSCE
Associate Professor of Dermatology
Hospital of the University of Pennsylvania
Philadelphia, PA

Melanoma Literature Update. Dr. Michalel E. Ming.

Chen Q, Zheng M, Ling C. Incidence trends of lentigo maligna and lentigo maligna melanoma in the United States from 2000 to 2019. *Int J Dermatol.* Jan 2024 doi:10.1111/ijd.16982

- SEER (Surveillance Epidemiology and End Results) database from 2000-2019
- Incidence of LM and LMM increased for all ages between 2001-2015
  - But trend seems to be different in recent years
    - Trend for incidence rate is decreasing from 2015-2019 for males, females, and overall
    - This is expansion of a trend seen in SEER from 2006-2015, when the overall rate for melanoma was increasing, but younger people (those less than 30 yo) had a decreasing rate

Lentigo maligna melanoma rates in US

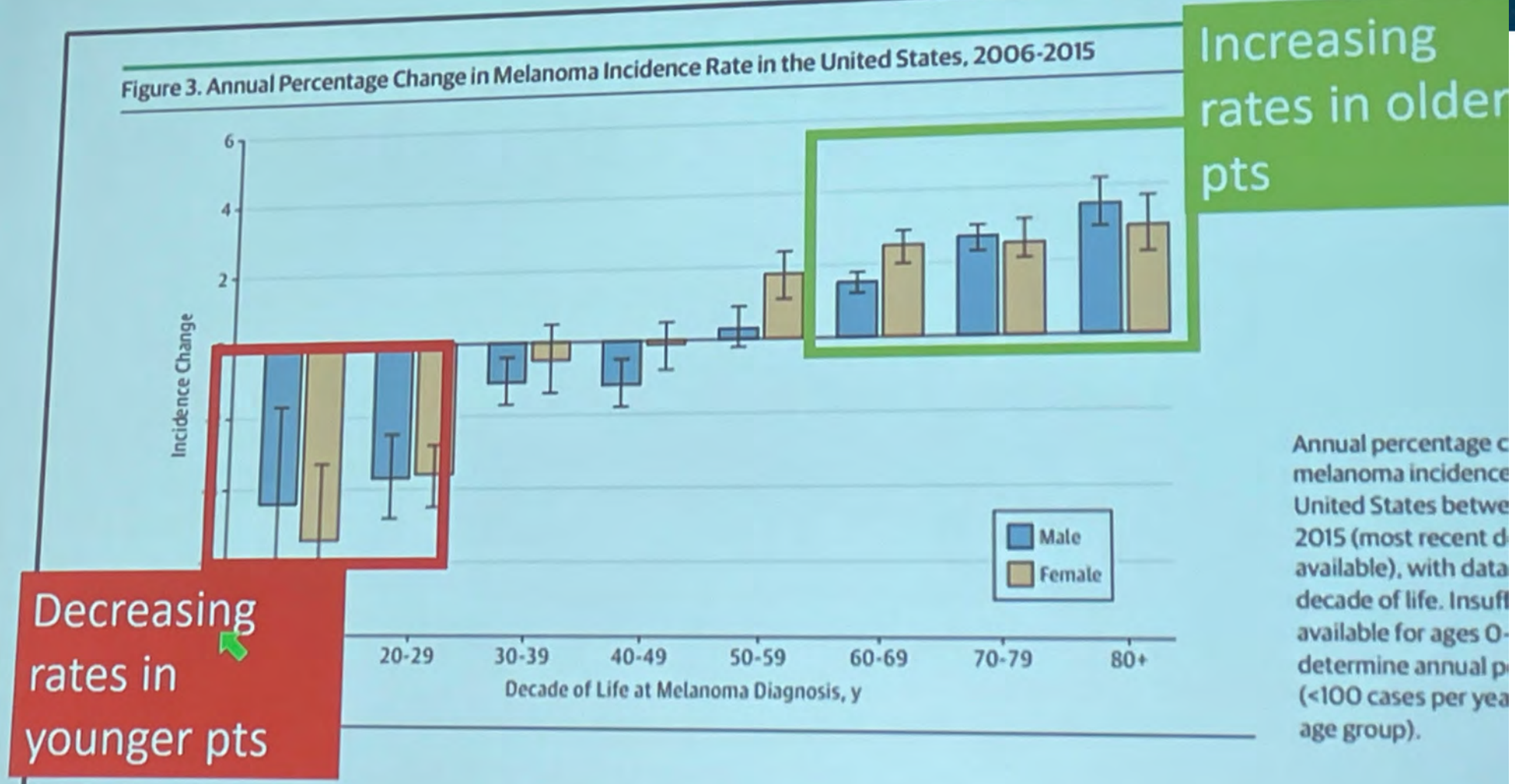
Melanoma Literature Update. Dr. Michalel E. Ming.

Berk-Krauss J, Sharma M, Polsky D, Geller AC. Cutaneous melanoma incidence-Evidence of a flattening curve. *J Am Acad Dermatol. .* 2023 doi:10.1016/j.jaad.2023.12.010

- Also used SEER (Surveillance Epidemiology and End Results) database from 2000-2019
  - Thin (T1) melanoma incidence rate for 70+ yo increased from 2000-2014, but the rate decreased from 2014-2019
  - Thick (T4) melanoma incidence rate for 70+ yo increased throughout 2000-2019, but the slope of the increase flattened after 2010

- These data along with the prior article seem to indicate that melanoma incidence rate may be decreasing
  - This could be from effective public health messaging about sun avoidance
  - We will see what future trends are

2006-2015



(JAMA Dermatol. 2020;156(1):57-64. doi:10.1001/jamadermatol.2019.33

Melanoma Literature Update. Dr. Michalel E. Ming.

Shifai N, van Doorn R, Malvehy J, Sangers TE. Can ChatGPT Vision diagnose melanoma? An exploratory diagnostic accuracy study. *J Am Acad Dermatol.* In press doi:10.1016/j.jaad.2023.12.062

- Can ChatGPT Vision diagnose melanoma?
  - No, it can not
    - Specificity, sensitivity, and accuracy were all less than 40% in distinguishing melanoma from nevi

NO

Melanoma Literature Update. Dr. Michalel E. Ming.

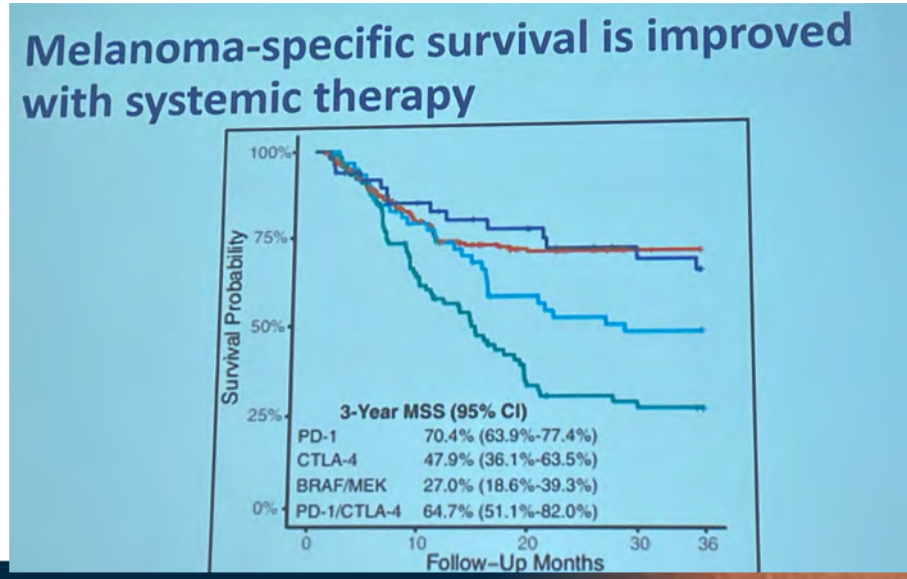
Young JN, Ross O'Hagan, Poplausky D, et al. The utility of ChatGPT in generating patient-facing and clinical responses for melanoma. *J Am Acad Dermatol. .* 2023;89(3):602-604. doi:10.1016/j.jaad.2023.05.024

- ChatGPT can provide general information like you might find on a website
  - But it can not provide specifics that a doctor would provide (eg, frequency of follow up)
    - It can not replace a medical visit

Melanoma Literature Update. Dr. Michalel E. Ming.

Kim DY, Swetter SM, Huhmann L, et al. Real-world effectiveness of immune checkpoint inhibitors and BRAF/MEK inhibitors among veteran patients with cutaneous melanoma. *J Am Acad Dermatol. .* 2024;90(3):620-623. doi:10.1016/j.jaad.2023.10.051

- Immunotherapy and targeted therapy with BRAK/MEK inhibitors were shown in clinical trials to be effective against melanoma, resulting in FDA approval
- This study used a VA population to show that these therapies were also effective in the real world, with significant improvements in survival



New Systematic Therapies and Trends in Cutaneous Melanoma Deaths Among US Whites, 1986–2016

Juliana Berk-Krauss, MD, Jennifer A. Stein, MD, PhD, Jeffrey Weber, MD, PhD, David Polsky, MD, PhD, and Alan C. Geller, RN, MPH

Objectives. To determine the effect of new therapies and trends toward reduced mortality rates of melanoma.

Methods. We reviewed melanoma incidence and mortality among Whites (the group most affected by melanoma) in 9 US Surveillance, Epidemiology, and End Results registry areas that recorded data between 1986 and 2016.

Results. From 1986 to 2013, overall mortality rates increased by 7.5%. Beginning in

We coded incident melanomas of the skin according to the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3; Geneva, Switzerland: World Health Organization; 2000), histological tumor classification. We obtained overall age-adjusted

(Am J Public Health. 2020;110: 731–733. doi:10.2105/AJPH.2020.305567)

Melanoma Literature Update. Dr. Michalel E. Ming.

Approved melanoma therapies

2010:

- Dacarbazine
- Interferon-alfa
- IL-2

2024:

- **Ipilimumab**
- **Verumafenib**
- **Talimogene laherparepvec**
- **Pembrolizumab**
- **Nivolumab (for Stage II disease)**
- **Debrafenib**
- **Nivolumab and ipilimumab**
- **Trametinib**
- **Trametinib/dabrafenib**
- **Azetolizumab/cobimetinib/ vemurafenib**
- **Encorafenib/bimetinib**
- **Cobimetinib/vemurafenib**
- **Nivolumab/relatlimab**
- **Lifelucel (Feb 2024)**

Melanoma Literature Update. Dr. Michalel E. Ming.

Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *N Engl J Med. .* 2022;386(1):24-34. doi:10.1056/NEJMoa2109970

Relatlimab/nivolumab

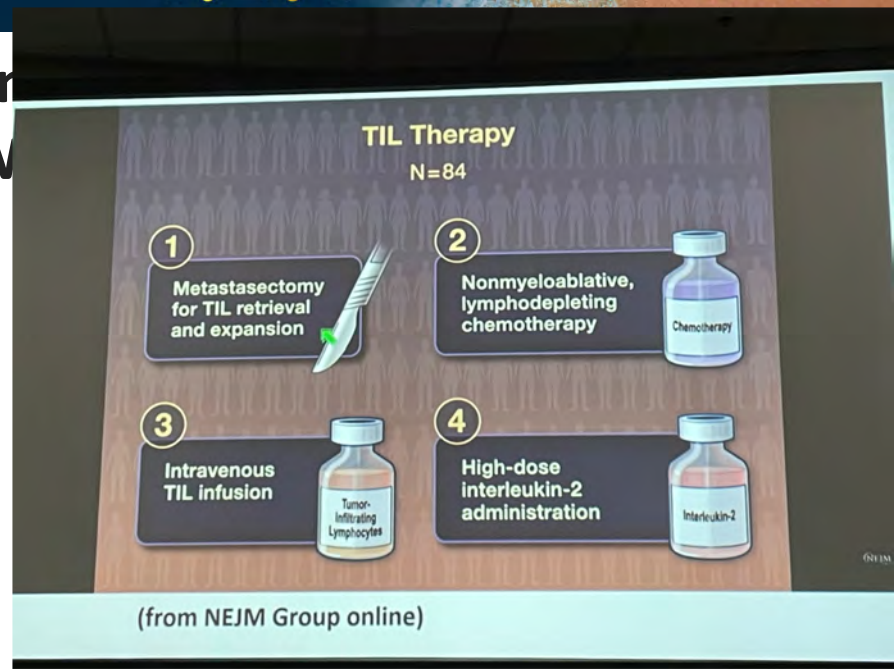
- Immunotherapy with 2 agents
  - Nivolumab – PD-1 inhibitor
    - Already approved in 2014 as a single agent
    - Approved in 2015 in combination with ipilimumab
      - Combo works better but more side effects
  - Relatlimab – monoclonal antibody against LAG-3 (lymphocyte activation gene 3 protein)
    - LAG-3 receptor is expressed on T-cells and inhibits T-cell immune response

Relatlimab/nivolumab

- This paper described a randomized controlled trial of 714 pts with unresectable Stage III or Stage IV melanoma
  - Relatlimab/nivolumab vs nivolumab only
- Relatlimab/nivolumab was better than nivolumab alone
  - Progression-free survival at 12 months was 47% vs 36%
  - Median progression-free survival was 10.1 months vs 4.6 months
  - More serious side effects with combination therapy (19% vs 10%)

Melanoma Literature Update. Dr. Michalel E. Ming.

Rohaan MW, Borch TH, van den Berg JH, et al. Tumor-Infiltratin
Lymphocyte Therapy or Ipilimumab in Advanced Melanoma. *N*
Engl J Med. . 2022;387(23):2113-2125.
doi:10.1056/NEJMoa2210233



(from NEJM Group online)

Lifeleucel

- Adoptive cell therapy with tumor-infiltrating lymphocytes
  - "TIL therapy"
  - Uses patient's own T-cells
    - First such T-cell therapy approved for a solid cancer

Lifeleucel

- The process is:
  - Metastases are removed and T-cells extracted in the lab
  - Pt has nonmyeloablative, lymphodepleting chemotherapy to reduce their own T-cells
  - The extracted T-cells are expanded in the lab and given intravenously to the patient along with IL-2

Melanoma Literature Update. Dr. Michalel E. Ming.

Lifeleucel

- This paper describes a randomized controlled trial of 168 pts with unresectable Stage IIIC or Stage IV melanoma
  - 86% had failed immunotherapy already with either nivolumab or pembrolizumab
  - TIL therapy vs ipilimumab
    - TIL therapy group did better by many measures, including 20% complete response vs 7% for ipi group

Weber JS, Carlino MS, Khattak A, et al. Individualised neoantigen therapy mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy in resected melanoma (KEYNOTE-942): a randomised, phase 2b study. *Lancet.* . 2024;403(10427):632-644. doi:10.1016/S0140-6736(23)02268-7

Melanoma vaccine?

- Not a vaccine in the usual way we think of a vaccine
  - Not preventing disease from occurring
  - Used for metastatic disease, where the tumor can be removed and analyzed
- Creating an mRNA vaccine personalized against up to 34 specific neoantigens present on that patient's melanoma
  - 91% of patients had all 34 neoantigens
- Given with pembrolizumab to block immune system inhibition

- This paper described a phase 2 trial: 157 patients with Stage IIIB-IV melanoma
- RCT for vaccine + pembro vs pembro alone
- Improved recurrence-free survival and 18-month survival
- Not yet FDA approved, phase III trial is next step

Emerging therapeutic options for higher-risk melanoma

John Miura
Assistant Professor of Surgery
Hospital of the University of Pennsylvania

March 8, 2024

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Approved therapies for melanoma

Immunotherapy

Imlygic (talimpogene laherparapvec "T-vec")
Intron A (high dose IFNalpha-2b)
Keytruda (pembrolizumab)
Opdivo (nivolumab)
Opdivo (nivolumab) and Yervoy (ipilimumab)
Opdualag (Nivolumab/relatlimab)
Proleukin/IL-2
Sylatron (peginterferon alpha-2b)
Yervoy (ipilimumab)

Targeted therapies

Braftovi (encorafenib) and Mektovi (binimetinib) Combination
Cotellic (cobimetinib) and Zelboraf (vemurafenib) Combination
Mekinist (trametiinib)
Mekinist (trametinib) and Tafinlar (dabrafenib)
Tafinlar (Dabrafenib)
Zelboraf (vemurafenib)

Adjuvant Trials For Stage III/IV Melanoma: Current Landscape

Trial	Regimen	HR RFS	HR DMFS	HR OS
Immunotherapy				
EORTC 18071	Ipilimumab 10 mg/kg vs. placebo	0.76	0.76	0.72
EORTC 1325	Pembrolizumab 200 mg vs. placebo	0.57	0.53	NA
CheckMate 238	Ipilimumab 10 mg/kg vs. nivolumab 3 mg/kg	0.65	0.73	NA
ECOG 1609	Ipilimumab 10 mg/kg vs. ipilimumab 3 mg/kg vs. IFN-α2b	1	NA	NA
Targeted therapy				
BRIM-8	Vemurafenib vs. placebo	0.54 (IIC-IIIB); 0.8 (IIIC)	NA	NA
COMBI-AD	Dabrafenib + trametinib vs. placebo	0.47	0.51	0.57

Abbreviations: DMFS, distant metastatic-free survival; HR, hazard ratio; OS, overall survival; RFS, recurrence-free survival

Patel et al. JSO 2022; 125: 38-45.

- Adjuvant immunotherapy or targeted therapy improved RFS

***Eligibility for adjuvant therapy among clinically node negative patients required a + SLN Biopsy**

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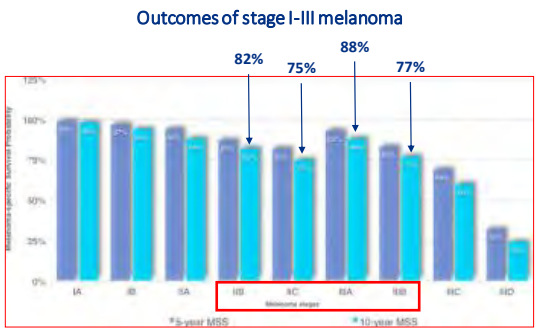
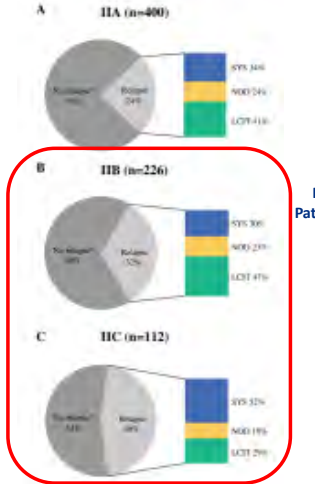
Treating melanoma in earlier stage disease



5/10yr MSS (AJCC 8th Edition)



Patterns of Relapse in Pathologic Stage II Patients

Napolitano et al cancer Treatment Rev 2018. Modified by: Gershenwald JE, et al. CA Cancer J Clin. 2017
Lee et al. Annals of Surg Onc 2017

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Adjuvant Immunotherapy Now FDA Approved for Pathologic Stage IIB/C Melanoma

Luke et al. Lancet 2022

KEYNOTE-716

Stage IIB/C (pT3b/T4a/bN0)

SLN Negative Patients

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Does Treatment Sequence Matter?

"Standard of Care"

Patel et al. ESMO 2022, NEJM 2023

Rationale for neoadjuvant therapy

- Pros
  - Earlier treatment of subclinical/micrometastatic disease
  - Tumor (antigens) present during treatment: “Immunopriming”
  - Allows assessment of response to therapy
  - Identify patients with rapidly progressive/ treatment unresponsive disease
  - Potential shrinkage of tumor => Easier/more feasible surgery
  - Neoadjuvant therapy may be associated with longer RFS

- Cons
  - Delays surgical intervention for resectable disease
  - Potential treatment toxicities

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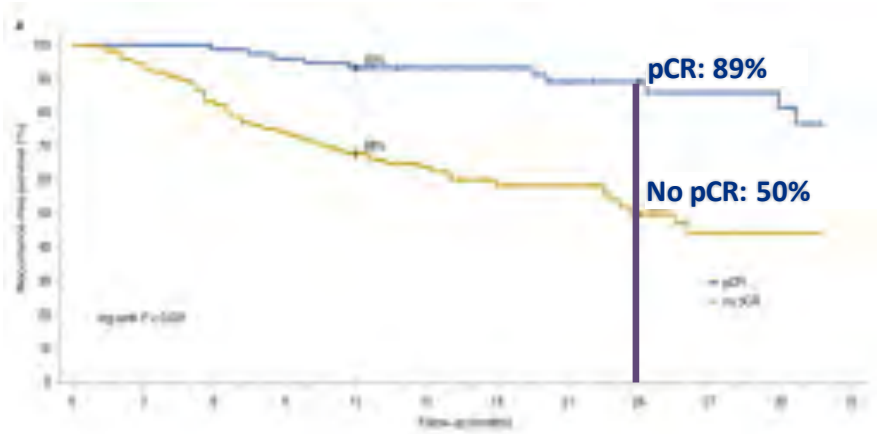
Neoadjuvant therapy associated with high pathologic response rates for clinical stage III melanoma

- Modern Melanoma NST Trials

Trial	Regimen	pCR (%)
Amaria Lancet Onc 2018	Dab/Tram	58
Long Lancet Onc 2019	Dab/Tram	49
Blank Nat Med 2018	Ipi+Nivo	33
Amaria Nat Med 2018	Ipi+Nivo Nivo	45 25
Huang Nat Med 2019*	Pembro	19
Rozeman Lancet Onc 2019	Ipi+Nivo	57

Menzies et al. Nature Med. 2021



- pCR results in a durable survival benefit

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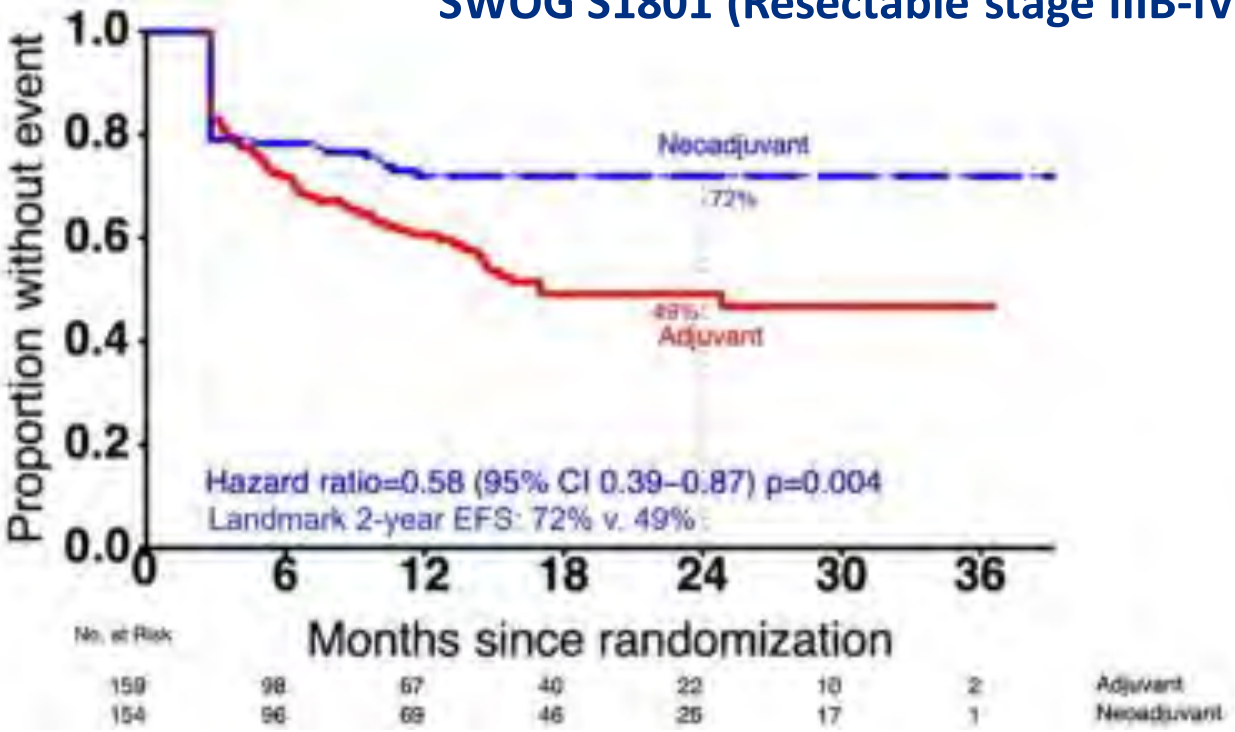
Neoadjuvant vs Adjuvant: Which is better?

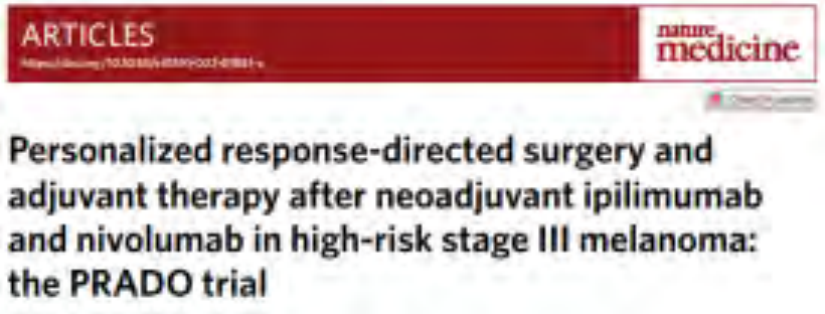
SWOG S1801 (Resectable stage IIIB-IV)



"A neoadjuvant approach may be more effective at preventing relapses than adjuvant therapy"

Patel et al. ESMO 2022, NEJM 2023

Neoadjuvant therapy may allow for de-escalation of therapy in patients achieving a major pathologic response


ARTICLES

nature medicine

Personalized response-directed surgery and adjuvant therapy after neoadjuvant ipilimumab and nivolumab in high-risk stage III melanoma: the PRADO trial

TLND was omitted in 59 (60%) of patients!!!

- 99 Patients Enrolled
- Pathologic Response:
  - pRR: 70%
  - pMPR: 61%
- 2yr RFS
  - MPR: 93%
  - PR: 64%
  - NR: 71.4%

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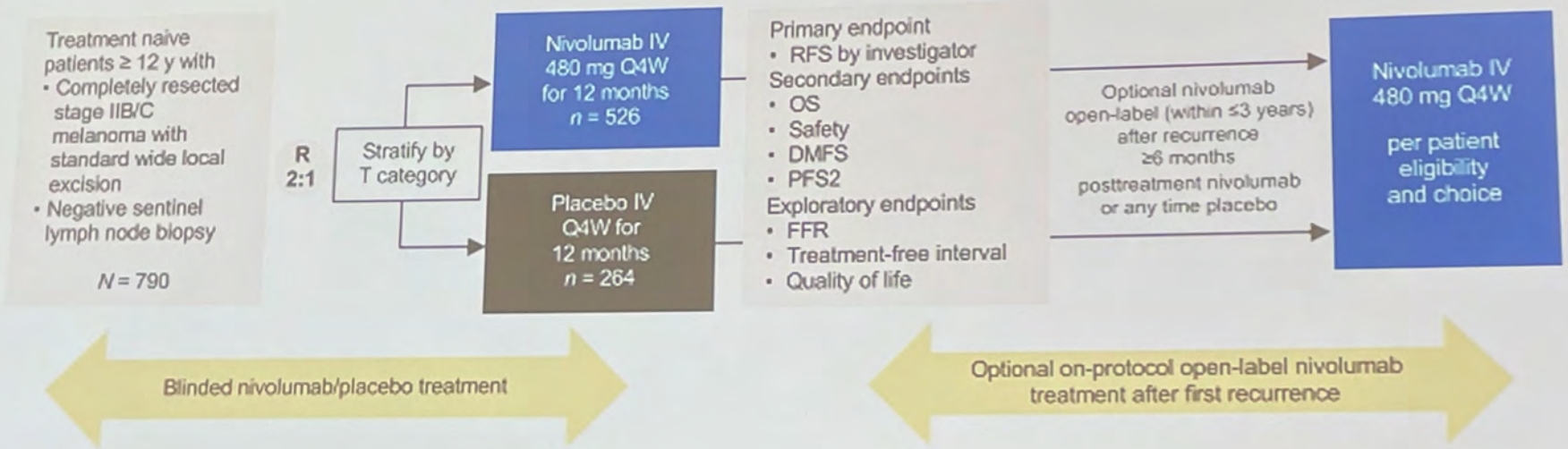
Reijers et al, Nature Medicine 2022

ADVANCED MELANOMA THERAPY. Laura K. Ferris

Article

Adjuvant nivolumab in resected stage IIB/C melanoma: primary results from the randomized, phase 3 CheckMate 76K trial

Nat Med. 2023 Nov;29(11):2835-2843.



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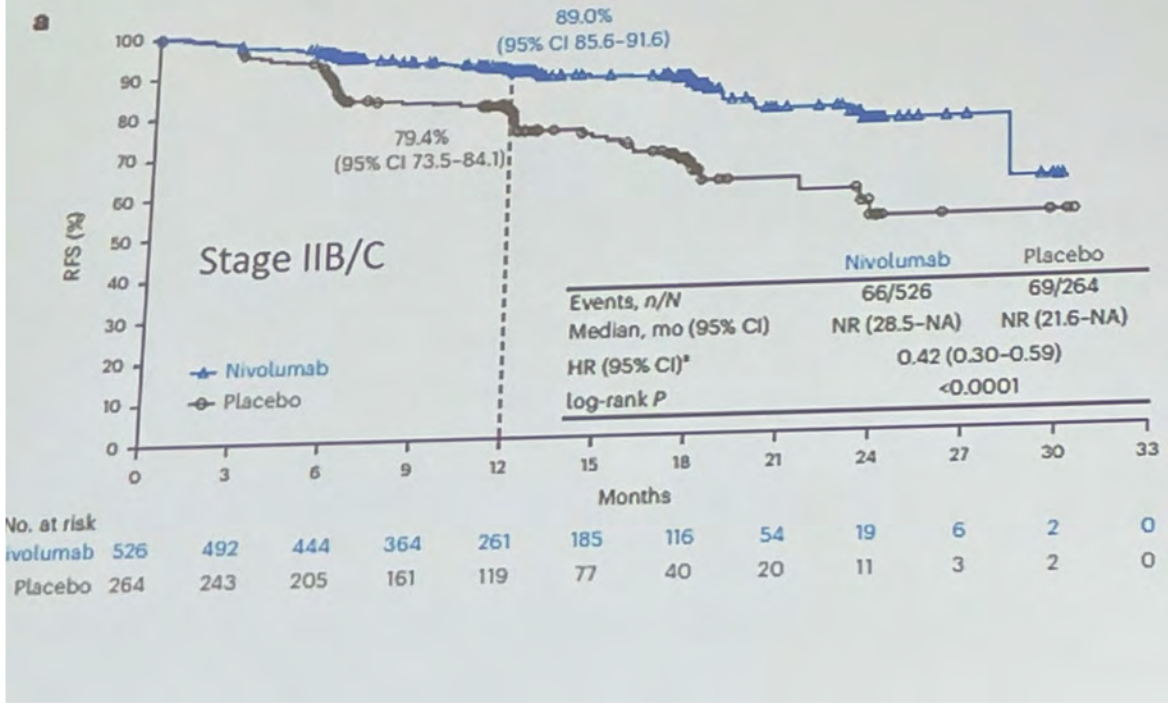
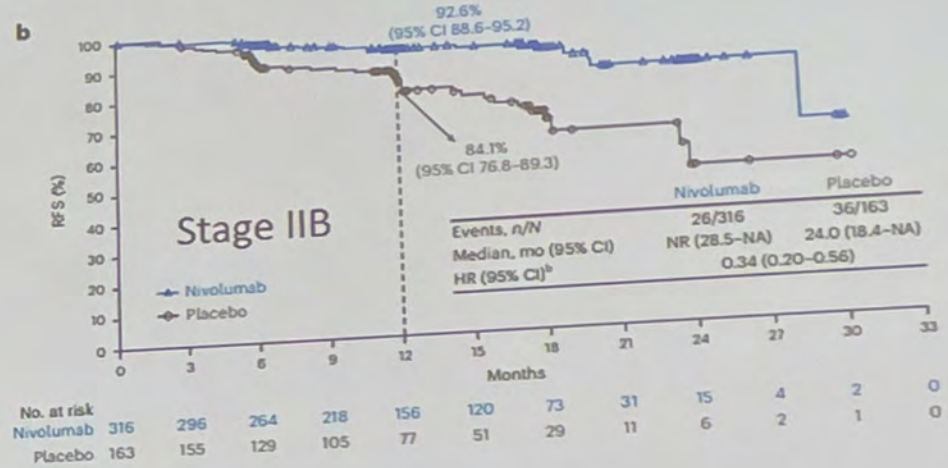
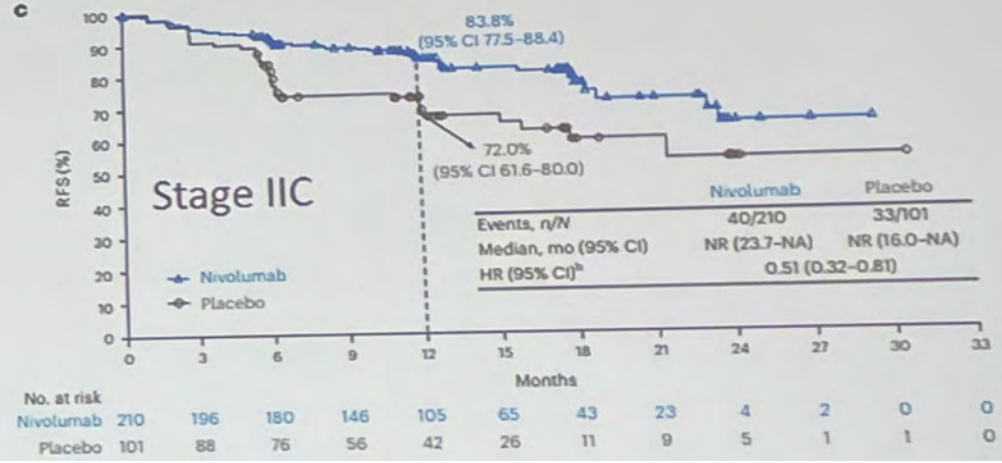


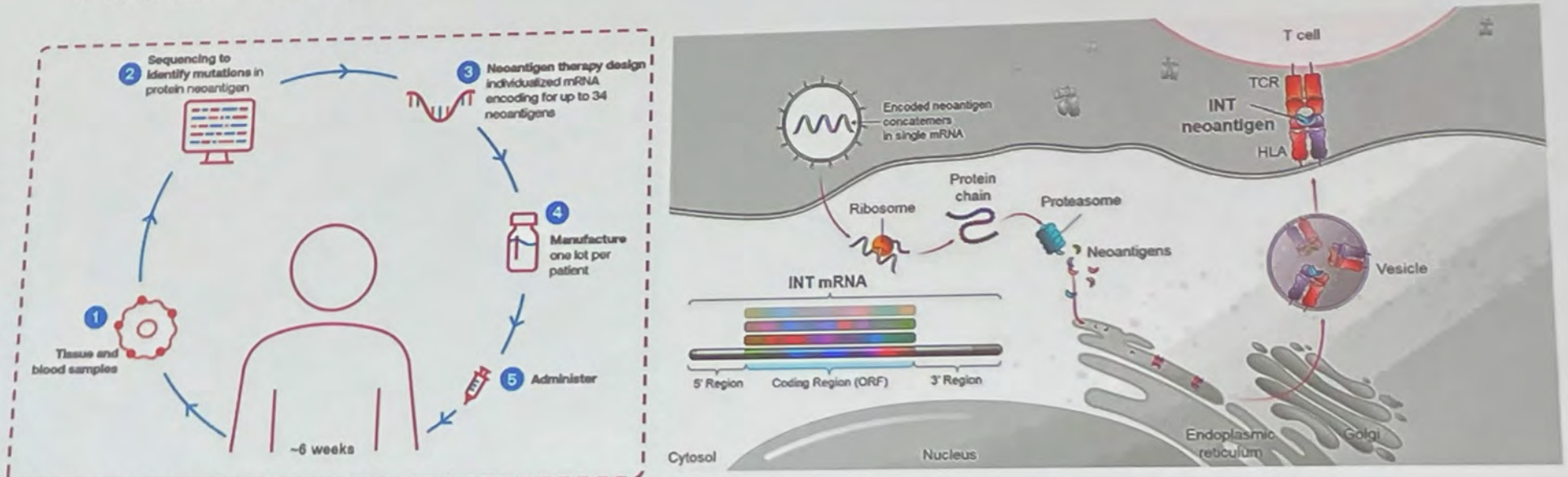




Individualized mRNA vaccine against melanoma

mRNA-4157 (V940) Mechanism of Action

- mRNA-4157 (V940) is **an individualized neoantigen therapy** designed to target an individual patient's unique tumor mutations and encodes up to 34 neoantigens[1,2]
- Therapies targeting neoantigens can increase endogenous **neoantigen T-cell responses and induce epitope spreading** to novel antigens with the ability **to drive antitumor responses** and **maintain memory** with cytolytic properties, potentially **producing long-term disease control** for patients[3-7]



HLA, human leukocyte antigen; INT, individualized neoantigen therapy; ORF, open reading frame.

1. Burris HA, et al. *J Clin Oncol*. 2019;37(suppl 15). Abstract 2523. 2. Zhong S, et al. *Cancer Res*. 80(suppl 16). Abstract 6539. 3. Wirth TC, Kühnel F. *Front Immunol*. 2017;8:1848. 4. Ott PA, et al. *Nature*. 2017;547:217-221. 5. Hu Z, et al. *Nat Med*. 2021;27:515-525. 6. Ott PA, et al. *Cell*. 2020;183:347-362. 7. Palmer CD, et al. *Nat Med*. 2022;28:1619-1629.

mRNA-4157-P201/KEYNOTE-942 (NCT03897881) Study Design

Randomized, phase 2, open-label study in adjuvant resected melanoma patients at high risk of recurrence

Key eligibility criteria

- Resected stage IIIB,[a] IIIC, IIID, or IV cutaneous melanoma
- Complete surgical resection within 13 weeks prior to first pembrolizumab dose
- Disease-free at study entry
- ECOG PS score 0-1
- Tissue available for NGS

2:1 Randomization

Stratified by disease stage[b]

Combination treatment arm: mRNA-4157 (V940) + pembrolizumab
Up to 1 year of pembrolizumab treatment
mRNA-4157 (V940) 1 mg IM Q3W for up to 9 doses +
pembrolizumab 200 mg IV Q3W for up to 18 cycles
(n = 107)

Control treatment arm: pembrolizumab monotherapy
Up to 1 year of pembrolizumab treatment
pembrolizumab 200 mg IV Q3W for up to 18 cycles
(n = 50)

Primary endpoint:
RFS[c,d]

Secondary endpoints:
DMFS,[e]
safety, tolerability

Follow-up:
up to 3 years following the first dose of pembrolizumab

Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1)
DMFS analysis was prespecified for testing following positive RFS in the ITT population[f]
Median follow-up[g]: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab monotherapy

[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. [b]According to the 8th edition of the American Joint Committee on Cancer Staging Manual. [c]The primary endpoint was investigator-assessed RFS (defined as the time from first dose of pembrolizumab until the date of first recurrence [local, regional, or distant metastasis], a new primary melanoma, or death from any cause) in the intention-to-treat population. [d]The primary analysis for RFS was specified to occur after all patients completed ≥12

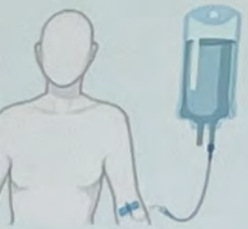
Cardiac toxicity associated with TIL therapy

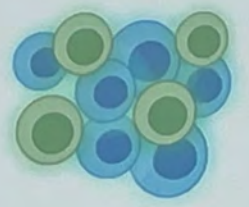
TIL cardiotoxicity timeline

1 **Lymphodepletion**
Cyclophosphamide and fludarabine

2 **TIL infusion**
TIL cells

3 **IL-2 doses**
Recombinant IL-2





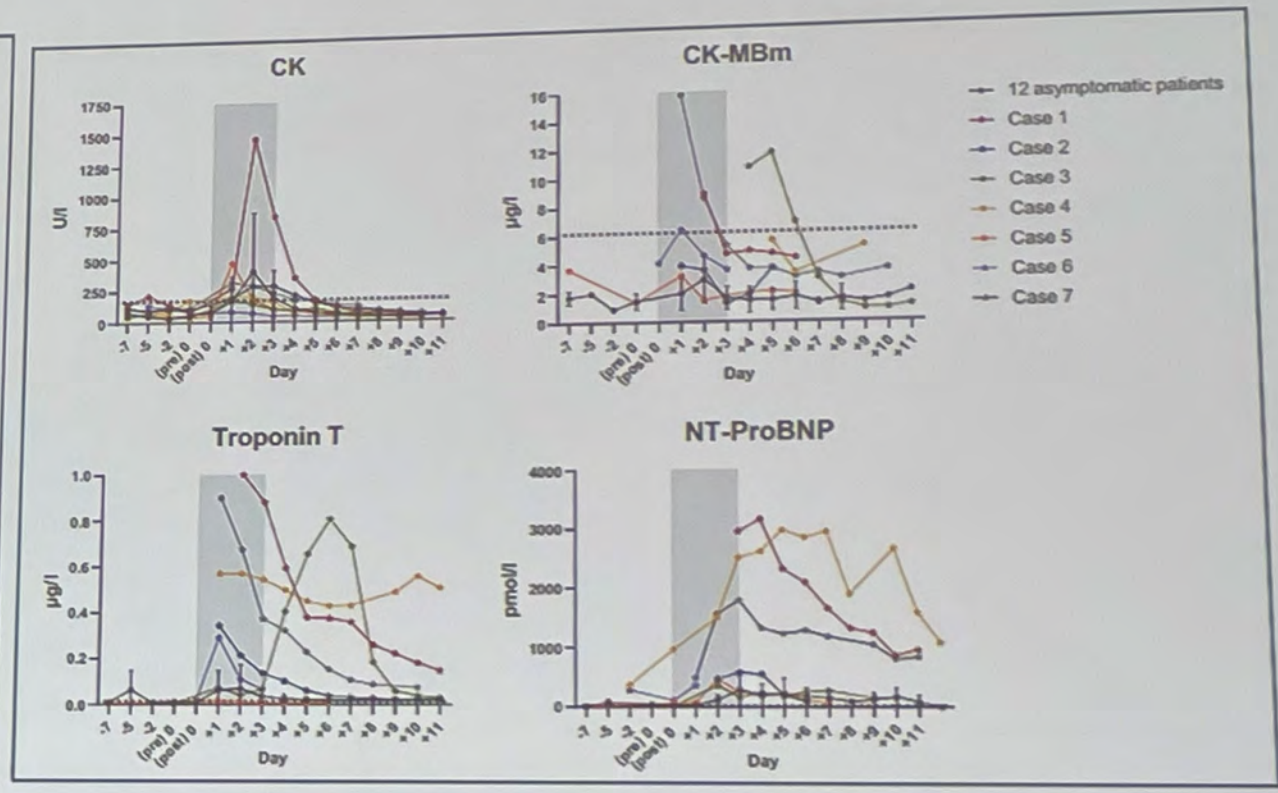
- clophosphamide-
- uced heart failure
- hythmias
- ractory hypotension
- morrhagic)
- carditis
- carditis
- gestive heart failure

- Dyspnea
- Tachycardia
- Arrhythmias

- Capillary leak syndrome
- Arrhythmias
- Angina pectoris
- Heart failure
- Myocardial infarction
- Peri-/myocarditis
- Tachycardia
- Hypotension

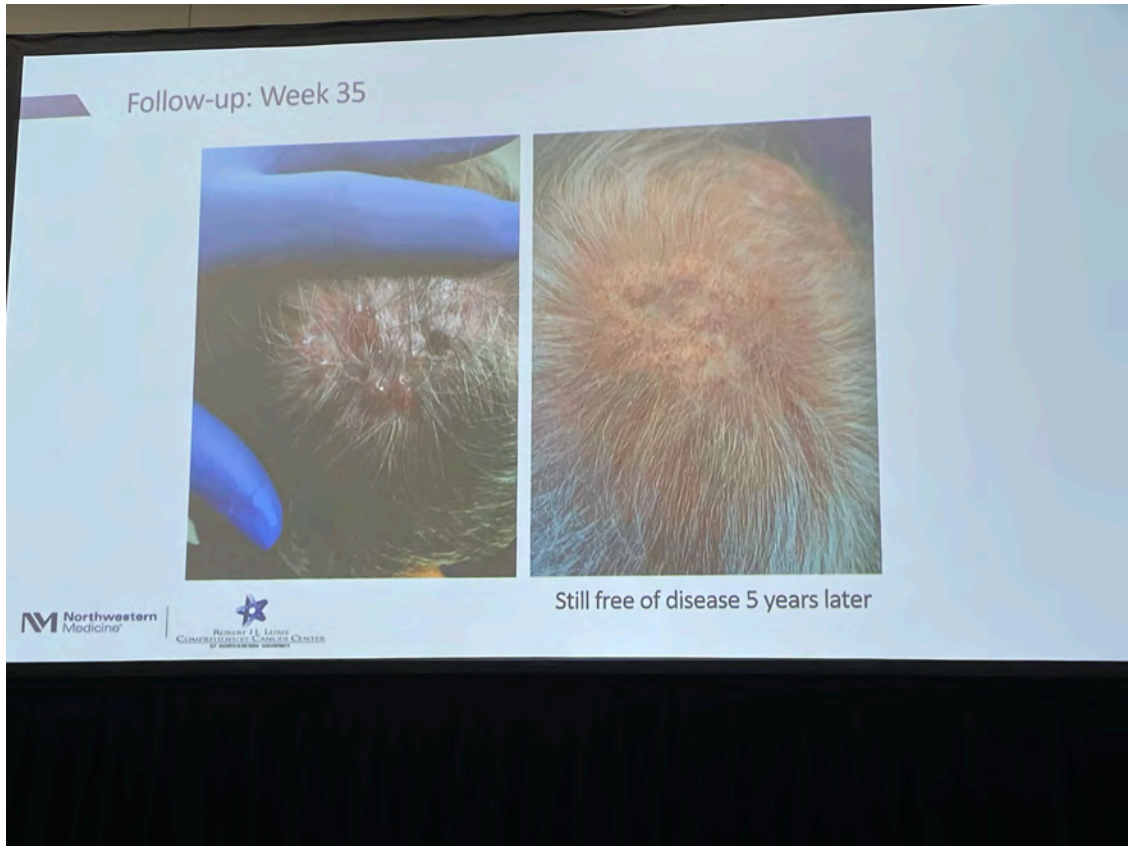
Immune suppression

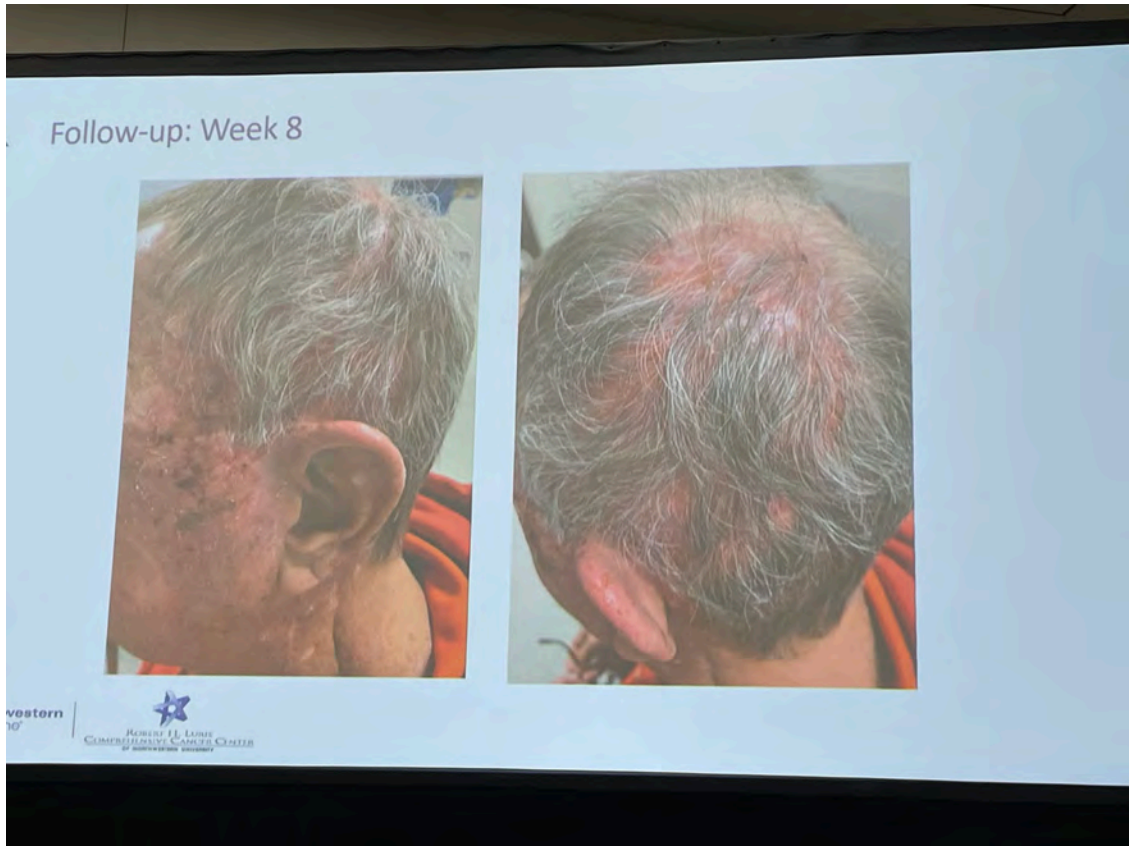
Inflammation



ESMO Open. 2024 Feb 15;9(2):102383.

Cutaneous Metastases in Cancer patient. The Role of the Dermatologist: More Than Just Diagnosis. Dra Jennifer N. Chol





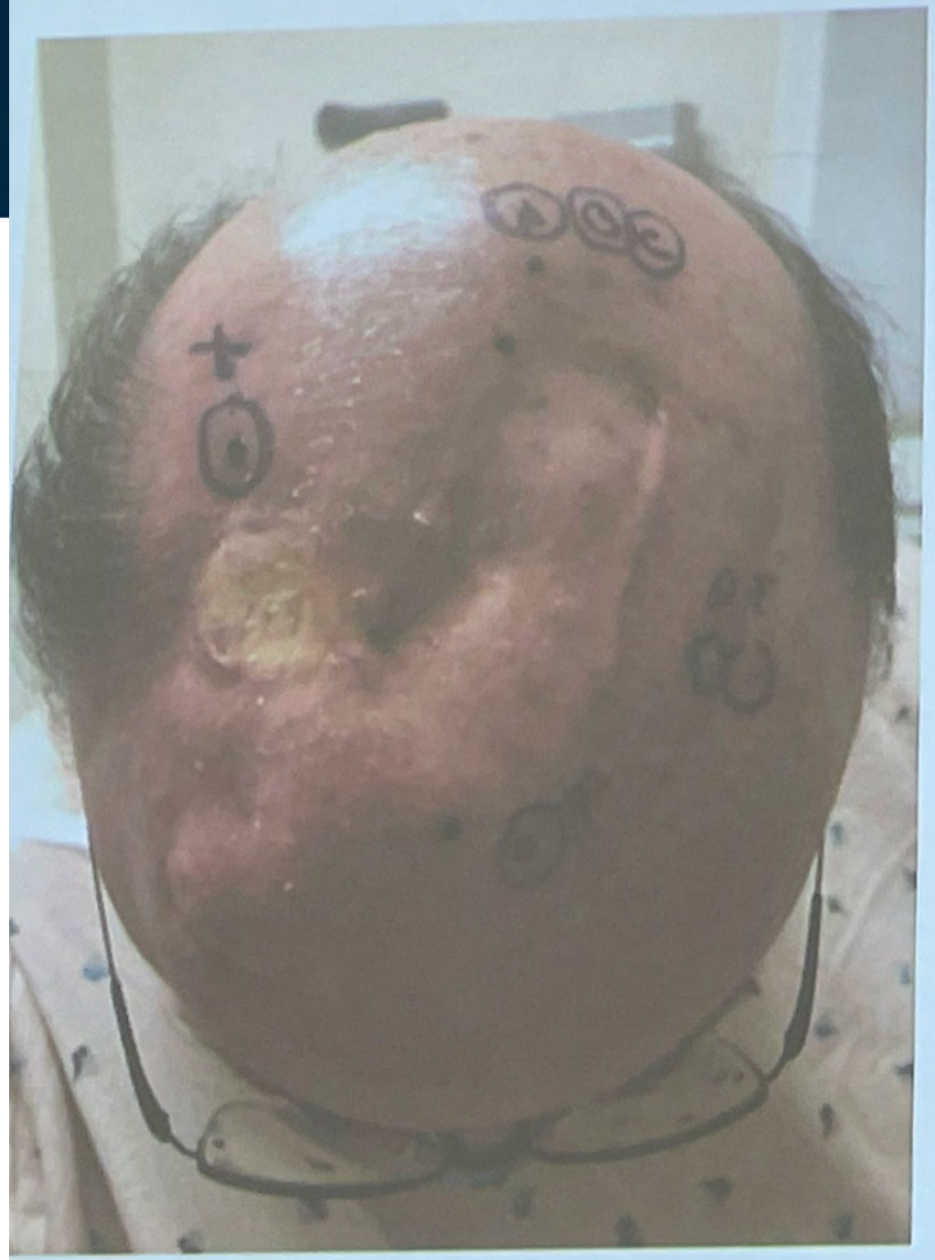
In-transit cutaneous metastatic melanoma

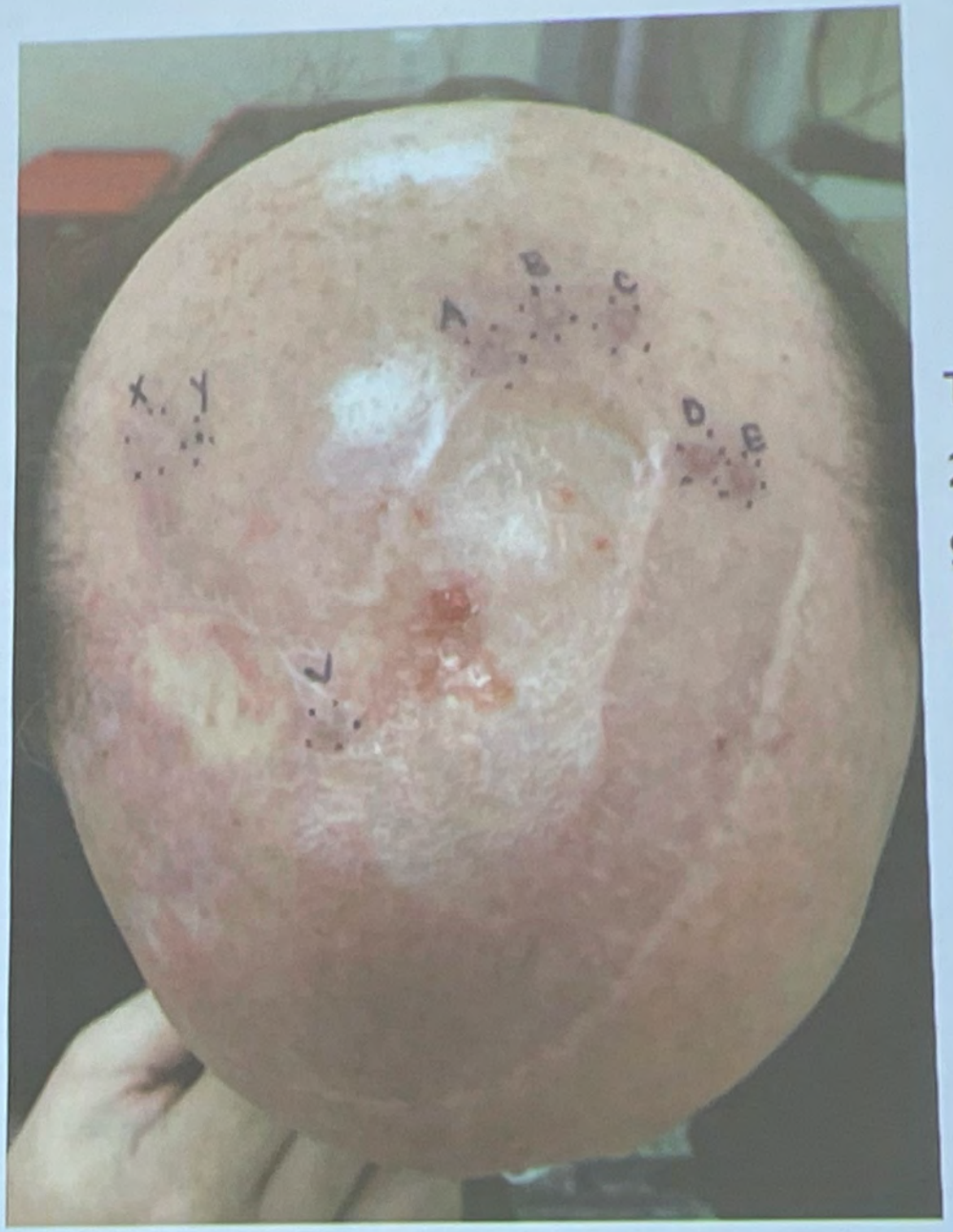
- Any skin or subcutaneous metastases that are more than 2 cm from the primary lesion but are not beyond the regional nodal basin
- Occur in 2.3 – 13% of patients diagnosed with invasive melanoma
- Treatments include:
  - Surgical excision
  - Radiotherapy
  - Isolated limb infusion/perfusion
  - Cryotherapy
  - Electrochemotherapy
  - Laser therapy
  - Topical therapy (imiquimod cream, diphencyprone)
  - Intralesional (BCG, IL-2, GM-CSF, T-VEC)
  - Targeted kinase inhibitors
  - Immune checkpoint inhibitors

IMIQUIMOD

Imiquimod adjuvant therapy

- Prior studies show that imiquimod can be added as an adjuvant to other intralesional therapies in the treatment of in-transit cutaneous melanoma metastases:
  - **Intralesional BCG + imiquimod**: 9 patients, significant clinical improvement in disease (retrospective case series)
  - **Intralesional IL-2 + imiquimod**: 13 patients, regression of cutaneous disease in approximately 50% of patients (phase I clinical trial)
  - **Intralesional IL-2 + imiquimod + retinoid:** 11 patients, 100% complete local clinical response rate (retrospective case series)





T-VEC:

20 injection cycles

9 months

Imiquimod 5% crean

Series of 5 patients with in-transit melanoma metastases

-VEC + imiquimod 5% cream

4 on head (scalp/cheeks/nose)

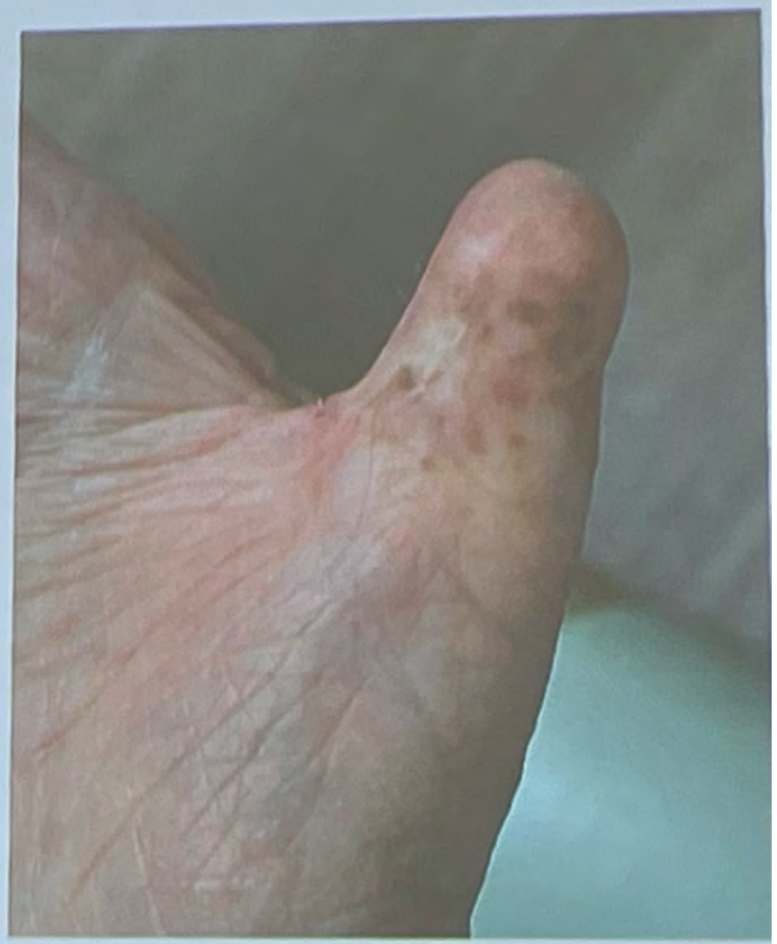
1 on finger

Median # of lesions injected: 12 (range 9-20)

Median # of treatments: 13 (range 8-20)

2/5 developed systemic disease

/5 clear of disease (3-5 years)



RESPECT THE DORMANT BEAST: OPTIMIZE YOUR MANAGEMENT OF HIGH –RISK CUTANEOUS SCCs room 28B 3:30

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

DR VISHAL PATEL

GW

Finer BWH

Research

JAMA Dermatology | Original Investigation

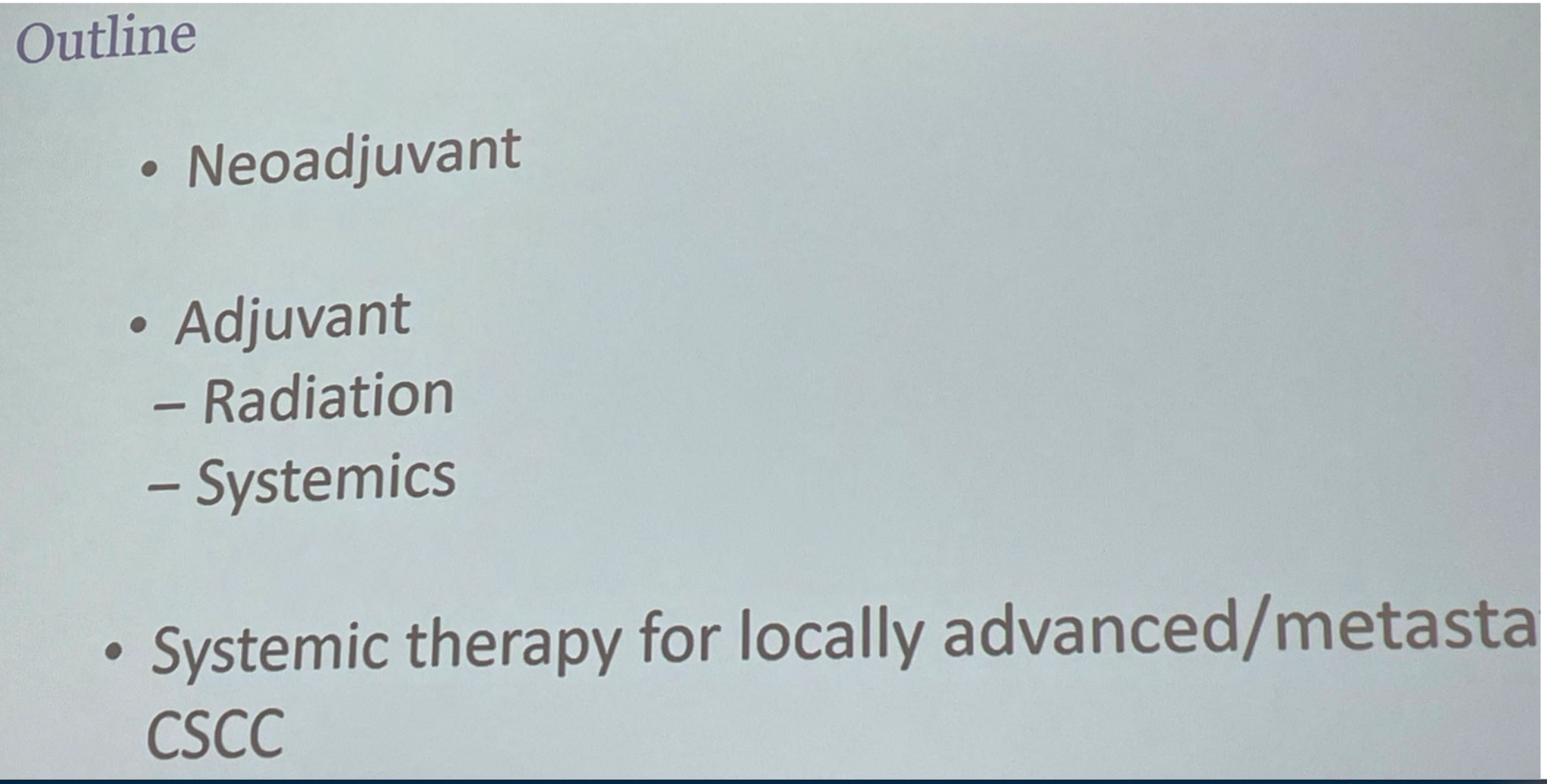
Extensive Perineural Invasion vs Nerve Caliber to Assess Cutaneous Squamous Cell Carcinoma Prognosis

Paul R. Massey, MD, MPH; David M. Wang, MD; Fadi Murad, MD, MPH; Patrick Mulvaney, MD, MPH; Kevin Moore, MD; Jean-Phillip Okhovat, MD; Eleanor Russell-Goldman, MD, PhD; William M. Lin, MD; Adriano Piris, MD; Shyamala C. Huilgol, MBBS (Hons); Emily S. Ruiz, MD, MPH; Chrysalyne D. Schmults, MD, MSCE

- This retrospective cohort study of 140 patients with CSCC w performed at a single tertiary care institution and compare assessments:
  - nerve caliber
  - number of involved nerves per section
  - PNI maximal depth
  - PNI location with respect to tumor.
- Of the 4 PNI assessments studied, only involvement of multip was associated with poor outcomes.
- Perineural invasion of 5 or more distinct nerves (extensive P was independently associated with:
  - local recurrence (subhazard ratio [SHR], 13.83 [95%CI, 3.5 < .001)
  - disease-specific death (SHR, 6.20 [95%CI, 1.59-24.21]; P
  - any poor outcome (SHR, 10.21 [95%CI, 2.88-36.15]; P <
- ***A revised BWH staging system with substitution of ePNI for la PNI resulted in improved area under the curve and test chara compared with current BWH staging criteria that use nerve c measure of PNI.***

Valorar el número de IPN
En vez del calibre

RESPECT THE DORMANT BEAST: OPTIMIZE YOUR MANAGEMENT OF HIGH –RISK CUTANEOUS SCCs room 28B 3:30

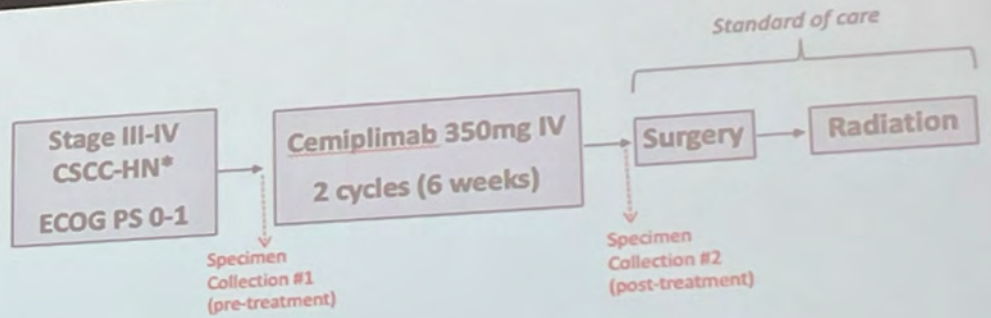


Treatment Paradigm for resectable high-risk CSCC

Pilot Phase II Trial of Neoadjuvant Immunotherapy in Locoregionally Advanced, Resectable Cutaneous Squamous Cell Carcinoma of the Head and Neck

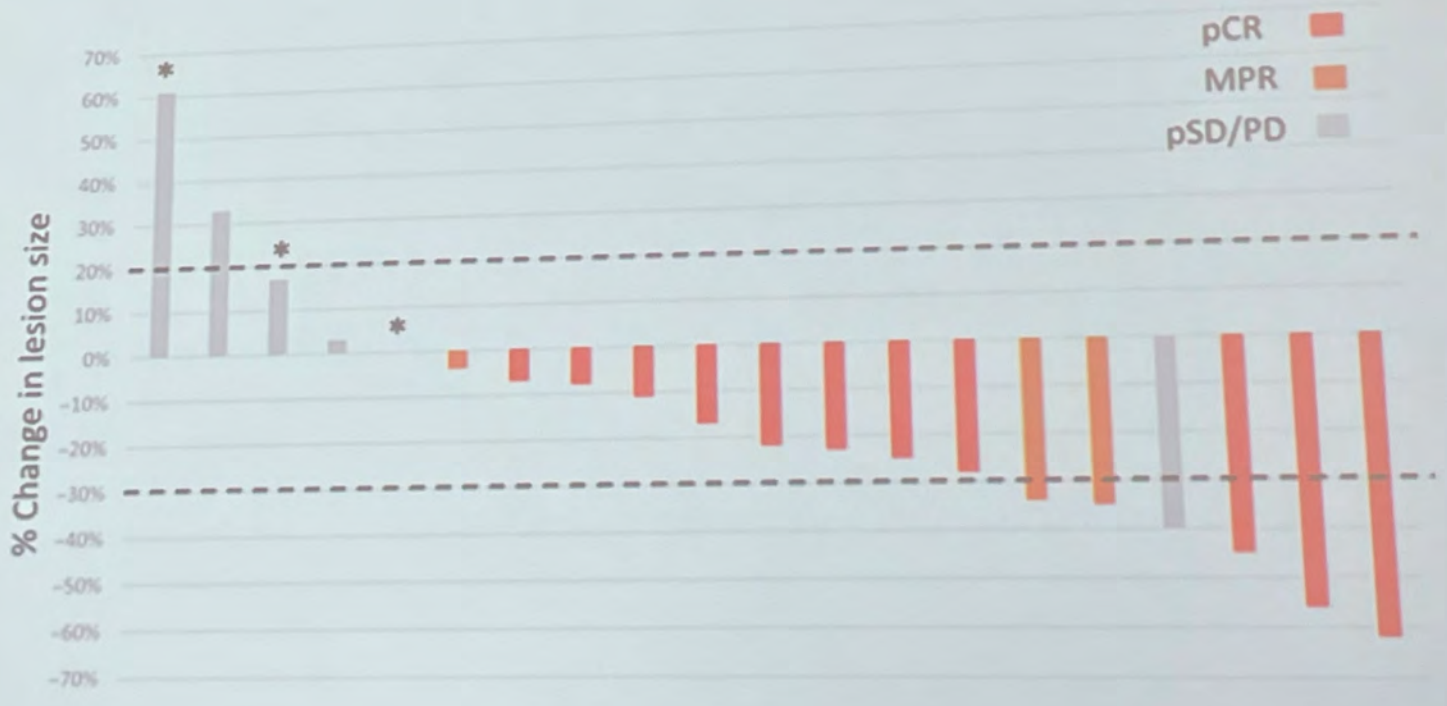
Renata Ferrarotto[1], Moran Amit[2], Priyadharsini Nagarajan[3], M. Laura Rubin[4], Ying Yuan[4], Diana Bell[3], Adel K. El-Naggar[3], Jason M. Johnson[5], William H. Morrison[6], David I. Rosenthal[6], Bonnie S. Glisson[1], Faye M. Johnson[1,7], Charles Lu[1], Frank E. Mott[1], Bita Esmaeli[8], Eduardo M. Diaz Jr[2], Paul W. Gidley[2], Ryan P. Goepfert[2], Carol M. Lewis[2], Randal S. Weber[2], Jennifer A. Wargo[9], Sreyashi Basu[10], Fei Duan[10], Shalini S. Yadav[10], Padmanee Sharma[11], James P. Allison[10], Jeffrey N. Myers[2], and Neil D. Gross[2]

Clin Cancer Res; 27(16) August 15, 2021



Pathologic Classification:

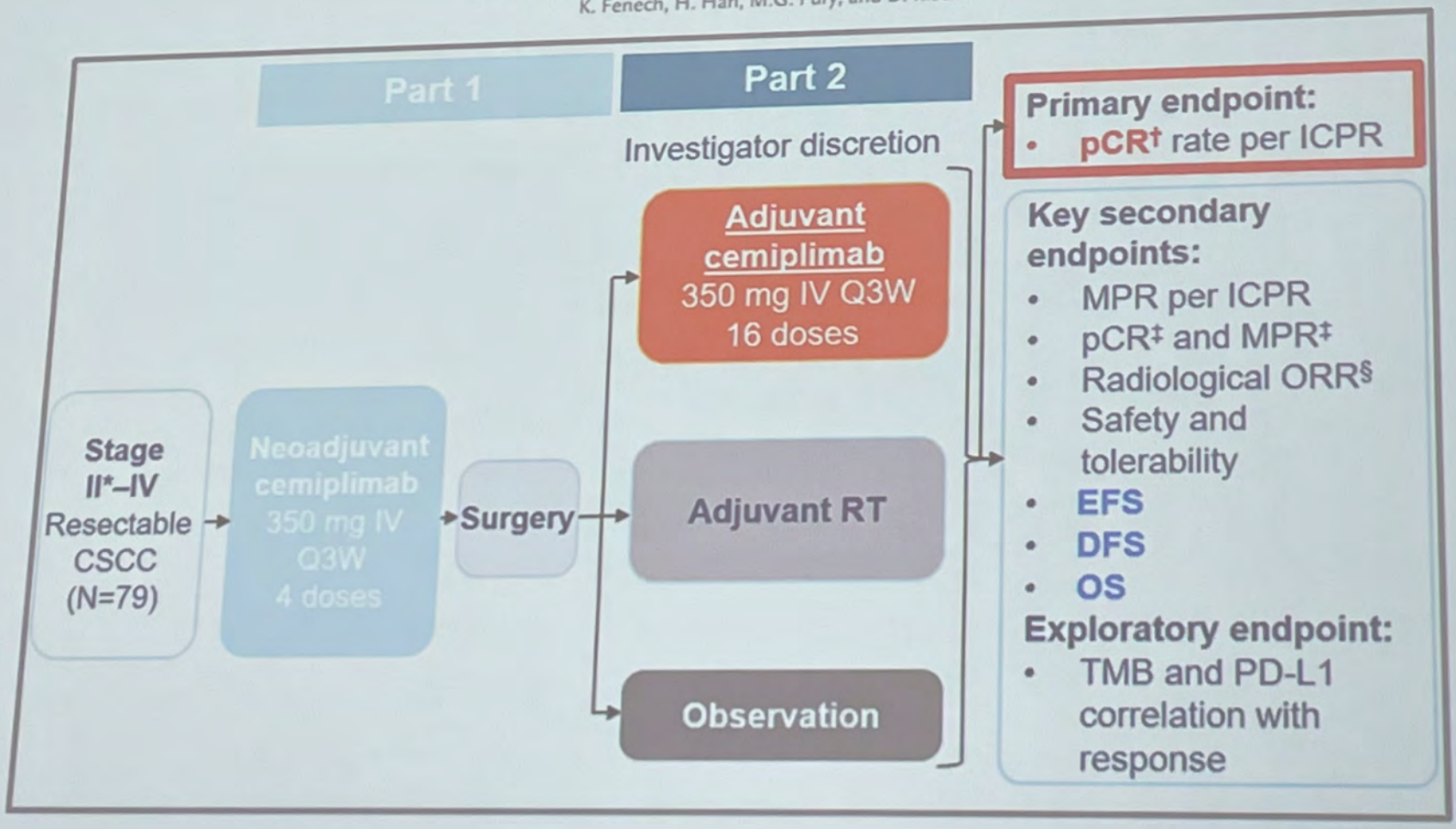
pCR: No viable tumor
MPR: ≤ 10% viable tumor
pPR: >10% but ≤ 50% viable tumor
SD or PD: >50% viable tumor

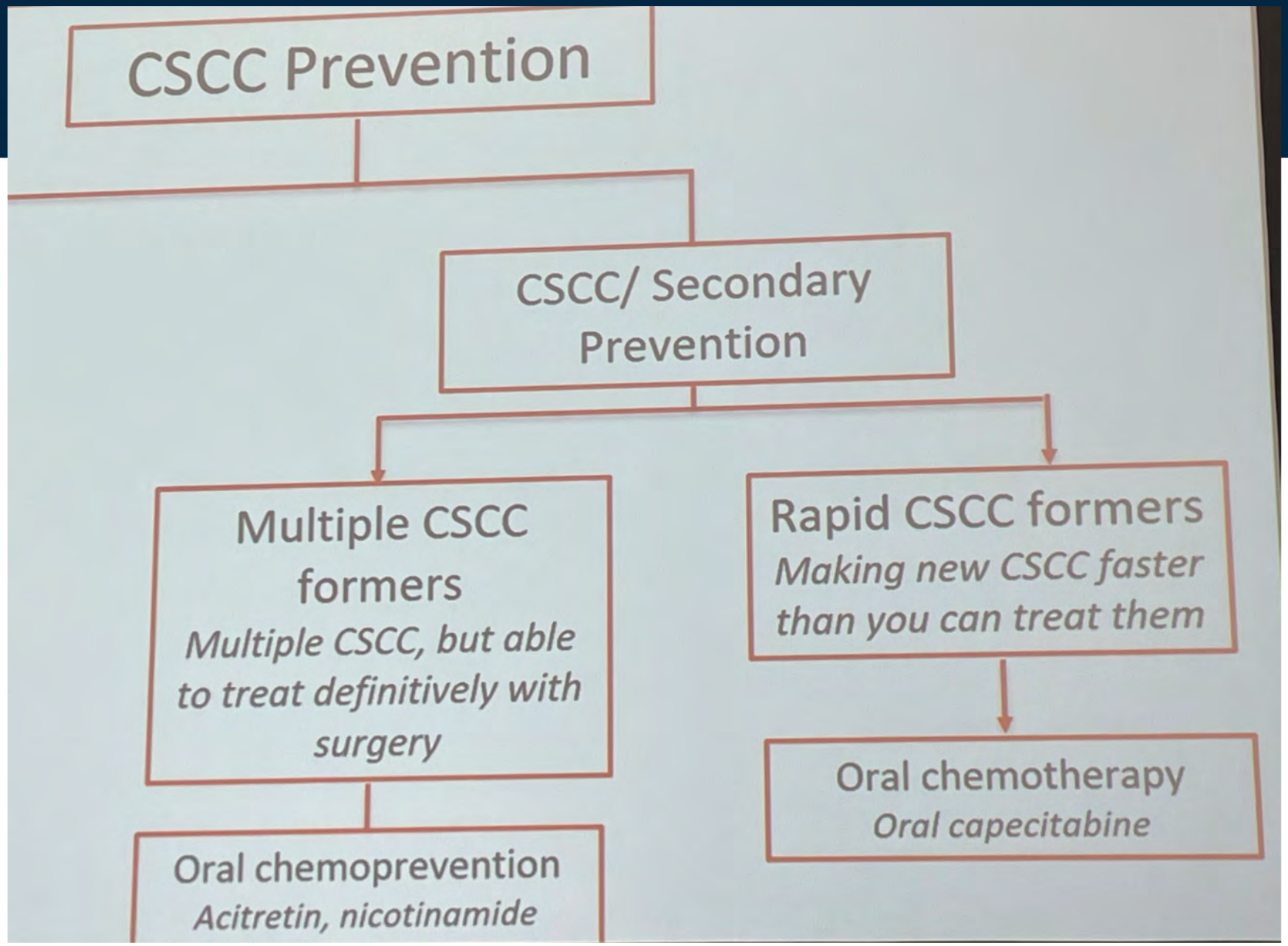


ORIGINAL ARTICLE

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

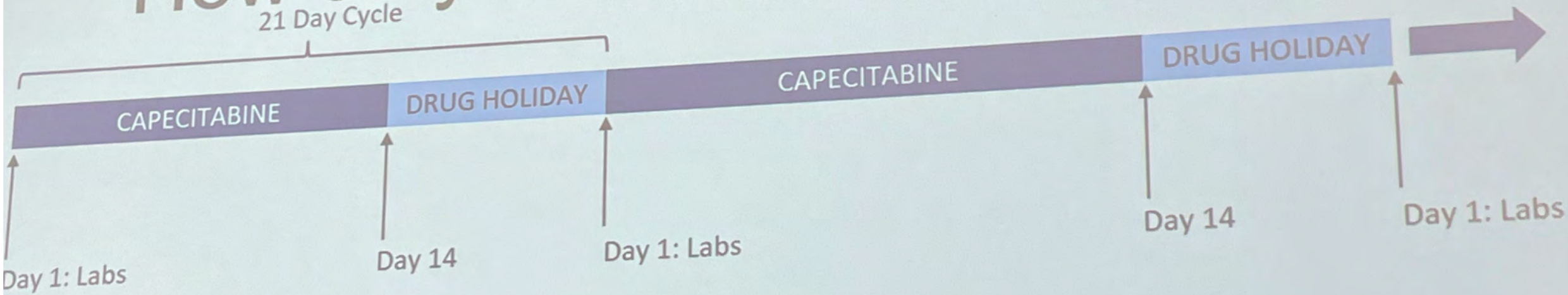
N.D. Gross, D.M. Miller, N.I. Khushalani, V. Divi, E.S. Ruiz, E.J. Lipson, F. Meier, Y.B. Su, P.L. Swiecicki, J. Atlas, J.L. Geiger, A. Hauschild, J.H. Choe, B.G.M. Hughes, D. Schadendorf, V.A. Patel, J. Homsi, J.M. Taube, A.M. Lim, R. Ferrarotto, H.L. Kaufman, F. Seebach, I. Lowy, S.-Y. Yoo, M. Mathias,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




CSCC Prevention
CSCC/ Secondary Prevention
Multiple CSCC formers
Multiple CSCC, but able to treat definitively with surgery
Oral chemoprevention
Acitretin, nicotinamide
Rapid CSCC formers
Making new CSCC faster than you can treat them
Oral chemotherapy
Oral capecitabine

The University of Texas at Austin
Dell Medical School

How do you dose capecitabine?



- Target dose 1000mg BID
  - Start 500mg BID x 1 cycle

- Treat for 6-8 months
  - Often multiple courses are needed

Courtesy of Dr. Emily Ruiz

CA BASOCELULAR LOCALMENTE AVANZADO

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

NeoBCC: Phase 2 Trial of Neoadjuvant T-VEC in Difficult-to-Resect Primary BCC

- *Histologically confirmed BCC*
- *Difficult-to-resect* BCC*

N = 18

T-VEC
6 cycles in 13 weeks†

Surgery

End of treatment

Follow-up

Primary objective: to evaluate number of pts with BCC that becomes resectable after 6 cycles of T-VEC with primary wound closure without requiring skin flaps or skin grafts

Baseline Patient Characteristics	Patients (N = 18)
Female, n (%)	11 (61.0)
Male, n (%)	7 (39.0)
Median age, y (range)	74.50 (49-92)
Median height, m (range)	1.68 (1.50-1.85)
Histopathological BCC subtype, n (%)	
Nodular	9 (50.0)
Infiltrative	9 (50.0)
BCC localization, n (%)	
Head and neck	13 (72.0)
Lower extremities	2 (11.0)
Trunk	3 (17.0)
Median longest tumor diameter, cm (range)	1.42 (0.70-13.70)
Serum HSV IgG, n (%)	
Negative	1 (6.0)
Positive	17 (94.0)

*Assessed by an expert panel to require either a skin flap or graft for wound closure.

†Initial dose of 10^6 PFU/mL, 10^8 PFU/mL 3 weeks later, remaining 4 doses of 10^8 PFU/mL given once every 2 weeks (total treatment period: 13 weeks).

HSV, herpes simplex virus; IgG, immunoglobulin G; PFU, plaque-forming unit; T-VEC, talimogene laherparepvec.

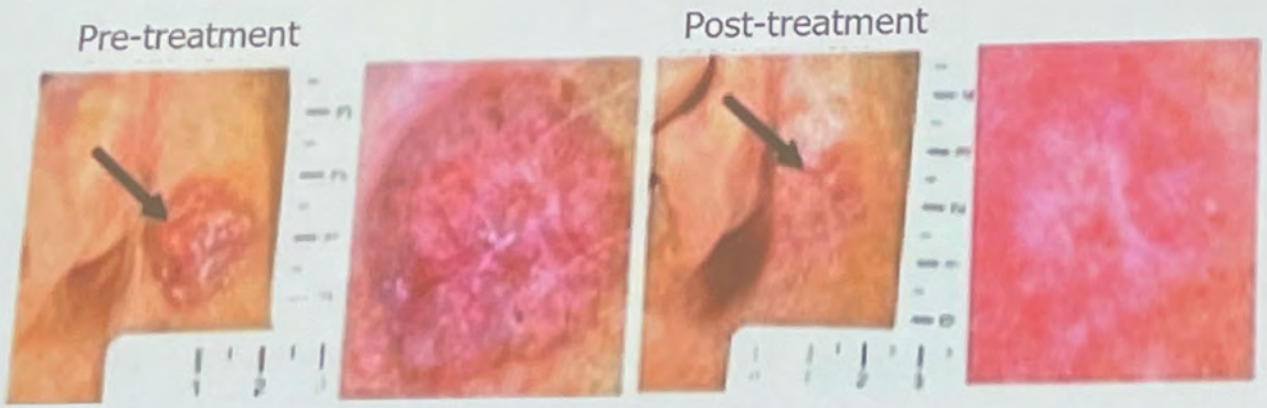
Ressler JM, et al. Presented at: ESMO Congress 2022; September 9-13, 2022; Paris, France. Presentation 794P.

hool of Medicine
Health Sciences
EORGE WASHINGTON UNIVERSITY

smhs.gwu.edu

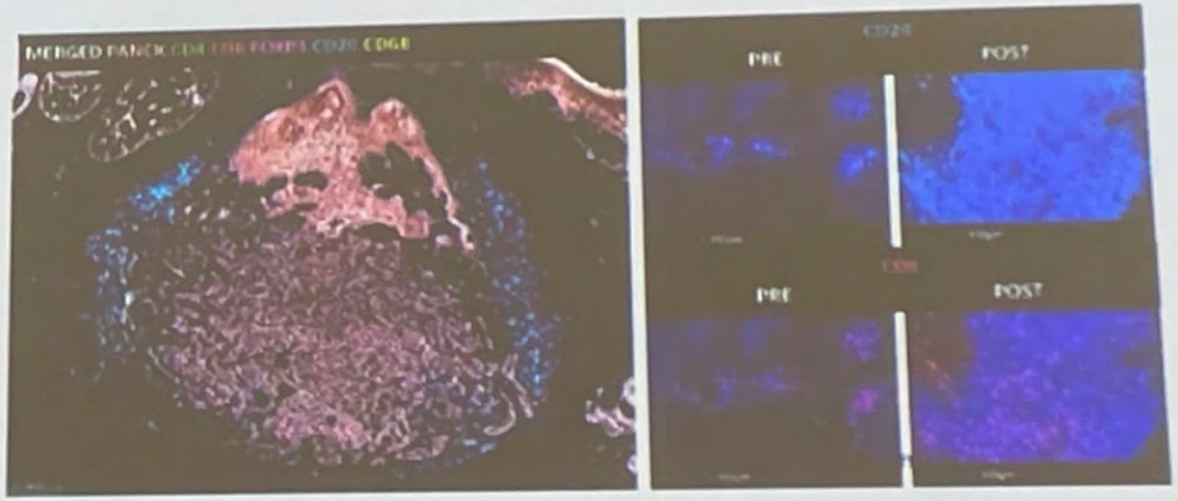
NeoBCC: Response to Neoadjuvant T-VEC

Neoadjuvant T-VEC Showed High Activity in BCC



Clinical response		Pathologic response	
SD	41.2%	Non-pCR	64.71%
PR	23.5%	pCR	35.29%
CR	35.3%		

Significant Increase of CD8+ T Cells and CD20+ B Cells in Complete Responders Upon T-VEC Treatment



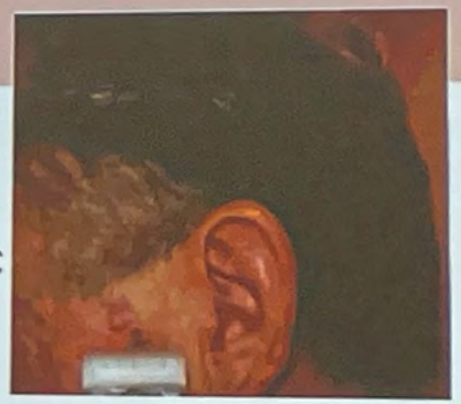
Ressler JM, et al. Presented at: ESMO Congress 2022; September 9-13, 2022; Paris, France.

Proposed Solution for Efficacy without Adverse Effects	Apply the HH inhibitor to the Skin
PRELIMINARY Results	TOPICAL HH inhibitors CAN shrink existing BCCs and reduce new Development of New BCCs
Patidegib topical 2%	Phase 2 trial Phase 3 trial

Before vismodegib

During vismodegib

Adverse Effects Hair Loss ->
Plus Taste Loss, Severe Muscle Cramps, etc



Baseline

Month 4 on drug

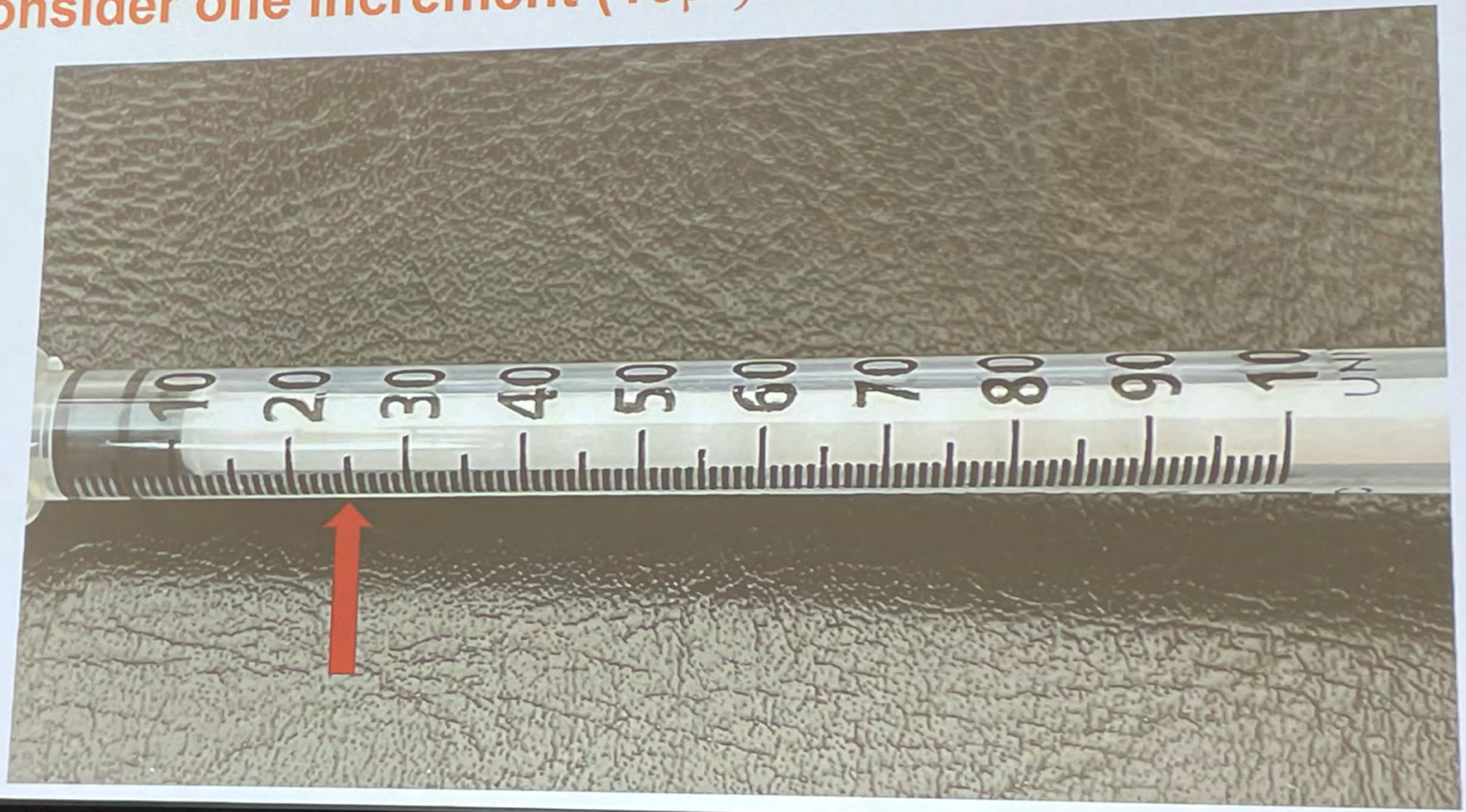
A Phase 1 Study of Pre-Operative Cemiplimab (REGN2810), Administered Intralesionally, for Patients With Cutaneous Squamous Cell Carcinoma (CSCC) or Basal Cell Carcinoma (BCC)

Michael R. Migden, MD

Professor, Departments of Dermatology and Head and Neck Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA

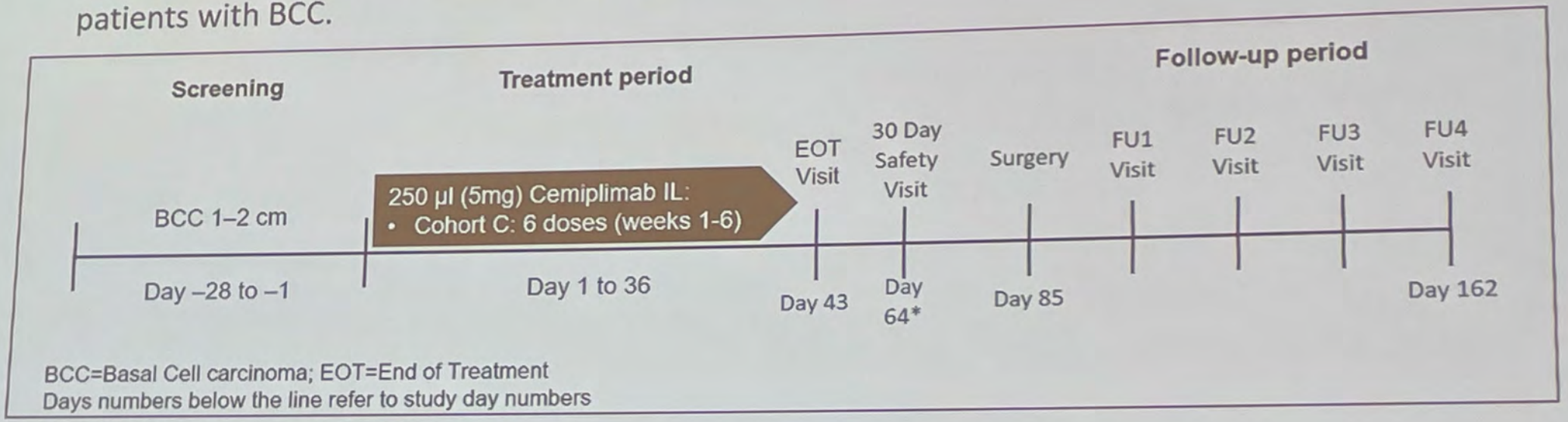
Injection should be very slow, over 2-3 minutes

Consider one increment (10μl) at a time (each 5-6 sec.)



Study Design for Cohort C in patients with BCC

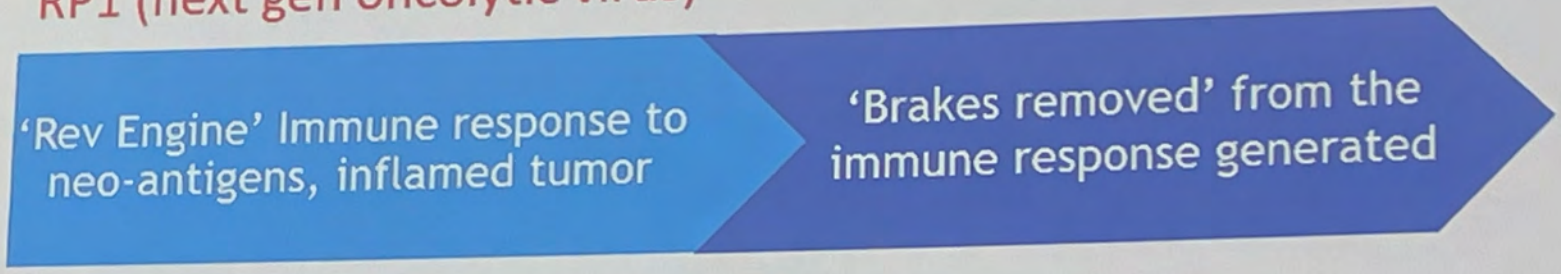
- Cohort C: 5 mg cemiplimab intralesional administration on weeks 1-6 for a total of 6 doses in patients with BCC.



- If there are more than 1 lesion, one lesion will be selected as the "index lesion" for the treatment in the study
- All other lesions will be considered as "non-index lesions" and will not be injected with study drug
- No requirement of recurrent disease

Oncolytic immunotherapy + checkpoint blockade:

RP1 (next gen oncolytic virus)



Oncolytic and immune-based efficacy in its own right

Patient-specific neo-antigen vaccine generated in situ

Without a pre-existing neo-antigen response, nothing to remove the brakes from

Only some patients respond

Oncolytic immunotherapy is a logical combination partner for checkpoint blockade

Randomized controlled Phase 2 study in CSCC (CERPASS)

Cemiplimab as a single agent and in combination with RP1 in patients with advanced CSCC

(Ignite trial of RP1 +/- nivolumab, incl. 15 CSCC, Prelim: CR ~2X single agent nivo, TTCR ~2X faster)

Key eligibility criteria:

- Locally advanced/metastatic CSCC
- ECOG PS 0 or 1
- No active autoimmune disease
- No prior treatment with a PD-1/ PD-L1 inhibitor
- No prior treatment with other immune-modulating agents (including CTLA-4)
- No untreated brain metastases

2:1
N=240

RP1 IT Q3W x 8 doses†
($1x10^6$ PFU/mL for one dose followed by $1x10^7$ PFU/mL for seven doses)
+
Cemiplimab 350 mg Q3W IV

Cemiplimab 350 mg Q3W IV

3-year survival follow-up

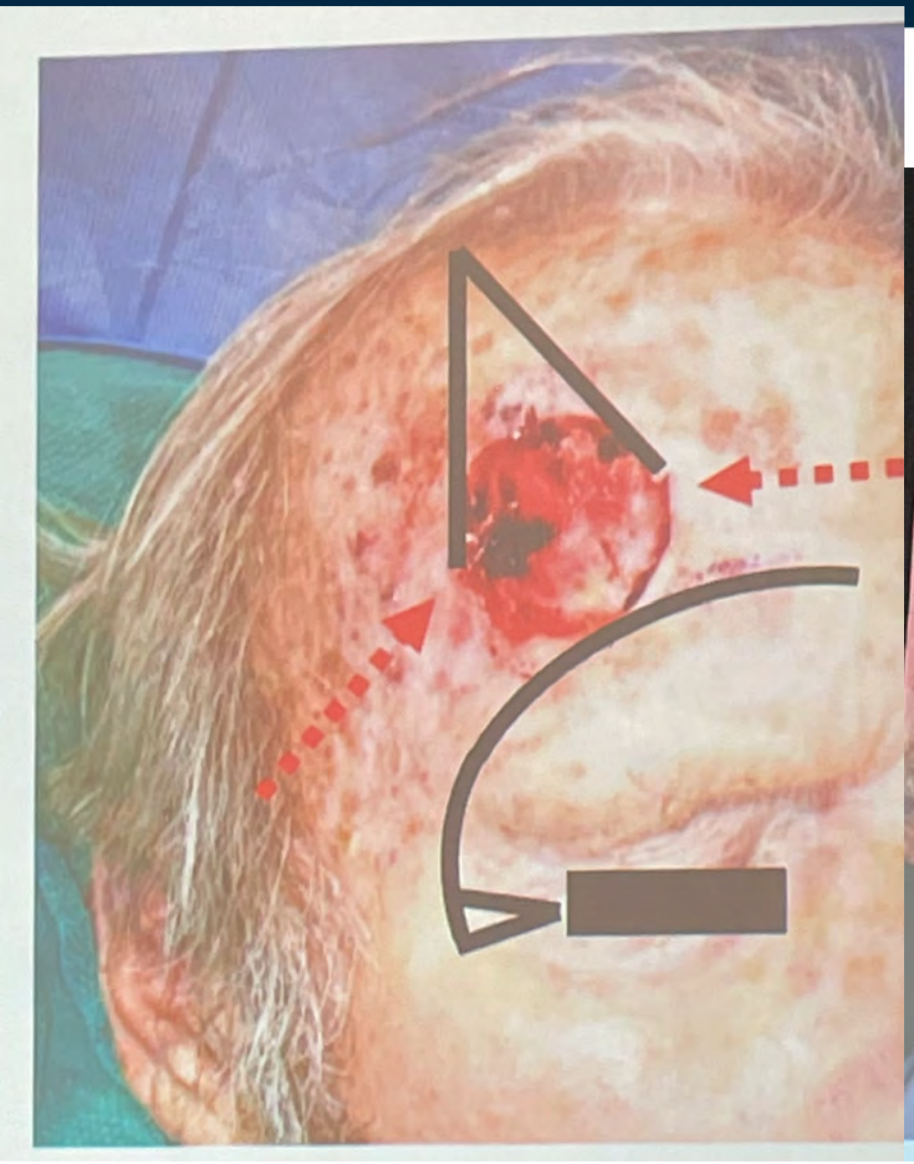
57 weeks treatment‡

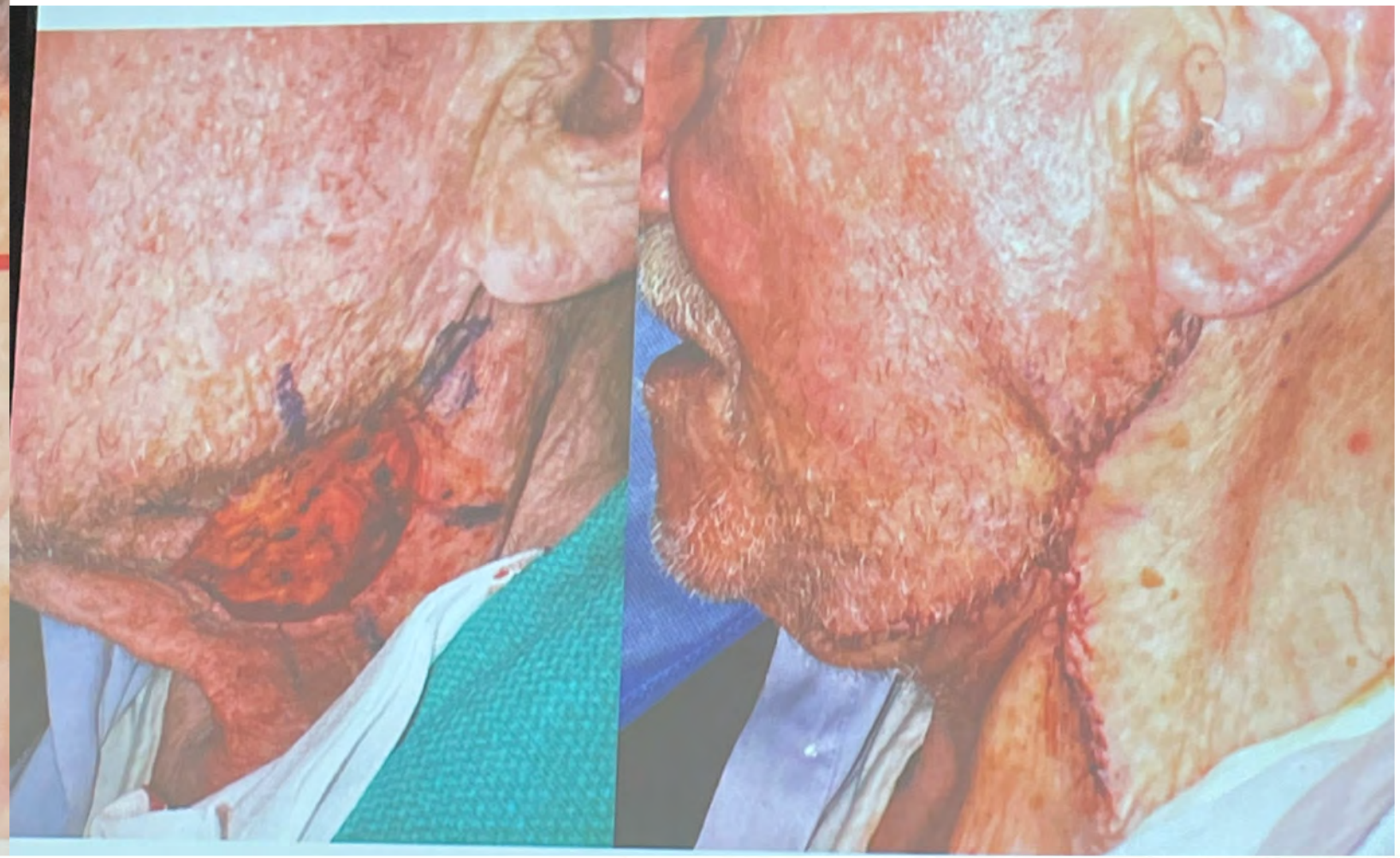
Key endpoints

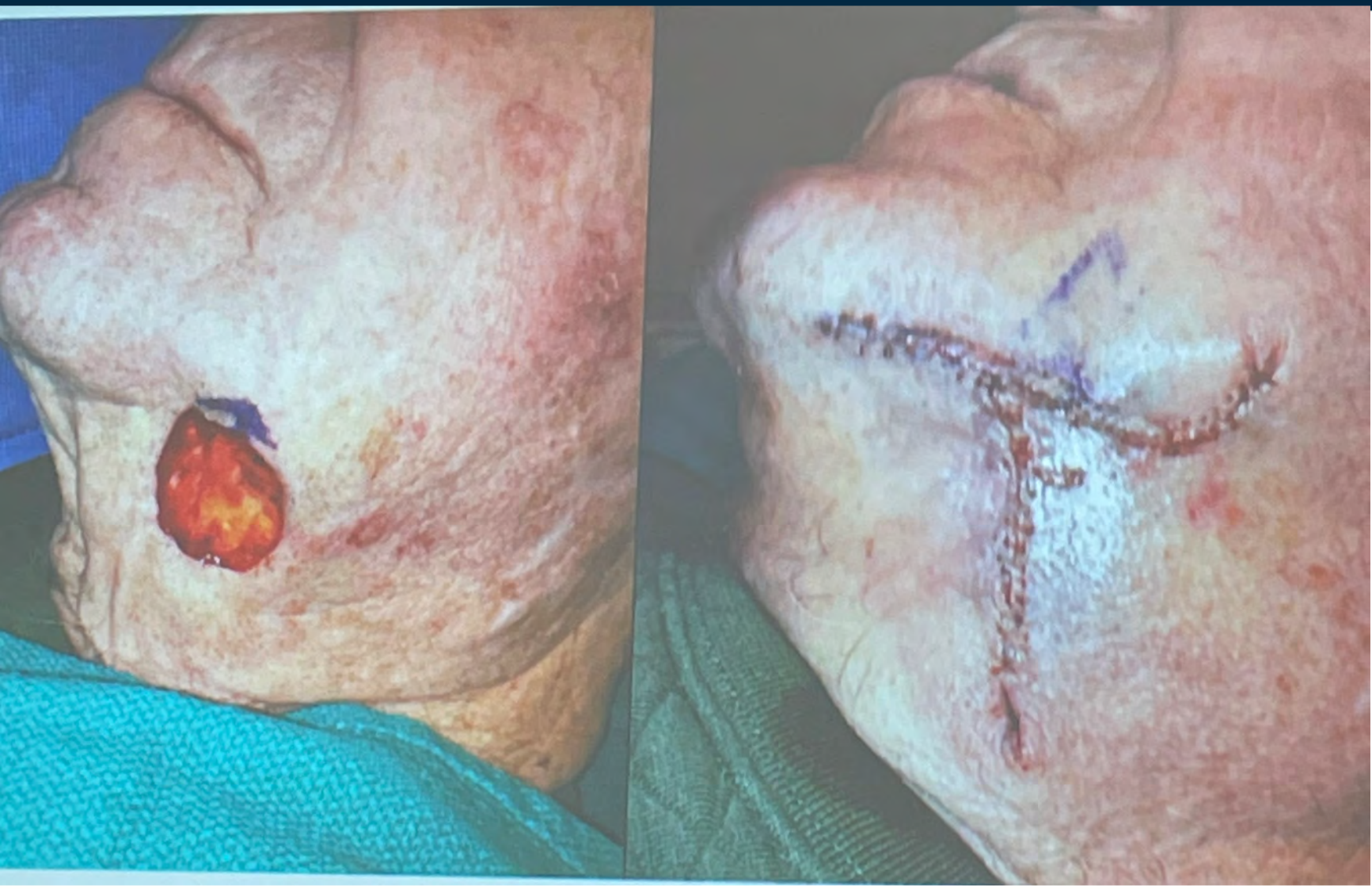
Primary: ORR (RECIST 1.1)
Secondary: DOR, PFS, overall survival, disease-specific survival, safety/tolerability

†First dose of RP1 to be given as monotherapy with cemiplimab to be given with second dose of RP1.
‡57 weeks treatment for the combination arm; treatment duration for cemiplimab-only arm is 54 weeks.
CLTA, cytotoxic T-lymphocyte-associated protein; CSCC, cutaneous squamous cell carcinoma; DOR duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IT, intratumoral; IV, intravenous; ORR, objective response ra programmed cell death-1; PD-L1, PD-ligand 1; PFS, progression-free survival; PFU, plaque-forming unit; Q3W, every 3 weeks; REC

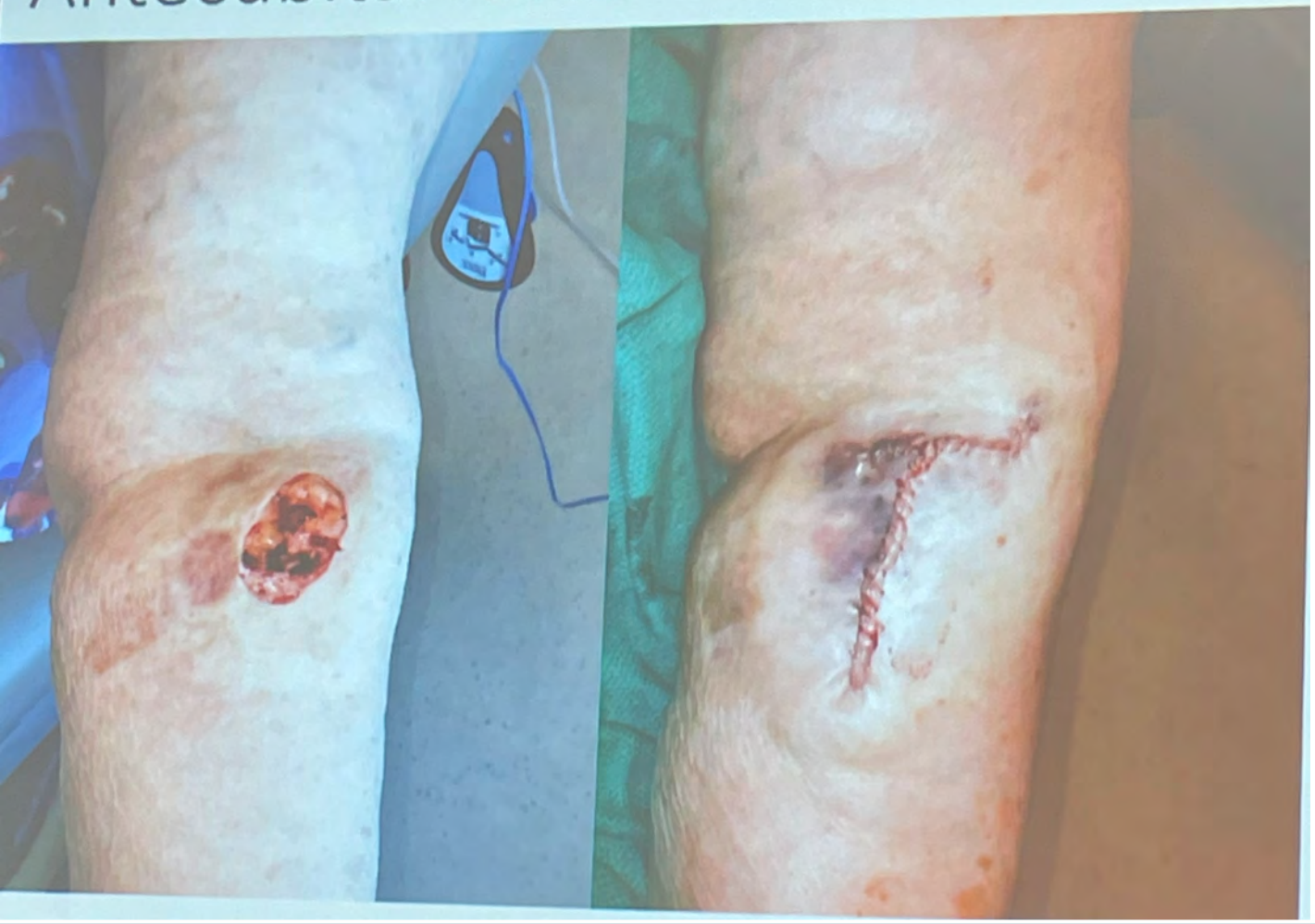
DERMATOLOGIC SURGERY PEARLS FOR NON-MOHS SURGEON ROOM 31B 4:30



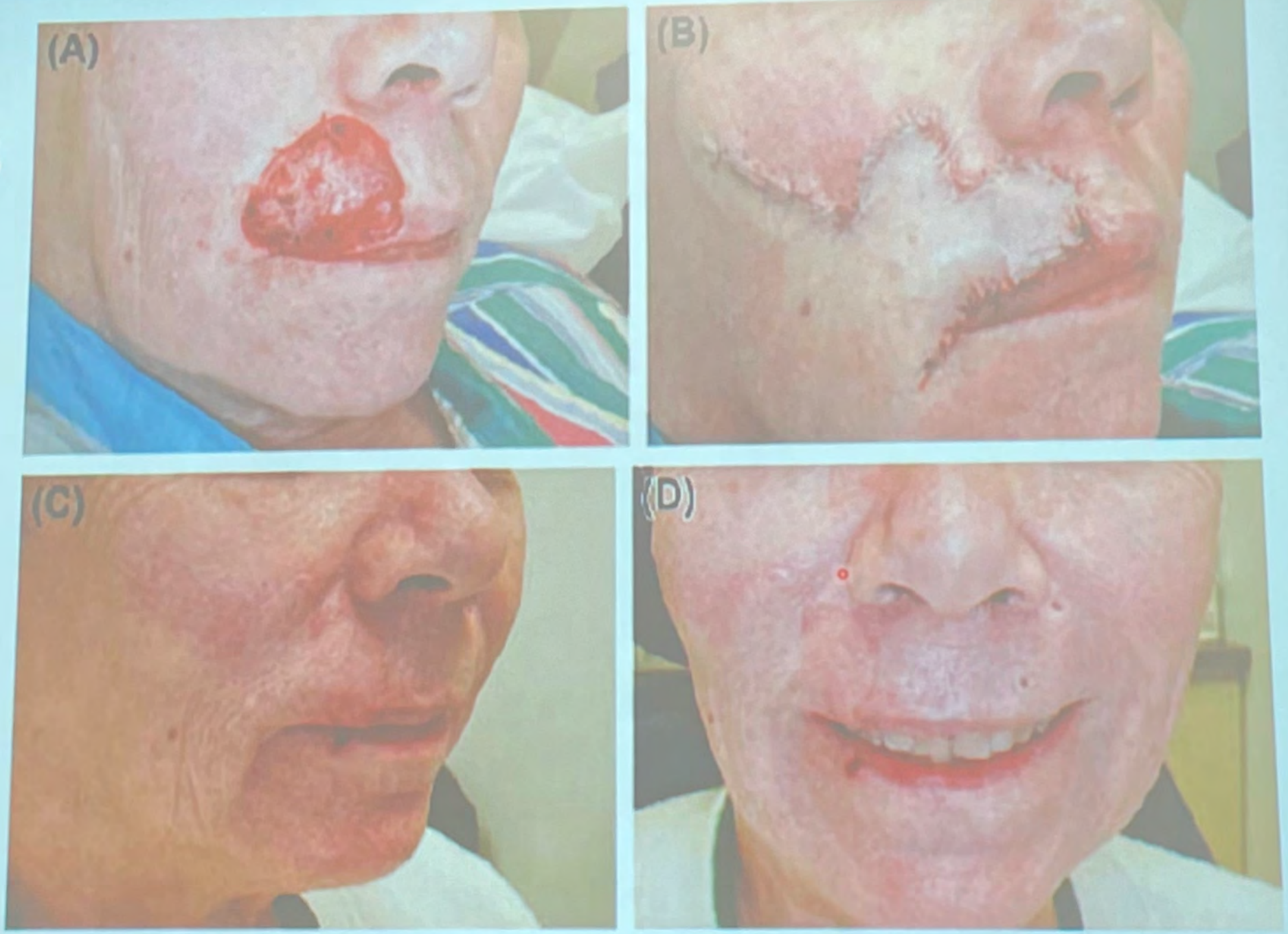




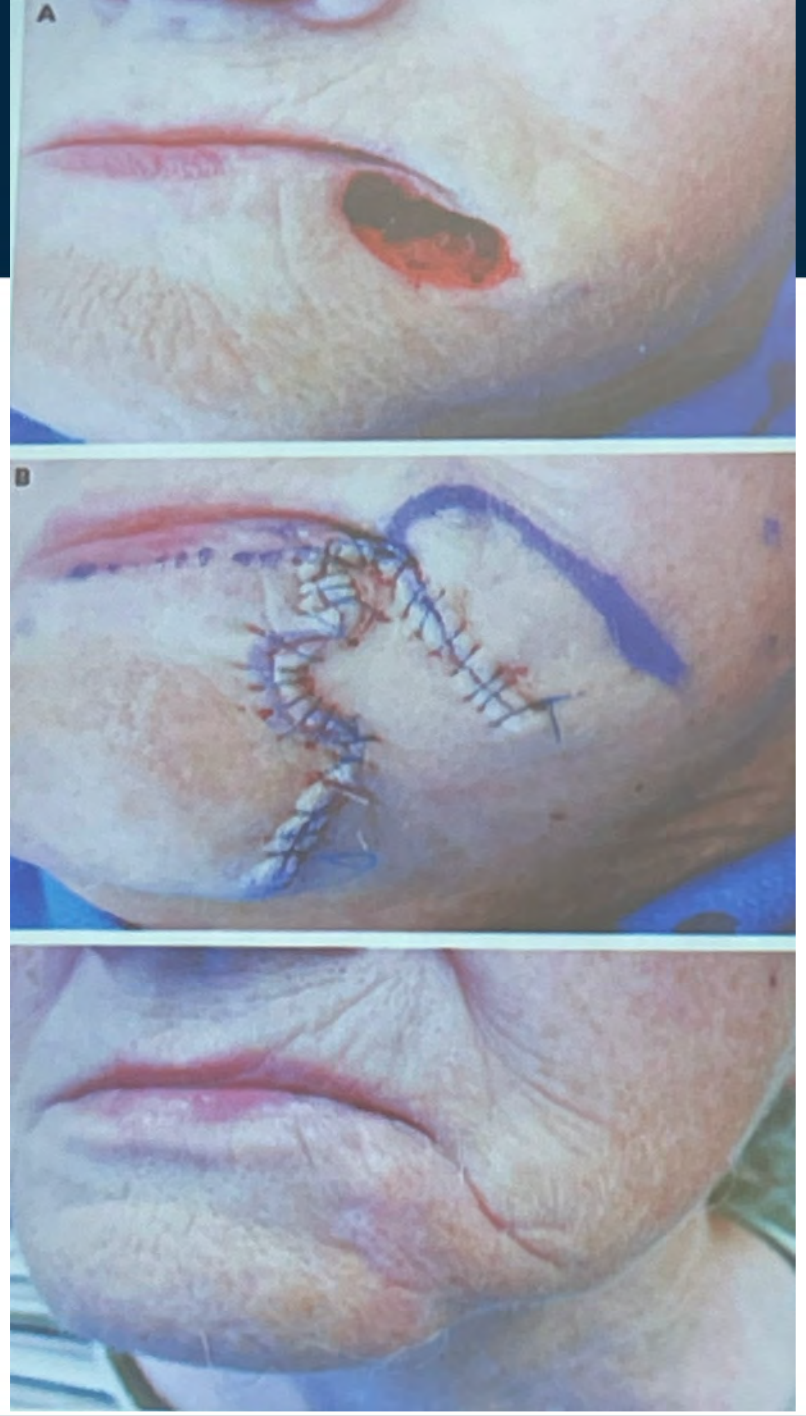
Antecubital fossa

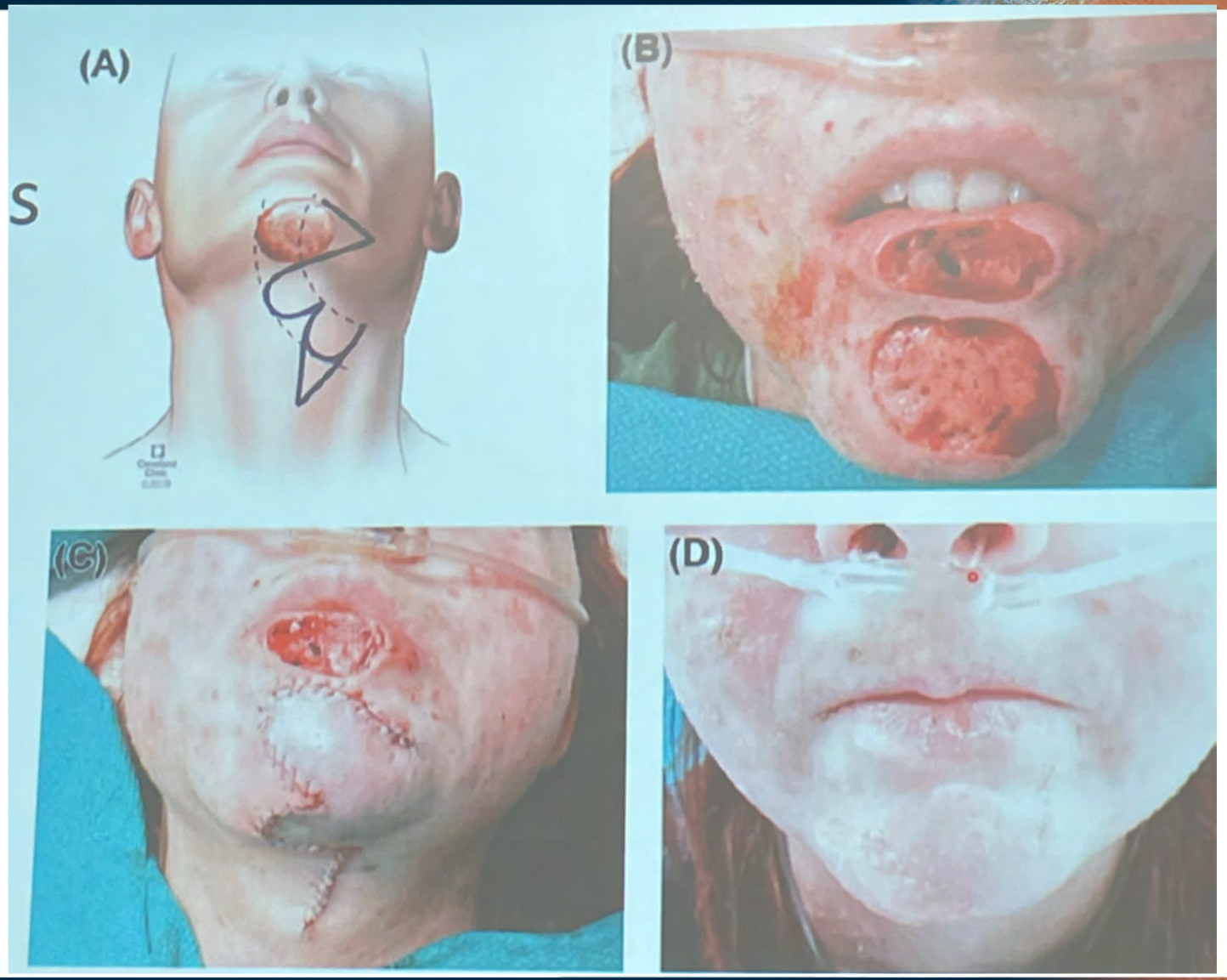


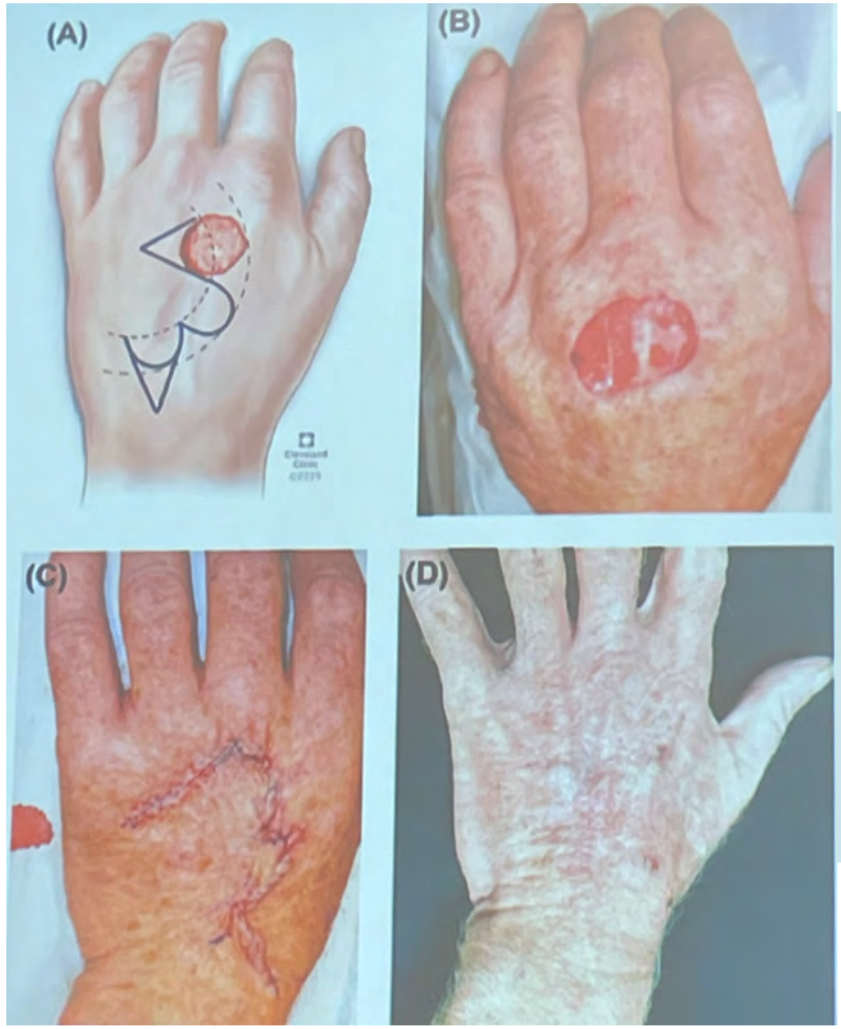
Upper Cutaneous Lip Defects



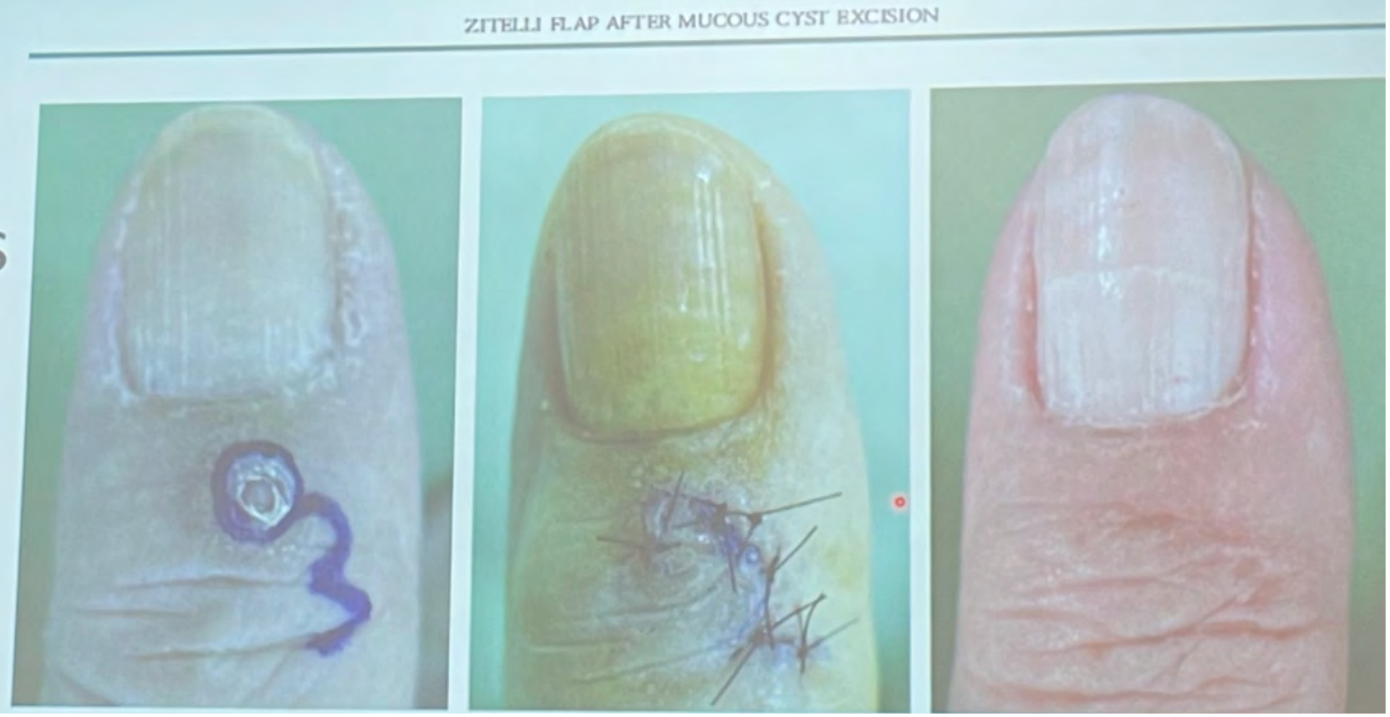
eele et al.

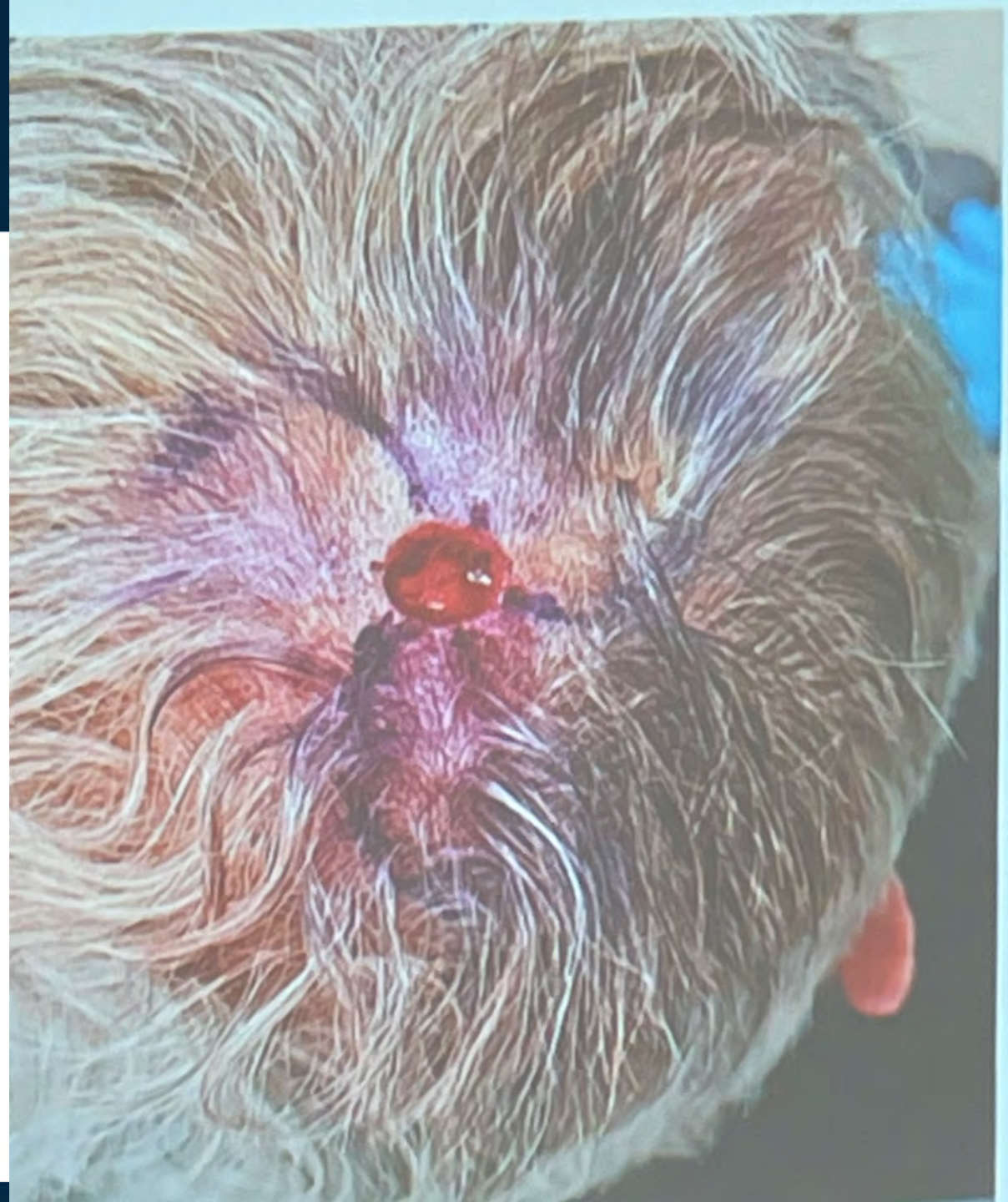

A
B

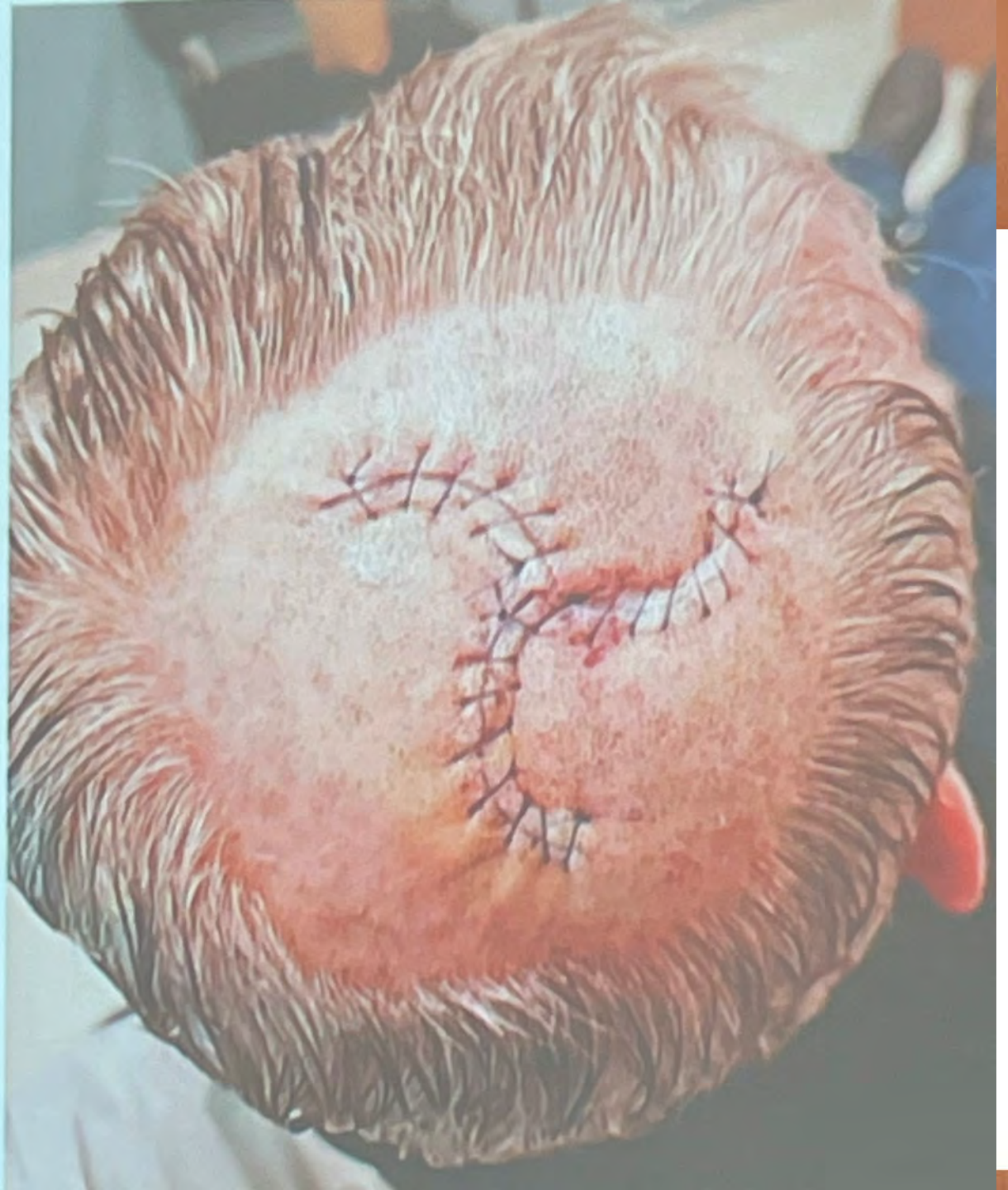

(A)
(B)
(C)
(D)



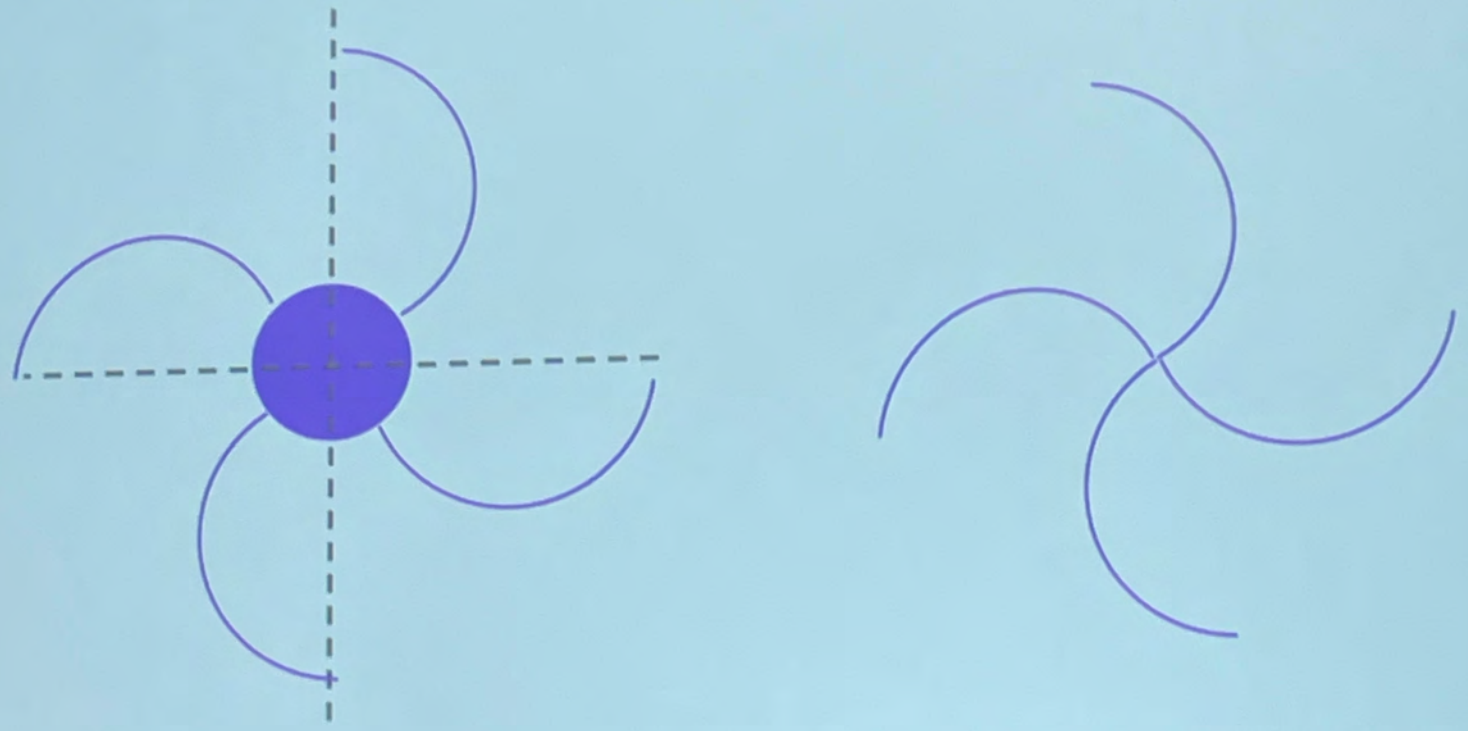
Distal Finger Defects

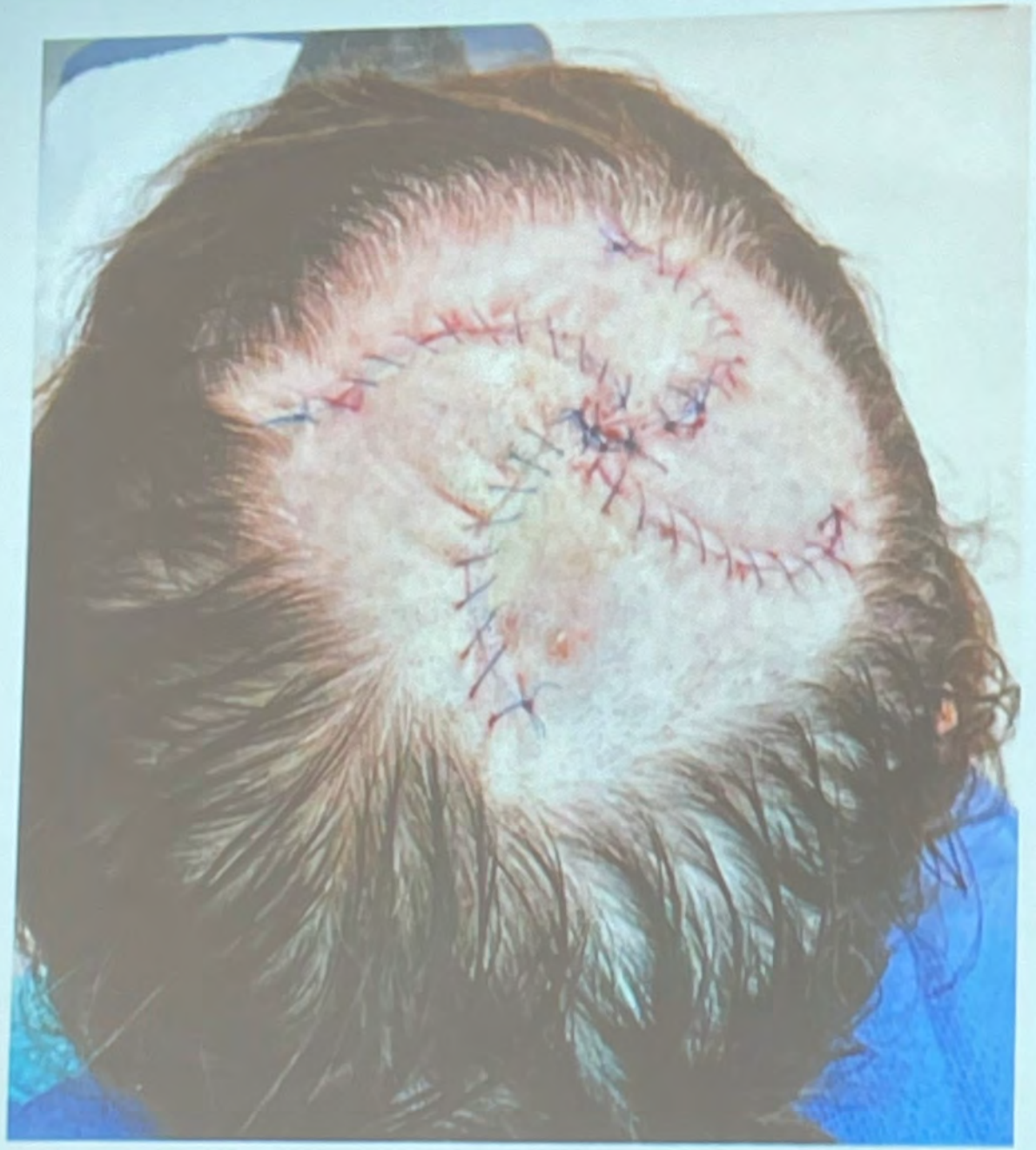


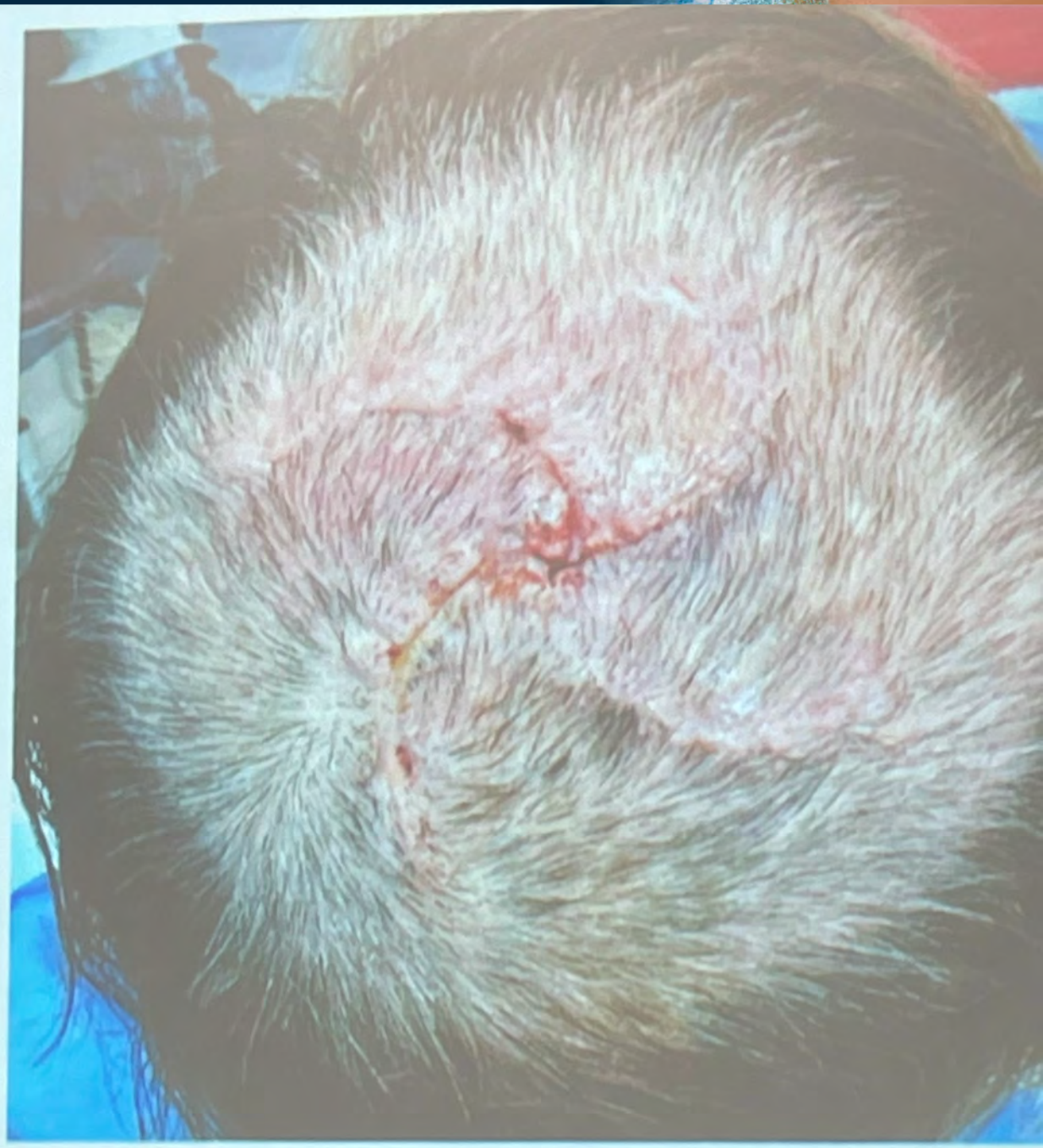




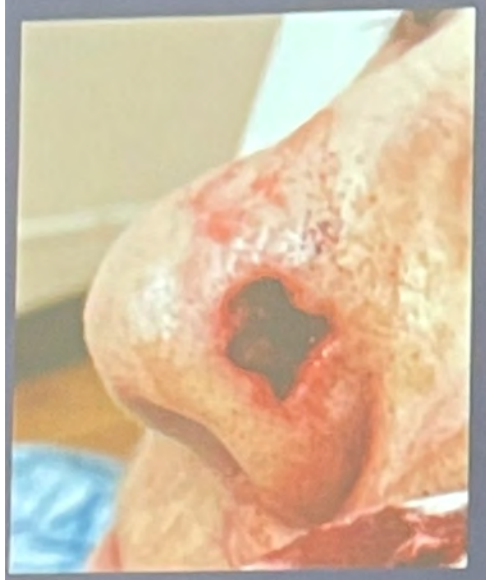
Pinwheel flap

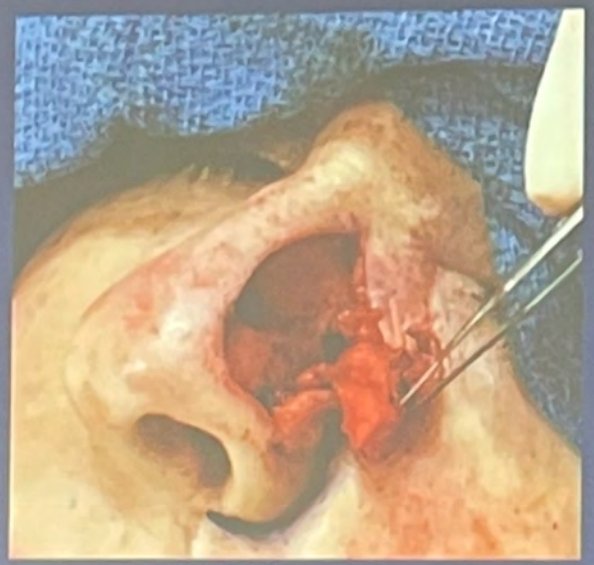


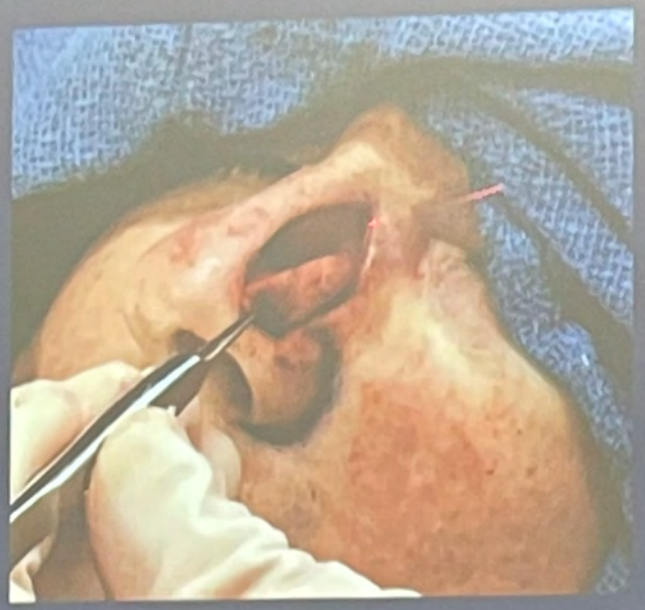


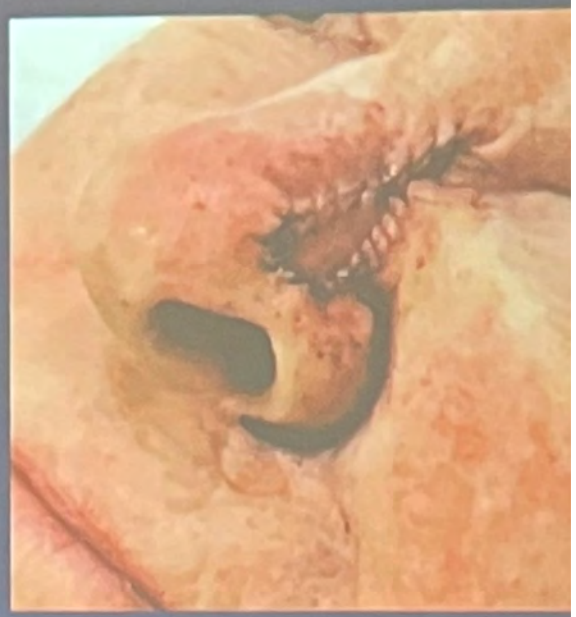


V to Y Advancement Flap/Muscle Sling









AAD **ANNUAL** MEETING

AEDV highlights

SAN DIEGO
8-12 MARZO

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2024.

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