

Outside the Box: Injectable Therapy for Advanced Melanoma

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Creighton University

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Disclosures

- No financial disclosures

Objective

- Discuss emerging injectable therapy options in advanced melanoma through case-based learning.

Cutaneous Melanoma

Rate of New Cancers in the United States, 2021

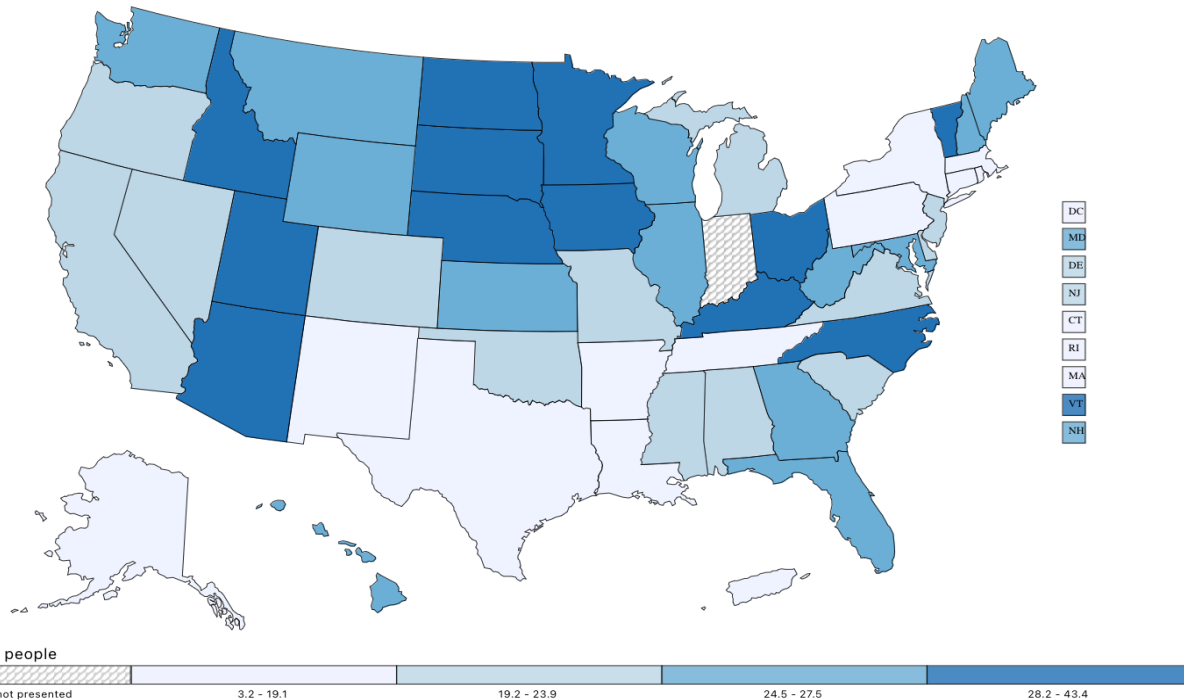
Melanomas of the Skin, All Ages, All Races and Ethnicities, Male and Female

US:
6th most common
among new cancers

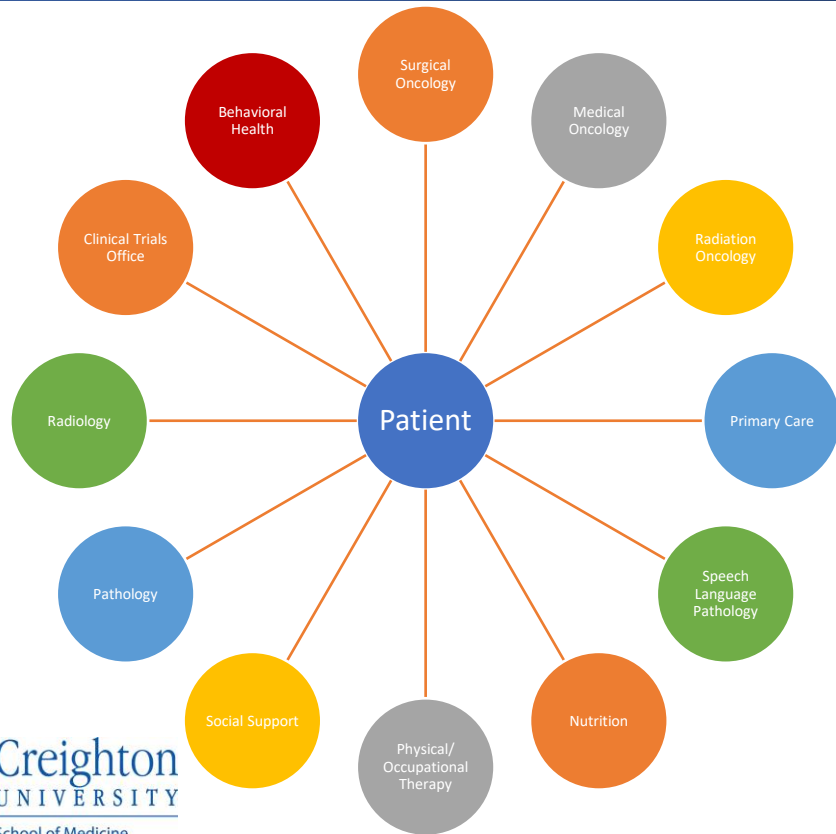
90,000 new cases/
year

8,000

About 8,000 people in the
U.S. die from melanoma
each year.



Patient-Centered Multidisciplinary Care for Cutaneous Melanoma



Scientific Progress, but...

- Patients with advanced disease (Stage III-IV melanoma) experience poor survival outcomes
- Expanded treatment options needed

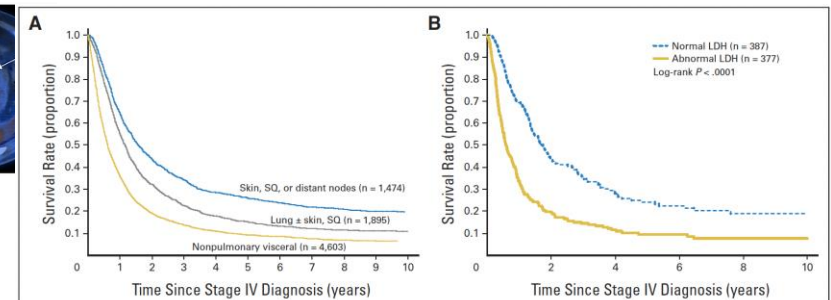
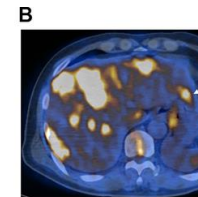
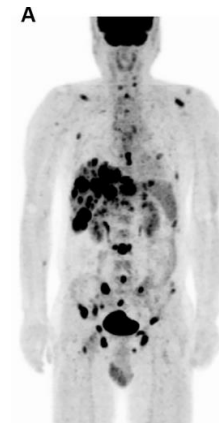
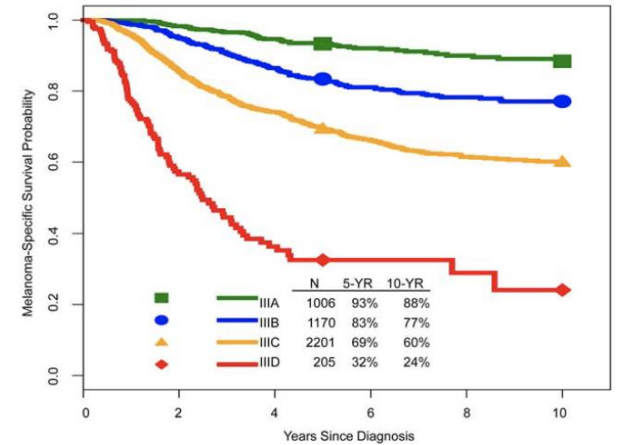
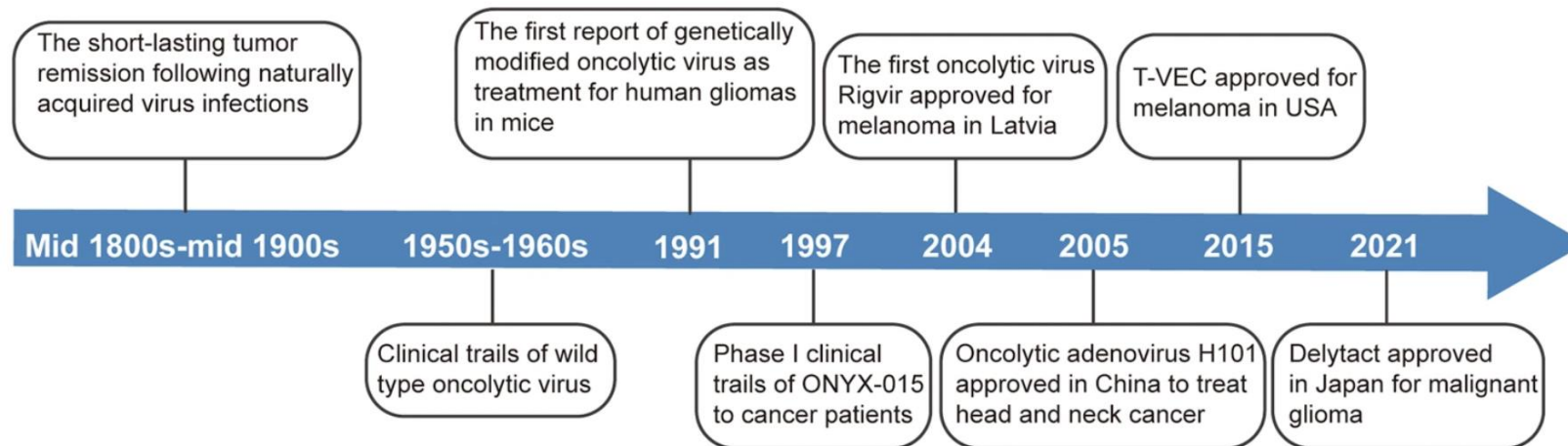


Fig 2. Survival curves of 7,635 patients with metastatic melanomas at distant sites (stage IV) subgrouped by (A) the site of metastatic disease and (B) serum lactate dehydrogenase (LDH) levels. LDH values are not used to stratify patients. Curves in (A) are based only on site of metastasis. The number of patients is shown in parentheses. SQ, subcutaneous.

Balch CM, et al. Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol. 2009 Dec 20;27(36):6199-206.

Oncolytic Viral Therapy

1896: First report of spontaneous regression of “myelogenous leukemia” after presumed influenza episode



T-VEC for Melanoma

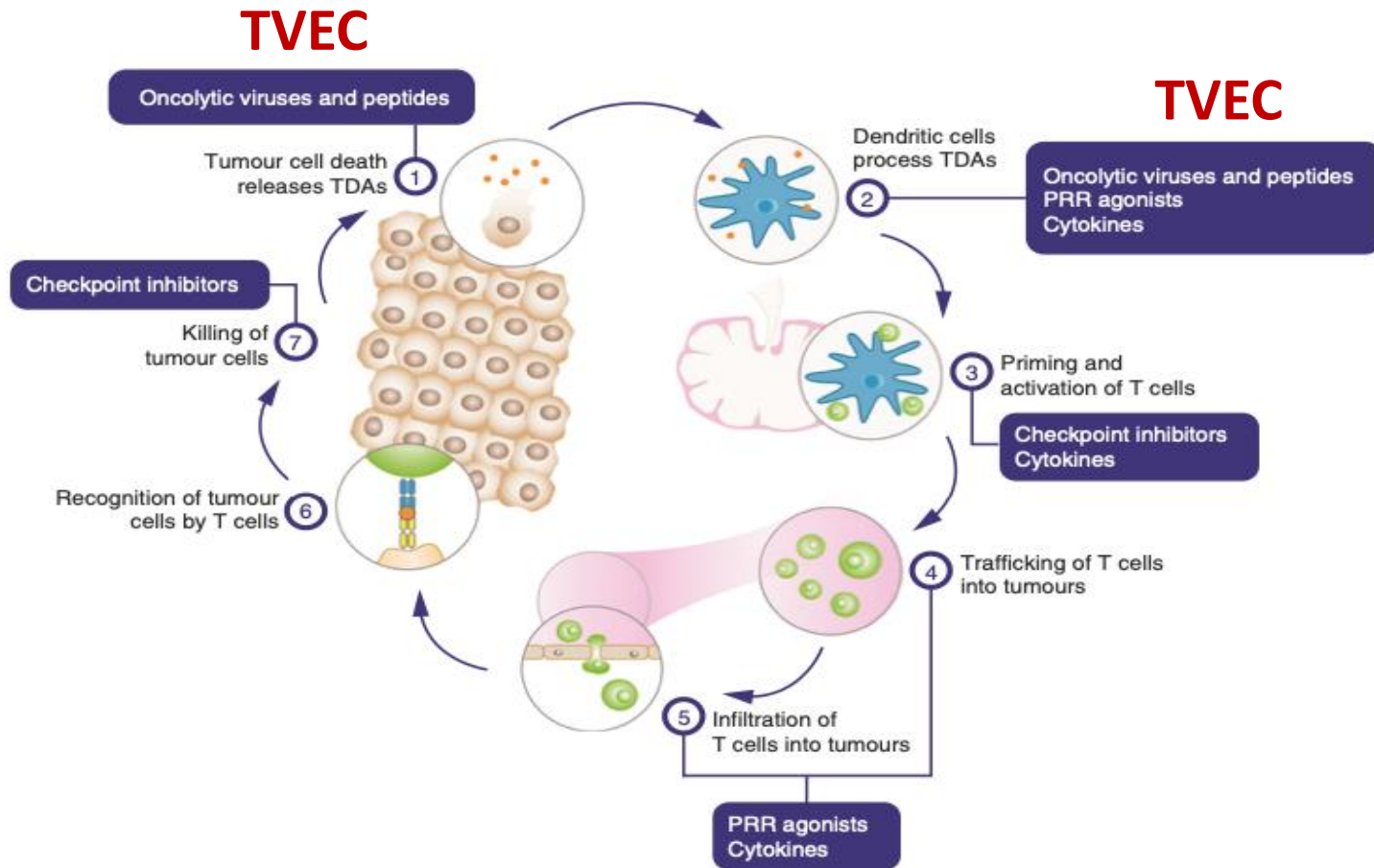
Talimogene laherparepvec (T-VEC): Modified Herpes Simplex Virus-1

HSV-1: common virus that results in cold sores

Oncolytic therapy using weakened, genetically modified HSV-1:

FDA approved for advanced melanoma in 2015



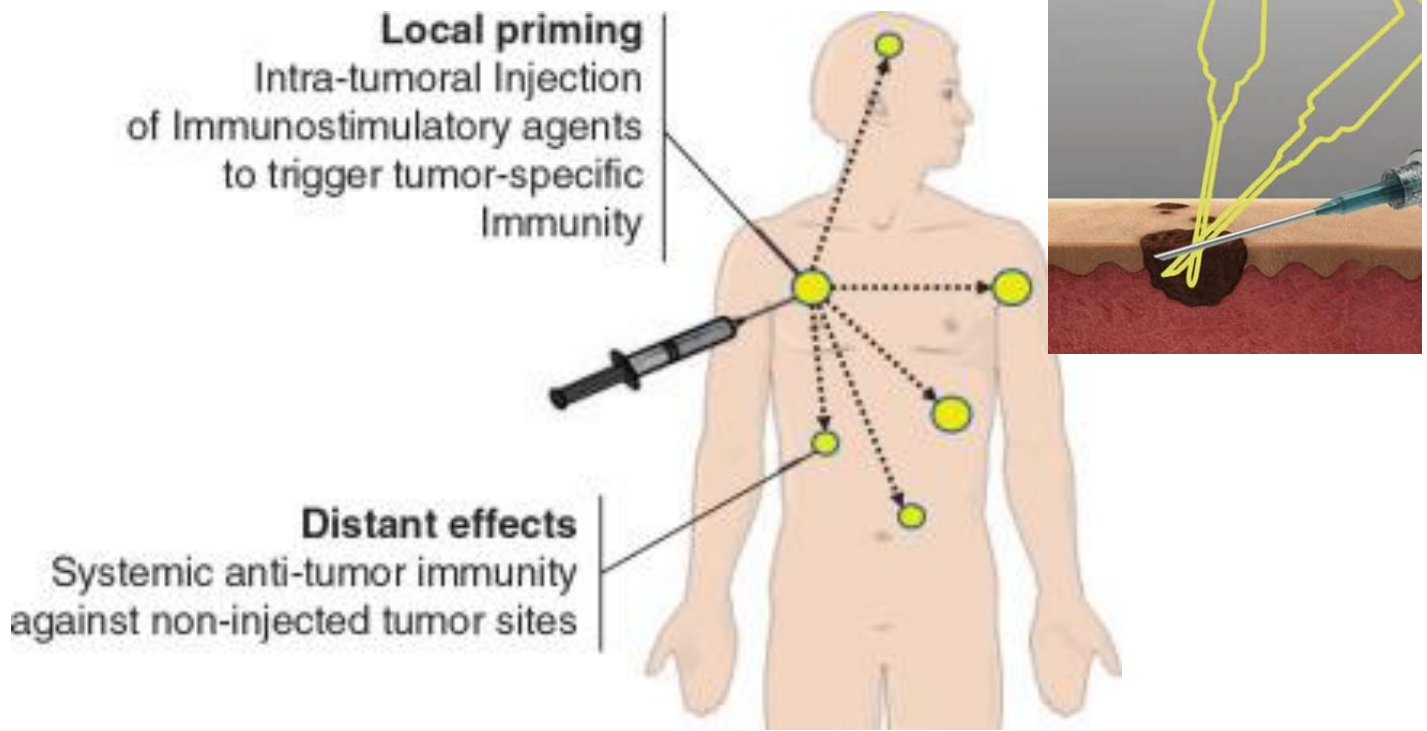


T-VEC: directly injected into tumor deposits in skin, subcutaneous tissue or lymph glands

Infects and multiplies in tumor cells

Triggers immune system

- Increased GM-CSF signal
- Results in tumor cell death

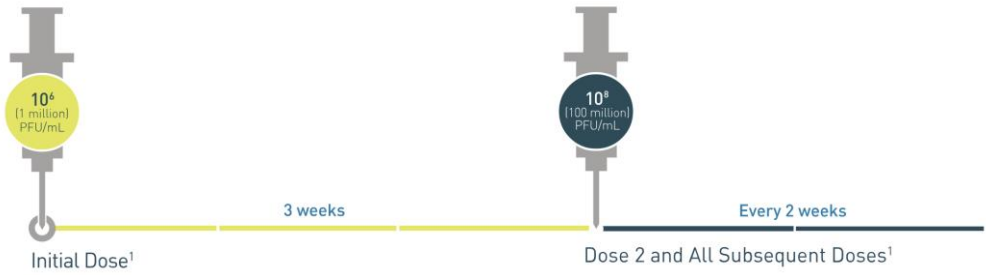


T-VEC: directly injected into tumor deposits in skin, subcutaneous tissue or lymph glands

Injection usually every 2 weeks, up to 6 months duration

Usually well tolerated

Mild symptoms common: tiredness, fever, joint pain, muscle aches.



Intratumoral Immunotherapy: TVEC trials

- **OPTiM trial (Randomized, Phase III): led to FDA approval**
 - Unresectable stage IIIB-IV melanoma TVEC vs subcutaneous recombinant GM-CSF
 - ORR 31.5% vs 6.4%
- **Masterkey-265 (Phase 1B)**
 - T-VEC +Pembrolizumab: ORR 61.9%
- **KEYNOTE-034 (Randomized, Phase III)**
 - Pembrolizumab Vs TVEC + Pembrolizumab
 - ORR 41.3% vs 48.6%
 - PFS 8.5 vs 14.3 months

Clinical Case 1

Case example 1: TVEC + pembrolizumab



3 weeks after first injection

TVEC + Pembro
Q3W



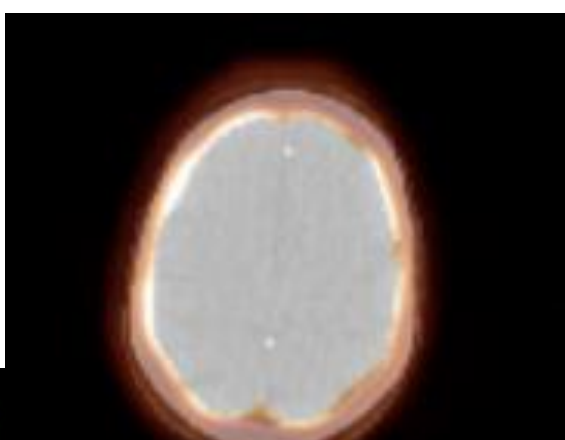
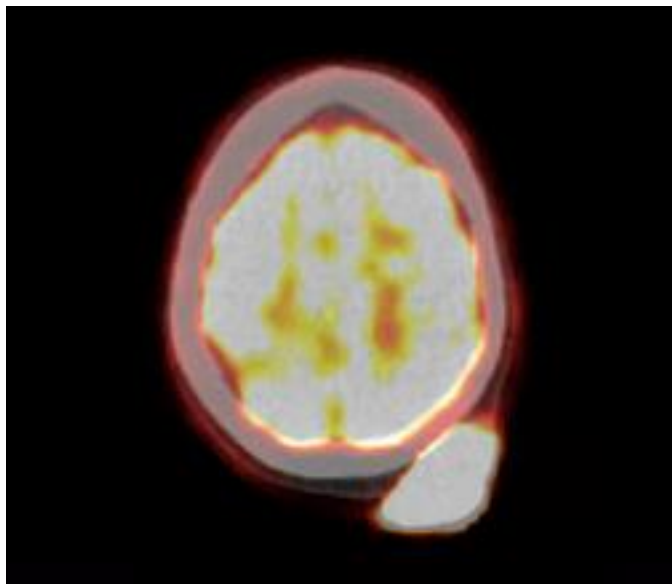
6 months after first injection

Pembro alone
Q6W



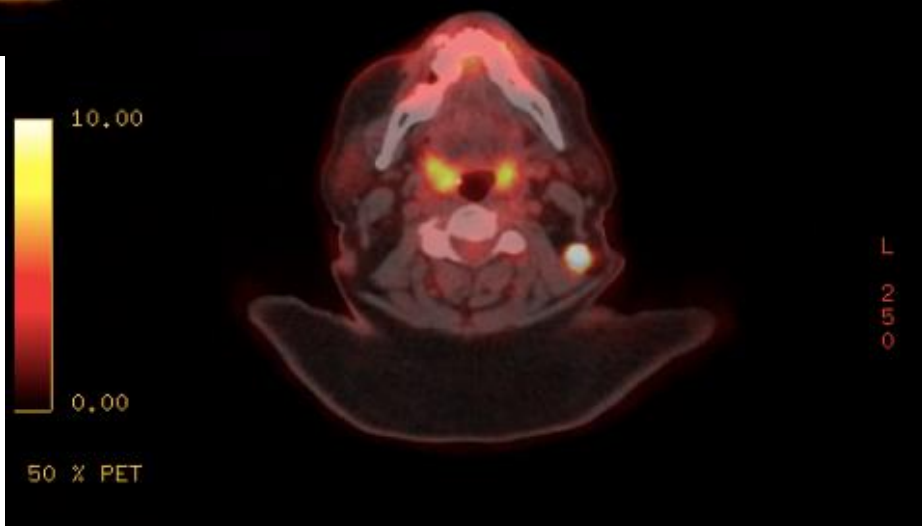
1 year after first injection (1/2022)

Clinical Case 1



Volume 1 SCOTT GARY
IX 6292 A 250 UVM Health Network at CVPH
M 69 455848
DoB: Oct 16 1951
Ex: Dec 15 2020

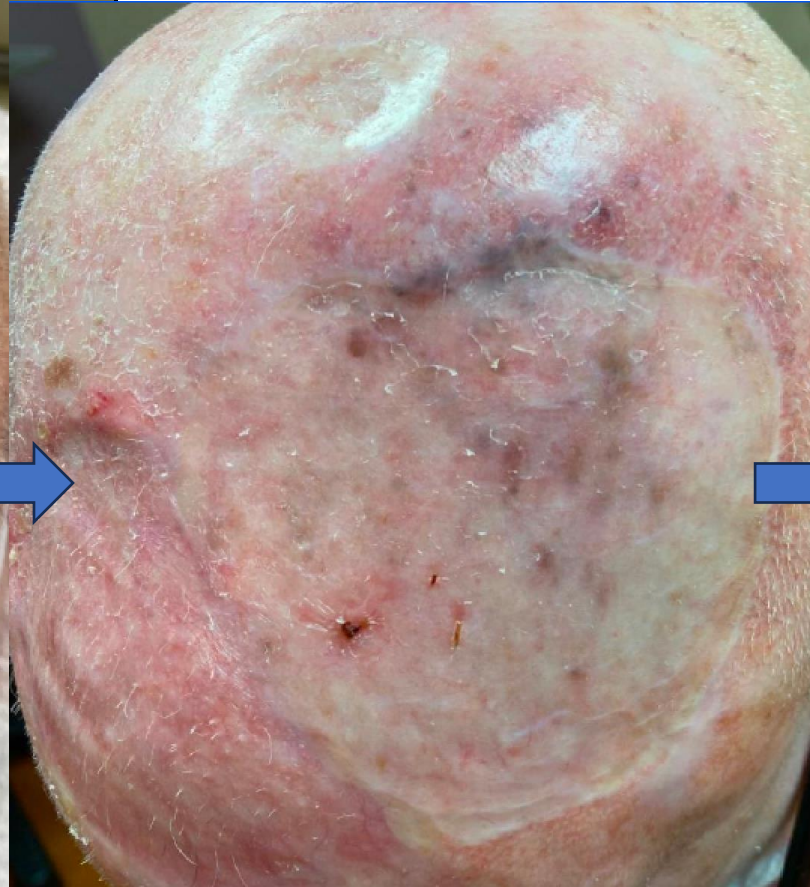
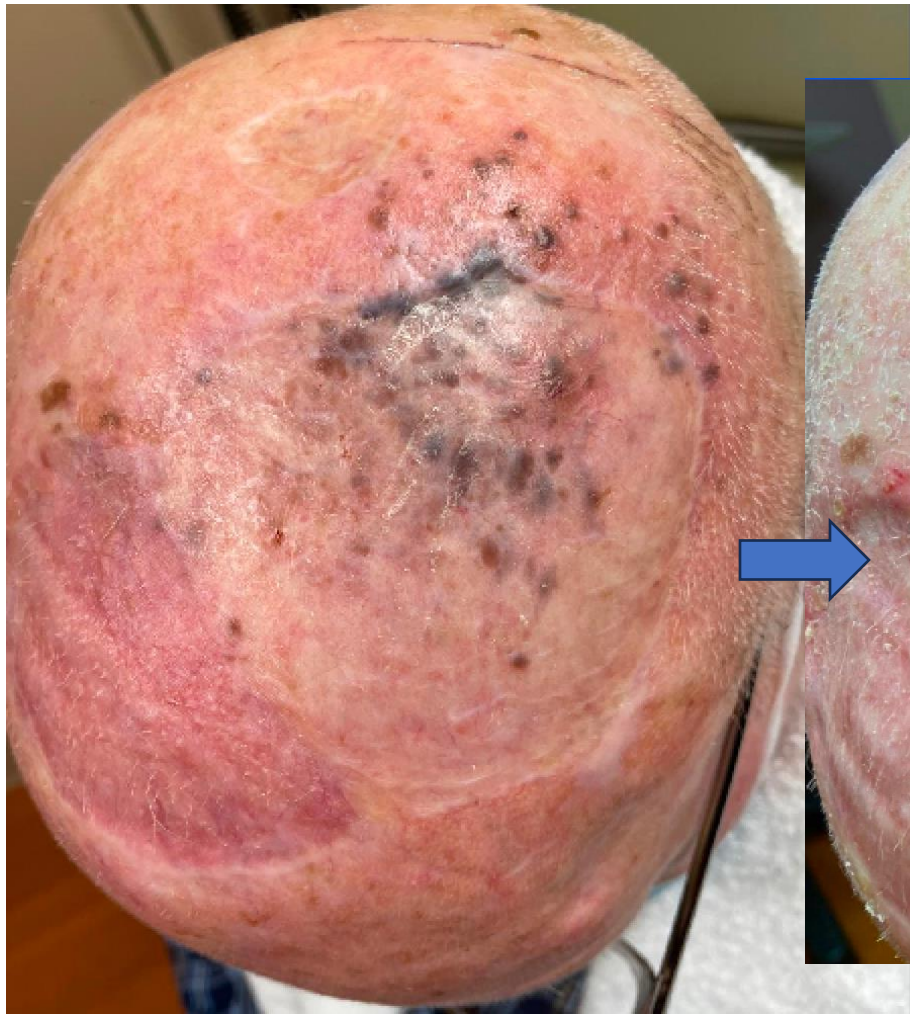
Before



After



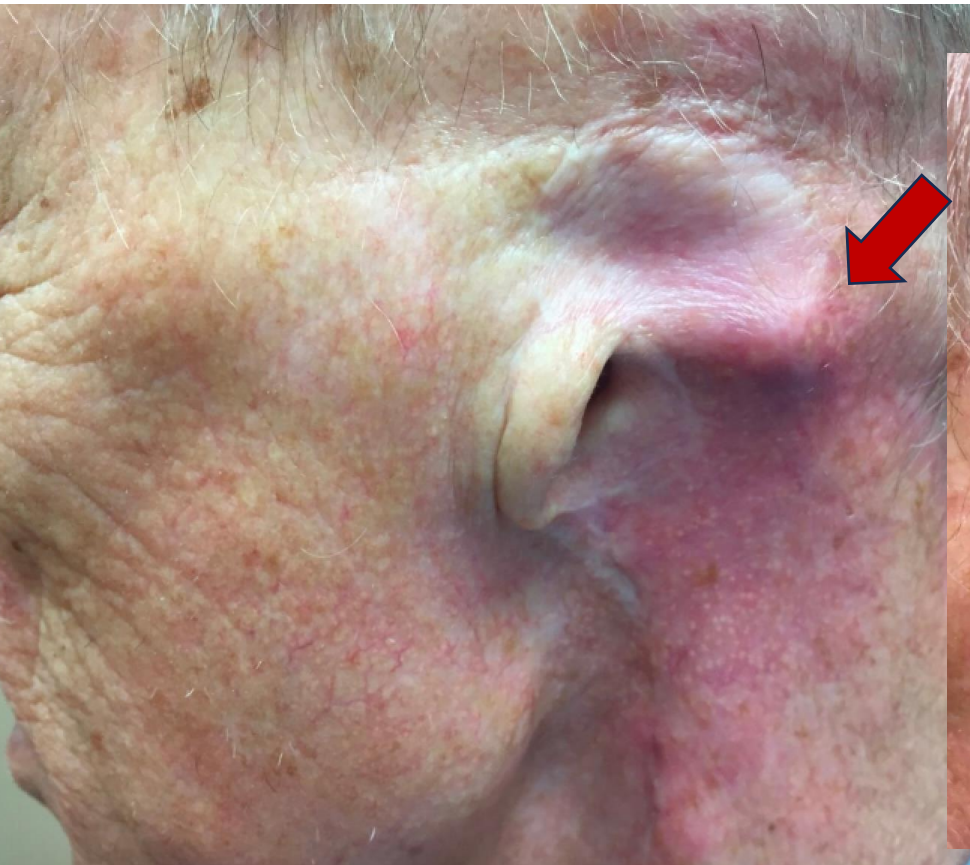
Clinical Case 2: Male, 90s, Multiple prior surgical treatments
T-VEC therapy with 4 years of disease-free survival



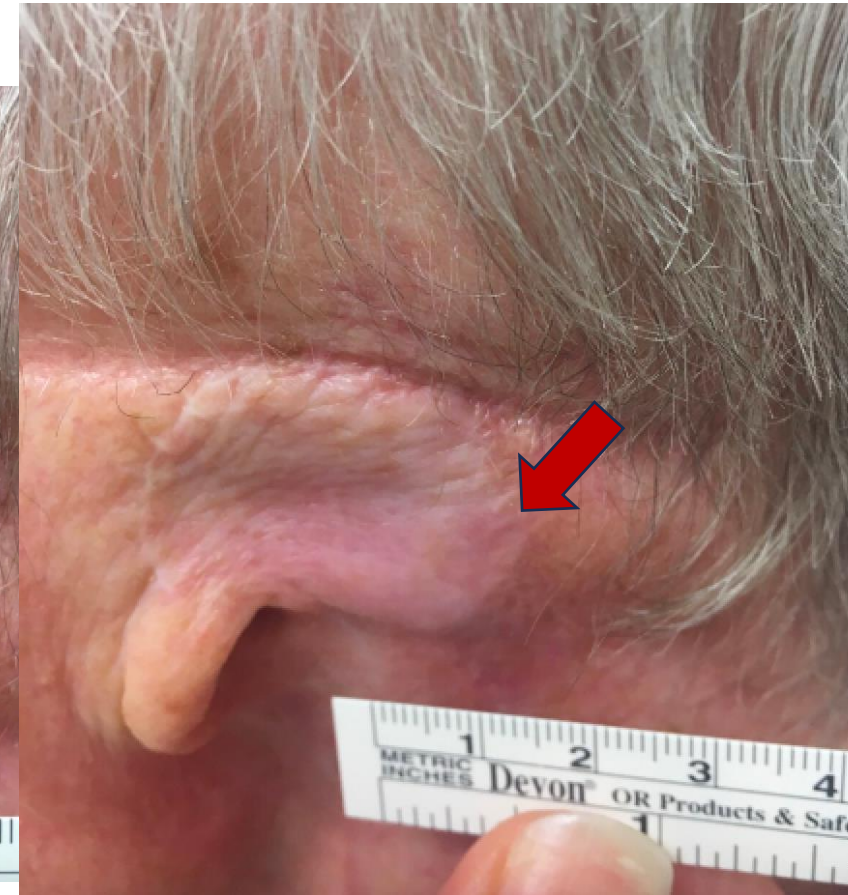
Pre-treatment

Post-treatment

Clinical Case 3: Male, 70s, Prior surgery and radiotherapy
T-VEC therapy with 8 years of disease-free survival



Pre-treatment



Post-treatment

Clinical Case 3: Male, 70s, Prior surgery + Immunotherapy
T-VEC therapy with 7 years of disease-free survival



Recap

- Patients with advanced melanoma:
 - Inferior outcomes
 - Need for expanded treatment options
- Intra-tumoral injectable therapy with T-VEC:
Promising option for some patients
- Optimal treatment requires multidisciplinary care
- Encourage clinical trial participation

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