



Society for Immunotherapy of Cancer

# Advances in Cancer Immunotherapy™

## Case Study

Elizabeth Buchbinder

Dana-Farber Cancer Institute

#LearnACI

# Disclosures

- Consulting as an advisory board member for Novartis, Apixigen, Shionogi, BMS and Nektar.
- Clinical trial support from Lilly, Novartis, Partners Therapeutics, Genentech and BVD.
- I will be discussing non-FDA approved indications during my presentation.

## 80 yo male

- At the age of 40 had a melanoma removed from right calf and was told it was pretty “advanced”. No adjuvant therapy done at that time.
- 2016 noted growing mass proximal to his previous melanoma
- 2018 presented to dermatology with 5 X 4 cm mass on right medial calf, biopsy confirmed recurrent melanoma
- PET/CT with numerous nodules

# PET/CT and clinical images



# 80 yo male treatment course

- 11/18 –  
Started on  
nivolumab  
without  
benefit



## 80 yo male treatment course

- 4/19 – Started on encorafenib and binimetinib with nice response to therapy
- 11/19 - stopped for malignant hypertension and concern for possible cardiac toxicity
- Subsequently started progressing again in his leg lesions



# PET/CT and clinical imaging



# 80 yo male treatment course

- 1/20 – Started on injection T-VEC therapy



# PET/CT and clinical imaging





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## Case Study

**Patrick A Ott, MD, PhD**

Clinical Director, Melanoma Center

Dana Farber Cancer Institute

Associate Professor of Medicine

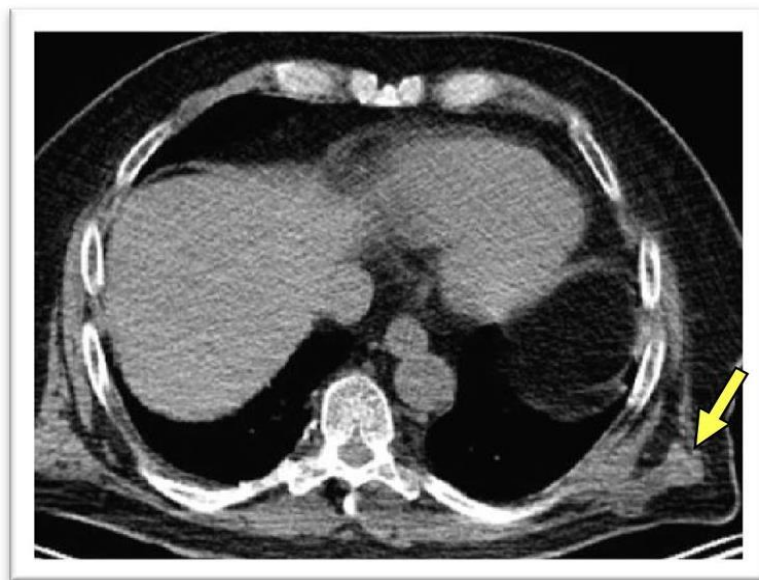
Harvard Medical School

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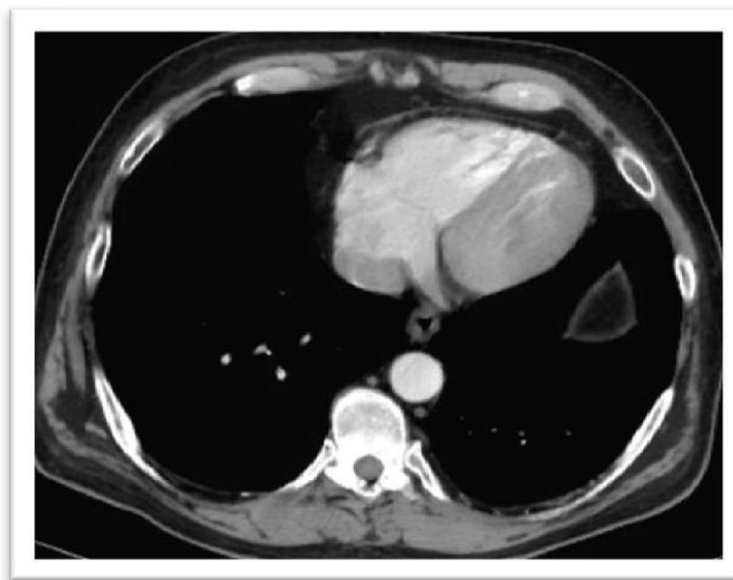
## ML, 57 yo male

- **Jan 2012** Initial diagnosis of 2.2 mm melanoma on chest wall
- **March 2012:** wide local excision and sentinel lymph node biopsy =
- **March 2015** CT demonstrates a 2 cm lung nodule
- **May 2015:** enrollment on 13-240 NeoVax study
- **May 2015:** lung nodule resection
- **Aug 2015:** Initiation of vaccination
- **Jan 2016:** chest wall recurrence - initiation on pembrolizumab monotherapy
- **April 2016:** complete response to treatment
- **March 21, 2018:** pembrolizumab discontinued

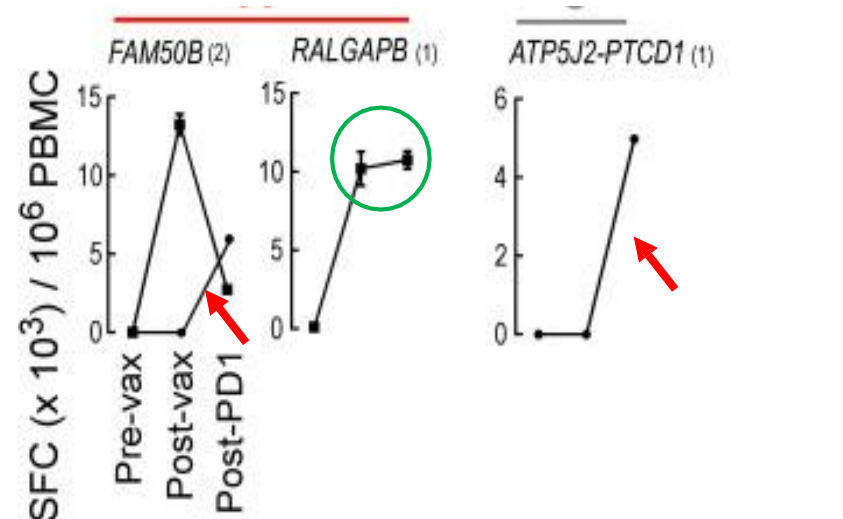
Post-vaccine pre pembrolizumab



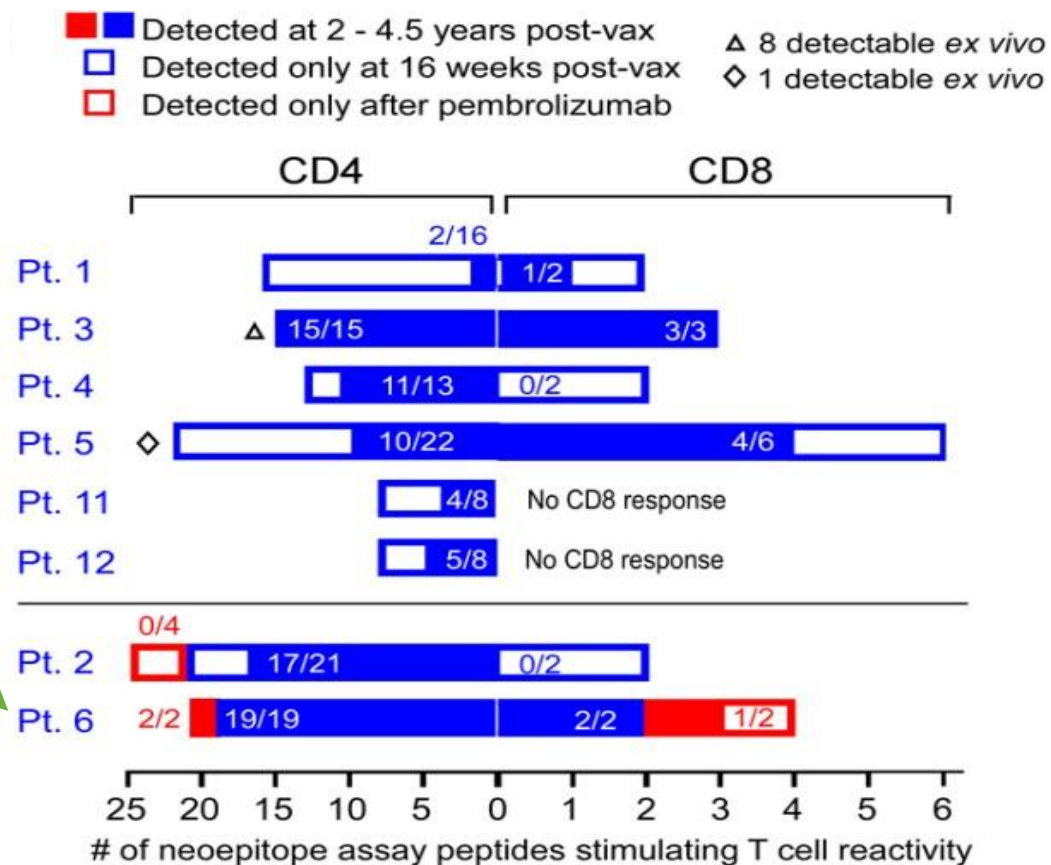
3 months post pembrolizumab



# Broadening of T cell response after PD-1 inhibition



## Vaccine-induced neoantigen specific T cells persist over several years







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# Case Study

Virginia Seery, NP

Beth Israel Deaconess Medical Center

# Disclosures

- Advisory Board or Panel: Exelixis, Aveo
- Speaker's Bureau: Clinigen
- Consultant: Apricity Health
- I will be discussing non-FDA approved indications during my presentation.

## 58 y.o. male

- Hx of IIB melanoma in 2012
- Presented in 2018 w/new scalp primary melanoma, pT4b w/satellites
- PET scan showed FDG avidity in scalp/cervical nodes
- Planned for surgery

## 58 y.o. male w/melanoma

- Massive disease progression within 2 weeks - unresectable





## 58 y.o. male w/melanoma





## 58 y.o. male w/melanoma

- Started pembrolizumab x 2 cycles
- New scalp nodules noted w/progression of pre-existing nodules
- TVEC added to pembro
- Significant disease regression after 2 cycles of TVEC

## 58 y.o. male w/melanoma

- TVEC stopped after 4 months
- Pembro stopped after one year d/t colitis
- PET scan shows no active disease x 2.5 years after pembro stopped

# Post TVEC



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# 2 years after TVEC



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# mRNA-2752 plus durvalumab in patient with melanoma

## Case Presentation:

### 57 yo M multiple SQ nodules and regional adenopathy

- 2018:
  - Shave biopsy right medial pretibial lesion: 1.1 mm, SSM, non-ulcerated, 12 mits
  - WLE: 0.7 mm residual melanoma, completely excised
  - SLE: no involvement of four right inguinal SLNs
- 2020:
  - Recurrence (in transit) near WLE site; PET/CT, MRI brain NED elsewhere
  - TVEC x 6 doses, progression in regional nodes, flattening of injected lesion
  - Commenced pembrolizumab – no response with new SQ and nodal progression on imaging



## Case Presentation:




### 57 yo M multiple SQ nodules and regional adenopathy

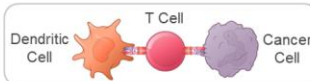
- Enrolled onto Phase 1 trial of intralesional mRNA-2752 with durvalumab
- Baseline lesions on leg



# Advances in Cancer Immunotherapy™

## Immune modulation with OX40L/IL-23/IL-36 $\gamma$

	IL-23	IL-36 $\gamma$	OX40L
	Proinflammatory cytokine of the IL-12 family	Proinflammatory cytokine of the IL-1 family	Transmembrane T cell co-stimulatory protein
	<ul style="list-style-type: none"> <li>Reported to prime DC</li> <li>Activates other cells that bridge innate to adaptive immunity (NKT, ILCs, <math>\gamma\delta</math> T cells)</li> </ul>	<ul style="list-style-type: none"> <li>Acts on DCs to promote maturation and <math>\uparrow</math> cytokine/chemokines</li> </ul>	
	<ul style="list-style-type: none"> <li>Expands and maintains Th17</li> <li>Acts on antigen experienced T cells</li> </ul>	<ul style="list-style-type: none"> <li>Enhances T cell proliferation, Th1, Th9 differentiation</li> </ul>	<ul style="list-style-type: none"> <li>Promotes Th1, Th2, Th9; suppresses Treg</li> <li>Enhances expansion and survival of CD4 and CD8 T cells <math>\rightarrow</math> promotes memory</li> </ul>
 <i>Rationale as IO Therapeutic?</i>	<ul style="list-style-type: none"> <li>Monotherapy efficacy established and reported (pre-clinical)</li> <li>Clear role in human barrier immunity and inflammatory disease</li> </ul>	<ul style="list-style-type: none"> <li>Reported to enhance anti-cancer immunity (pre-clinical)</li> <li>Clear role in human barrier immunity and inflammatory disease</li> </ul>	<ul style="list-style-type: none"> <li>Monotherapy efficacy established and reported (pre-clinical)</li> </ul>



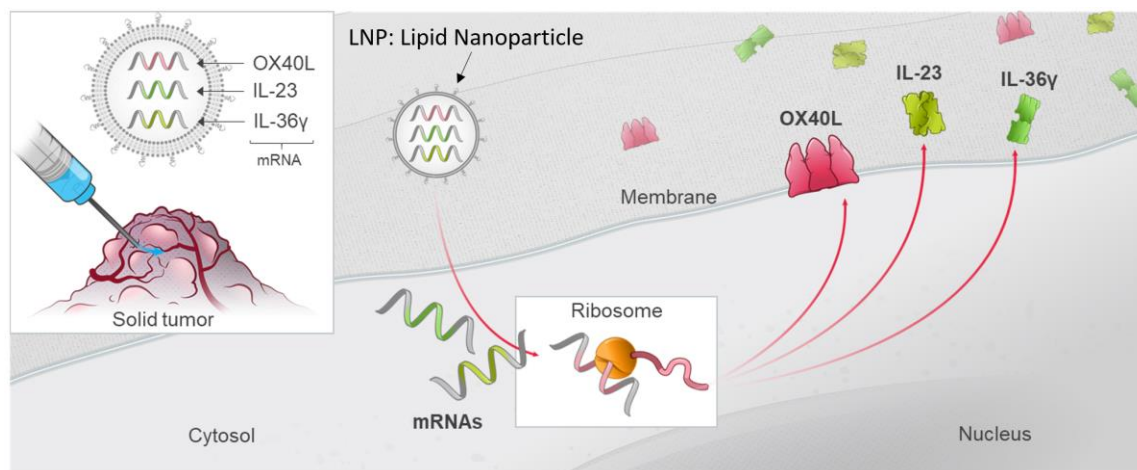
**Arm A**  
mRNA-2752 Monotherapy Dose Escalation  
(Superficial/Palpable Lesions)

**Arm B**  
mRNA-2752  
+Durvalumab  
Combination  
Dose Escalation  
(Superficial/Palpable Lesions)

**Arm B**  
mRNA-2752  
+Durvalumab  
Combination  
Dose Confirmation  
(Visceral Lesions)

**Arm B Expansion Cohorts:**  
IO-refractory Melanoma  
IO-refractory NSCLC  
NHL  
HNSCC  
Urothelial ca.  
TNBC

**Arm C Schedule Exploration**  
mRNA-2752 Weekly administration  
+/- Durvalumab in Neoadjuvant Melanoma



## Objectives:

- Assess the safety and tolerability of mRNA-2752 +/- durvalumab
- Characterize the pharmacokinetics of mRNA-2752 +/- durvalumab
- Characterize protein expression from introduced mRNAs and biomarkers of immune response
- Assess preliminary anti-tumor activity in select expansion cohorts of TNBC, HNSCC, NHL, urothelial carcinoma, and immune checkpoint refractory-melanoma and -NSCLC



C1D1

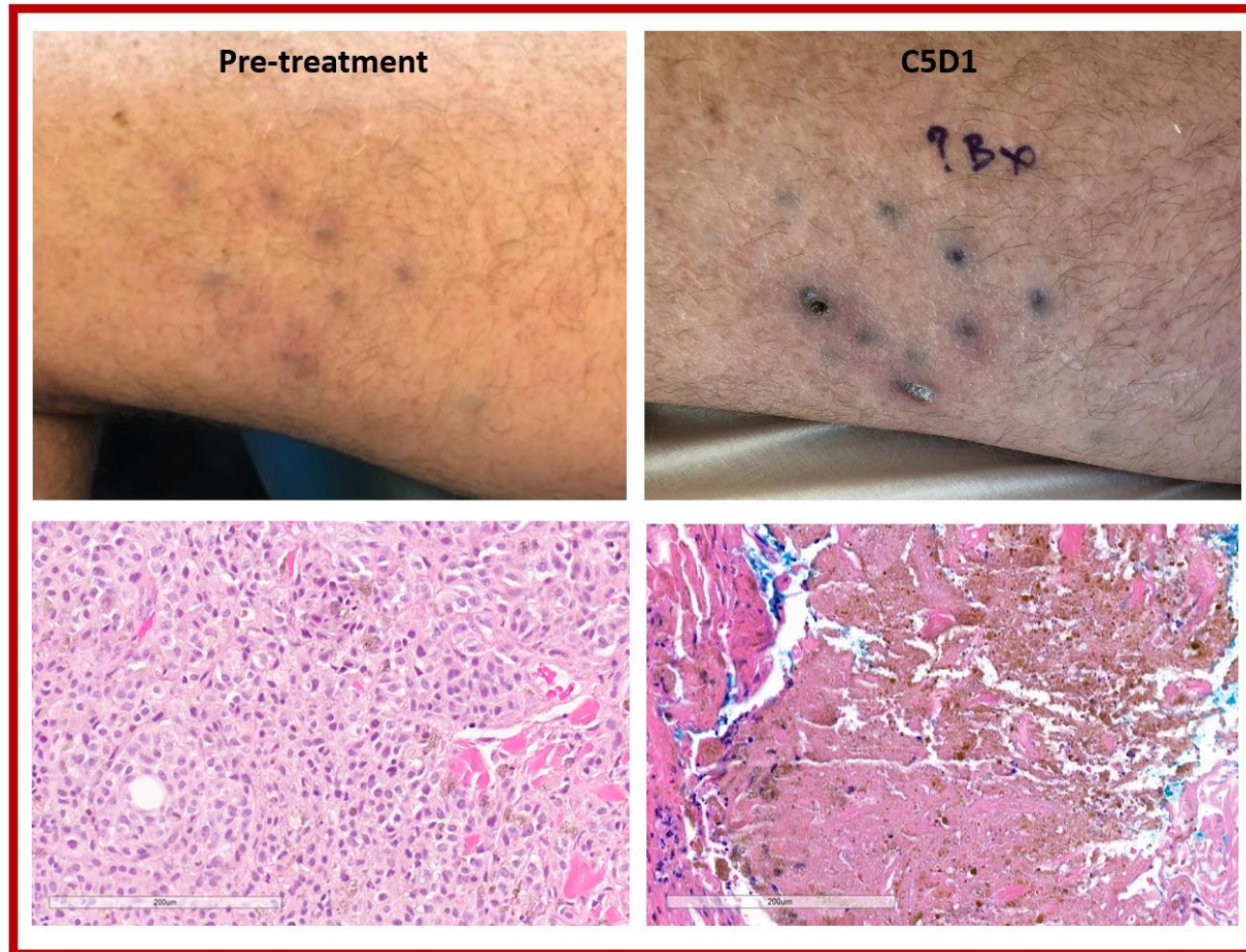
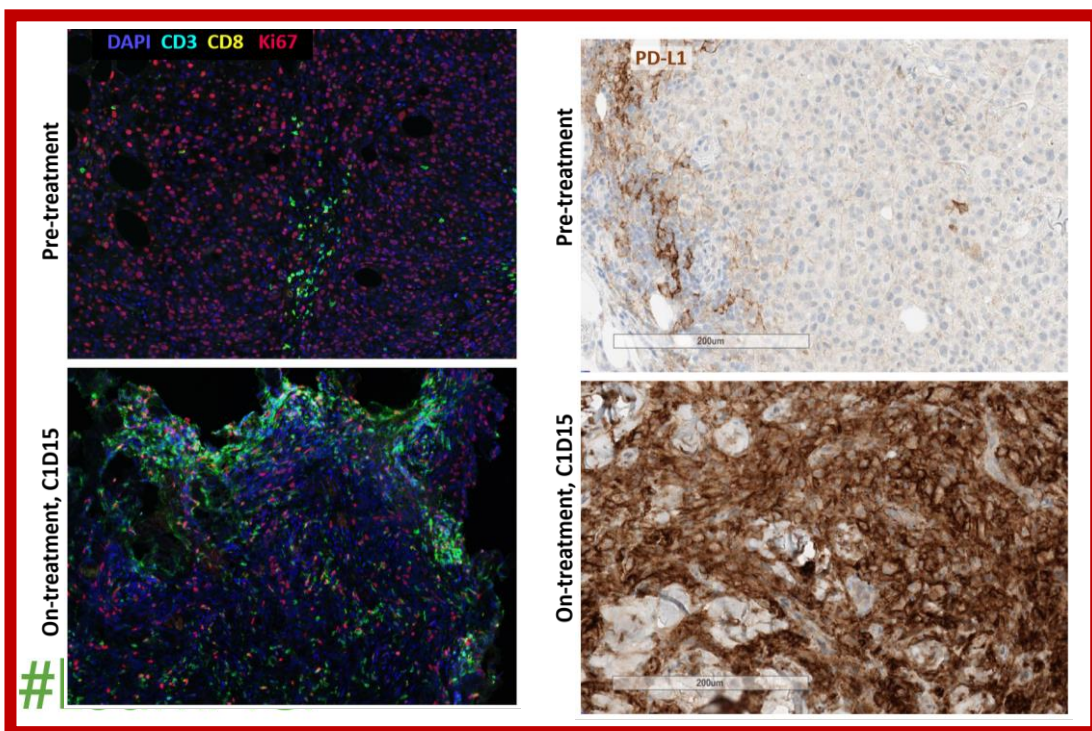


C5D1





Early on treatment biopsy shows evidence of increase infiltration of proliferating T cells



Pretreatment biopsy showed sheets of tumor cells. C5D1 biopsy shows necrosis, minimal viable tumor cells, and numerous pigment-laden macrophages

## Case Presentation:

### 57 yo M multiple SQ nodules and regional adenopathy

- After 7 injections, he had resolution of palpable, injectable lesions; he continued with four more cycles of durvalumab before documented PD in right inguinal region and gallbladder.
- He is now NED following right groin dissection and cholecystectomy