# Immunotherapy for the Treatment of Skin Cancers

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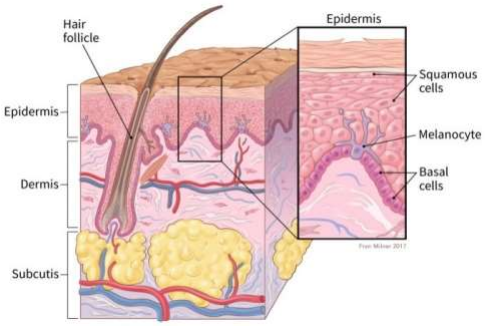
## Disclosures

- Consulting Fees: Castle, Kimera Labs, Array
- Contracted Research: BMS, Replimune, Novartis, Regeneron, Immunocore, Iovance
- I will be discussing non-FDA approved indications during my presentation.

# Background

- Skin cancer is the most common type of cancer
- Three most common types of skin cancers:
  - Basal cell carcinoma
  - Squamous cell carcinoma
  - Melanoma
- Melanoma was one of the foundational disease states for testing immunotherapies






# Approved cytokines in melanoma

| Drug | Indication | Dose |
|---|---|---|
| High-dose interferon alfa-2b | Adjuvant – high risk for systemic recurrence | Induction: 20m IU/$m^2$ IV 5x/wk for 4 wks<br>Maintenance: 10m IU/$m^2$ s.c. 3x/wk for 48 wks |
| Interleukin-2 (Aldesleukin) | Stage IV | 600k IU/kg/dose Q8hr, up to 14 doses; 9 days of rest; can repeat up to 28 doses per course |
| Pegylated Interferon alfa-2b (Sylatron) | Adjuvant – microscopic or gross nodal involvement | 6 mcg/kg/wk s.c. for 8 doses, then 3 mcg/kg/wk s.c. for up to 5 years |

# Approved checkpoint inhibitors in melanoma

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Ipilimumab | 2011 | Unresectable/Metastatic melanoma: newly diagnosed or after progression | 3 mg/kg Q3W for 4 doses |
| | 2015 | Adjuvant therapy in stage III melanoma after complete resection | 10 mg/kg Q3W for 4 doses, then 10 mg/kg Q12W for 3 years |
| | 2017 | Unresectable/Metastatic melanoma: newly diagnosed or after progression, all patients ≥ 12 yr | 3 mg/kg Q3W for 4 doses |

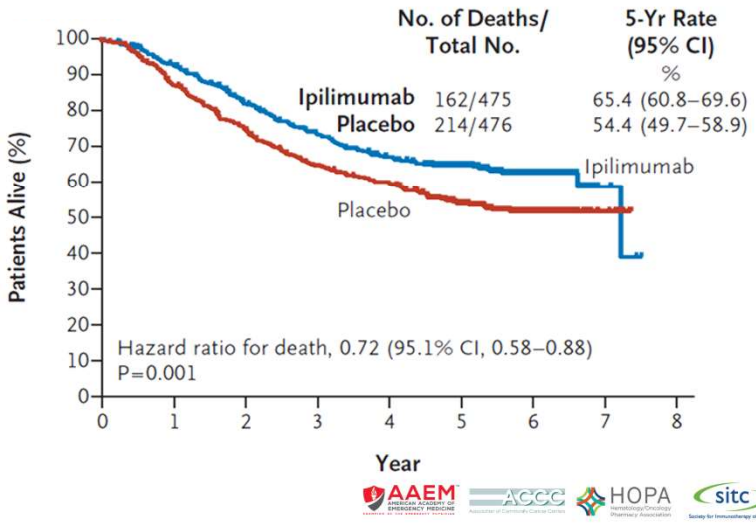


# Approved checkpoint inhibitors in melanoma

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Ipilimumab | 2011 | Unresectable/Metastatic melanoma: newly diagnosed or after progression | 3 mg/kg Q3W for 4 doses |
| | 2015 | Adjuvant therapy in stage III melanoma after complete resection | 10 mg/kg Q3W for 4 doses, then 10 mg/kg Q12W for 3 years |
| | 2017 | Unresectable/Metastatic melanoma: newly diagnosed or after progression, all patients ≥ 12 yr | 3 mg/kg Q3W for 4 doses |
| | 2020 | Adjuvant therapy in stage III after complete resection 3mg/kg vs 10 mg/kg vs high dose interferon alpha-2b | 3 mg/kg dose superior to interferon alpha-2b |

# Adjuvant Ipilimumab in High-Risk Stage III Melanoma

- EORTC 18071 phase III trial
  - NCT00636168
  - Adjuvant ipilimumab vs placebo
  - Ipilimumab 10mg/kg Q3W for four doses, then every 12 weeks for up to 3 years




Eggermont, NEJM 2016.

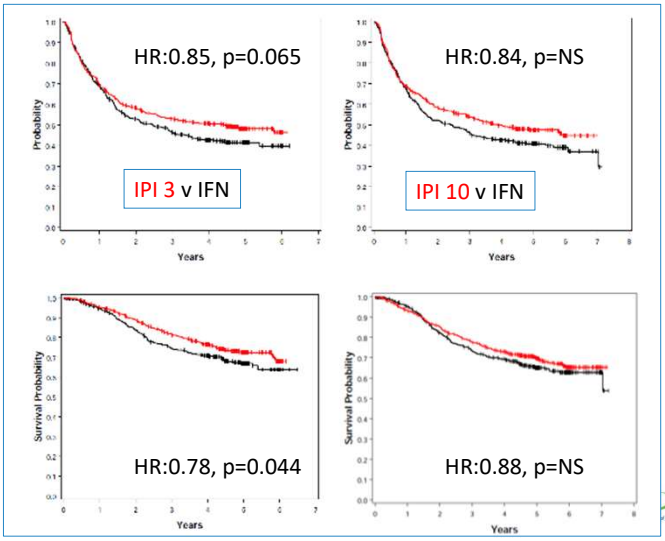


# Adjuvant Ipilimumab in High-Risk Stage III Melanoma

- ECOG 1609
  - NCT01274338
  - Adjuvant interferon (IFN) vs ipilimumab 3 mg/kg (IPI 3) vs ipilimumab 10 mg/kg (IPI 10)
  - Ipilimumab Q3W for four doses, then every 12 weeks for up to 3 years
  - IPI 3 "better than IFN", IPI 10 "not better than IFN"
  - IPI3 better tolerated than IPI 10

RFS

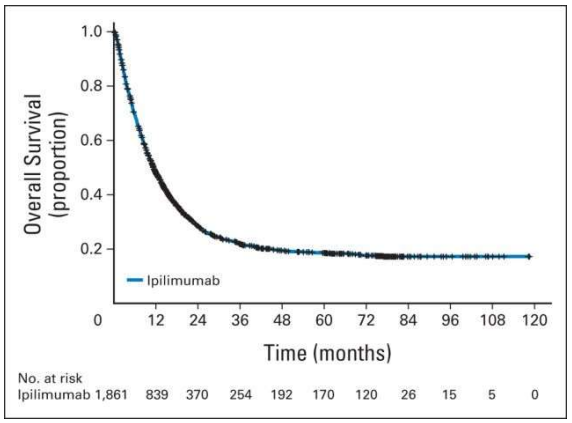
OS




Tarhini, ASCO Annual Meeting 2019.

# Ipilimumab in Stage III/IV Melanoma

- Pooled OS data from 10 phase II/III trials
  - Previously treated (n = 1,257) or treatment-naïve (n = 604)
  - Ipilimumab 3 mg/kg (n = 965) or 10 mg/kg (n = 706)




Schadendorf, JCO 2015.



# Approved checkpoint inhibitors in melanoma

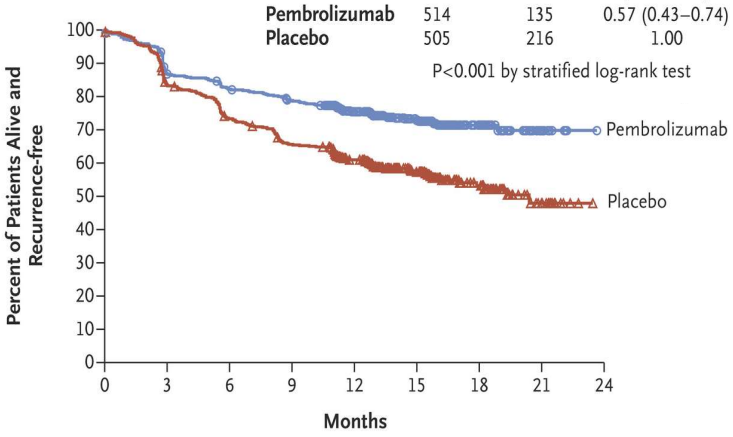
| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Pembrolizumab | 2014 | Advanced/unresectable melanoma with progression after other therapy | 200 mg Q3W* |
| | 2015 | 1st line unresectable/metastatic melanoma | 200 mg Q3W* |
| | 2019 | Adjuvant therapy of melanoma following complete resection | 200 mg Q3W |
| *Original approvals were 2 mg/kg Q3W – updated to flat dosing regimen | | | |

# Adjuvant Pembrolizumab in High-Risk Stage III Melanoma

- EORTC 1325/KEYNOTE-054 phase III trial
  - NCT02362594
  - Adjuvant pembrolizumab vs placebo
  - Pembrolizumab 200mg Q3W for up to 1 year (~18 total doses)

| | Total No. | No. with Event | Hazard Ratio (98.4% CI) |
|---|---|---|---|
| Pembrolizumab | 514 | 135 | 0.57 (0.43–0.74) |
| Placebo | 505 | 216 | 1.00 |

P<0.001 by stratified log-rank test

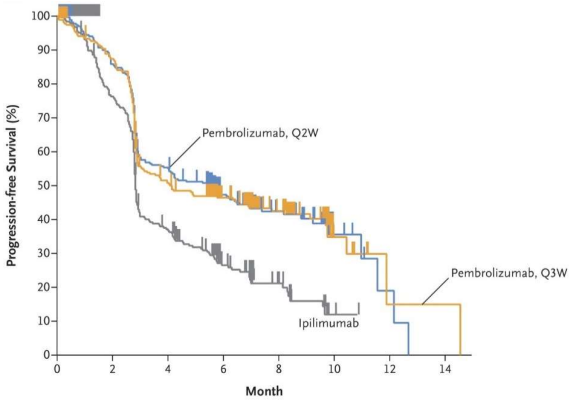


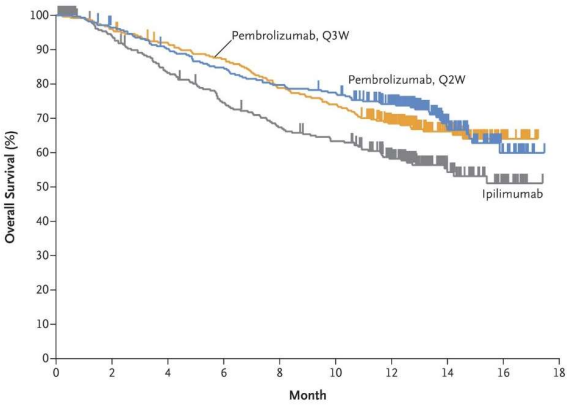

Eggermont, NEJM 2018.



# Pembrolizumab in Stage III/IV Melanoma

## Phase III KEYNOTE-006 Trial




Robert, NEJM 2015.

# Approved checkpoint inhibitors in melanoma

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Nivolumab | 2014 | Unresectable/metastatic melanoma with progression after other therapy | 240 mg Q2W or 480 mg Q4W* |
| | 2017 | Adjuvant treatment of melanoma after complete resection | 240 mg Q2W or 480 mg Q4W |
| *Original approval was 3 mg/kg Q2W, updated to flat dosing regimen | | | |

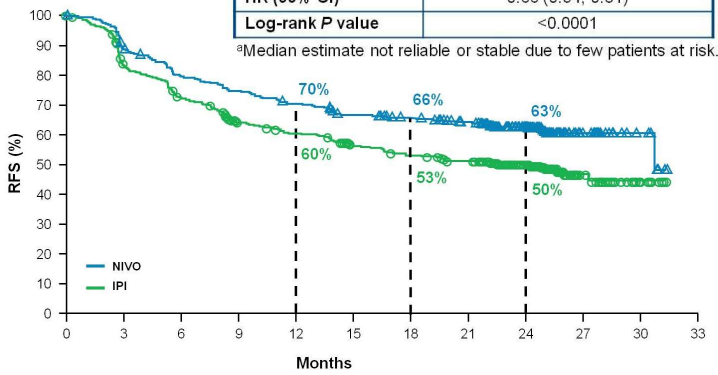


# Adjuvant Nivolumab vs Ipilimumab in High-Risk Stage III Melanoma

- CheckMate 238 phase III trial
  - NCT02388906
  - Ipilimumab 10mg/kg Q3W for four doses, then every 3 months for up to 1 year
  - Nivolumab 3mg/kg Q2W for four doses, then every 3 months for up to 1 year

| | NIVO | IPI |
|---|---|---|
| Events/patients | 171/453 | 221/453 |
| Median (95% CI) | 30.8 (30.8, NR)[a] | 24.1 (16.6, NR) |
| HR (95% CI) | 0.66 (0.54, 0.81) | |
| Log-rank *P* value | <0.0001 | |

[a]Median estimate not reliable or stable due to few patients at risk.




Miller, ASCO 2018.

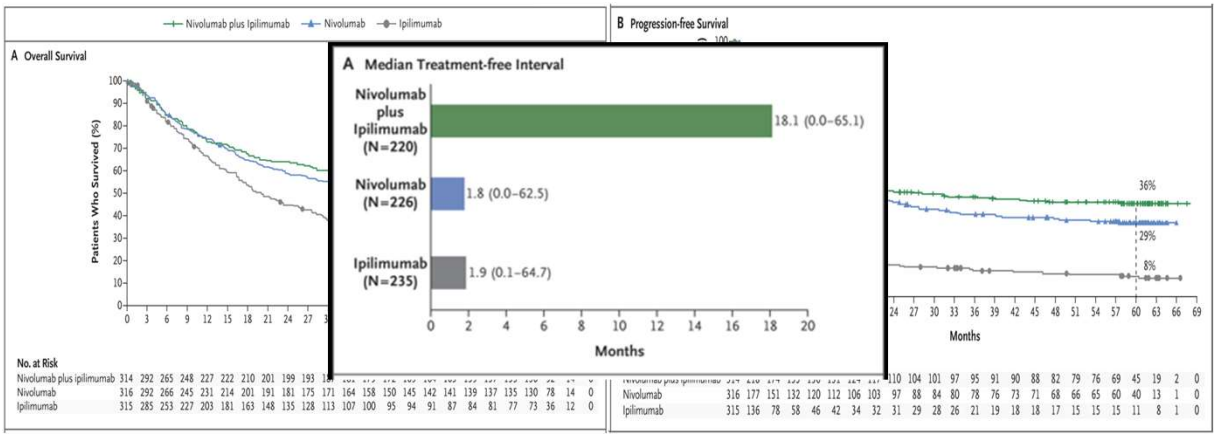
# Approved checkpoint inhibitors in melanoma

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Nivolumab + Ipilimumab | 2015 | BRAF V600 WT unresectable/metastatic melanoma | 1 mg/kg nivolumab + 3 mg/kg ipilimumab Q3W for 4 doses, then nivolumab 240 mg Q2W or 480 mg Q4W |
| | 2016 | BRAF V600 WT or mutant unresectable/metastatic melanoma | 1 mg/kg nivolumab + 3 mg/kg ipilimumab Q3W for 4 doses, then nivolumab 240 mg Q2W or 480 mg Q4W |



## Combination Ipilimumab +Nivolumab in Stage III/IV Melanoma

Phase III CheckMate 067 Trial




Larkin J et al. N Engl J Med 2019; 381:1535-1546

# A phase II study to evaluate the need for >2 doses of nivolumab + ipilimumab combination immunotherapy in patients with unresectable stage III/IV melanoma

## Results

**Two doses**
**nivolumab (1mg/kg) + ipilimumab (3mg/kg)**

**Week 6 Scan**

**No tumor burden growth*** — **68% (41/60)**

*7 patients only had 1 total dose of nivo + ipi

**Tumor burden growth > 4%** — **32% (19/60)**

**Among the 19, no patients had subsequent RECIST response****

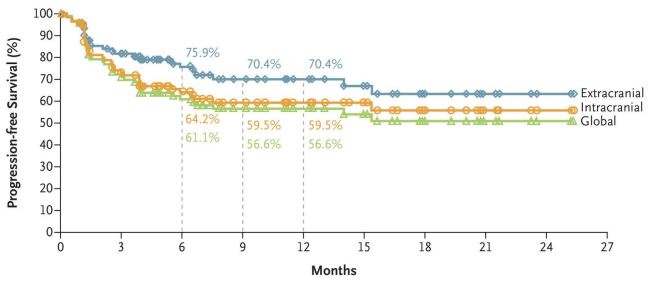
**12/19 patients received ≥3 total doses of nivo + ipi

Postow, ASCO 2020.



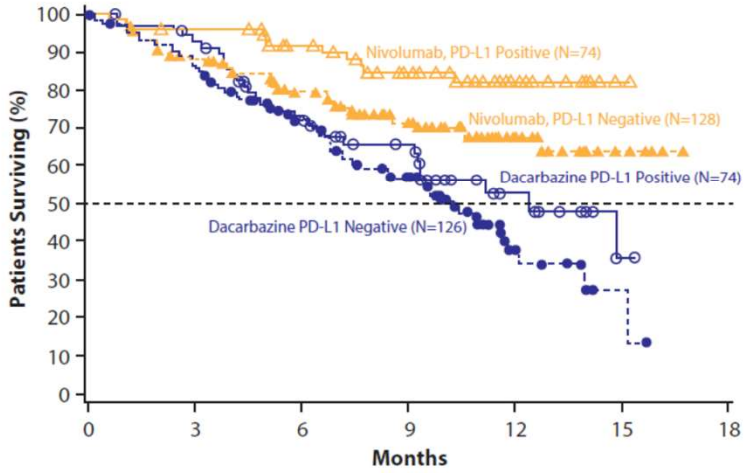
# Combination Ipilimumab + Nivolumab for Patients with Asymptomatic Brain Metastases

| Variable | Intracranial (N=94) | Extracranial (N=94) | Global (N=94) |
|---|---|---|---|
| Best overall response — no. (%)* | | | |
| Complete response | 24 (26) | 7 (7) | 8 (9) |
| Partial response | 28 (30) | 40 (43) | 40 (43) |
| Stable disease for ≥6 mo | 2 (2) | 6 (6) | 5 (5) |
| Progressive disease | 31 (33) | 28 (30) | 33 (35) |
| Could not be evaluated† | 9 (10) | 13 (14) | 8 (9) |
| Objective response‡ | | | |
| No. of patients | 52 | 47 | 48 |
| Percent of patients (95% CI) | 55 (45–66) | 50 (40–60) | 51 (40–62) |
| Clinical benefit§ | | | |
| No. of patients | 54 | 53 | 53 |
| Percent of patients (95% CI) | 57 (47–68) | 56 (46–67) | 56 (46–67) |




Tawbi, NEJM 2018.

# Importance of Tumor PD-L1 Status with Anti-PD-1 Monotherapy

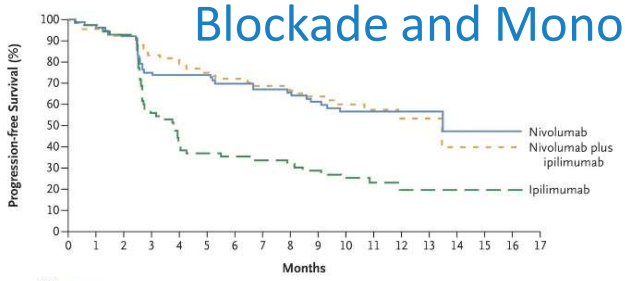



| | Patients Who Died *n/N* | Median Survival *mo (95% CI)* |
|---|---|---|
| Nivolumab PD-L1 Positive | 11/74 | N.R. |
| Nivolumab PD-L1 Negative | 37/128 | N.R. |
| Dacarbazine PD-L1 Positive | 29/74 | 12.4 (9.2–N.R.) |
| Dacarbazine PD-L1 Negative | 64/126 | 10.2 (7.6–11.8) |

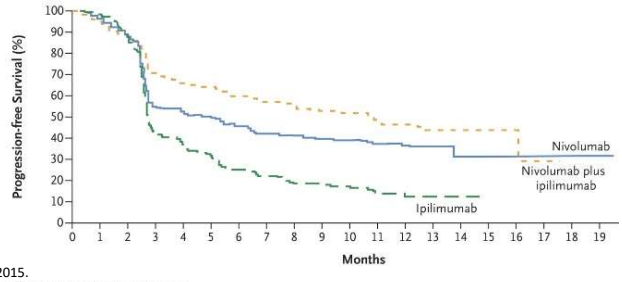
Robert, NEJM 2015.



# Importance of Tumor PD-L1 Status between Combination Checkpoint Blockade and Monotherapy



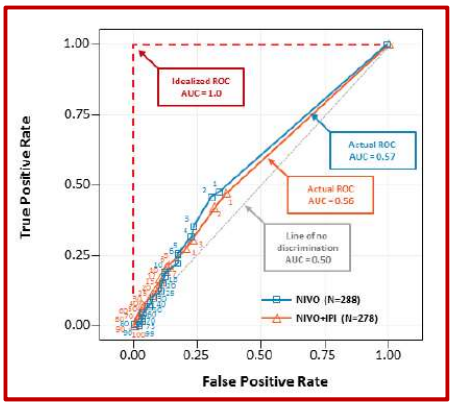

Tumor PD-L1 Positive Patients




Tumor PD-L1 Negative Patients

Larkin, NEJM 2015.

# The use of PD-L1 status to predict overall survival is poor with single-agent PD-1 or combined ipi/nivo…




| PDL-1 (%) | ≥ 1 | < 1 | ≥ 5 | < 5 | ➢ 10 | < 10 |
|---|---|---|---|---|---|---|
| Ipilimumab | 19% | 18% | 21% | 17% | 20% | 18% |
| Nivolumab | 54% | 35% | 58% | 42% | 58% | 44% |
| Ipi/Nivo | 65% | 54% | 72% | 56% | 85% | 55% |

…but, PD-L1 status predicts higher response rate with combo at every PD-L1 expression cut-off

Wolchok, NEJM 2017.



# Approved combination therapy in melanoma

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Atezolizumab + cobimetinib + vemurafenib | 2020 | BRAF V600 mutation-positive unresectable or metastatic melanoma | 28-day cycle of vem/cobi, then atezo 840 mg Q2W + cobi 60 mg Q1D (21 D on, 7 D off) + vem 720 mg twice daily |

**IMspire150 – BRAFV600-positive melanoma**

Atezolizumab + cobimetinib + vemurafenib vs Placebo + cobimetinib + vemurafenib

Median PFS: 15.1 vs 10.6 months

AEs leading to discontinuation: 13% vs 16%

Gutzmer, Lancet 2020

# Evaluation of atezolizumab (A), cobimetinib (C), and vemurafenib (V) in previously untreated patients with BRAFV600 mutation-positive advanced melanoma: Primary results from the phase 3 IMspire150 trial

- Previously untreated, advanced *BRAF*$^{V600}$ mutation–positive melanoma
- ECOG PS 0 to 1
- Measurable disease by RECIST v1.1

**Randomized 514 patients**

Randomization stratified by:
- Geographic region and
- Centrally tested LDH level (≤ ULN versus > ULN)

R 1:1

| | 28-day doublet period; cycle 1 | | Triple combination period; cycle 2 onward |
|---|---|---|---|
| → | Days 1–21: Vemurafenib 960 mg BID plus Cobimetinib 60 mg QD | Days 22–28: Vemurafenib 720 mg BID plus vemurafenib placebo | 28-day cycle: Atezolizumab 840 mg on days 1 and 15 plus Vemurafenib 720 mg BID plus vemurafenib placebo BID plus Cobimetinib 60 mg QD on days 1–21 |
| → | Days 1–21: Vemurafenib 960 mg BID plus Cobimetinib 60 mg QD | Days 22–28: Vemurafenib 960 mg BID | 28-day cycle: Atezolizumab placebo on days 1 and 15 plus Vemurafenib 960 mg BID plus Cobimetinib 60 mg QD on days 1–21 |

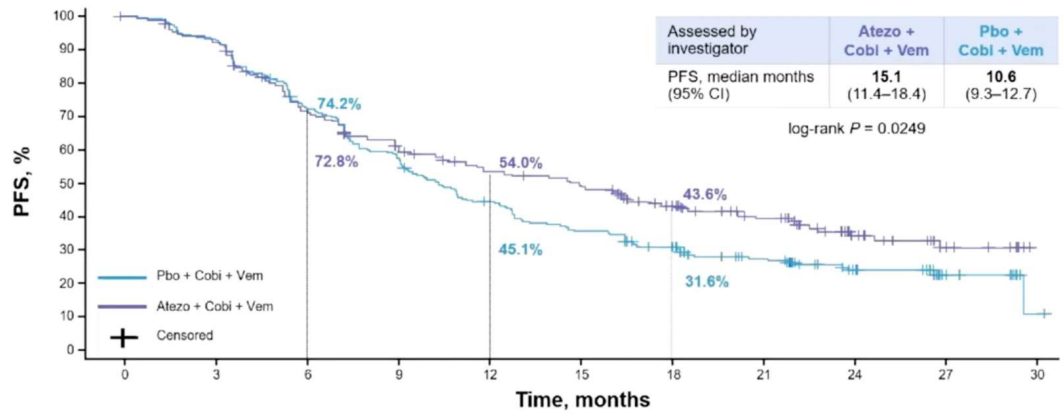
**Primary endpoint**
- Investigator-assessed PFS

**Key secondary endpoints**
- PFS assessed by an IRC
- Objective response (confirmed by observations at least 4 weeks apart)
- DOR
- OS

McArthur, AACR 2020.



# Results – Investigator-assessed PFS




| Assessed by investigator | Atezo + Cobi + Vem | Pbo + Cobi + Vem |
|---|---|---|
| PFS, median months (95% CI) | **15.1** (11.4–18.4) | **10.6** (9.3–12.7) |

log-rank $P = 0.0249$

McArthur, AACR 2020.

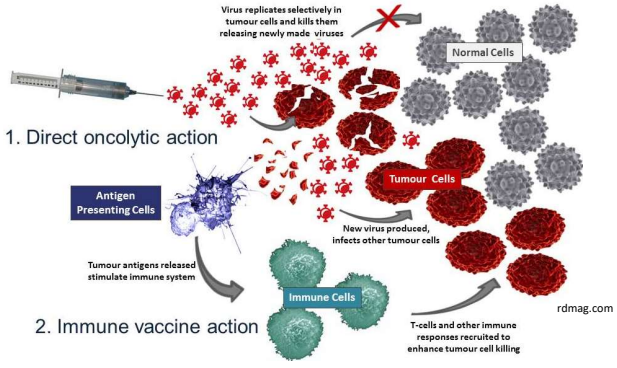
# **In development:** Neoadjuvant immunotherapy in advanced melanoma

| Trial | Regimen | N | pCR (%) | med RFS (mo) | med FU (mo) |
|---|---|---|---|---|---|
| Amaria Lancet Oncol 2018 | *Dab/Tram* | 21 | 58 | 19.7 | 18.6 |
| Long Lancet Oncol 2019 | *Dab/Tram* | 35 | 49 | 23.0 | 27.0 |
| Blank Nat Med 2018 | Ipi+nivo | 10 | 33 | NR | 32 |
| Amaria Nat Med 2018 | Nivo<br>Ipi+nivo | 12<br>11 | 25<br>45 | NR<br>NR | 20 |
| Huang Nat Med 2019 | Pembro | 30 | 19 | NR | 18 |
| Rozeman Lancet Oncol 2019 | Ipi+nivo | 86 | 57 | NR | 8.3 |

Menzies ASCO Annual Meeting 2019.



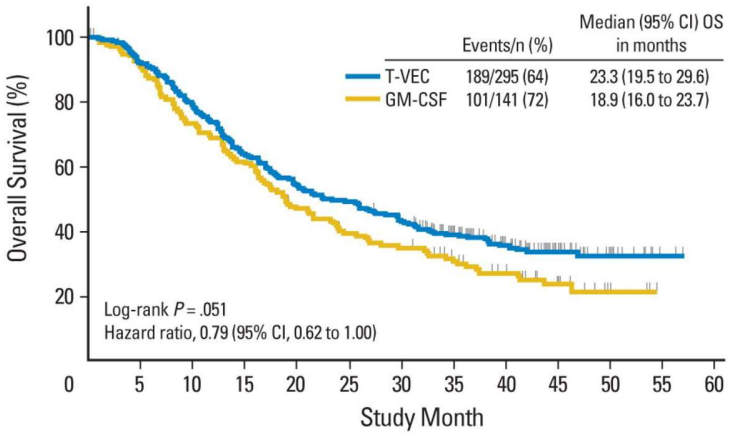
# Approved oncolytic virus in melanoma




| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Talimogene laherparepvec (T-Vec) | 2015 | Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in recurrent melanoma after surgery | Intralesional injection: ≤4 mL at $10^6$ PFU/mL starting; $10^8$ PFU/mL subsequent |

# Talimogene laherparepvec (T-VEC) in Stage III/IV Melanoma

- Phase III OPTiM Trial
  - Oncolytic, genetically-engineered herpes virus
  - Intralesional T-VEC 106 pfu/mL, 108 pfu/mL 3 weeks after initial dose, then Q2W
  - Subcutaneous GM-CSF




Andtbacka, Kaufman, JCO 2015.

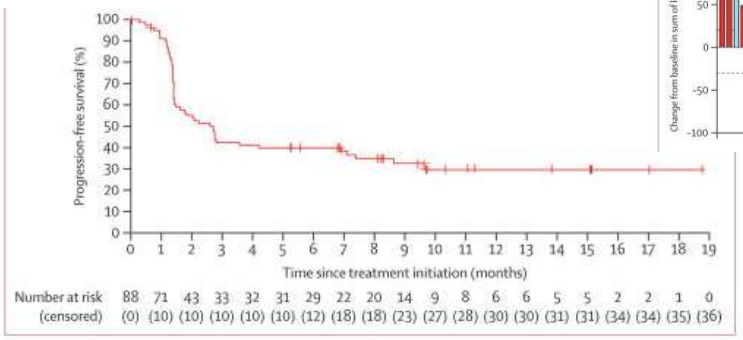


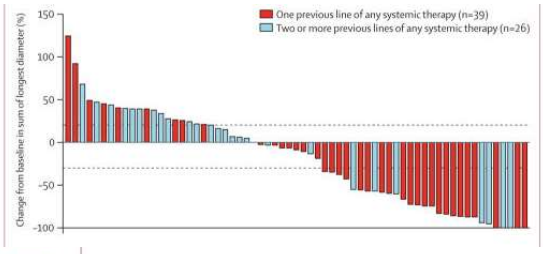
# Approved checkpoint inhibitors in other skin cancers

| Drug | Approved | Indication | Dose |
|---|---|---|---|
| Avelumab | 2017 | Patients >12 yr with metastatic **Merkel cell carcinoma** | 800 mg Q2W + premedication (first 4 cycles) |
| Pembrolizumab | 2018 | Adult/pediatric with recurrent advanced/metastatic **Merkel cell carcinoma** | Adults: 200 mg Q3W<br>Pediatric: 2 mg/kg (up to 200 mg) Q3W |
| Cemiplimab-rwlc | 2018 | Metastatic **cutaneous squamous cell carcinoma**, not candidate for curative therapies | 350 mg Q3W |

# Avelumab in 2nd-line metastatic Merkel Cell carcinoma

- 1st FDA-approved treatment for this status
- Avelumab 10 mg/kg Q2W
- ORR: 32%, CR: 9%; PR: 23%



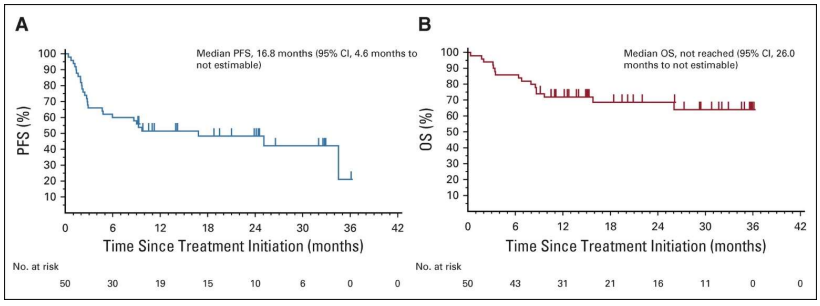




Kaufman, Lancet Oncol 2016.



# Pembrolizumab in 1st-line advanced Merkel Cell Carcinoma

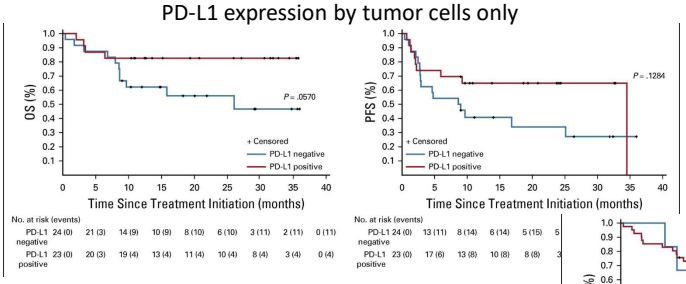
- KEYNOTE-017
- Pembrolizumab 2 mg/kg Q3W up to 2 years
- mPFS: 16.8 months (compared to 90 days for chemo)
- 24-month OS: 68.7%



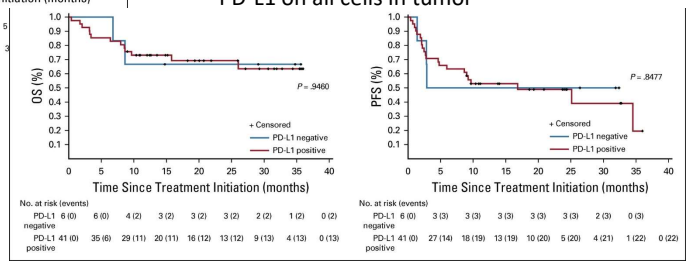

Nghiem, J Clin Oncol 2019.

# Pembrolizumab in 1st-line advanced Merkel Cell Carcinoma

PD-L1 expression by tumor cells only




PD-L1 on all cells in tumor

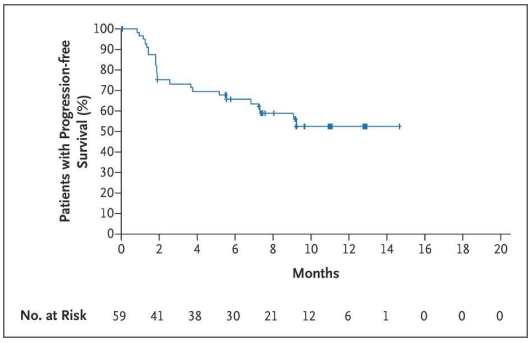


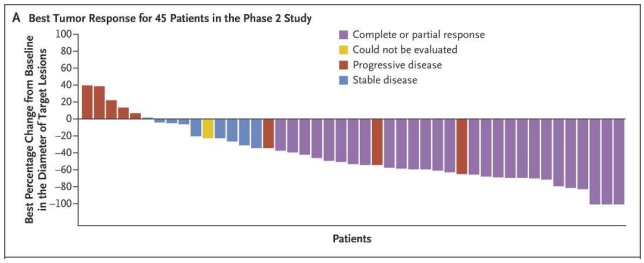

Nghiem, J Clin Oncol 2019.



# Cemiplimab in advanced/metastatic cutaneous squamous-cell carcinoma

- Cemiplimab 3mg/kg Q2W
- 47% response rate in metastatic patients
- 60% of locally advanced had objective response

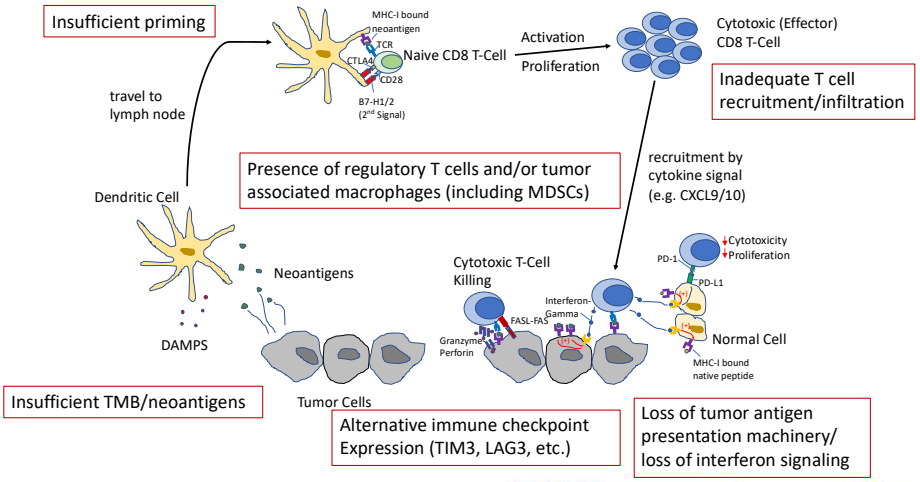



Migden, NEJM 2018.

# Developmental Immunotherapeutic Strategies for Melanoma

How does immune checkpoint inhibitor therapy fail?



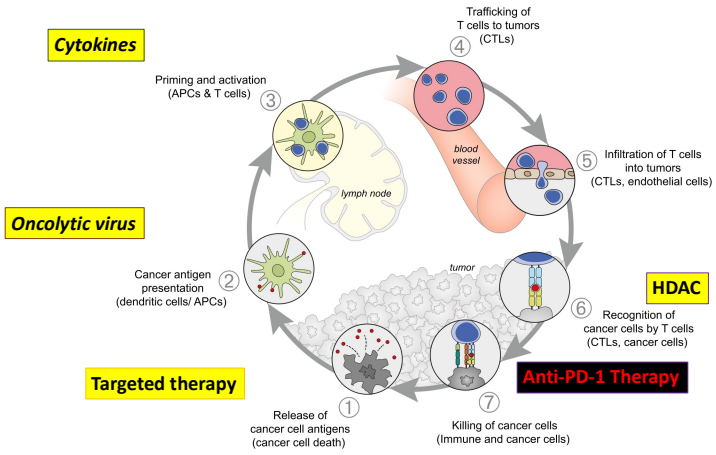

Modified from Liu, Jenkins, Sullivan. Amer J Clin Derm 2018.



# Developmental Immunotherapeutic Strategies for Melanoma

How do we overcome resistance?

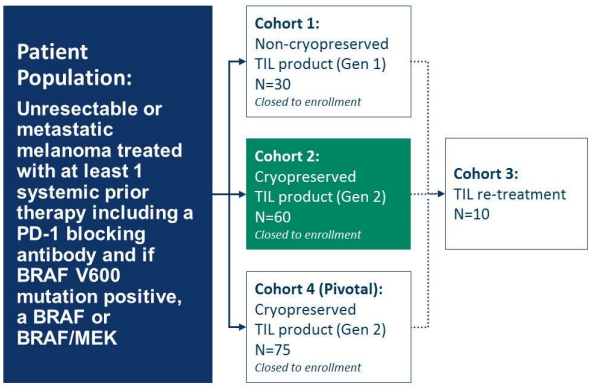
Combination therapy




Modified from Chen and Melman. Immunity 2015.

# Long-term follow up of lifleucel (LN-144) cryopreserved autologous tumor infiltrating lymphocyte therapy in patients with advanced melanoma progressed on prior therapies

## Study design




**Cohort 2 Endpoints:**
- Primary: Efficacy defined as investigator-assessed Objective Response Rate (ORR) following RECIST 1.1
- Secondary: Safety and efficacy

**Other Key Eligibility Criteria:**
- One tumor lesion resectable for TIL generation (~1.5cm in diameter) and ≥ one tumor lesion as target for RECIST 1.1 assessment
- Age ≥ 18 years at the time of consent
- ECOG Performance Status of 0-1

**Methods:**
- Data Extract: 23 April 2020 for Cohort 2
- Cohort 2 Safety and Efficacy sets: 66 patients who underwent resection for the purpose of TIL generation and received lifileucel infusion

Sarnaik, ASCO 2020.



# Results

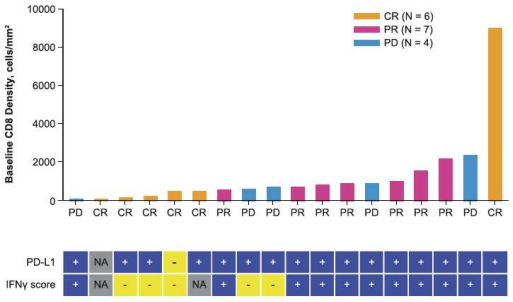
| RESPONSE | PATIENTS, N=66 n (%) |
|---|---|
| **Objective Response Rate** | **24 (36.4)** |
| Complete Response | 2 (3.0) |
| Partial Response | 22 (33.3) |
| Stable Disease | 29 (43.9) |
| Progressive Disease | 9 (13.6) |
| Non-Evaluable[1] | 4 (6.1) |
| Disease Control Rate | 53 (80.3) |
| **Median Duration of Response** | **Not Reached** |
| Min, Max (months) | 2.2, 26.9+ |

- After a median study follow-up of 18.7 months, median DOR was still not reached (range 2.2, 26.9+)
- Response was seen regardless of location of tumor resected
- Mean number of TIL cells infused: 27.3 x $10^9$

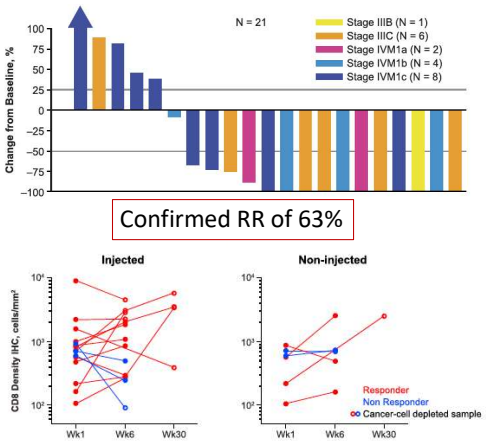
| | Cohort 2 (N=66) | | |
|---|---|---|---|
| PREFERRED TERM | Any Grade, n (%) | Grade 3/4, n (%) | Grade 5, n (%) |
| Number of patients reporting at least one Treatment-Emergent AE | 66 (100) | 64 (97.0) | 2 (3.0)* |
| Thrombocytopenia | 59 (89.4) | 54 (81.8) | 0 |
| Chills | 53 (80.3) | 4 ( 6.1) | 0 |
| Anemia | 45 (68.2) | 37 (56.1) | 0 |
| Pyrexia | 39 (59.1) | 11 (16.7) | 0 |
| Neutropenia | 37 (56.1) | 26 (39.4) | 0 |
| Febrile neutropenia | 36 (54.5) | 36 (54.5) | 0 |
| Hypophosphatemia | 30 (45.5) | 23 (34.8) | 0 |
| Leukopenia | 28 (42.4) | 23 (34.8) | 0 |
| Fatigue | 26 (39.4) | 1 ( 1.5) | 0 |
| Hypotension | 24 (36.4) | 7 (10.6) | 0 |
| Lymphopenia | 23 (34.8) | 21 (31.8) | 0 |
| Tachycardia | 23 (34.8) | 1 ( 1.5) | 0 |

Sarnaik, ASCO 2020.

# **In development:** Combined IO with Oncolytic Virus




Phase I: Pembrolizumab + TVEC




Confirmed RR of 63%

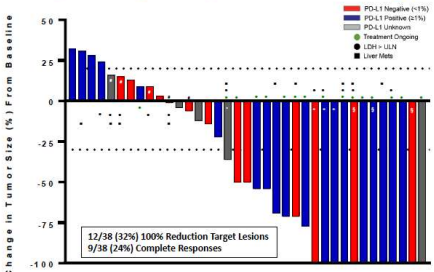
Ribas et al Cell 2017



# **In development:** Combined IO with IL-2 (NKTR-214)

Efficacy (response rate) data from non-randomized cohorts of urothelial bladder cancer, renal cell carcinoma, and melanoma looks promising

**Stage IV IO-Naïve 1L Melanoma Cohort at RP2D Best Overall Response by Independent Radiology**



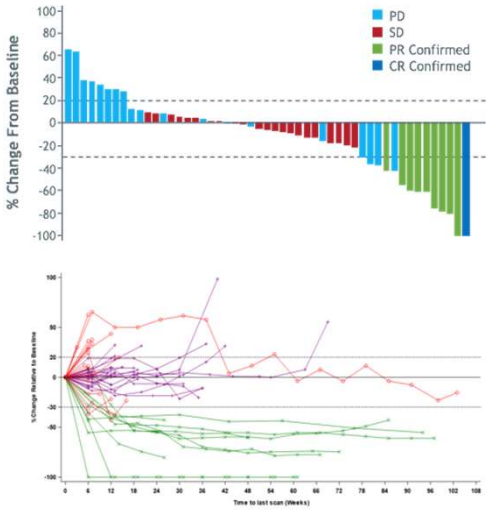

| 1L Melanoma (n=38 Efficacy Evaluable) | Overall Response Rate |
|---|---|
| Confirmed ORR (CR+PR) | 20 (53%) |
| CR | 9 (24%) |
| DCR (CR+PR+SD) | 29 (76%) |
| PD-L1 negative (n=14) | 6 (43%) |
| PD-L1 positive (n=19) | 13 (68%) |
| PD-L1 unknown (n=5) | 1 (20%) |
| LDH > ULN (n=11) | 5 (45%) |
| Liver metastases (n=10) | 5 (50%) |

**High level of concordance in ORR between independent central radiology (53%) and investigator-assessed 19/38 (50%).**

Diab et al, ASCO 2018.
Diab et al, SITC 2018.

# In development: Combined IO with HDAC inhibitor

- Entinostat + pembrolizumab
- 19% ORR (1 CR, 9 PR)
- Median duration of response: 13 mo
- 9 additional patients with SD for >6 mo



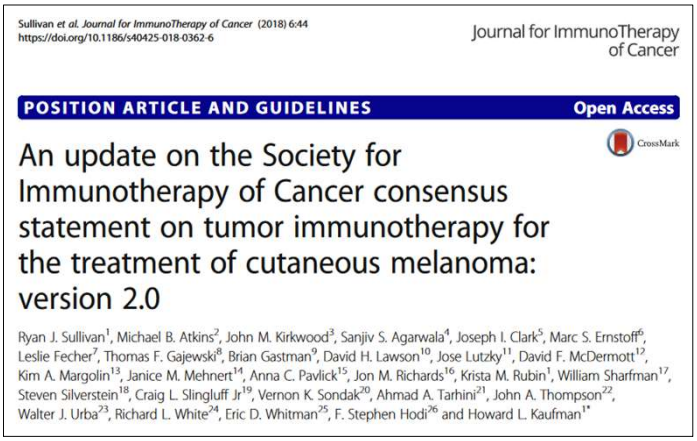

Sullivan et al, AACR 2019.



# Conclusions

- Melanoma was one of the foundational disease states for testing immunotherapies
- Immunotherapy has markedly improved outcomes in melanoma
- Avelumab and pembrolizumab are now approved for Merkel cell carcinoma, and cemiplimab is approved for cutaneous squamous cell carcinoma
- Combination immunotherapies may lead to higher response rate, more durable responses and may overcome resistance to single agent therapy

# Additional Resources



Sullivan et al. Journal for ImmunoTherapy of Cancer (2018) 6:44
https://doi.org/10.1186/s40425-018-0362-6

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES — Open Access

An update on the Society for Immunotherapy of Cancer consensus statement on tumor immunotherapy for the treatment of cutaneous melanoma: version 2.0

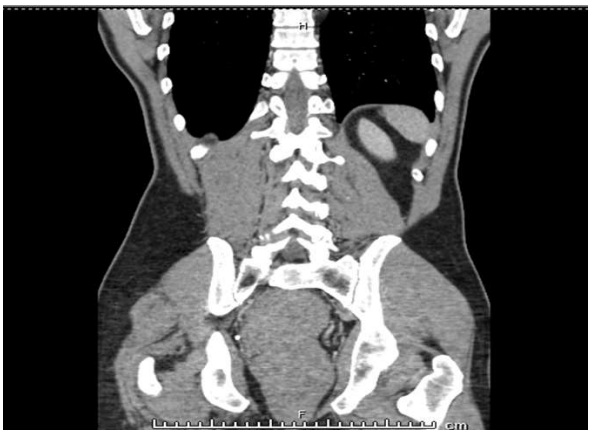
Ryan J. Sullivan[1], Michael B. Atkins[2], John M. Kirkwood[3], Sanjiv S. Agarwala[4], Joseph I. Clark[5], Marc S. Ernstoff[6], Leslie Fecher[7], Thomas F. Gajewski[8], Brian Gastman[9], David H. Lawson[10], Jose Lutzky[11], David F. McDermott[12], Kim A. Margolin[13], Janice M. Mehnert[14], Anna C. Pavlick[15], Jon M. Richards[16], Krista M. Rubin[1], William Sharfman[17], Steven Silverstein[18], Craig L. Slingluff Jr[19], Vernon K. Sondak[20], Ahmad A. Tarhini[21], John A. Thompson[22], Walter J. Urba[23], Richard L. White[24], Eric D. Whitman[25], F. Stephen Hodi[26] and Howard L. Kaufman[1*]



# Case Studies

# Case Study 1

- 50 year-old man presenting with increasing left lower quadrant pain, constipation and rectal bleeding. ECOG PS 1
- Colonoscopy revealed large ulcerated pigmented mass extensively involving the rectum.
- Biopsy: melanoma
- NGS: BRAF, NRAS, KIT all WT
- PET/CT and CT CAP: large hypermetabolic mass occupying entire anorectal area, hypermetabolic bilateral paraaortic LNs.
- MRI brain: no brain metastases





# Case Study 1

1. What would be your next step:

A. Radical surgical resection as needed to excise all disease followed by RT.

B. Limited surgical resection to achieve negative margins if possible

C. Systemic chemotherapy with dacarbazine because immunotherapy does not work for mucosal melanomas

D. Immunotherapy with ipilimumab plus nivolumab or either drug as single agent

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# Case Study 1

The patient was enrolled in a clinical trial with ipilimumab 3mg/kg + nivolumab 1 mg/kg every 3 weeks x 4 followed by nivolumab 3 mg/kg every 4weeks.

One week after cycle 1 he developed grade 2 colitis and grade 2 hepatitis, resolved after treatment with steroids.

2. What would you do now?

A. Continue treatment at reduced doses of both drugs

B. Stop treatment and reconsider surgery or chemotherapy

C. Switch to single agent immunotherapy

D. Once AEs resolve after steroid taper, resume combination immunotherapy

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# Case Study 1

Treatment resumed with no changes. One week after cycle 2 he developed grade 4 colitis treated with steroids and infliximab x 2.

3. The best approach now is to:

A. Complete the planned 4 cycles of ipi/nivo after AEs resolve

B. Slowly taper steroids over at least 4 weeks and hold further combination immunotherapy

C. Continue treatment after AEs resolve but give concomitant infliximab

D. Immediately start dacarbazine-based regimen

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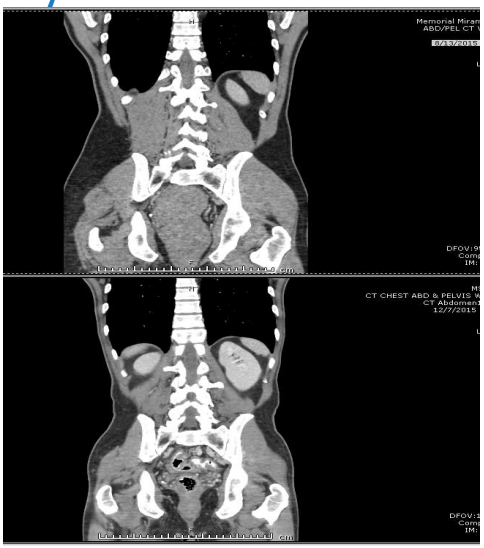
# Case Study 1

- Treatment was held, patient was put on a low steroid taper.
- Colitis eventually resolved.
- CT shows near CR; PET negative
- Colonoscopy showed NED
- He underwent colonoscopy that revealed one remaining focus of active disease.
- Colectomy was performed
- He is disease-free at 5-year f/u.



## Case Study 2

- 92 year-old woman with no known history of skin cancers until 2016 when she began to develop multiple, recurrent squamous cell carcinomas of the face.
- She underwent multiple resections with rapid recurrences at the resected site as well as dermal extension of the tumors to adjacent areas.
- Pathology was consistent with poorly differentiated squamous cell carcinoma.
- A lesion on the right cheek that had recurred multiple times was treated with radiation therapy.
- After a brief period of control, the right cheek tumor started to grow again
- Additional lesions in the nasal bridge, right eyebrow and right forehead appeared and grew rapidly.
- Right neck adenopathy was noted and biopsy revealed metastatic disease.



## Case Study 2

1. What is the best treatment option for this elderly patient ?

A. Further attempts at resection and radiation therapy

B. Systemic chemotherapy or EGFR inhibitors such as cetuximab

C. Anti-PD1 blocking antibody therapy

D. Intratumor oncolytic virus therapy

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## Case Study 2

- She enrolled in a clinical trial testing the efficacy of an anti PD-L1 antibody in patients with metastatic or unresectable squamous cell carcinoma.

- Six weeks after her treatment there was further growth of the lesions with increased erythema and tenderness to palpation.

## Case Study 2

2. What would you do now regarding her treatment?

A. Immediately stop treatment and reconsider chemo/cetuximab
B. Discuss palliative care options including hospice
C. Continue therapy as planned
D. None of the above



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2. What would you do now regarding her treatment?

A. Immediately stop treatment and reconsider chemo/cetuximab
B. Discuss palliative care options including hospice
C. Continue therapy as planned √
D. None of the above

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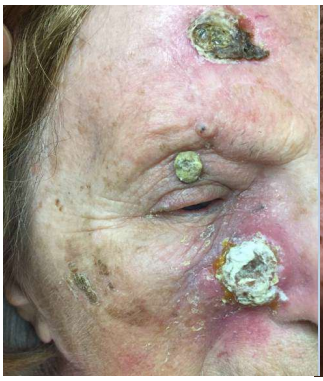
## Case Study 2

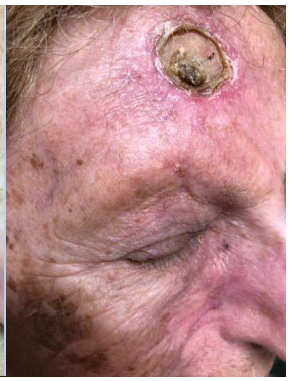
- Treatment was continued
- Over the following 4 weeks all lesions started to regress
- By week 12 all lesions had resolved
- A non-healing ulcer remained in the right forehead for 18 months
- Biopsy showed no residual SCC
- The patient has agreed to see a plastic surgery to graft the open wound.



## Case Study 2



August 2017



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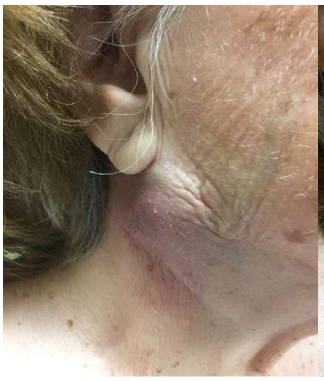

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