

IMMUNO-ONCOLOGY FOR THE PRIMARY CARE

DISCLOSURES

Honorarium/Speaker/Advisory boards

BMS

MERCK

IPSEN

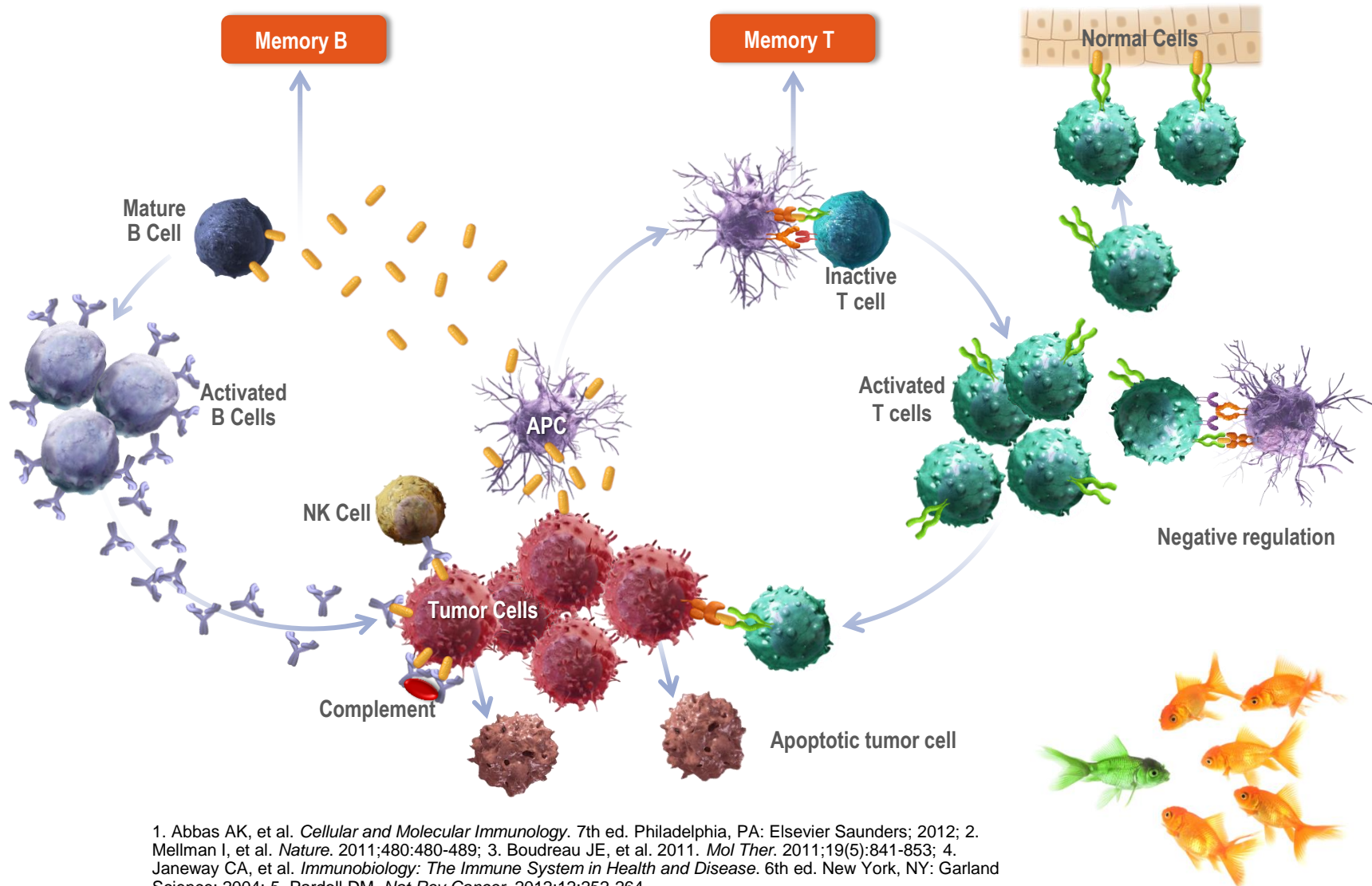
NOVARTIS

GENENTECH

AMGEN

ARRAY BIO

THE IMMUNE RESPONSE TO CANCER IS CHARACTERIZED BY A BALANCE BETWEEN CONTINUOUS ACTIVATION AND SUPPRESSION



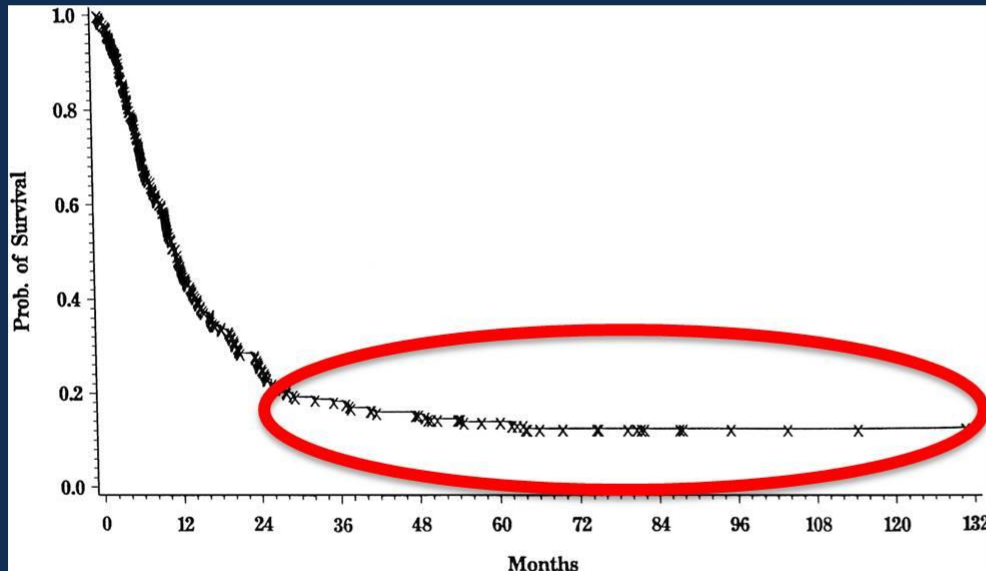
I-O Therapies Encompass a Wide Variety of Classes

Class	Example
Passive Immunotherapies¹⁻⁴	
Tumor-directed monoclonal antibodies^{5,6}	<ul style="list-style-type: none"> • Unconjugated • Conjugated • Single-armed
Cell therapy⁷⁻⁹	<ul style="list-style-type: none"> • Lymphokine-activated killer-cell therapy • Tumor-infiltrating lymphocyte with IL-2 • Gene-modified lymphocytes
Active Immunotherapies¹⁻⁴	
Vaccines¹⁰	<ul style="list-style-type: none"> • Dendritic-cell vaccines • Tumor-cell vaccines • Peptide/protein-based vaccines • Recombinant vector vaccines
Cytokines¹¹	<ul style="list-style-type: none"> • Interleukins • Interferons • Tumor necrosis factor-α • Granulocyte-colony stimulating factor • Immunocytokines
Immune checkpoint inhibitors and co-stimulatory pathway agonists¹²	<ul style="list-style-type: none"> • Immune checkpoints: CTLA-4, PD-1, PD-L1, LAG-3, B7-H3, B7-H4; Co-stimulatory pathways: OX40, CD28, CD40, CD137

1. Brody J, et al. *J Clin Oncol*. 2011;29:1864-1875; 2. Smits ELJM, et al. *Oncologist*. 2009;14:240-252; 3. Rescigno M, et al. *Biochimica Biophys Acta*. 2007;1776:108-123; 4. Mellman I, et al. *Nature*. 2011;480:480-489; 5. Weiner LM, et al. *Nat Rev Immunol*. 2010;10:317-327; 6. Merchant M, et al. *PNAS*. 2013;E2987-E2996; 7. West EJ, et al. *Br J Cancer*. 2011;105:787-795; 8. Chacon JA, et al. *PloS One*. 2013;8:e60031; 9. Rosenberg SA. *Sci Transl Med*. 2012;4(127ps8):1-5; 10. Schlom J. *J Natl Cancer Inst*. 2012;104:599-613; 11. List T, Neri D. *Clin Pharmacol*. 2013;5(suppl 1):29-45; 12. Pardoll DM. *Nat Rev Cancer*. 2012;12:252-264; 13. clinicaltrials.gov.

Immunotherapy– Early Days

IL-2 in metastatic melanoma: OS



- Difficult treatment regimen
- Highly selected patients
- Significant toxicity

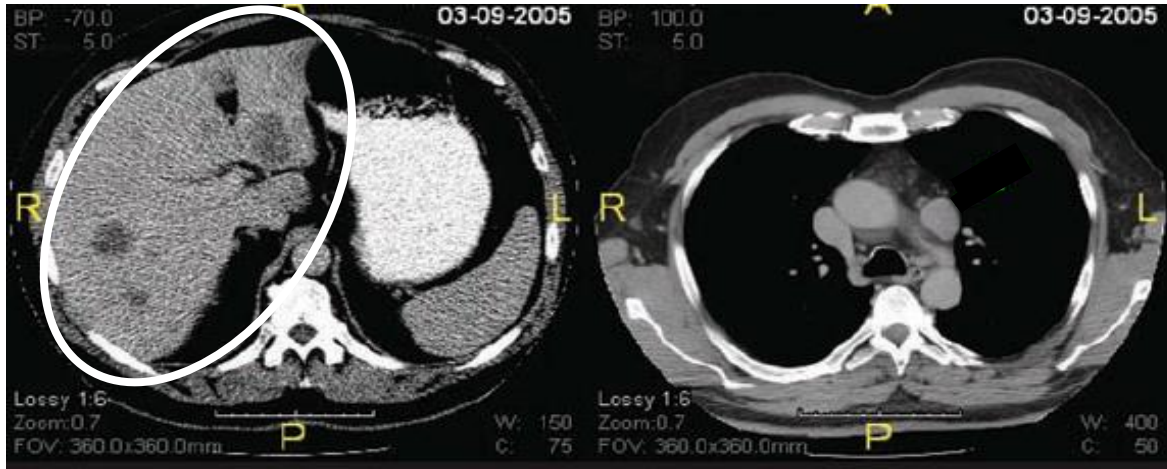
Atkins et al, J Clin Oncol 1999.

PRESENTED AT: ASCO-SITC **CLINICAL IMMUNO-ONCOLOGY SYMPOSIUM** | #ImmunoOnc18

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Presented by: Katy K. Tsai, MD

March 2005



History

- Dx: 6/2000 - T2a
- Recurrence 3/2005 – M1c

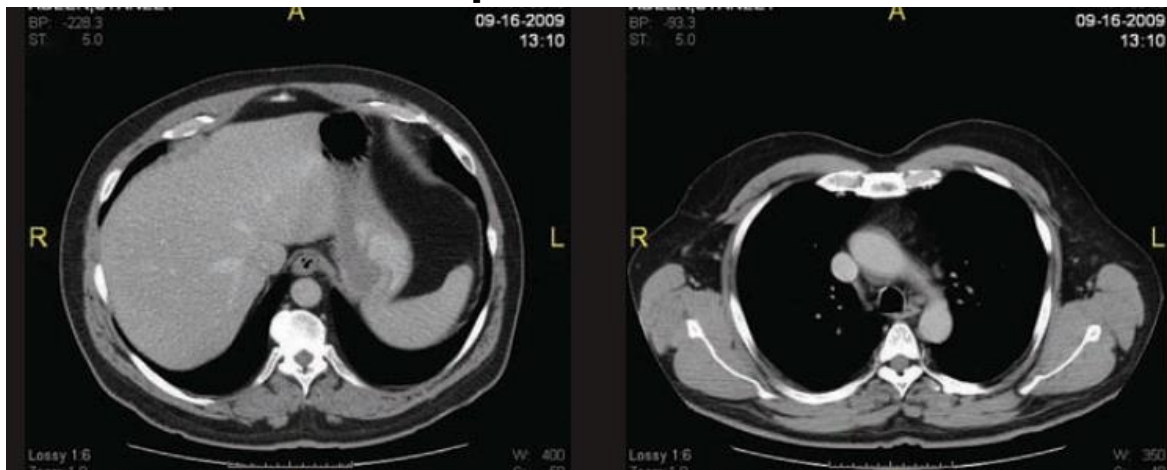
March 2005

- Heavy hepatic tumor burden/hepatic dysfunction
- Mediastinal LAD (shown) and a subpleural nodule (not shown)

Treatment & Outcomes

- 2005 – Proleukin x 3 courses
- 2006 - Resumed working
- 2008 - CT A/P – few small areas of liver attenuation

September 2009

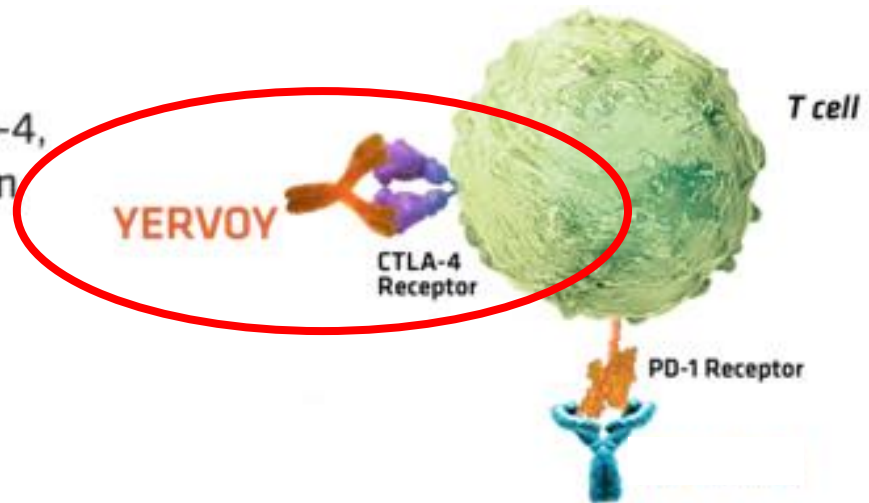


September 2009

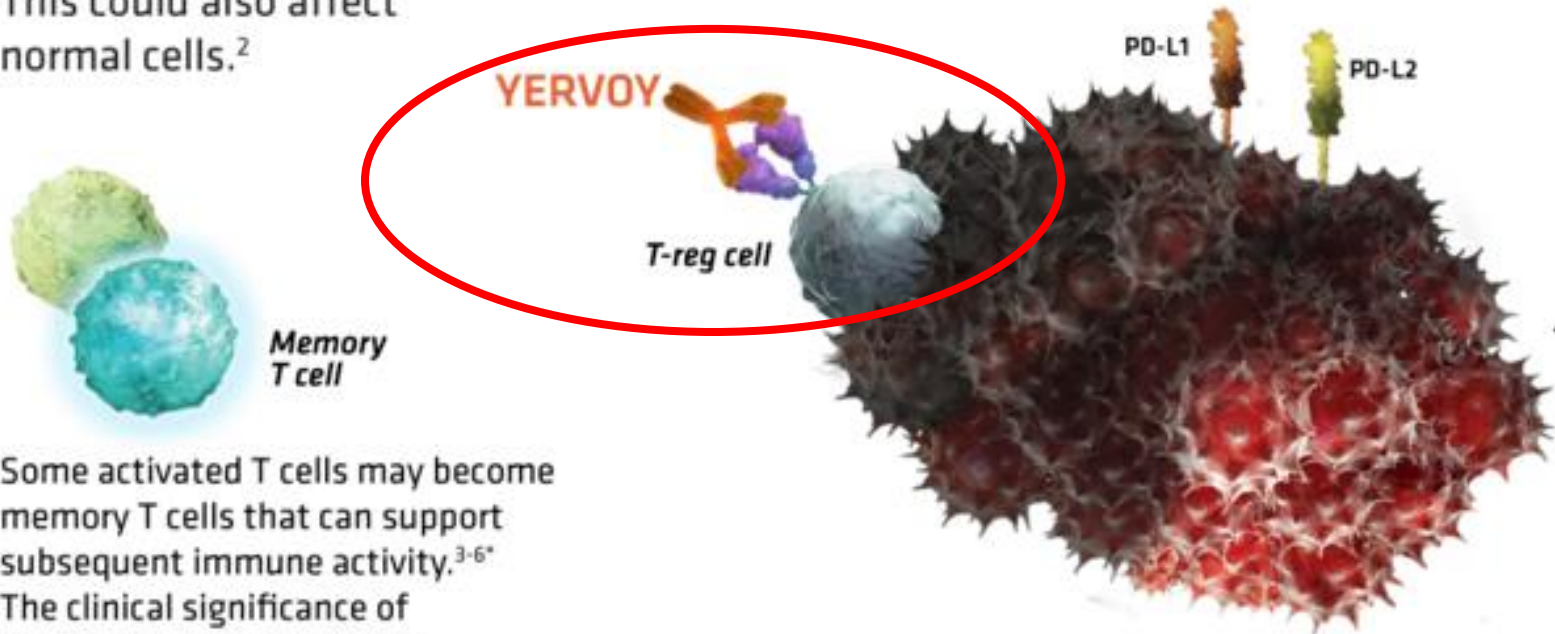
- No identifiable liver lesions and normal LFTs
- No mediastinal LAD

⚡ STIMULATE

YERVOY® (ipilimumab) blocks CTLA-4, helping to **stimulate** T-cell activation and proliferation.

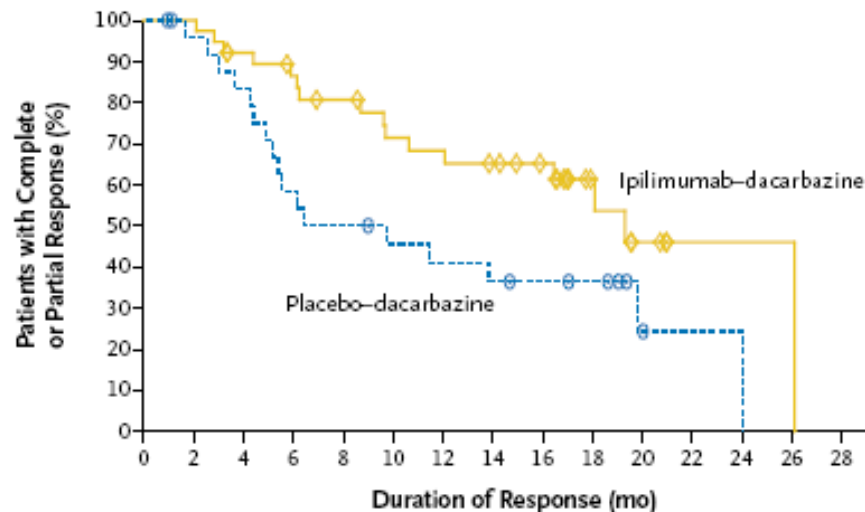
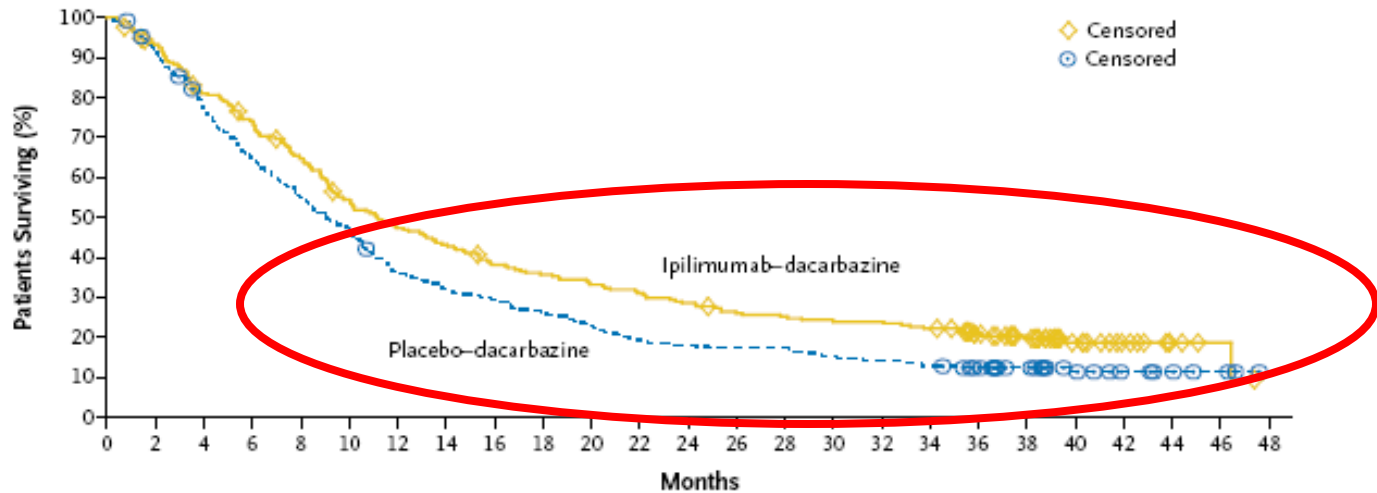


YERVOY can also block CTLA-4 on T-reg cells, reducing T-reg immune-suppressing activity in the tumor. This could also affect normal cells.²

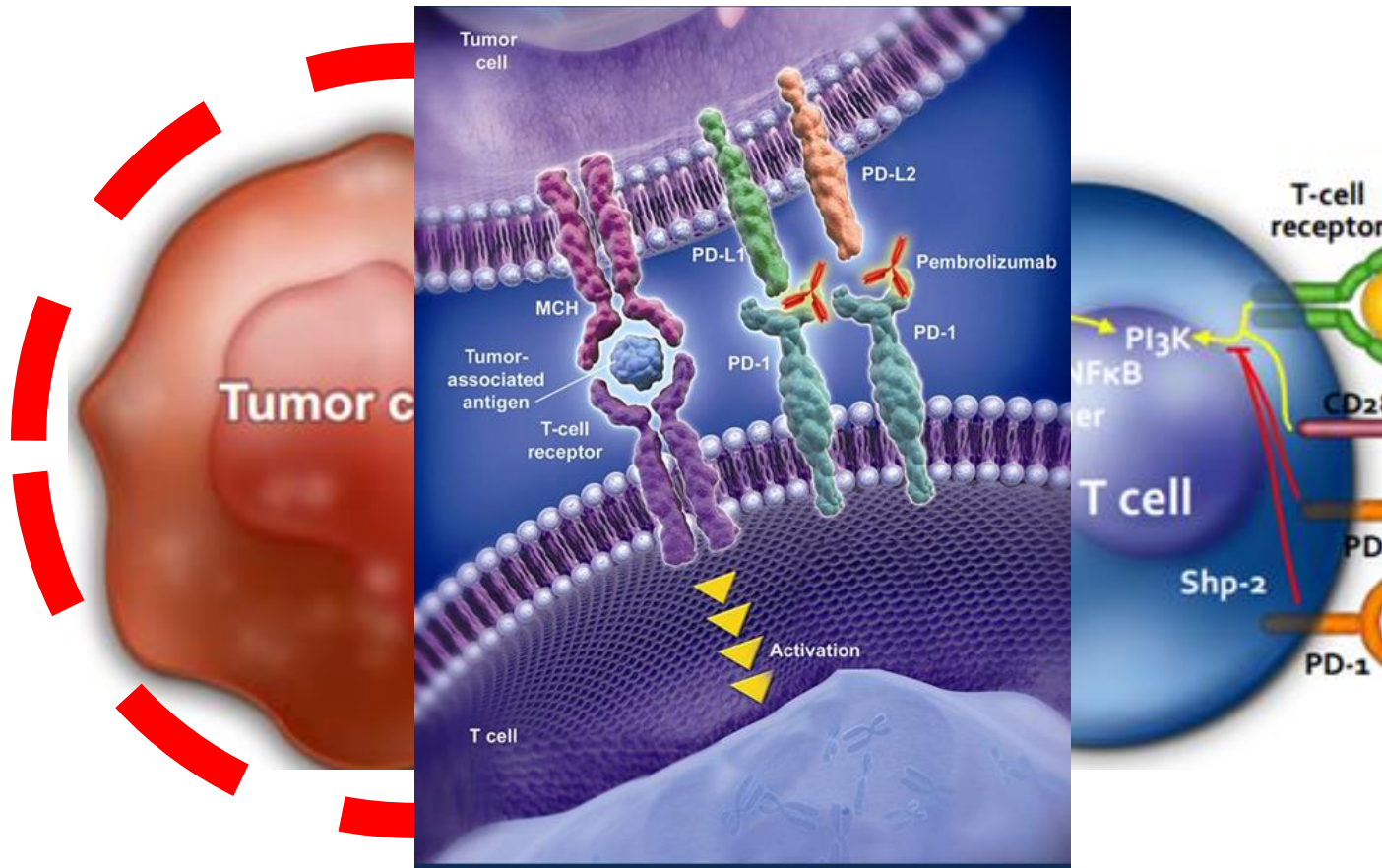


Some activated T cells may become memory T cells that can support subsequent immune activity.^{3-6*} The clinical significance of memory T cells is unknown.

NEJM – 2011 1ST LINE IPI/DTIC V DTIC



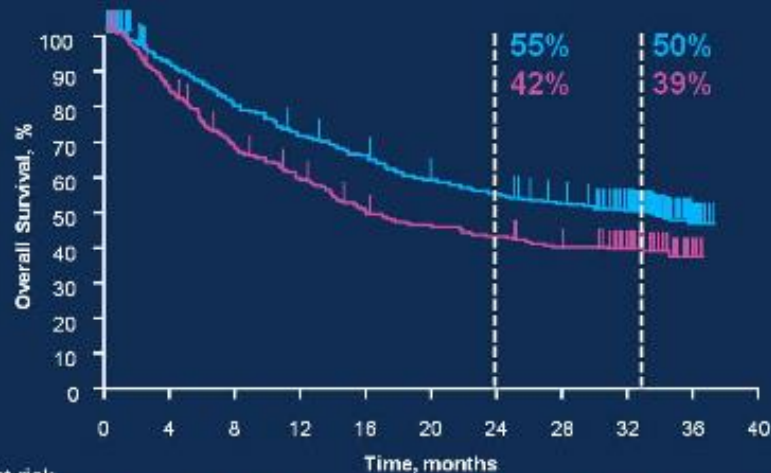
PD1 INHIBITORS – NIVOLUMAB/PEMBROLIZUMAB



Kaplan-Meier Estimates of Survival in Total Population (Median Follow-Up, 33.9 mo)

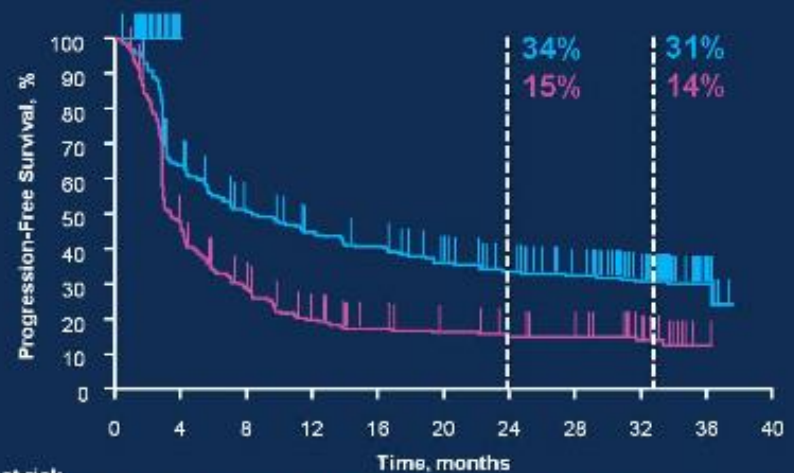
OS

Arm	Events, n	HR (95% CI)	Median, mo (95% CI)
Pembrolizumab	278	0.70 (0.58-0.86)	32.3 (24.5-NR)
Ipilimumab	155	—	15.9 (13.3-22.0)



PFS per irRC by Investigator

Arm	Events, n	HR (95% CI)	Median, mo (95% CI)
Pembrolizumab	369	0.56 (0.47-0.67)	8.3 (6.5-11.2)
Ipilimumab	204	—	3.3 (2.9-4.1)



PRESENTED AT: **ASCO ANNUAL MEETING '17** | **#ASCO17**

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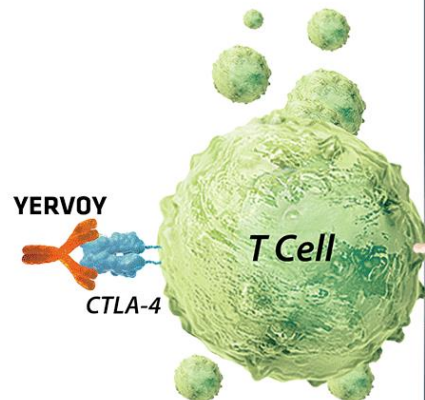
Analysis includes all randomized patients with measurable disease at baseline who received ≥ 1 pembrolizumab dose. Data cutoff date: Nov 3, 2016.

Complementary Inhibition Results in Enhanced T-Cell Function Greater Than the Effects of Either Antibody Alone¹

Dual Immune Checkpoint Inhibition Could Affect Both Normal and Tumor Cells¹⁻³

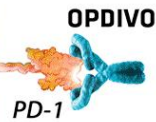
The Mechanism of Action Involves Complementary Inhibition of CTLA-4 and PD-1 Resulting in Increased Anti-tumor Activity

T-cell Activation and Proliferation



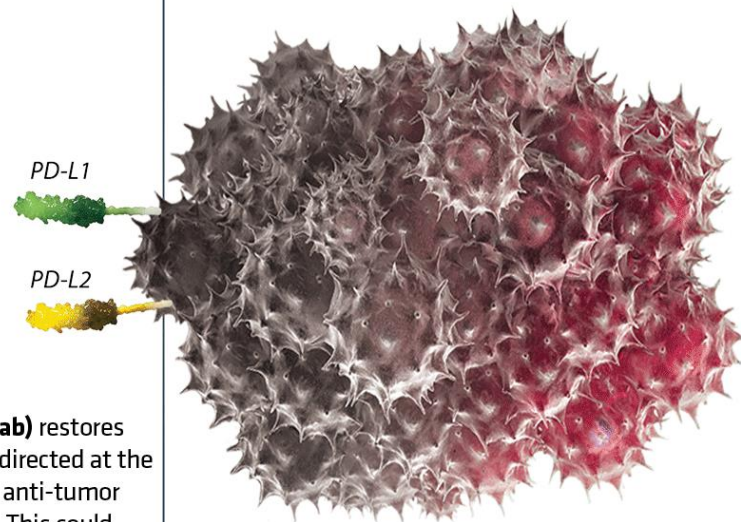
YERVOY® (ipilimumab) blockade of CTLA-4 has been shown to augment T-cell activation and proliferation^{2,3}

PD-1 Receptor Blockade



OPDIVO® (nivolumab) restores active T-cell response directed at the tumor to induce an anti-tumor immune response. This could also affect normal cells¹

Tumor Cell Degeneration

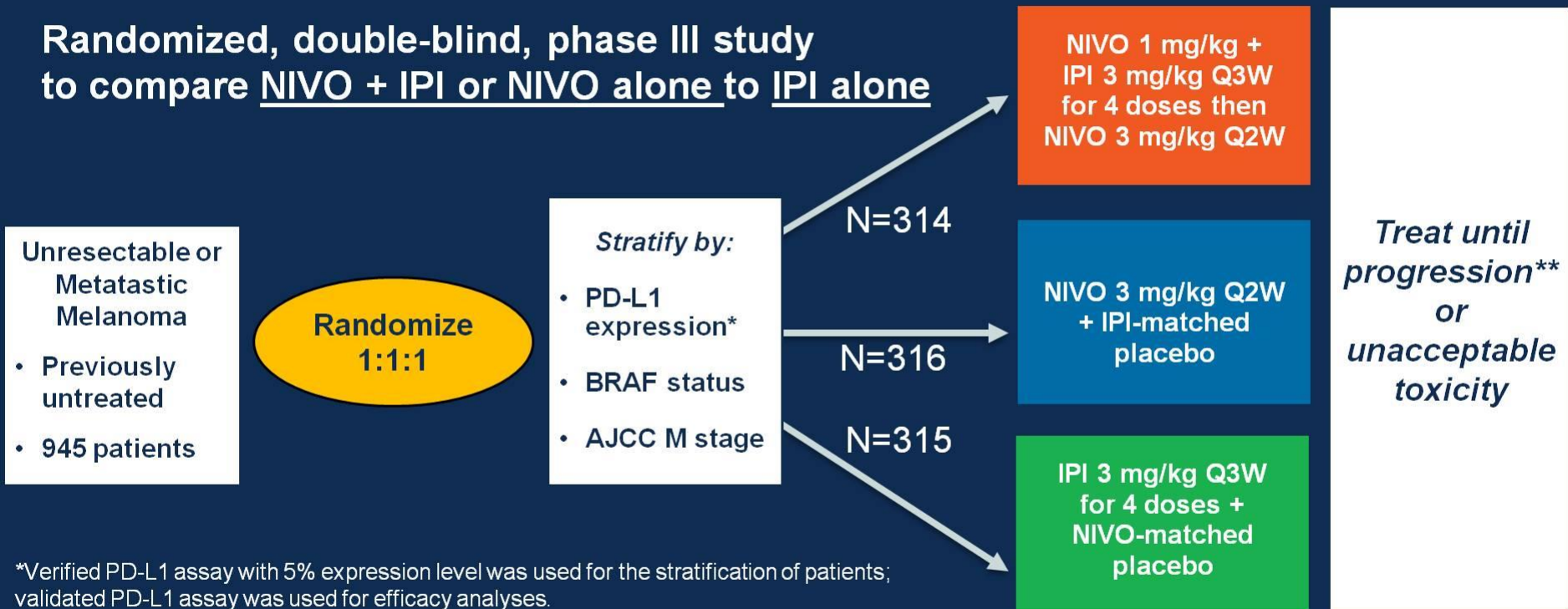


CTLA-4=cytotoxic T-lymphocyte antigen-4; PD-1=programmed death-1; PD-L1=programmed death ligand-1; PD-L2=programmed death ligand-2.

Please see Important Safety Information throughout this presentation.

CheckMate-067: Study Design

Randomized, double-blind, phase III study
to compare NIVO + IPI or NIVO alone to IPI alone



*Verified PD-L1 assay with 5% expression level was used for the stratification of patients; validated PD-L1 assay was used for efficacy analyses.

**Patients could have been treated beyond progression under protocol-defined circumstances.

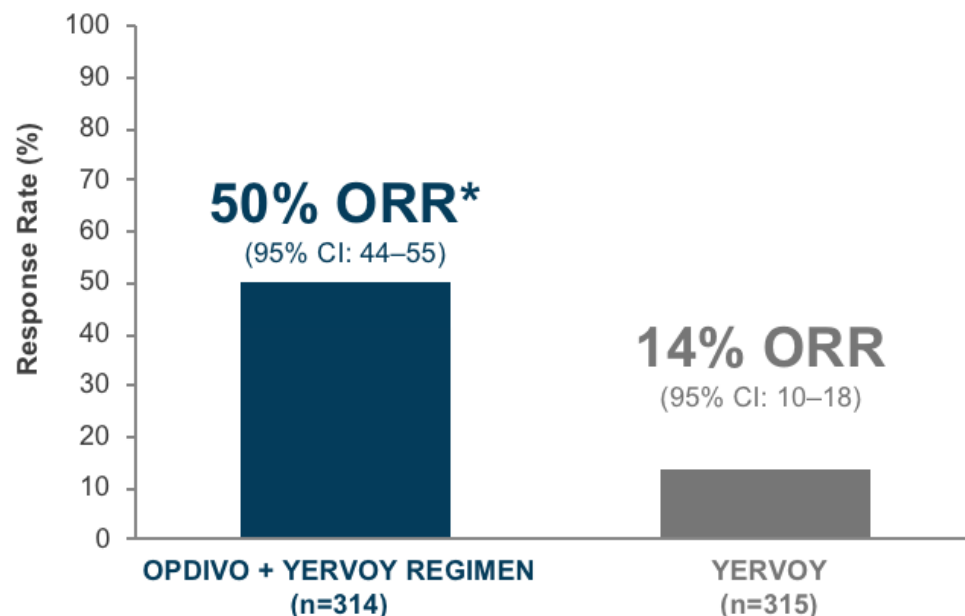
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Presented by: Katy K Tsai, MD

OPDIVO® (nivolumab) + YERVOY® (ipilimumab) Delivered a Significantly Superior Response vs YERVOY^{1,9}

Confirmed Objective Response Rate^{1*}



3 of 4 (76%) patients receiving the OPDIVO + YERVOY Regimen experienced a duration of response of at least 6 months (range: 1.2+ to 15.8+ months at the time of analysis)¹

Duration of Response \geq 6 months¹:

- OPDIVO Monotherapy: 74% (1.3+ to 14.6+)
- YERVOY Monotherapy: 63% (1.0+ to 13.8+)

Response Rates^{1*}:

- OPDIVO + YERVOY Regimen: CR: 8.9%; PR: 41%
- OPDIVO Monotherapy: ORR: 40% (95% CI: 34–46), $P < 0.0001$; CR: 8.5%; PR: 31%
- YERVOY Monotherapy: CR: 1.9%; PR: 12%

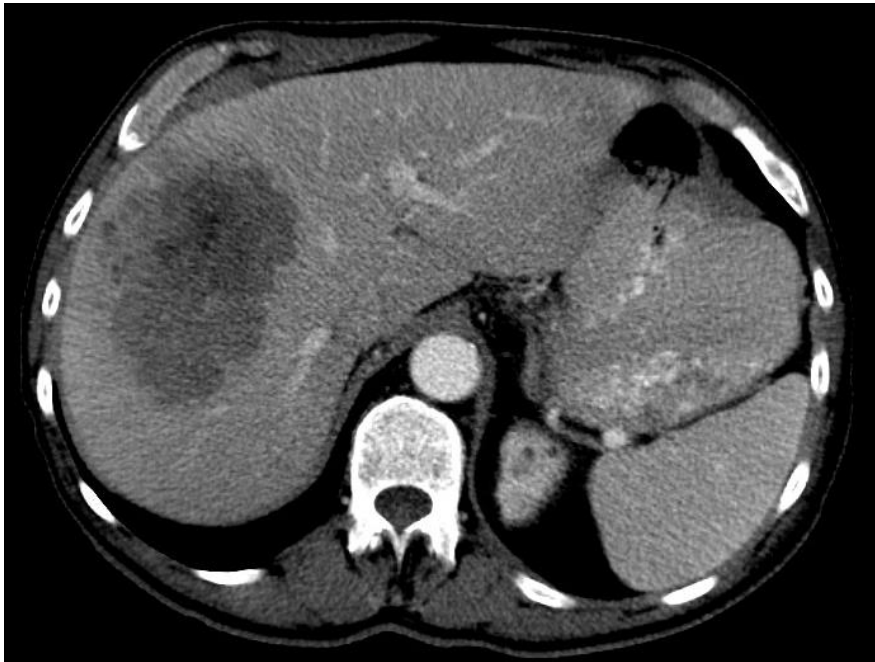
Select Important Safety Information

- In Checkmate 067, the most common ($\geq 20\%$) adverse reactions in the OPDIVO plus YERVOY arm (n=313) were fatigue (59%), rash (53%), diarrhea (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common ($\geq 20\%$) adverse reactions in the OPDIVO (n=313) arm were fatigue (53%), rash (40%), diarrhea (31%), and nausea (28%).

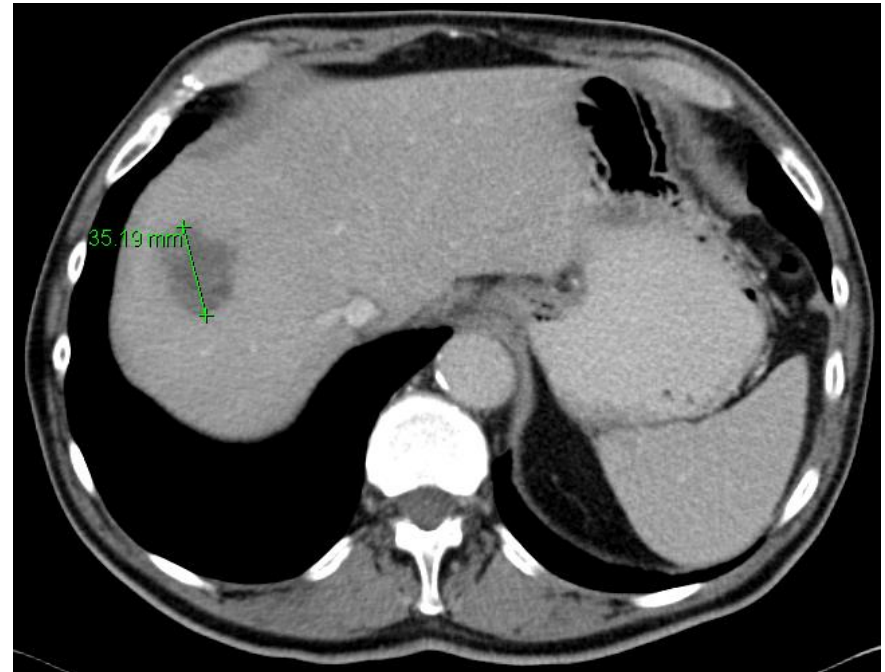
* Confirmed Objective Response per RECIST 1.1: Complete or partial responses may be confirmed if the criteria for each are met at a subsequent time point as specified in the protocol (generally 4 weeks later).⁹

CI: Confidence interval; CR: Complete response; ORR: Objective response rate; PR: Partial response; RECIST: Response Evaluation Criteria in Solid Tumors.

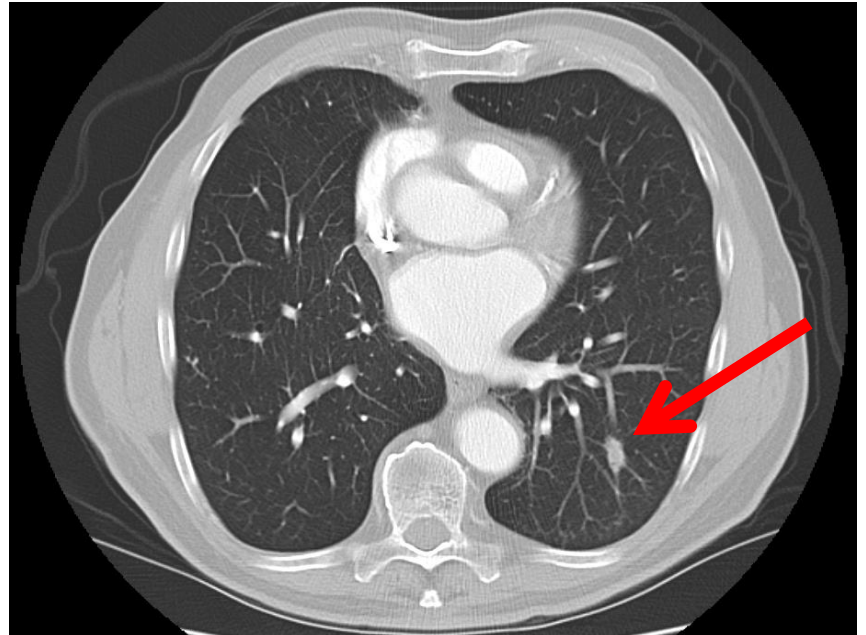
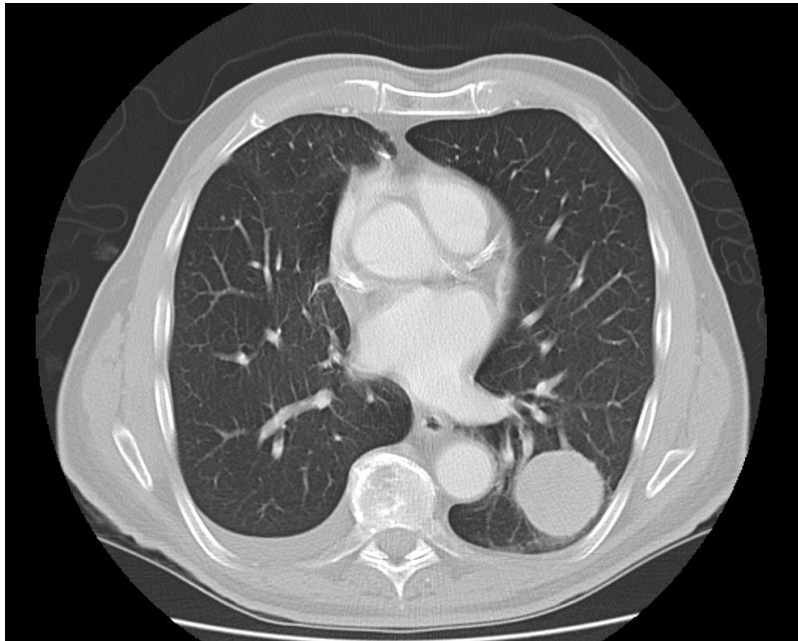
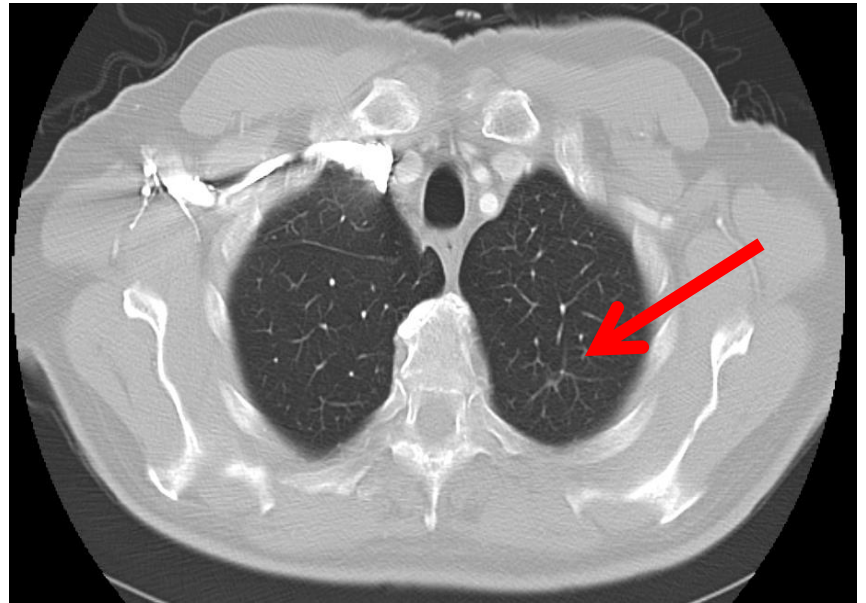
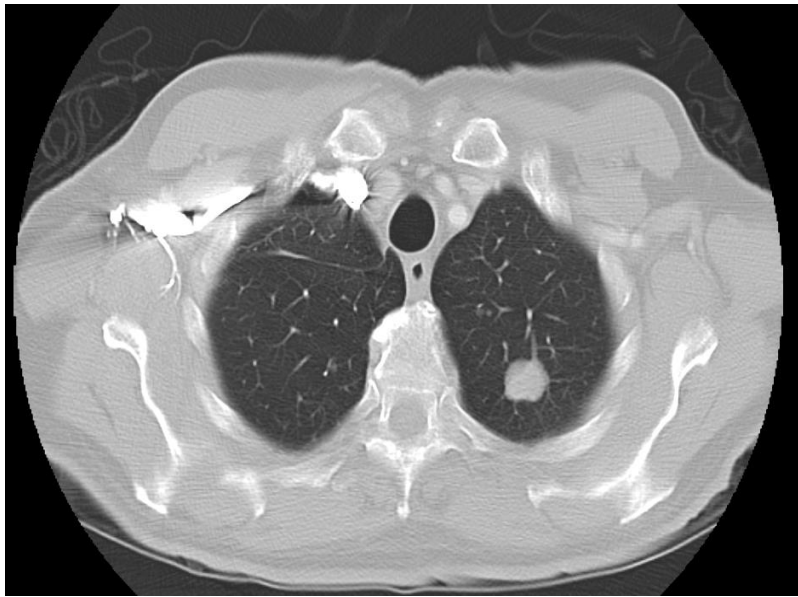
- 83 yo male with NRAS mutation C181A
- Progressed on prior Ipilimumab 6-9/2013



10/2013

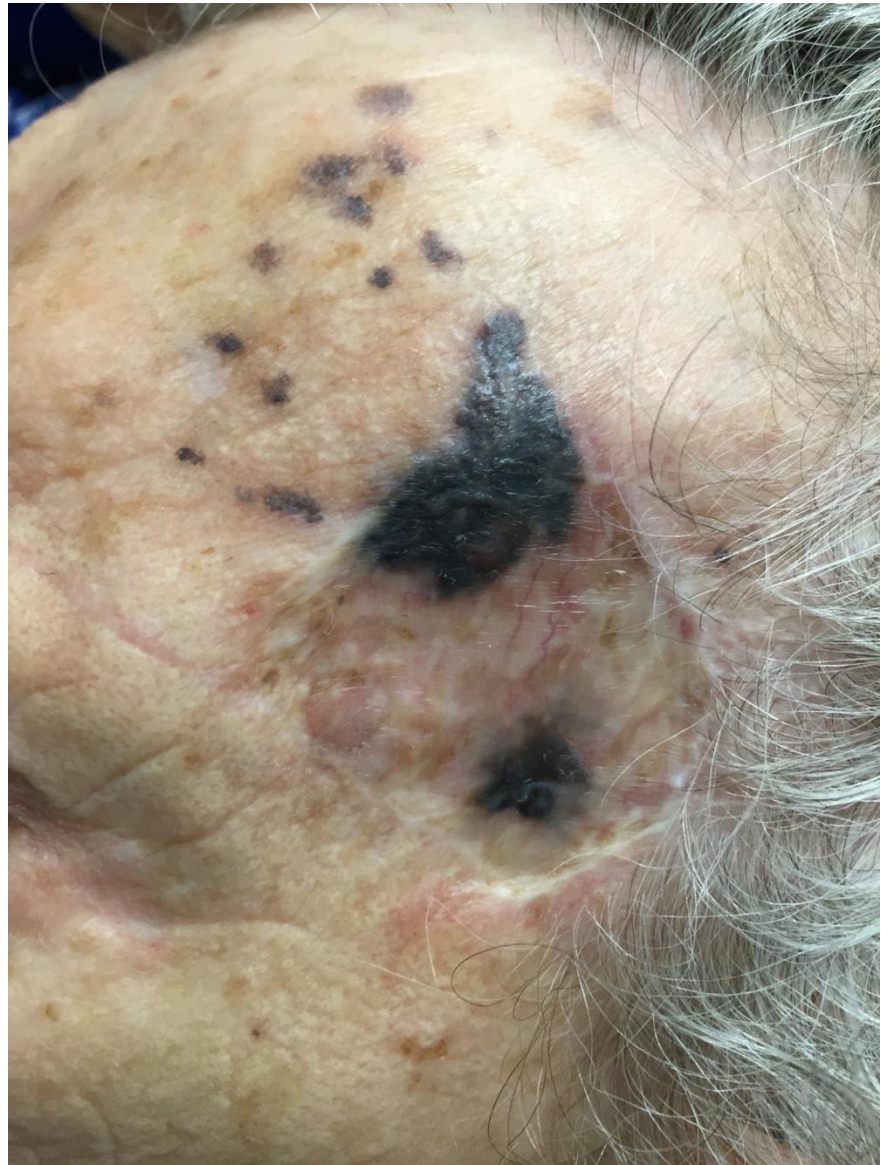
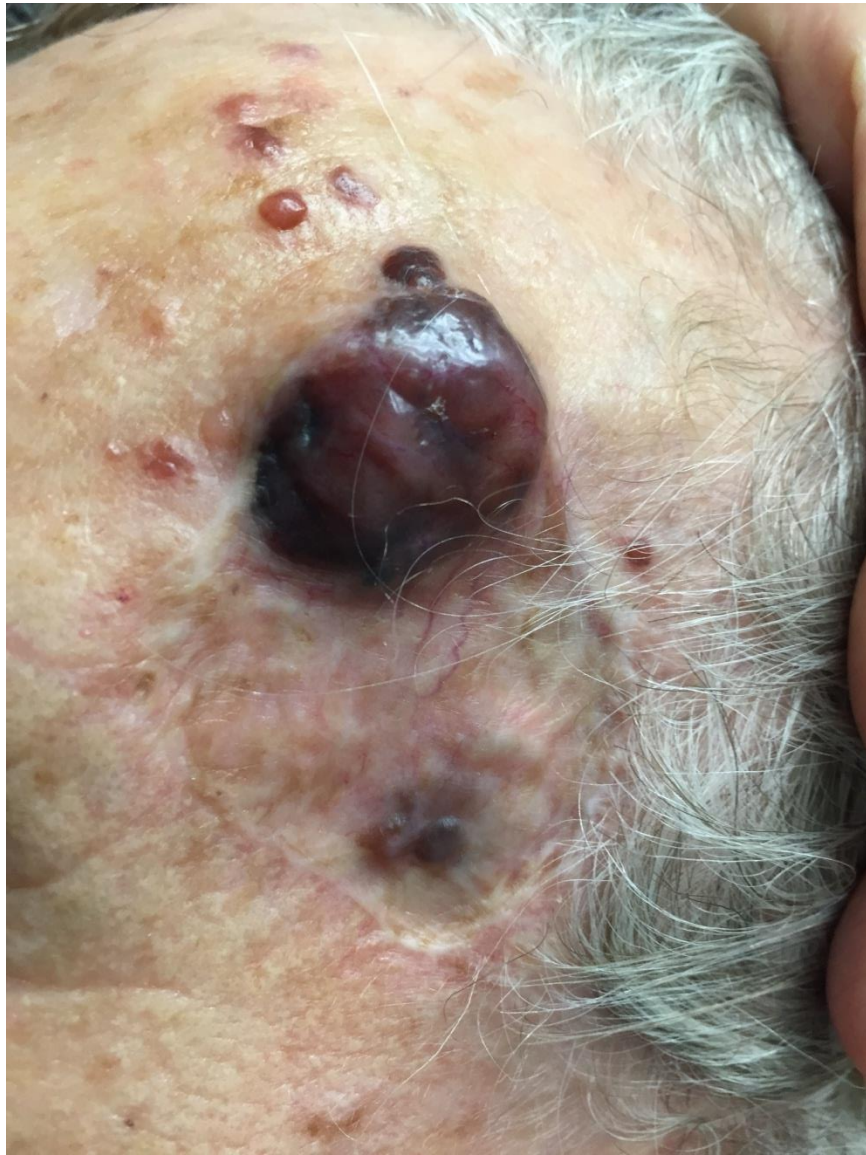


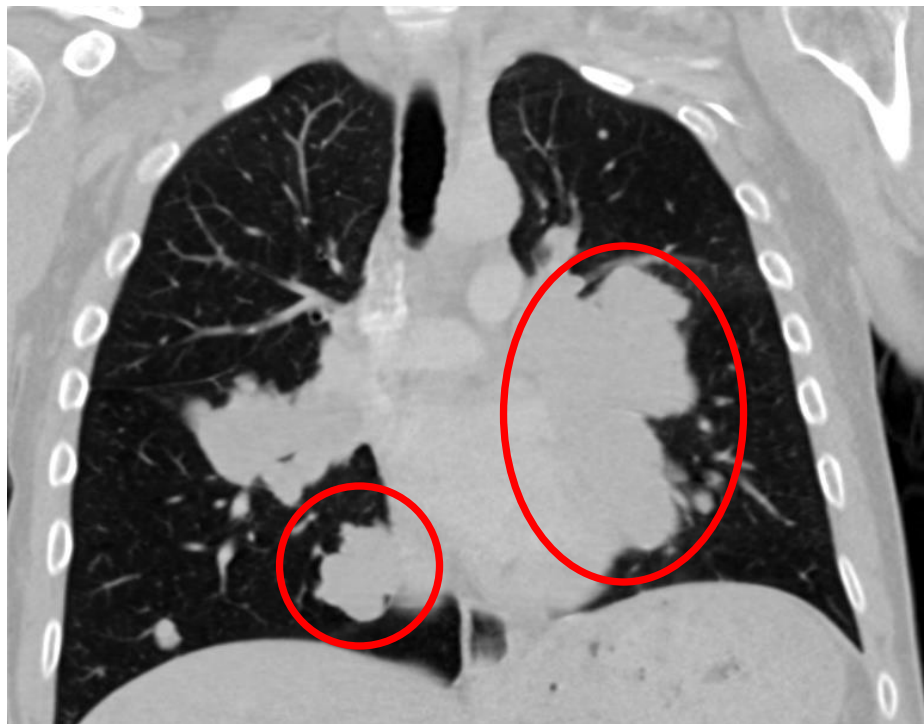
6/2014



8/2013

6/2014

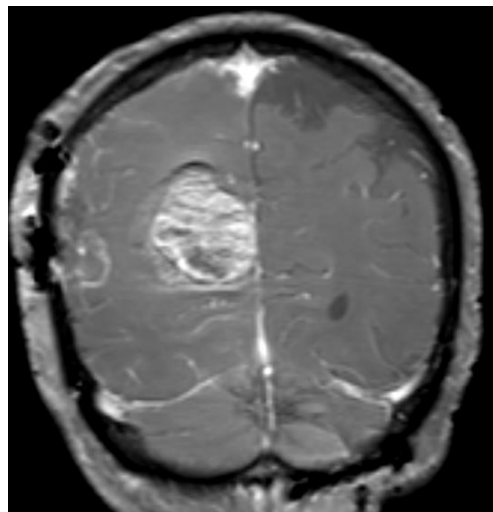




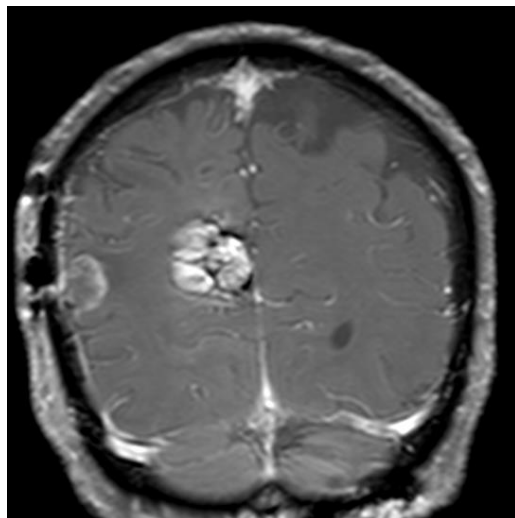
Feb 2015



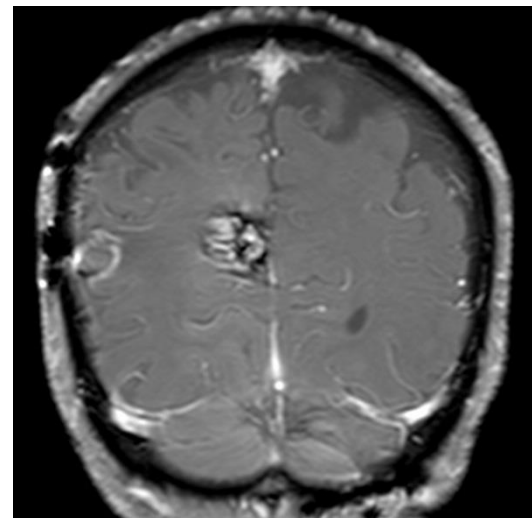
Sept 2015



Feb 2015



May 2015



Sept 2015

CNS METASTASIS ?

Trial Design

Key eligibilities

- ≥ 1 measurable, unirradiated MBM (0.5-3.0 cm)
- Prior SRT in ≤3 MBM
- Previous treatment with BRAFi/MEKi permitted

Induction

NIVO
1 mg/kg
Q3W × 4
+
IPI
3 mg/kg
Q3W × 4

Maintenance

NIVO
3 mg/kg
Q2W

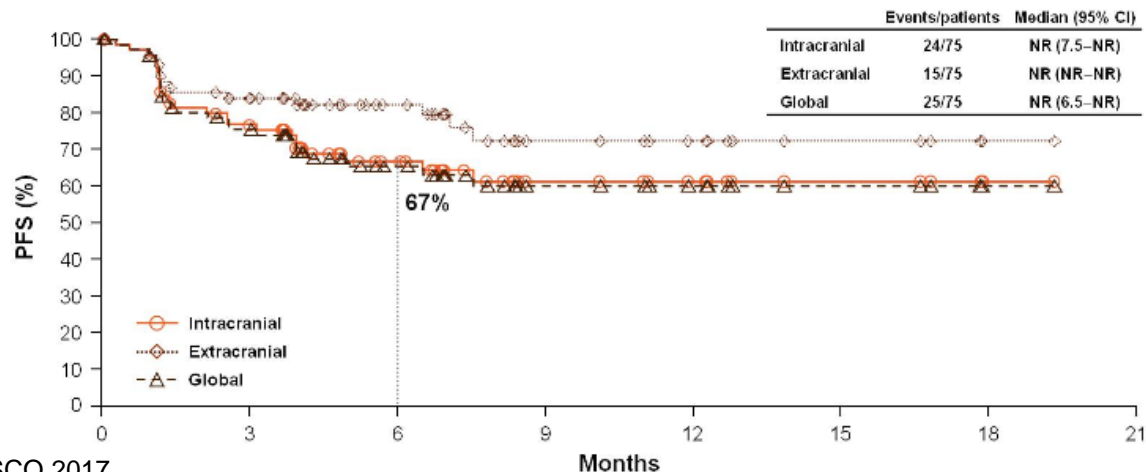
Treat until
progression or
unacceptable
toxicity
(maximum of
24 months)^a

- Exclusion criteria included neurological symptoms; steroids > 10 days; WBRT; prior treatment with checkpoint inhibitors; leptomeningeal disease
- Original planned enrollment of 110 asymptomatic patients

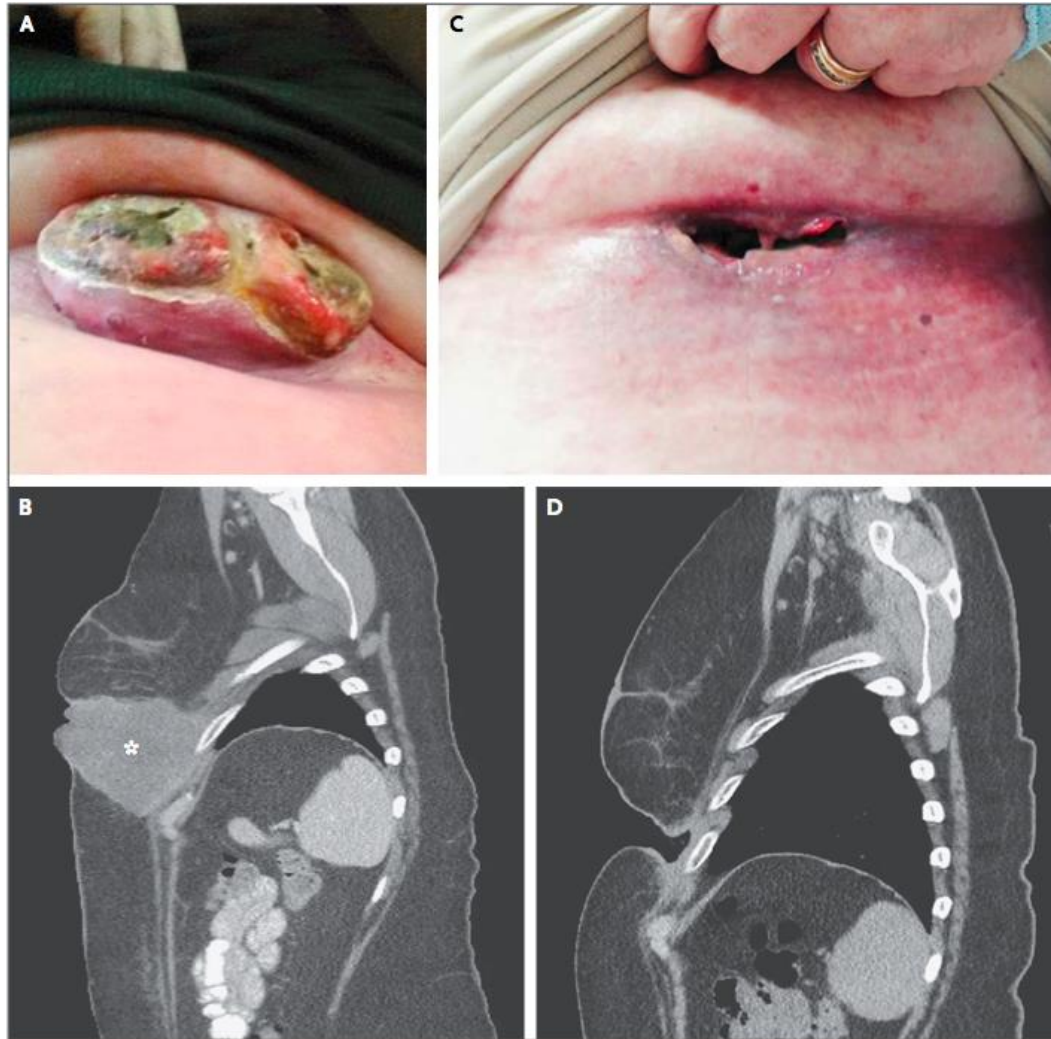
Response to Treatment – All Patients (N = 75)

	Global	Intracranial	Extracranial
Best overall response, n (%)			
Complete response	4 (5)	16 (21)	5 (7)
Partial response	36 (48)	25 (33)	32 (43)
Stable disease	4 (5)	4 (5)	2 (3)
Progressive disease ^a	18 (24)	18 (24)	16 (21)
Not evaluable ^b	13 (17)	12 (16)	20 (27)
Objective response rate, % (95% CI)	53 (41-65)	55 (43-66)	49 (38-61)
Clinical benefit rate^c, % (95% CI)	59 (47-70)	60 (48-71)	52 (40-64)

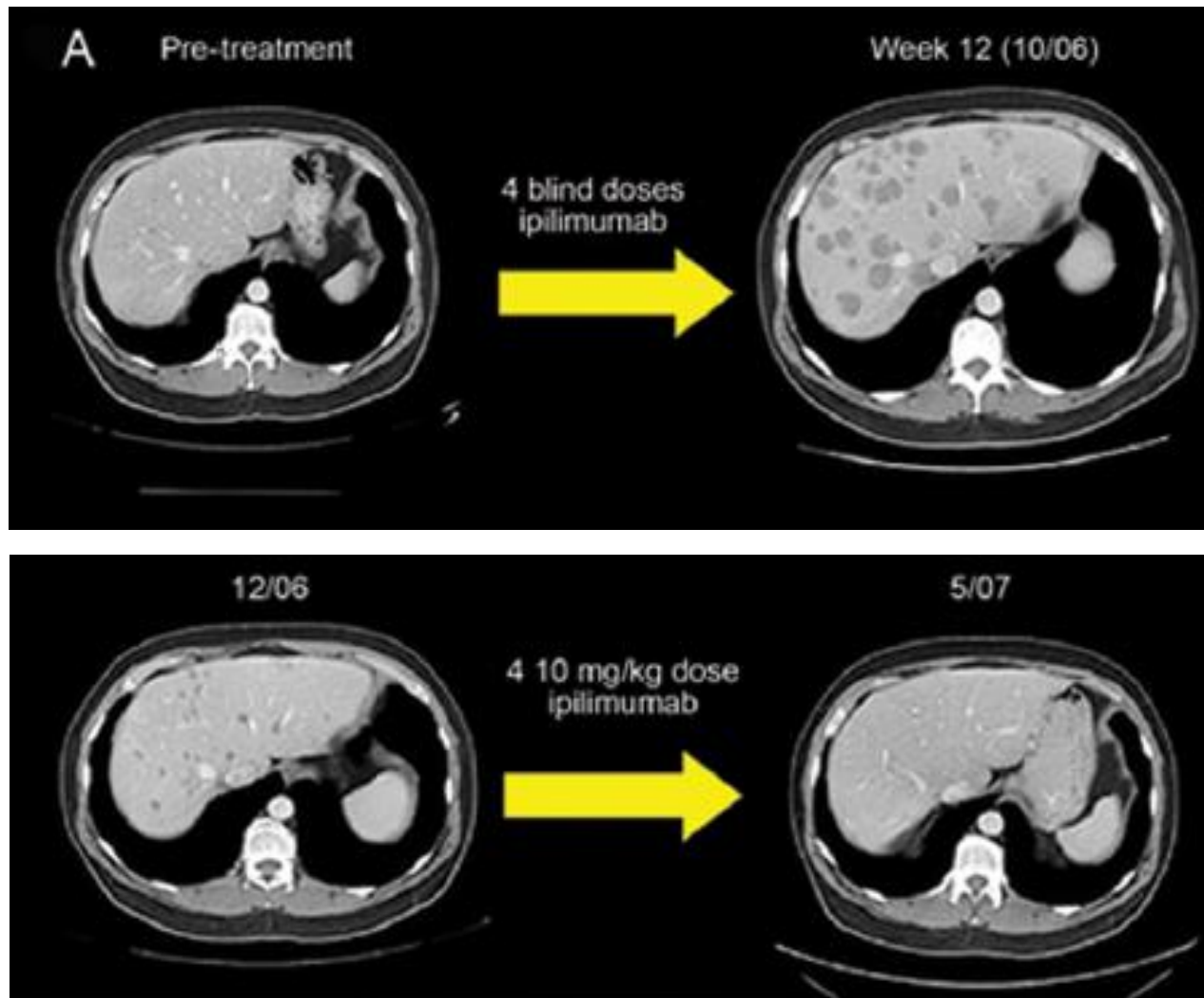
PFS



ONE DOSE OF IPI/NIVO !?!



VARIABLE RESPONSES TO IPI?



IMMUNE-MEDIATED ADVERSE REACTIONS

Follow color code to appropriate management guide section.

GASTROINTESTINAL

GO TO PAGE 6

Signs and symptoms such as

- Diarrhea
- Abdominal pain
- Blood or mucus in stool
- Bowel perforation
- Peritoneal signs
- Ileus

LIVER

GO TO PAGE 8

Signs such as

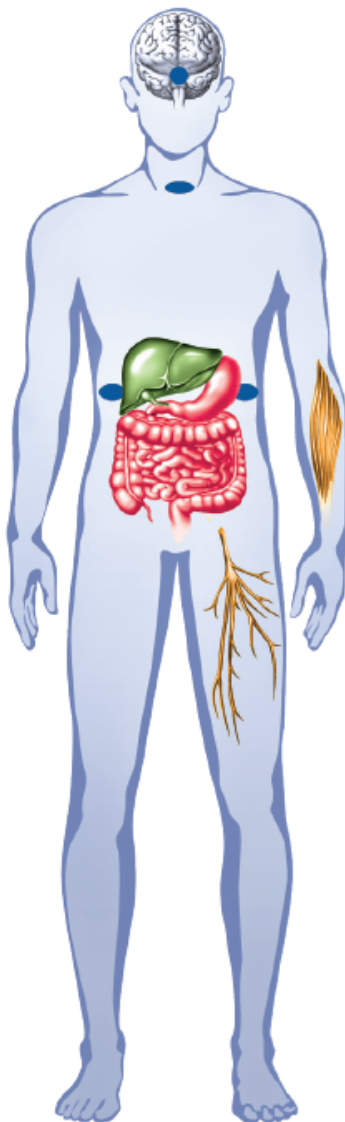
- Abnormal liver function tests (eg, AST, ALT) or total bilirubin

SKIN

GO TO PAGE 10

Symptoms such as

- Pruritus
- Rash



NEUROLOGIC

GO TO PAGE 12

Symptoms such as

- Unilateral or bilateral weakness
- Sensory alterations
- Paresthesia

ENDOCRINE

GO TO PAGE 14

Signs and symptoms such as

- Fatigue
- Headache
- Mental status changes
- Abdominal pain
- Unusual bowel habits
- Hypotension
- Abnormal thyroid function tests and/or serum chemistries

OTHER ADVERSE REACTIONS, including ocular manifestations

GO TO PAGE 16

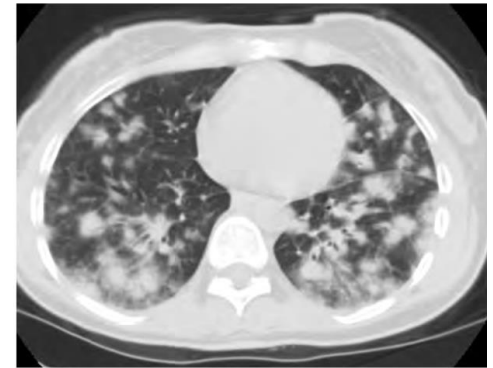
Please see each organ system section for related guidance.



Diarrhea and Colitis¹



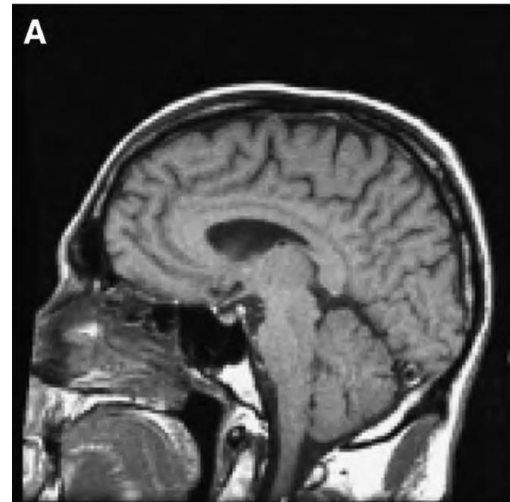
2/21/2011



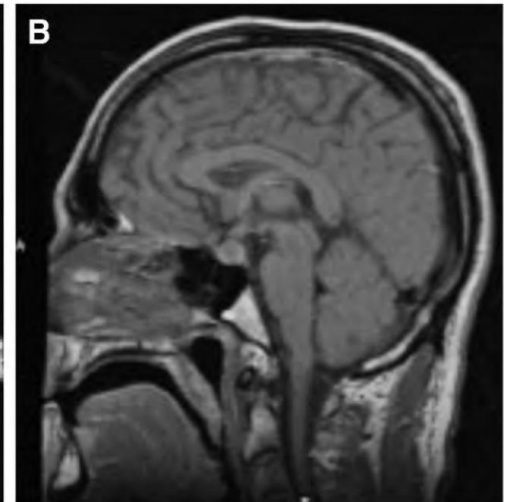
3/30/2011

- Two doses of ipilimumab and four doses of nivolumab

Hypophysitis Endocrinopathy¹



6/30/04 – Baseline (4.5 mm)

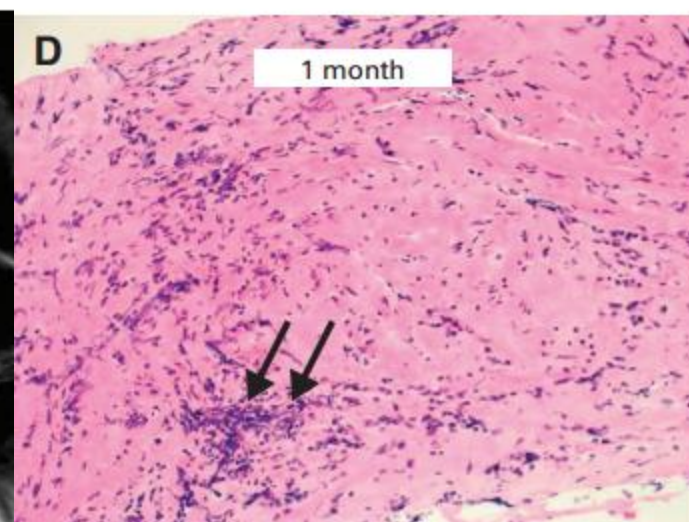
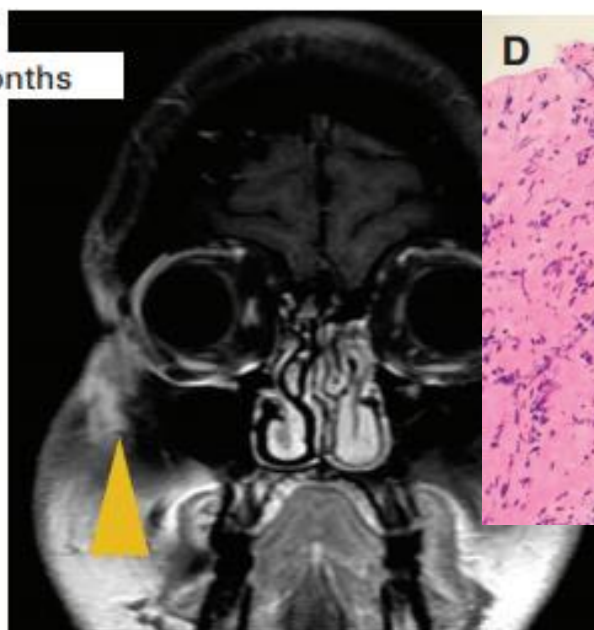
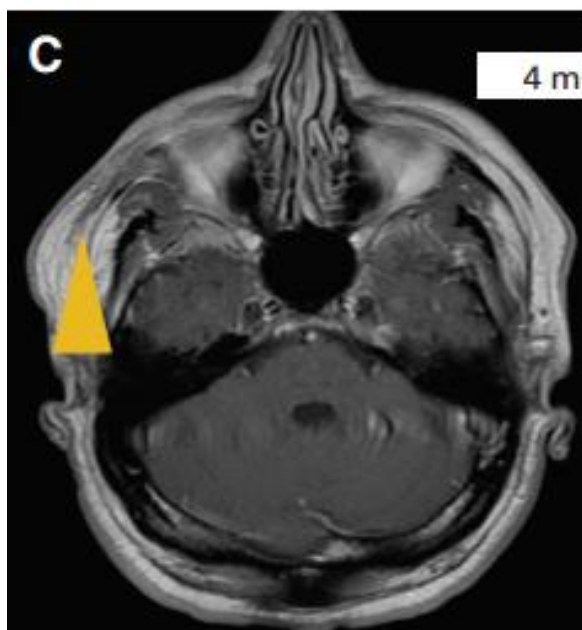
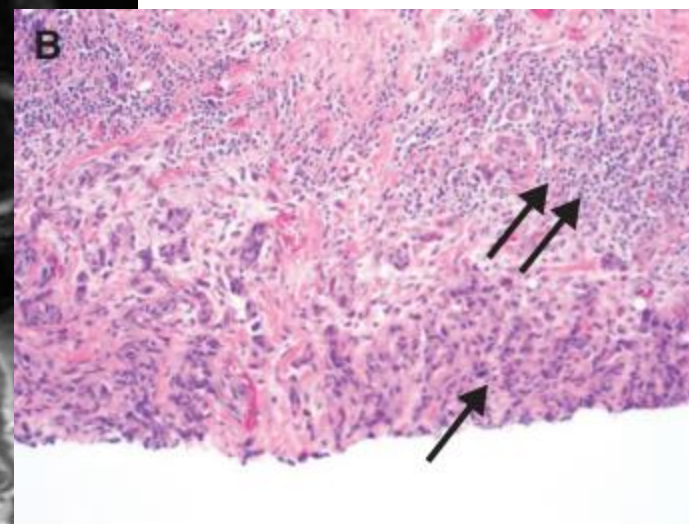
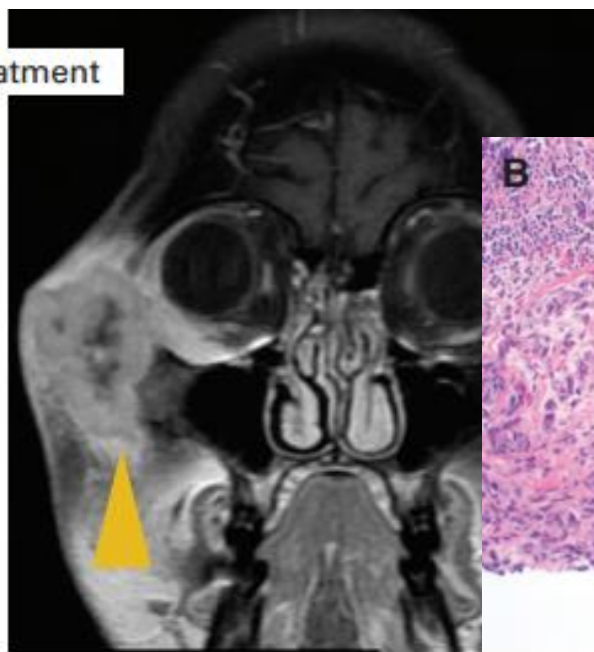
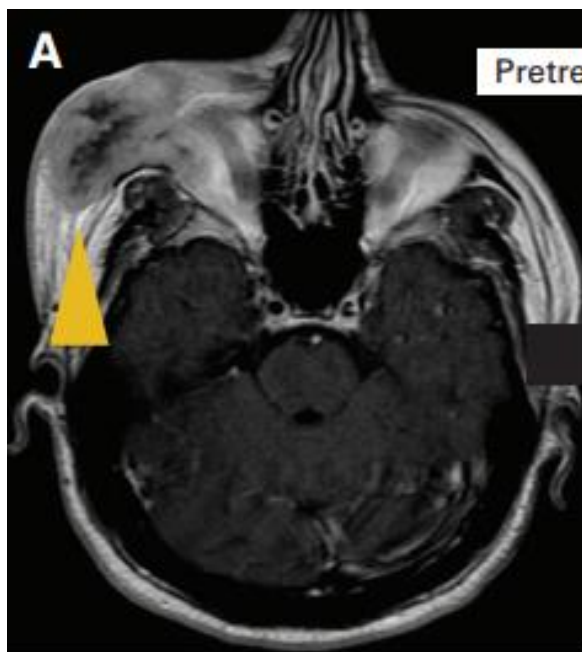


12/3/04 – Headache/fatigue (10.8 mm)

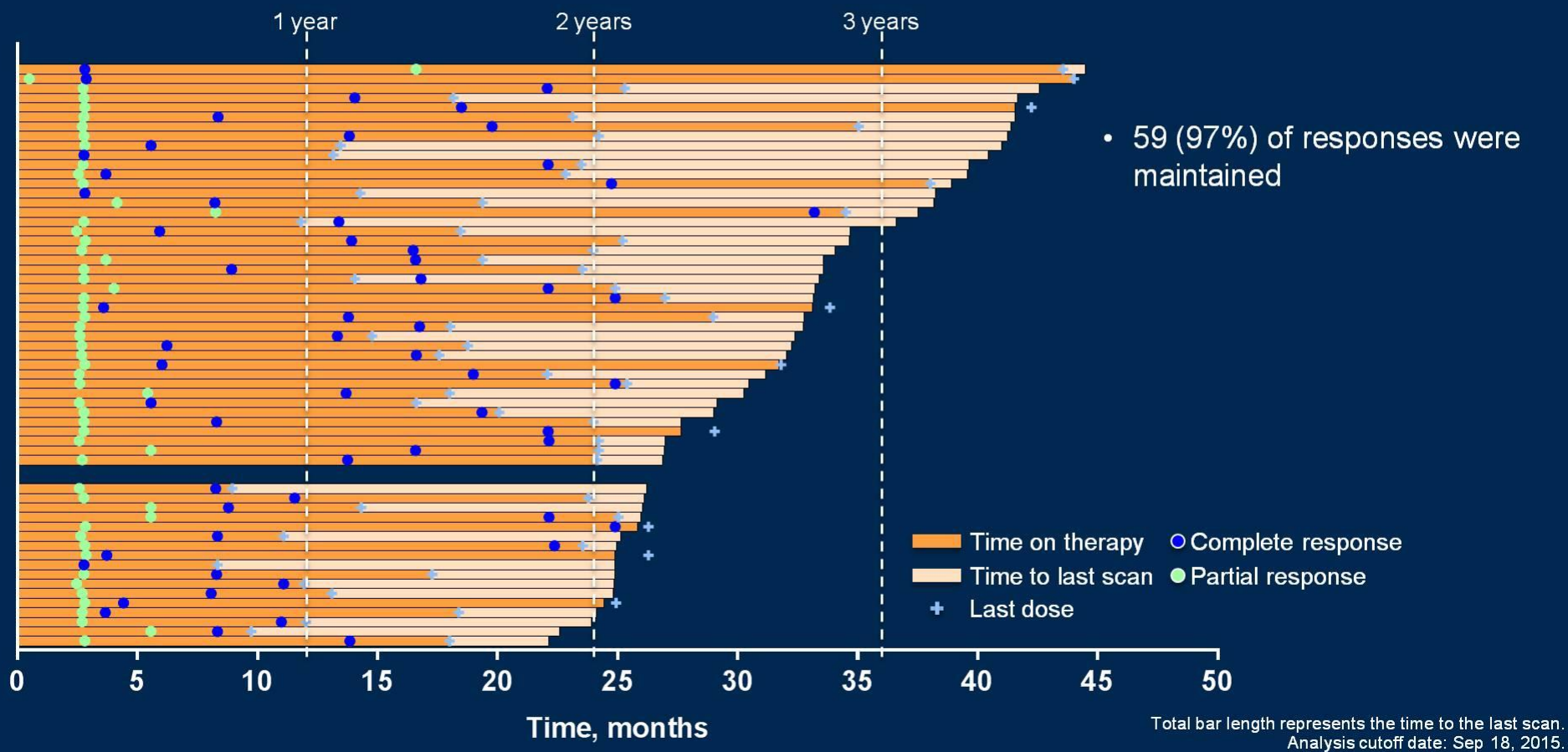
Toxicity Management: General Principles

- Low Grade
 - Monitor closely
 - Delay therapy
- Moderate Grade ?
- High Grade → Immunosuppression
 - Cease checkpoint inhibitor, consult sub-specialty and hospitalize
 - IV corticosteroids
 - Myophenolate
 - Infliximab (anti-TNF α)
 - Other → plasmapheresis, anti-thymocyte globulin

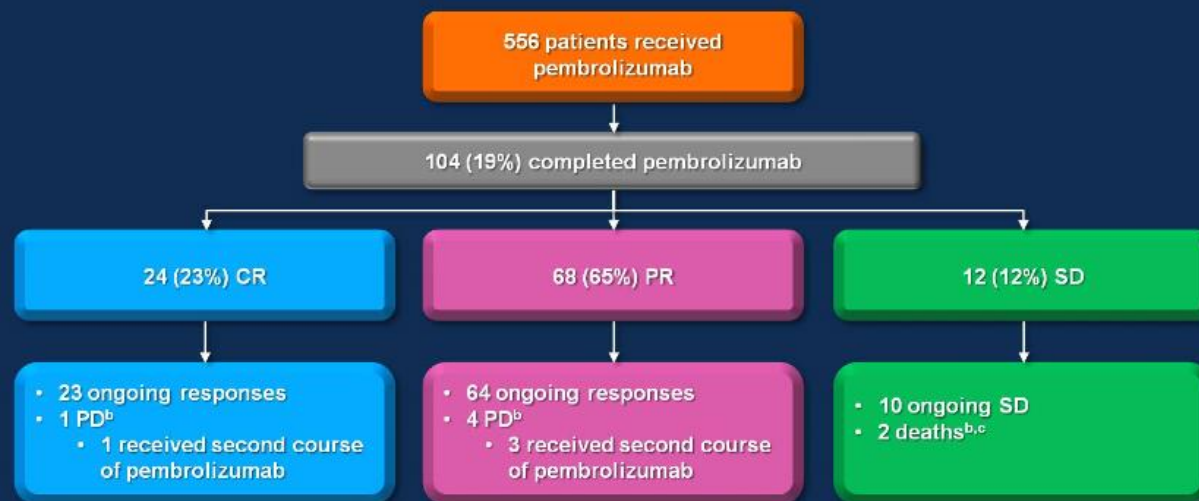




Complete Responders Who Stopped Pembrolizumab for Observation (N = 61)



Disposition of Patients Who Completed Protocol-Specified Time on Pembrolizumab^a (median follow-up, 9.7 mo)



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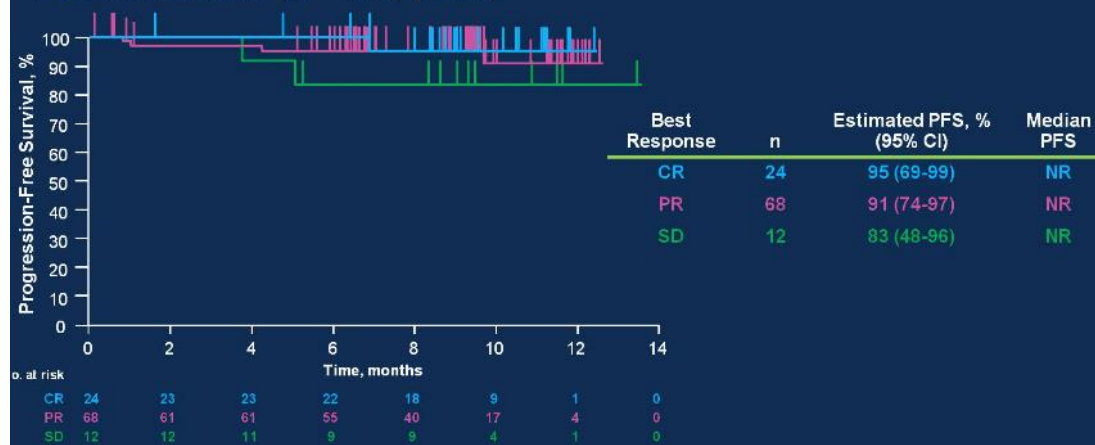
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^aIncludes patients completing ≥ 21.6 months of treatment.

^bFrom end of pembrolizumab treatment.

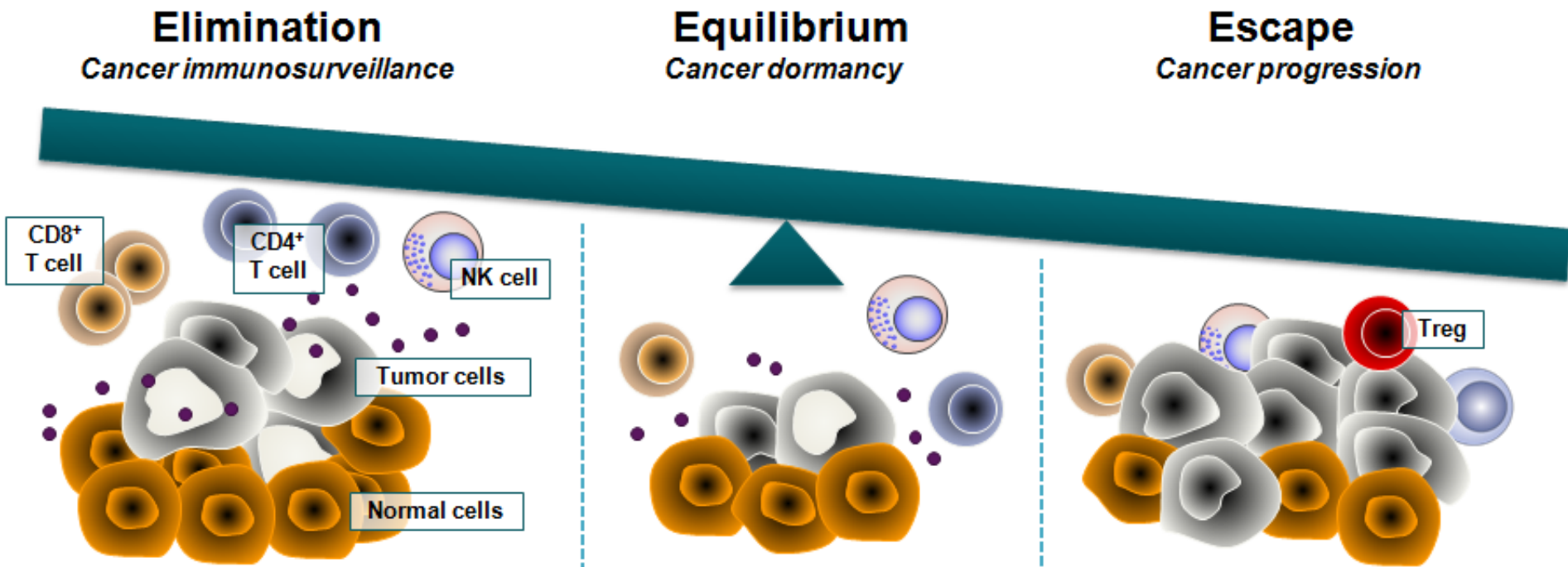
^cBoth deaths were a result of PD. Data cutoff date: Nov 3, 2016.

PFS (irRC, investigator) From Last Pembrolizumab Dose to PD or Death in Patients Who Completed Protocol-Specified Time on Pembrolizumab (n = 104) (cont)



EQUILIBRIUM VS ELIMINATION?

- There are 3 phases in tumor protection and promotion^{1,2}



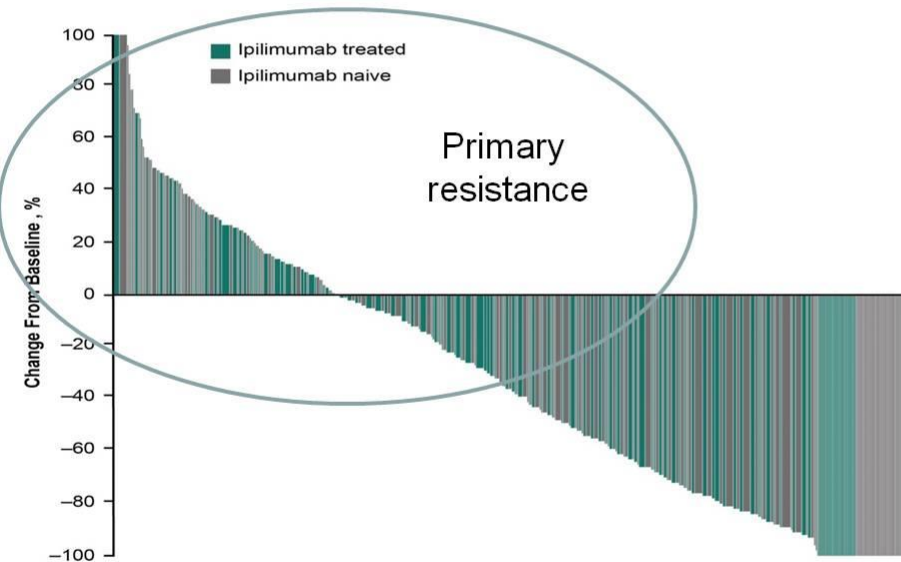
NK=natural killer; Treg=regulatory T cell.

1. Vesely MD, et al. *Ann Rev Immunol*. 2011;29:235-271. Figure republished with permission of Annual Reviews, from Vesely MD, et al, *Ann Rev Immunol*. 2011;29:235-271; permission conveyed through Copyright Clearance Center, Inc; 2. Schreiber RD, et al. *Science*. 2011;331:1565-1570.



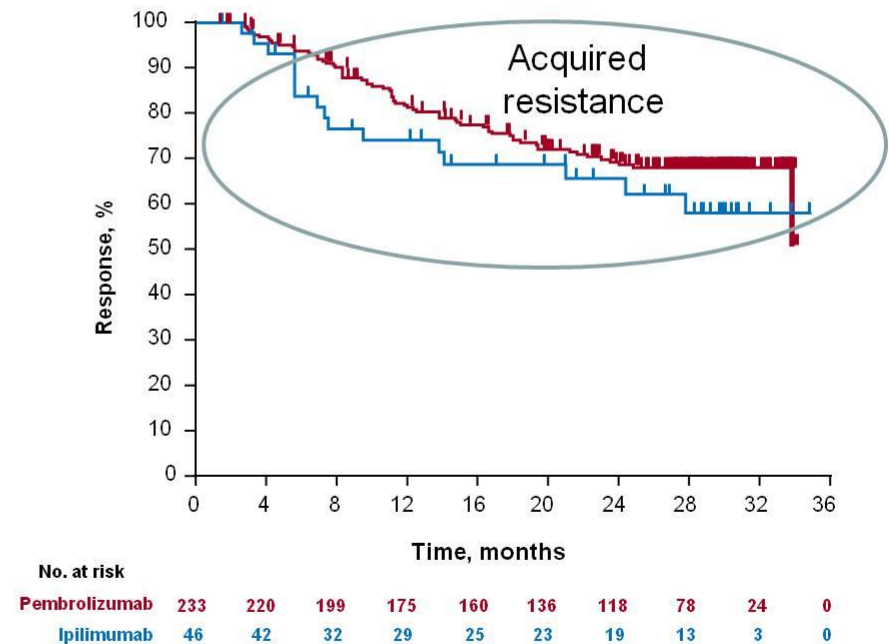
Primary and Acquired Resistance to PD-1 Blockade

Waterfall plot of RECIST responses in 510 patients treated with pembrolizumab in the Keynote 001 trial



Ribas *et al.* JAMA 2016 Apr 19; 315 (15): 1600-9.

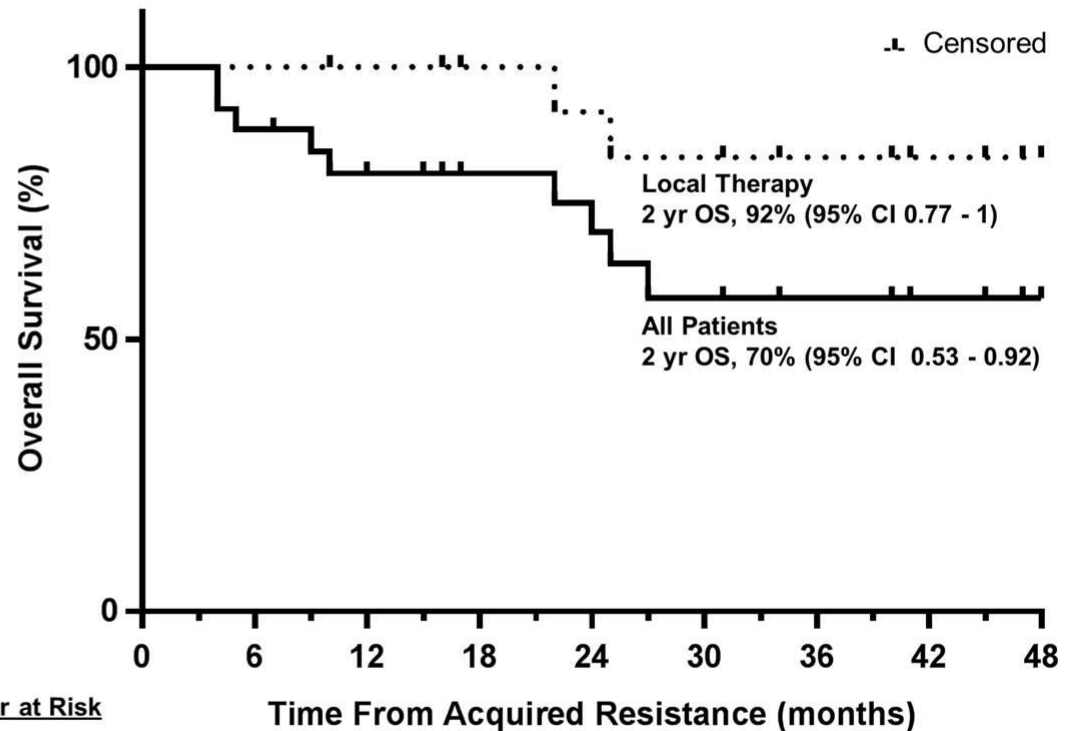
KM of duration of response in patients treated with pembrolizumab or ipilimumab in the Keynote 006 trial



Schachter J, et al. Lancet. 2017; 390: 1853-1862

Management of Acquired Resistance (n=26)

- 15 patients received local therapy to all sites of AR w/out alternative systemic Tx
 - 13 still alive (range 10-48 months from AR)
 - 10 patients at least 2 years from AR
 - 6 patients at least 3 years from AR

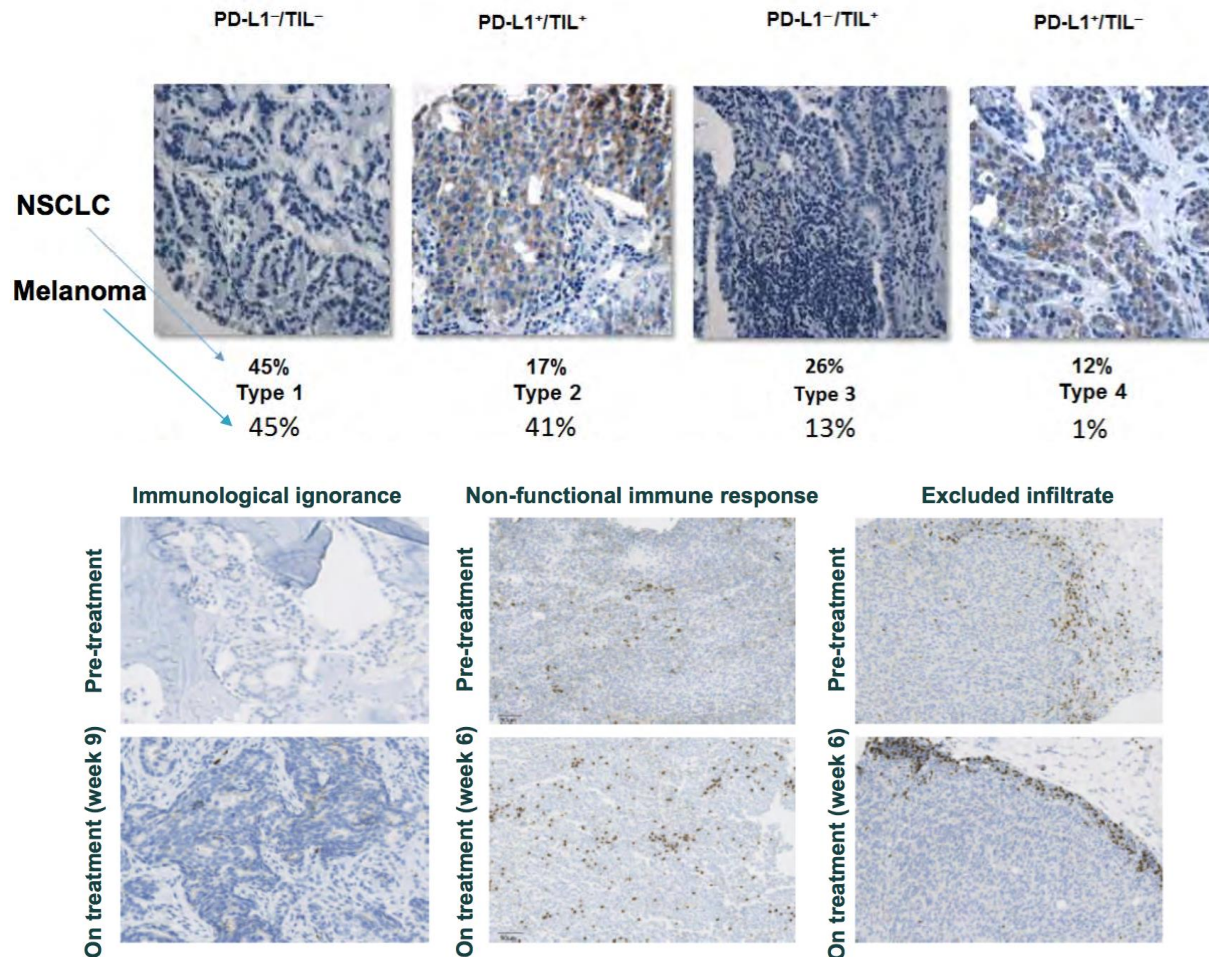


Number at Risk

All Patients	26	26	24	22	19	18	16	16	14	10	10	9	8	8	5	3	1
Local Therapy	15	15	15	15	15	15	13	13	12	11	11	9	8	8	5	3	1

Primary Resistance?

Presence of PD-L1 or TILs¹



Adapted from Dr Mario Sznol Melanoma Conference New York 2017

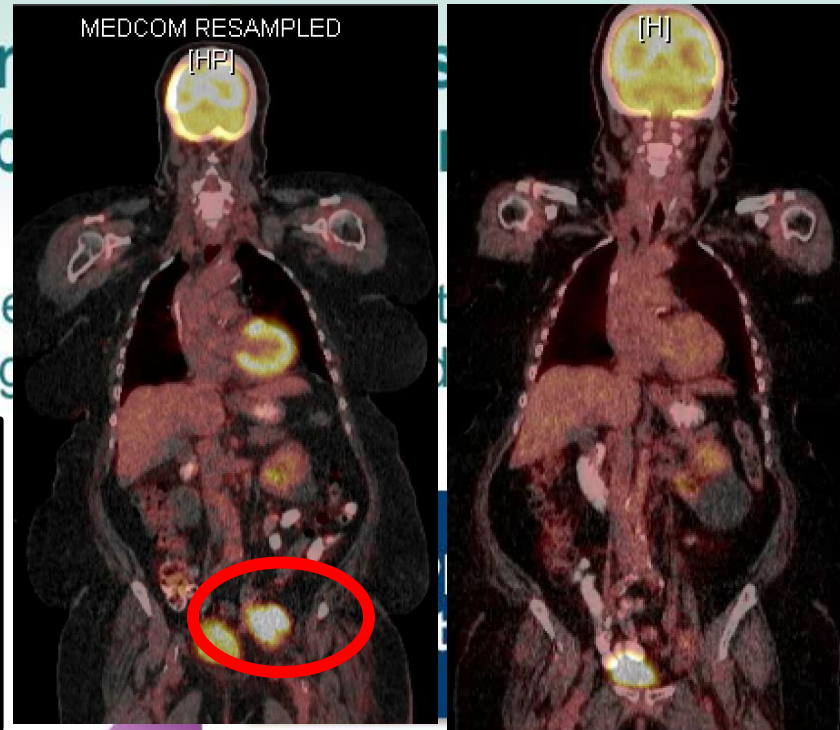
I-O Therapies Have The Potential To Be Monotherapy or Part of Combination

I-O research and development will continue to expand, including new targets and rationale for drug combinations

ORIGINAL ARTICLE

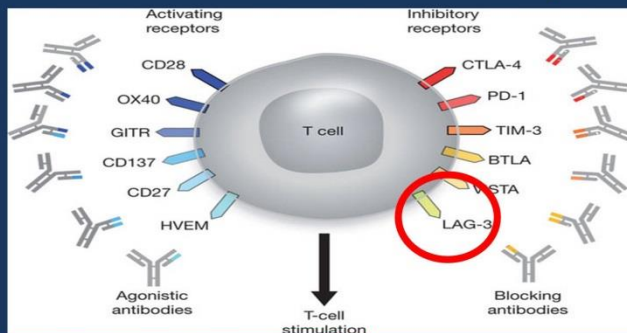
Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer

Leena Gandhi, M.D., Ph.D., Delvys Rodríguez-Abreu, M.D., Shirish Gadgil, M.B., B.S., Emilio Esteban, M.D., Enriqueta Felip, M.D., Ph.D., Flávia De Angelis, M.D., Manuel Domine, M.D., Ph.D., Philip Clingan, M.B., B.S., Maximilian J. Hochmair, Ph.D., Steven F. Powell, M.D., Susanna Y.-S. Cheng, M.D., Helge G. Bischoff, M.D., et al., for the KEYNOTE-189 Investigators*



I-O therapy

What about other T cell checkpoints?



Turning up The Activating

Blocking the Inhibiting

Mellman I, et al. *Nature*. 2011;480(7378):480-489.

Dabrafenib + Trametinib: BRAF V600 Melanoma



Week 0



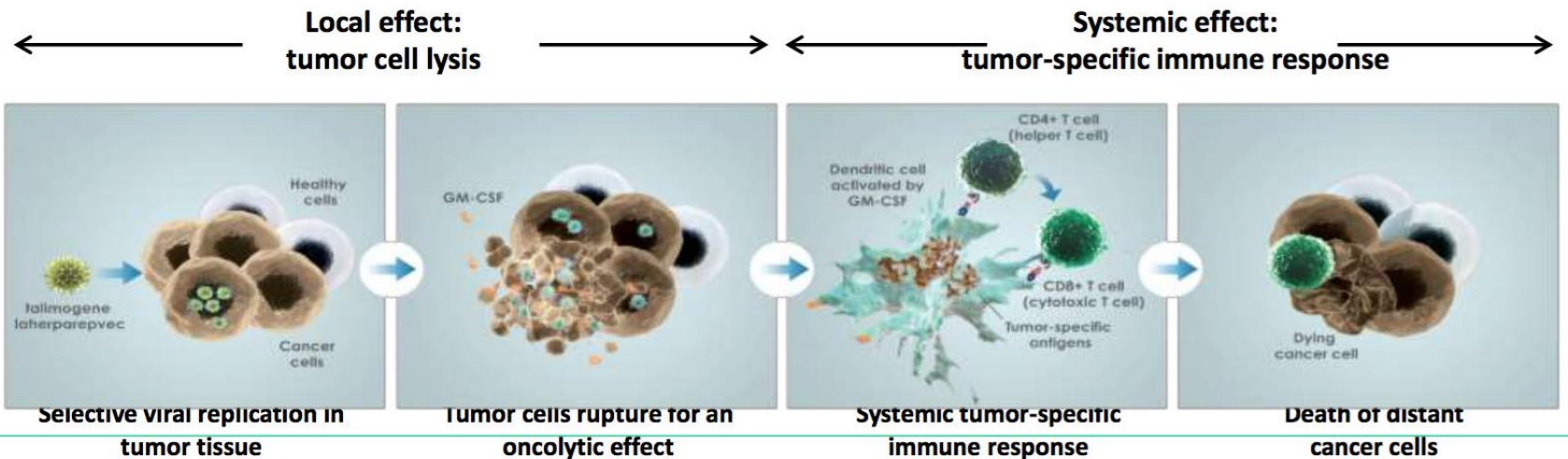
Week 8

Presented by Georgina V. Long

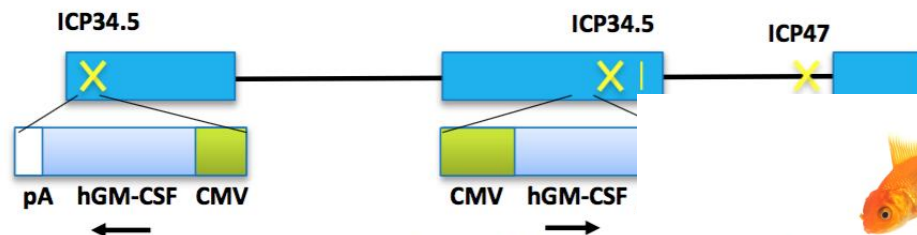
Talimogene Laherparecvec (T-VEC)

HSV-1 Derived Oncolytic Immunotherapy

Designed to Produce Local and Systemic Effects



T-VEC key genetic modifications:
JS1/ICP34.5-/ICP47-/hGM-CSF



ICP, infected cell protein; hGM-CSF, human granulocyte-macrophage colony-stimulating factor; CMV, cytomegalovirus; pA, polyadenylation (from bovine growth hormone)

1. Varghese S et al. *Cancer Gene Ther.* 2002;9:967-978. 2. Hawkins LK et al. *Lancet Oncol.* 2002;3:17-26. 3. Fukuhara H et al. *Curr Cancer Drug Ther.* 2011;19:335-344. 5. Liu BL et al. *Gene Ther.* 2003;10:292-303. 6. Melcher A et al. *Mol Ther.* 2011;19:1008-1016. 7. Fagoaga OR. In: *McDiagnosis and Management by Laboratory Methods*; 2011:933-953. 8. Dranoff G. *Oncogene.* 2003;22:3188-3192.

Adapted from Dr Merrick Ross Melanoma Conference N

TVEC RESPONSE

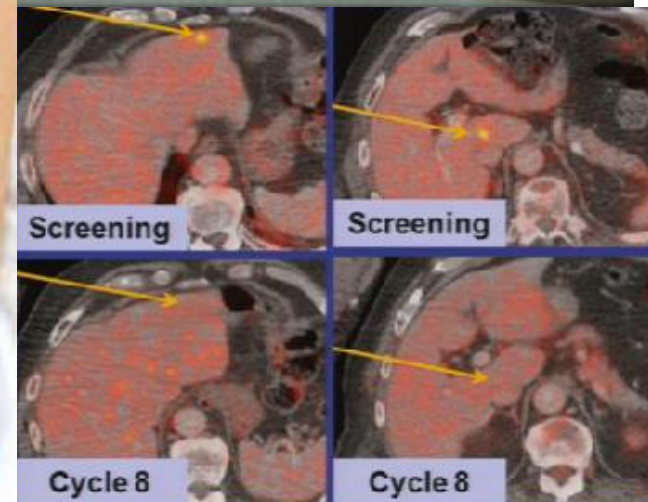


**Screening
(week 1)**

**First injection
(week 4)**

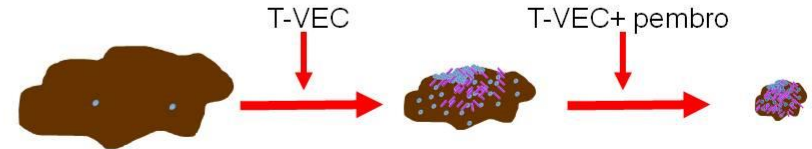
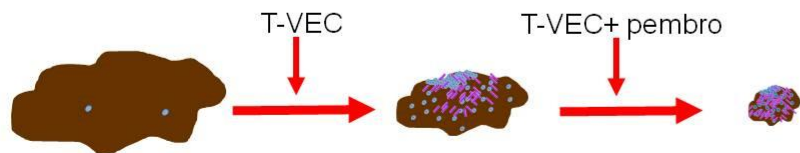
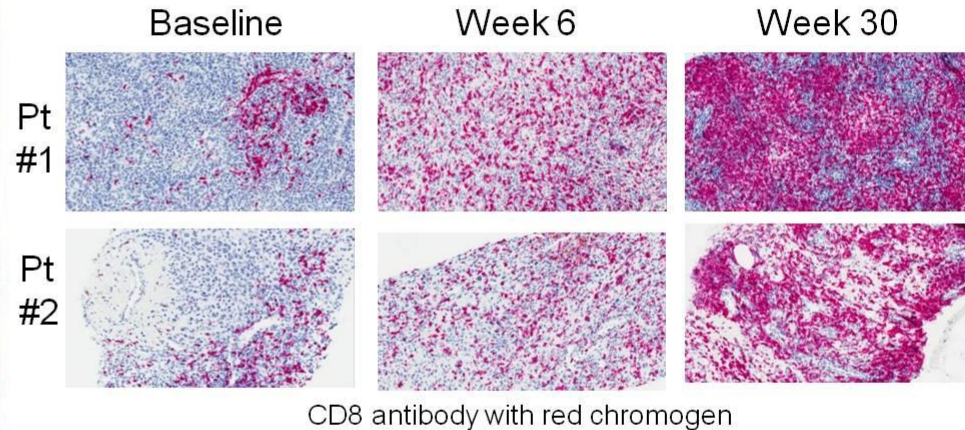
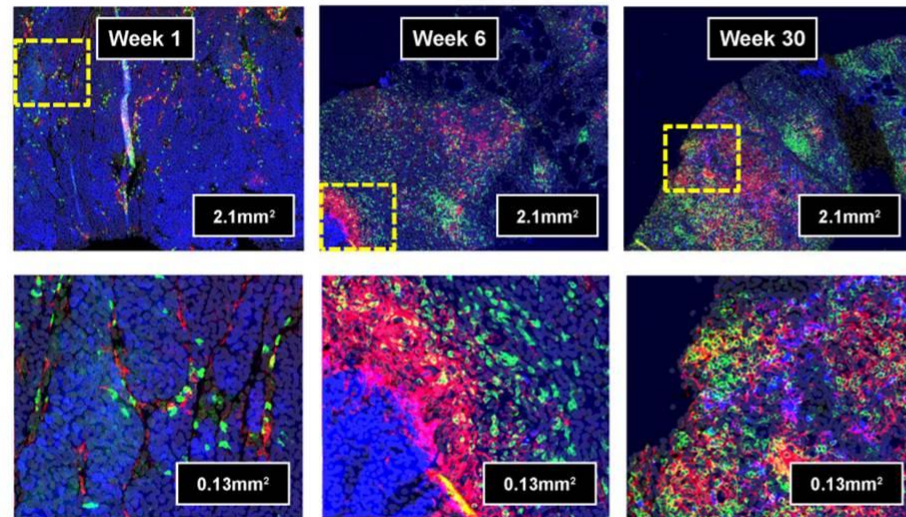
**Second injection
(week 6)**

**Eighth injection
(week 16)**



T-VEC increases tumor CD8 and PD-L1 in patients responding to combination with pembrolizumab

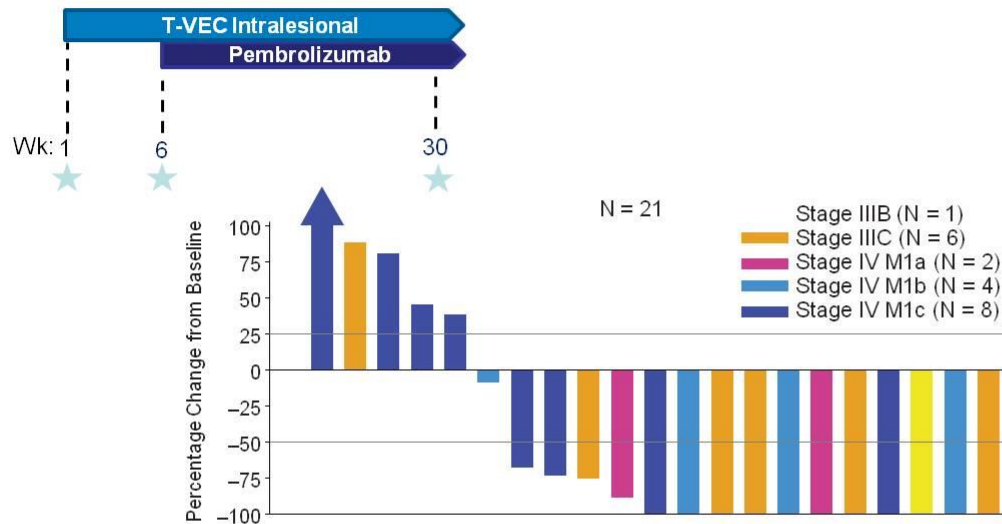
PD-L1 CD8 S100



Jennifer Gansert, Abraham Anderson, Kevin Gorski, Hajime Hilaragi, Jessica Stern

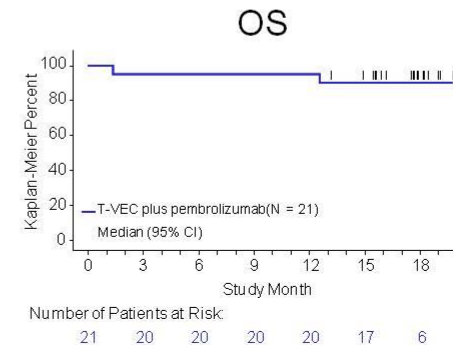
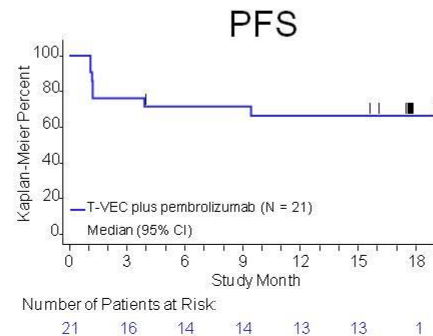
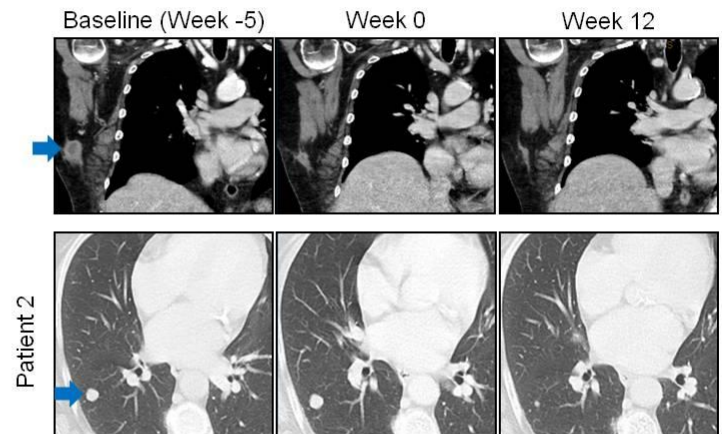
Ribas *et al.* Cell 2017 Sep 7; 170 (6): 1109-1119.e10.

MASTERKEY-265: T-Vec + pembrolizumab



62% objective response rate
33% complete response rate

Antoni Ribas, Reinhard Dummer, Igor Puzanov, Ari VanderWalde, Robert H. I. Andtbacka, Olivier Michielin, Anthony J. Olszanski, Josep Malvehy, Jonathan Cebon, Eugenio Fernandez, John M. Kirkwood, Thomas F. Gajewski, Lisa Chen, Kevin S. Gorski, Abraham A. Anderson, Scott J. Dieder, Michael E. Lassman, Jennifer Gansert, F. Stephen Hodi, Georgina V. Long. Cell 2017 Sep 7; 170 (6): 1109-1119.e10.



MASTERKEY-265 Phase 3 Study Design

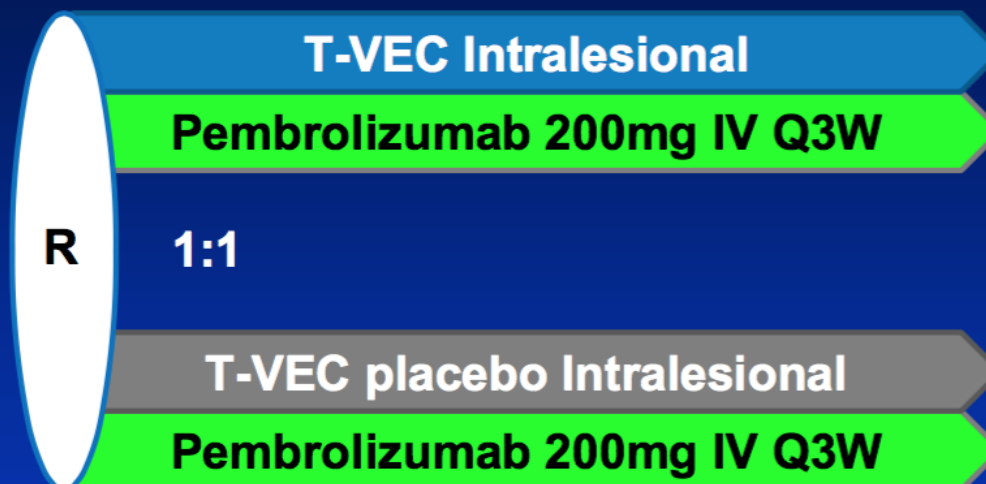
N = 660

- Unresectable stage III or IV melanoma
- Treatment naive
- Injectable lesions
- No clinically active brain mets
- No active herpetic skin lesions or prior complications from herpetic infection

T-VEC intralesional

- Up to 4 mL per treatment
- 1st dose 10^6 PFU/mL
- Then 10^8 PFU/mL Q2W x 4, then Q3W

N = 330



Treatment until whichever occurs first:

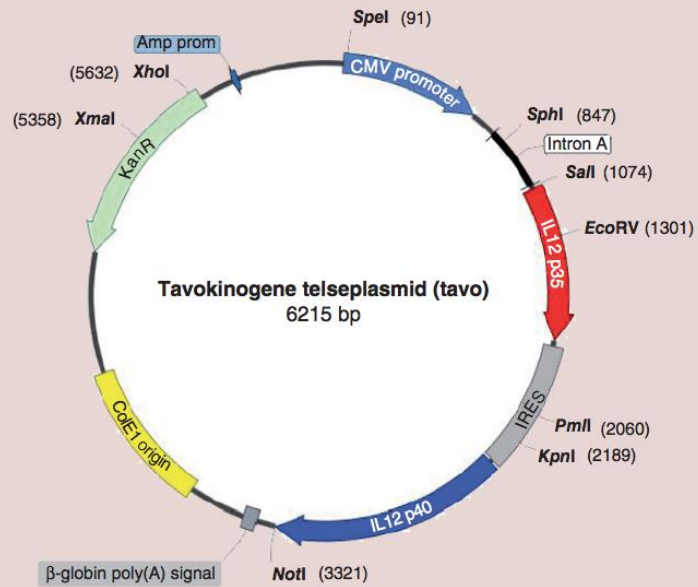
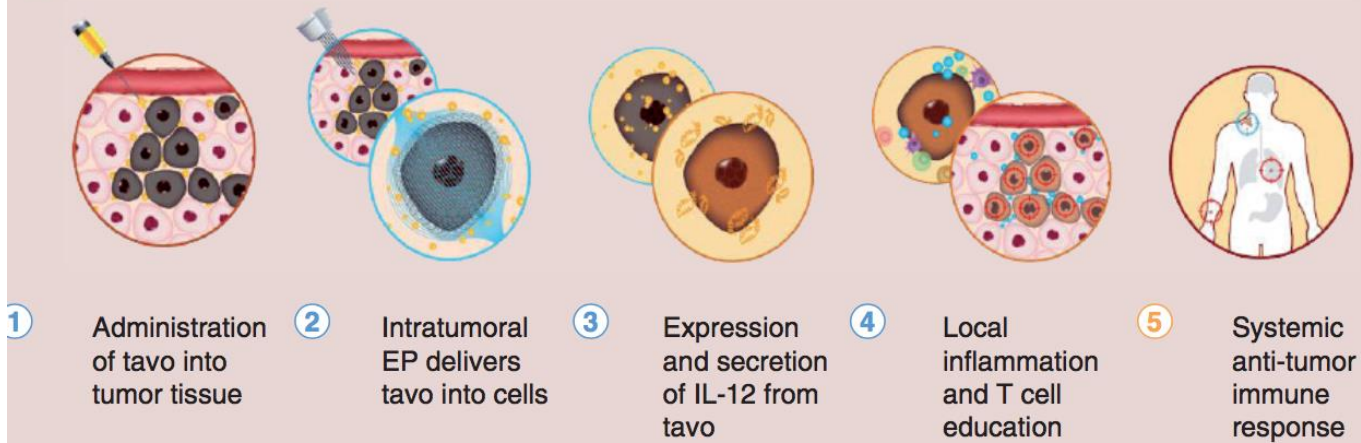
- Complete Response (CR)
- Progressive disease (PD) per irRC-RECIST
- Intolerance
- All injectable tumors disappeared (T-VEC/placebo only)
- 2 Years

N = 330

S
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30 (+7)
days after
end of
treatment

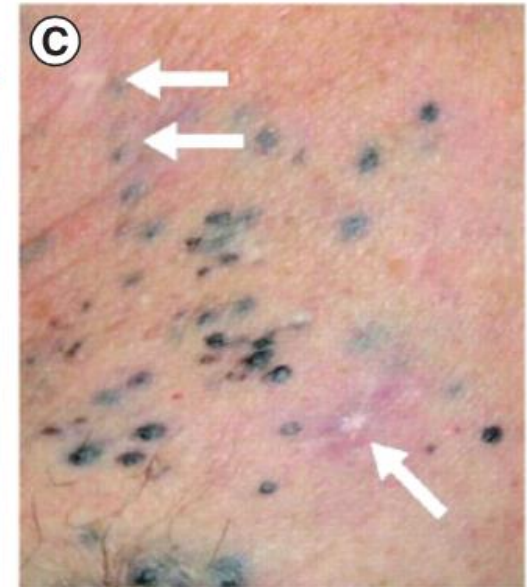
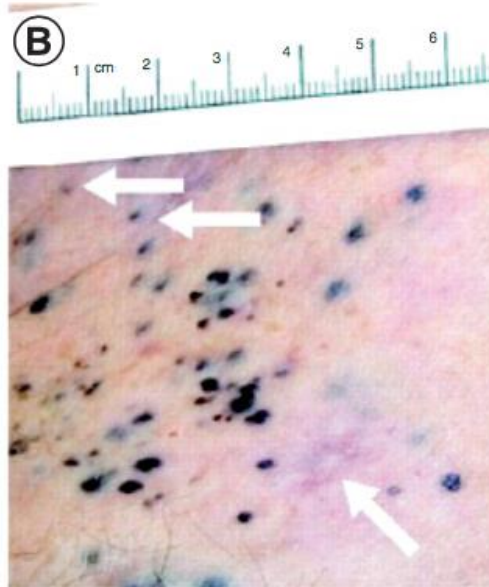
(A)**(B)****(C)**

Day 5

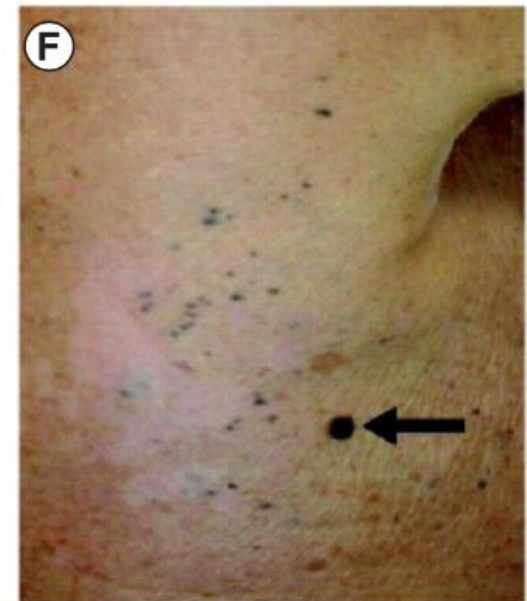
Day 256

Day 637

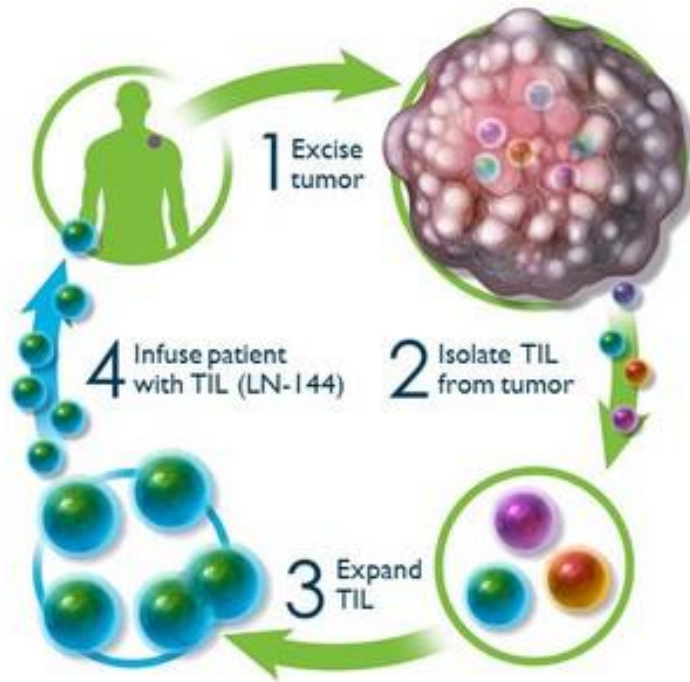
Right front chestwall



Right upper back

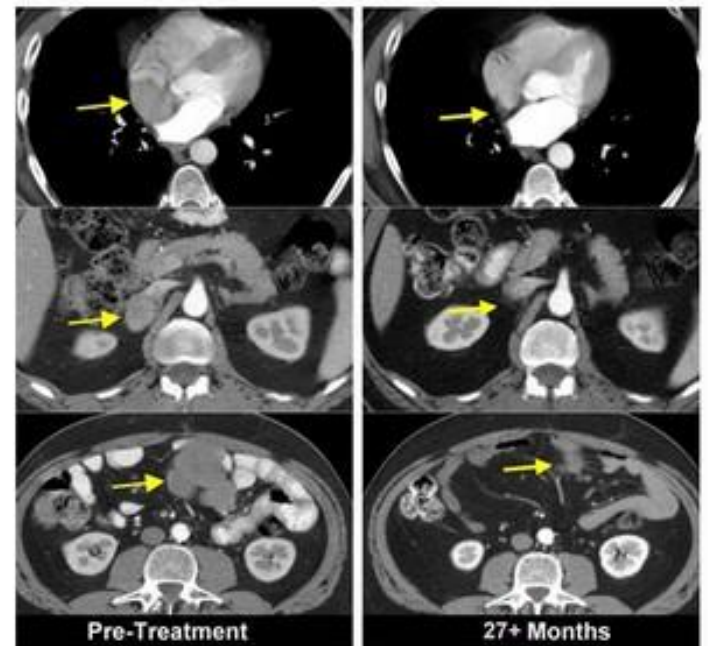


TIL Therapy Process



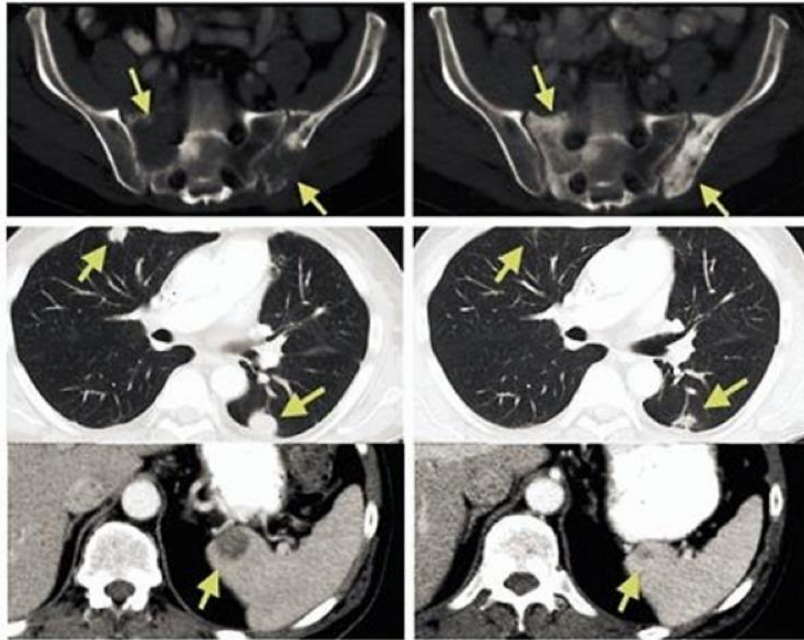
- **EXTRACTION:** Patient's TIL are removed from suppressive tumor microenvironment (via surgical resection of a lesion)
- **EXPANSION:** TIL expanded exponentially ex vivo to yield $10^9 - 10^{11}$ TIL
- **PREPARATION:** Patient receives non-myeloablative lymphodepletion, to eliminate potentially suppressive tumor microenvironment and maximize engraftment and potency of TIL therapy:
 - cyclophosphamide: 60 mg/kg x 2 doses
 - fludarabine: 25 mg/m² x 5 doses
- **INFUSION:** Patient is infused with their expanded TIL (LN-144) and IL-2 (600,000 IU/kg for up to 6 doses) to promote activation, proliferation, and anti-tumor cytolytic activity of TIL

NCI Study Melanoma Patient



Rosenberg, et al. Adoptive cell therapy for the treatment of patients with metastatic melanoma *Curr Opin Immunol*, 21(2), 233-240.

Compelling Results in Late-Stage Disease



Pretreatment

2 months posttreatment

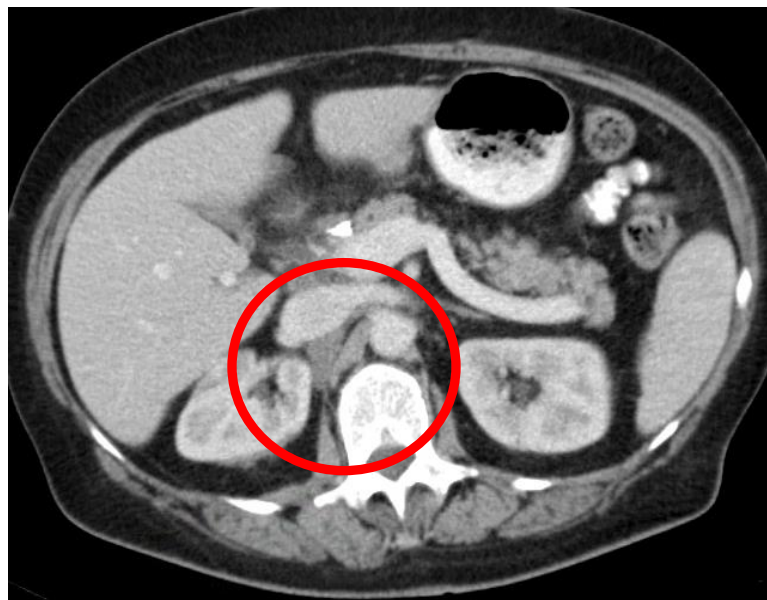
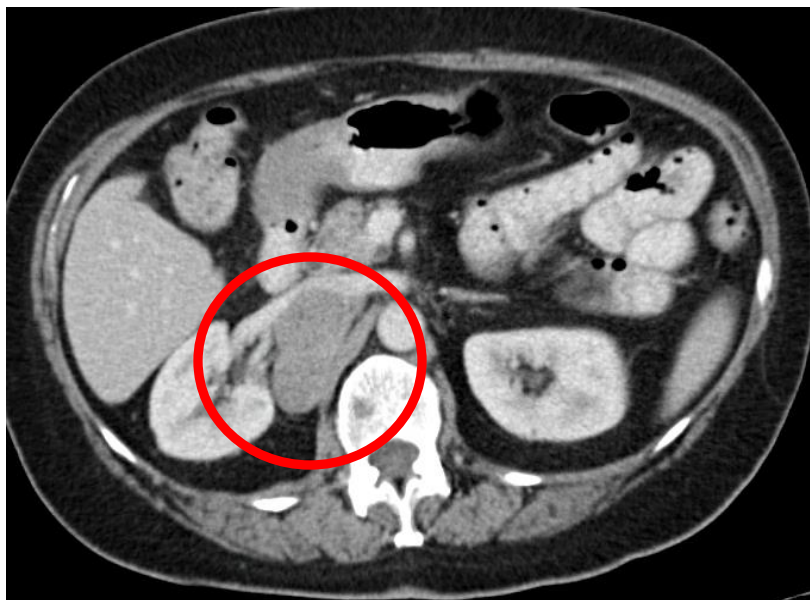
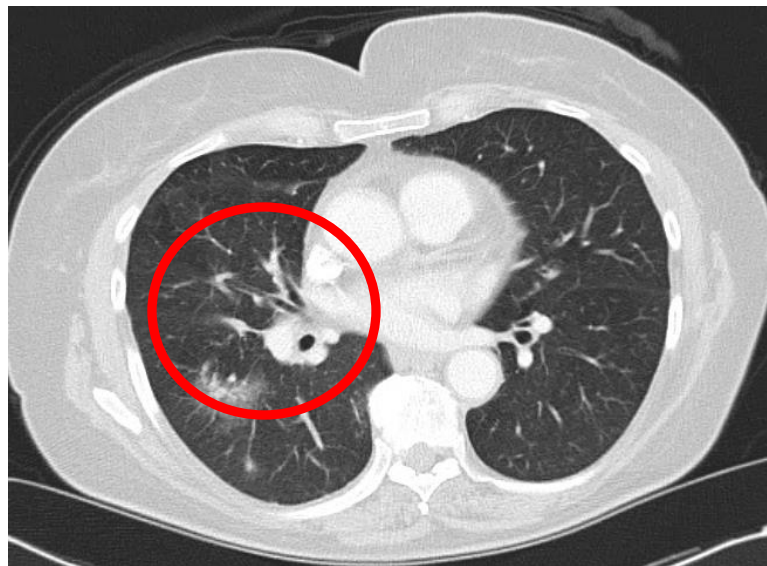
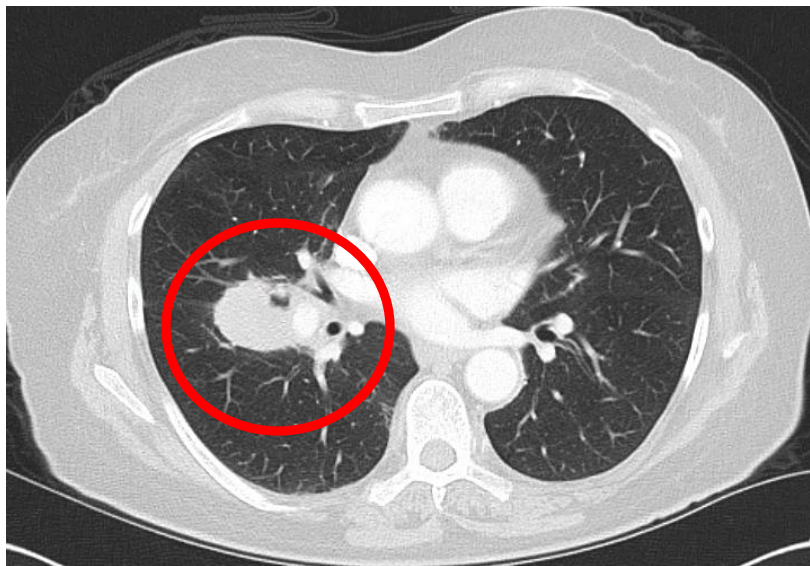


Day -9

Day +11

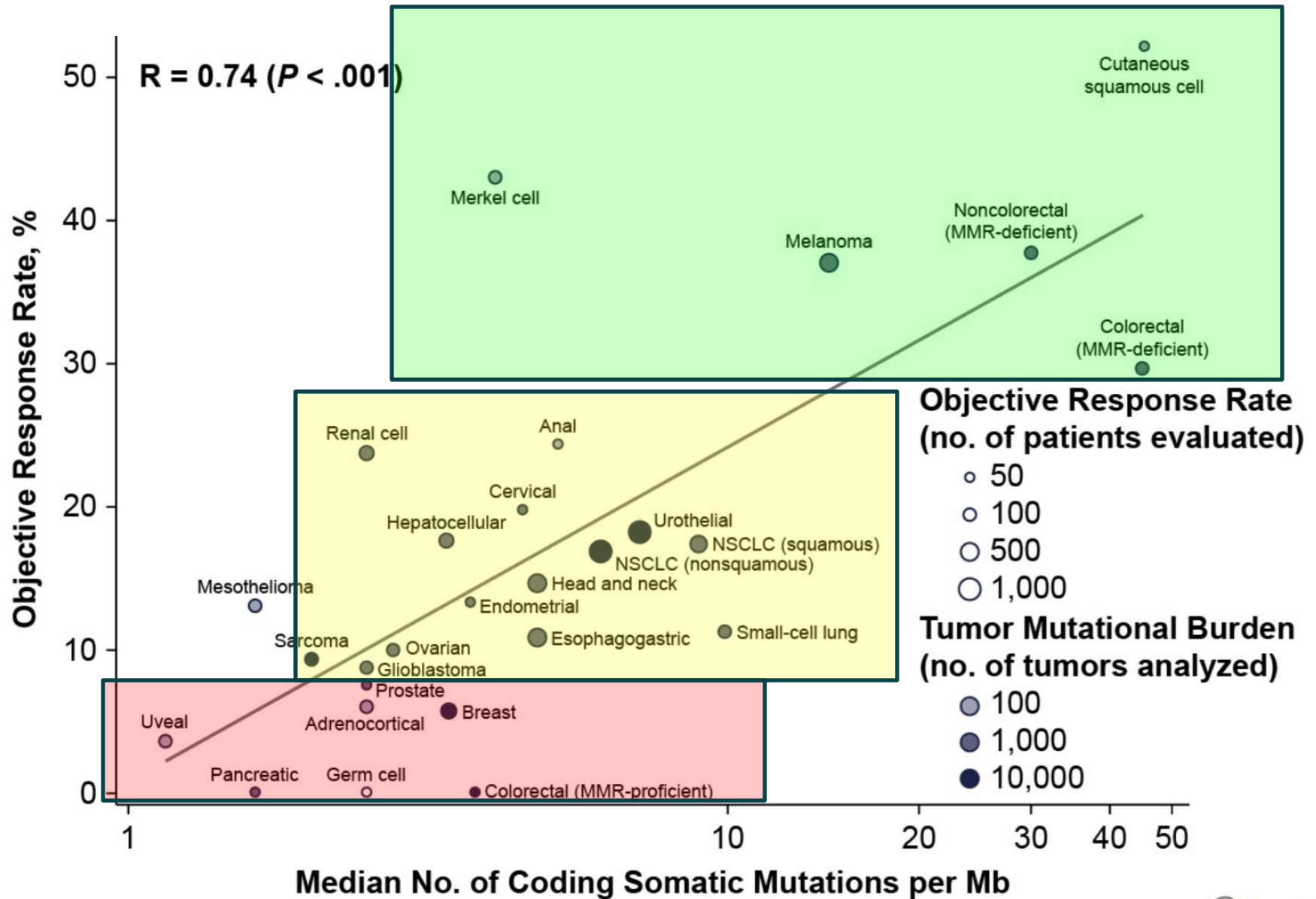
Day +76

Dudley, M. E., et al. (2010, December). CD8 Enriched "Young" Tumor Infiltrating Lymphocytes Can Mediate Regression of Metastatic Melanoma. *Clinical Cancer Research*, 16(24), 6122-6131.



March 2018

May 2018

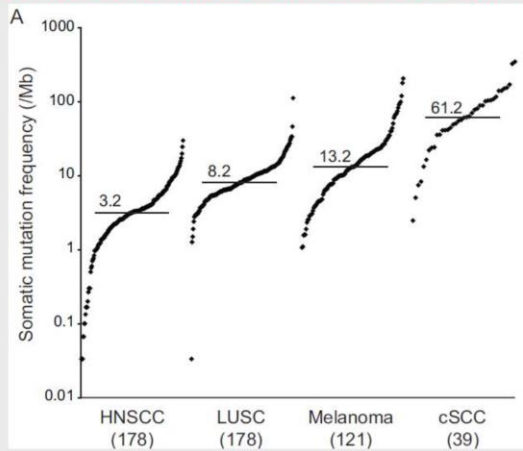


1. Yarchoan M et al. *N Engl J Med.* 2017;377:2500-2501.

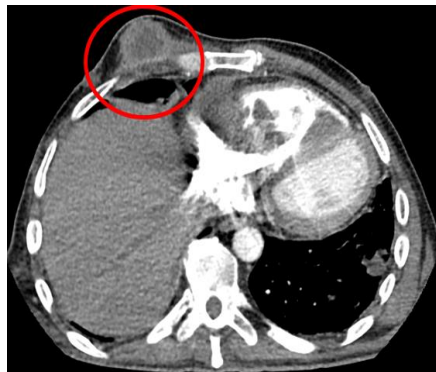
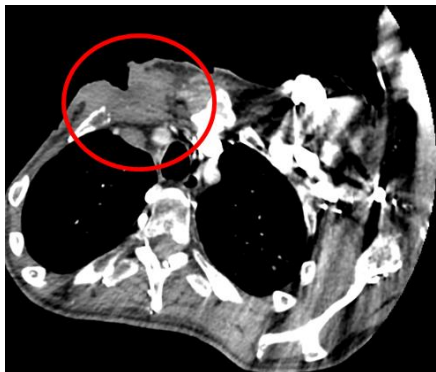
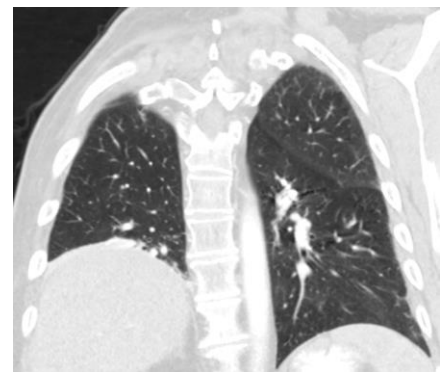
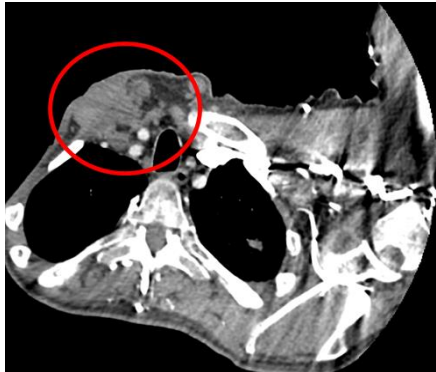
Cutaneous SCC



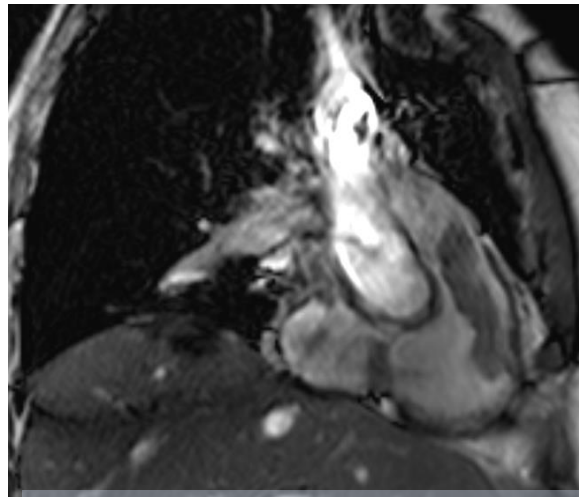
MUTATIONAL LANDSCAPE OF SCC (N= 39)



Cutaneous SCC



Cutaneous SCC



Partial response with avelumab

Baseline



At 5.3 mos



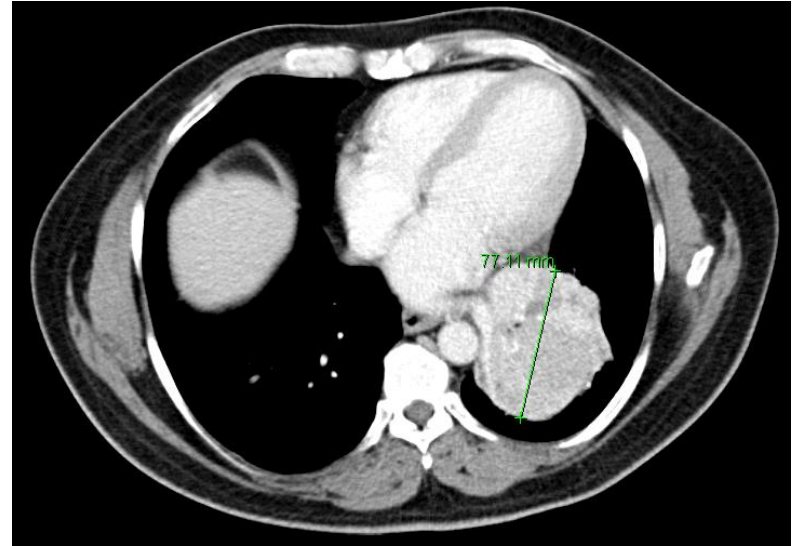
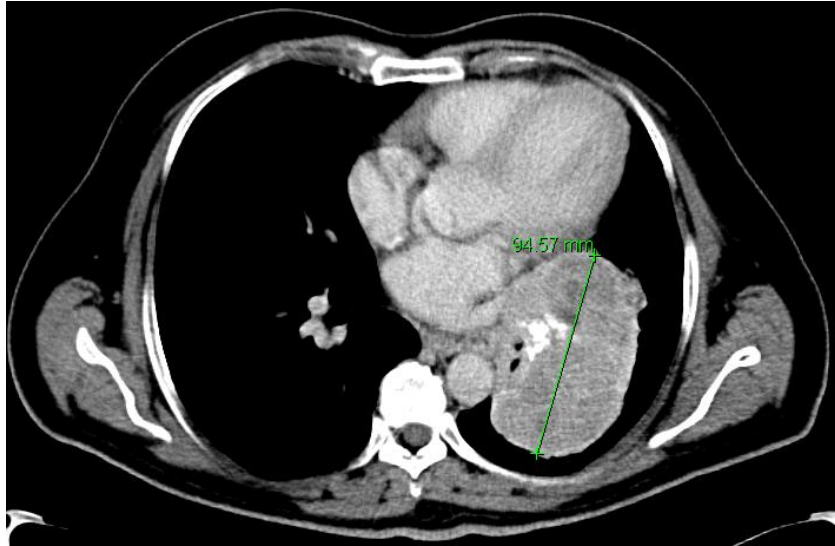
- 82-yo, ECOG PS 1 with visible lesions of the head and neck, MCC diagnosed 8.4 mos before trial enrollment
- Prior CTx with carboplatin/etoposide, resulting in PD
- PD-L1-, MCPyV-, no TILs present
- Received 7 doses of avelumab
- PR by IRC and RECIST v1.1
- At first tumor assessment (week 7), notable tumor regression and pathological CR
- Response ongoing 3.9+ mos (1.4 mos beyond treatment discontinuation)
- One TRAE: grade 1 diaphoresis

PRESENTED AT: **ASCO ANNUAL MEETING '16**

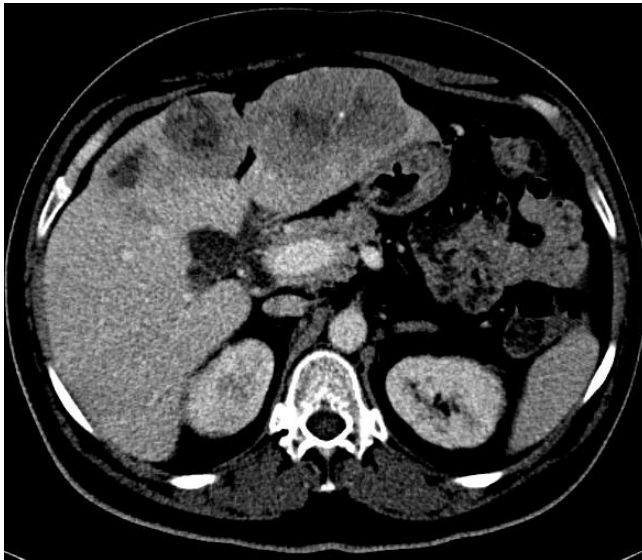
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Presented by: Howard Kaufman

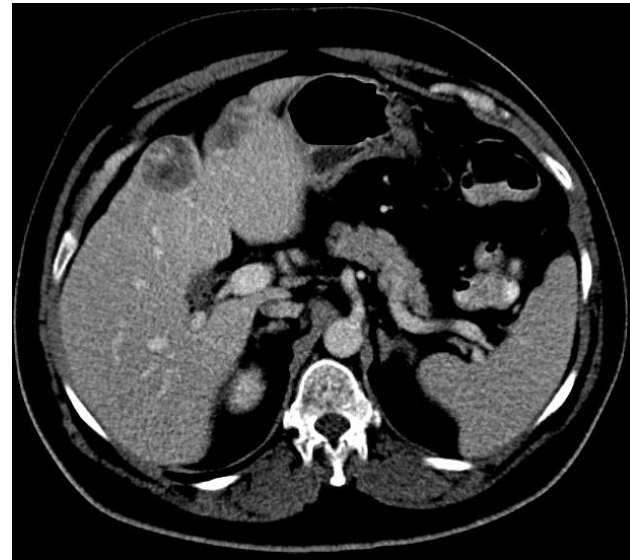
Low grade Pulmonary NET Ki67 of 1%



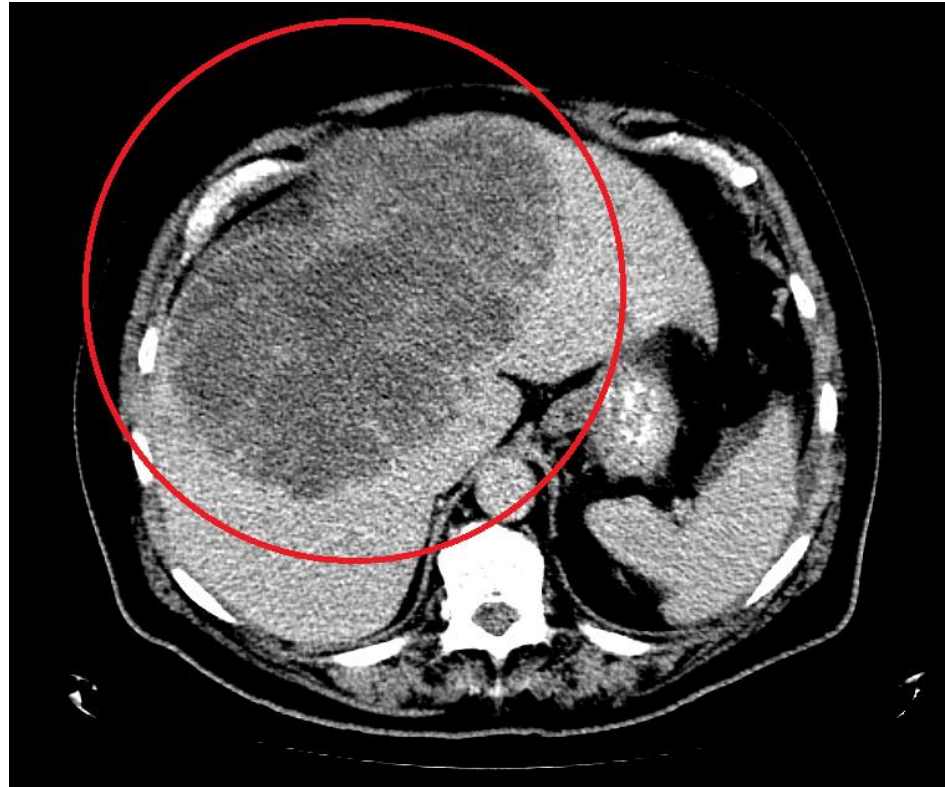
**May
2016**



**Dec
2016**



Pleomorphic Sarcoma

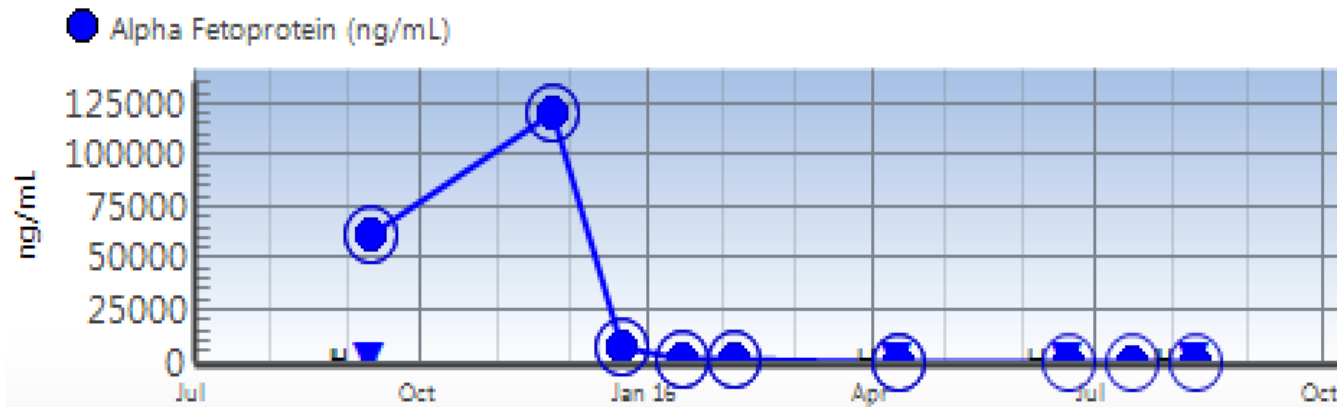


Cholangiocarcinoma



Hepatocellular carcinoma

Alpha Fetoprotein



Patient with metastatic HCC previously treated with multiple chemoembolization, radioembolization, and sorafenib. Treated with PD1 inhibitors when the AFP was greater than 100,000 with a dramatic biochemical response.

Mismatch repair deficiency

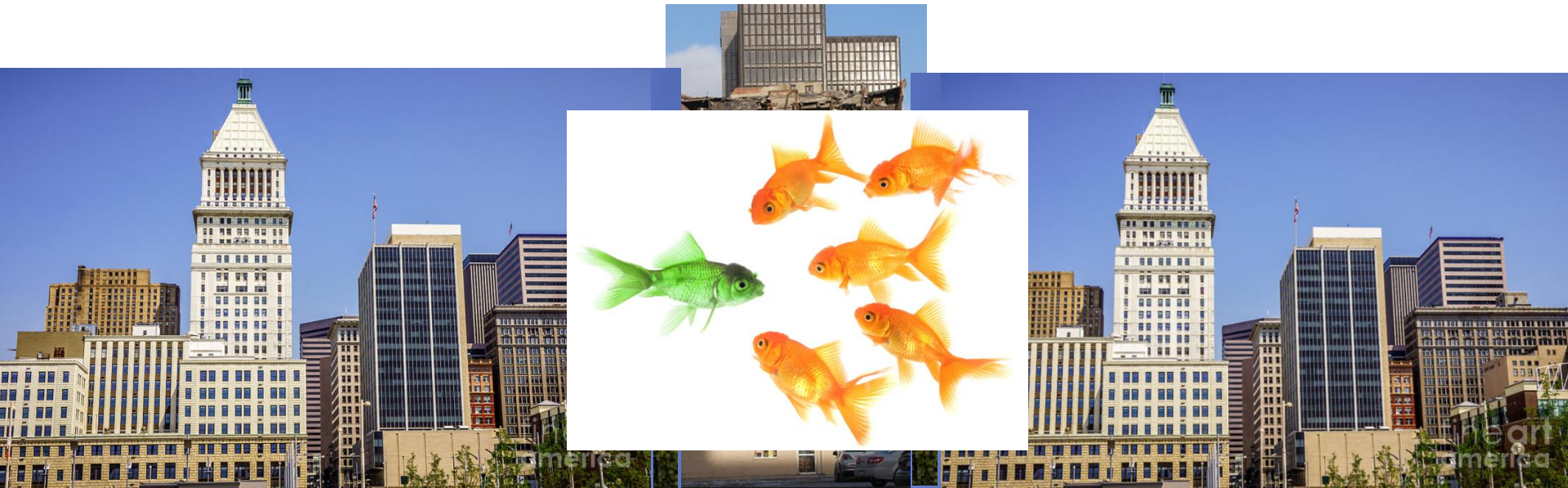
- **MSI – HIGH tumors 15 % of all colon cancers**

- MLH1/3
- MSH2
- PMS1/2
- MSH6

Mean somatic mutations

MSI
MSS

1782 somatic mutations
73 somatic mutations



Response by Tumor Type: Keynote-016

Ampulary	Cholangio	CRC	Endom	Gastric/ Eso	NET	Pancreas	Prostate	Small Intestine
N=4	N=11	N=40	N=15	N=5	N=1	N=8	N=2	N=5
25%	27%	52%	53%	60%	100%	62%	50%	80%

CRC:
RR 52%
2-yr OS 72%

Non-CRC:
RR 54%
2-yr OS 57%

Le DT, et al. *Science*. 2017;357(6349):409-413.

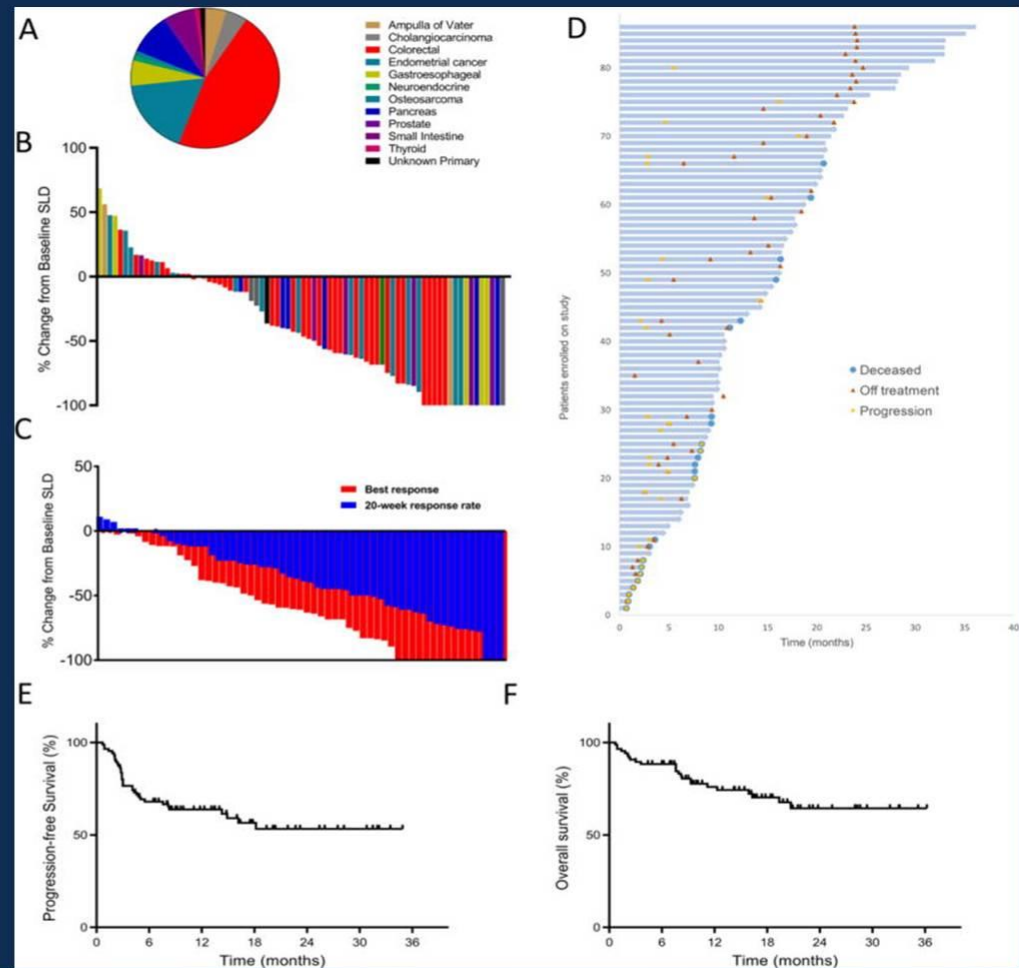
PRESENTED AT: ASCO-SITC **CLINICAL IMMUNO-ONCOLOGY SYMPOSIUM** | #ImmunoOnc18

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Presented by: E. Gabriela Chiorean

Keynote - 016 Pembrolizumab in MSI-High CRC and Non-CRC Cancers

MSI-high by PCR
dMMR by IHC
n=86



Le DT, et al. *Science*. 2017;357(6349):409-413.

PRESENTED AT: ASCO-SITC CLINICAL IMMUNO-ONCOLOGY SYMPOSIUM | #ImmunoOnc18

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Presented by: E. Gabriela Chiorean

FDA approves first cancer treatment for any solid tumor with a specific genetic feature

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**For Immediate
Release**

May 23, 2017

Release

The U.S. Food and Drug Administration today granted accelerated approval to a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.

Keytruda (pembrolizumab) is indicated for the treatment of adult and pediatric patients with unresectable or metastatic solid tumors that have been identified as having a biomarker referred to as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR). This indication covers patients with solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options and patients with colorectal cancer that has progressed following treatment with certain chemotherapy drugs.

Spectrum of PD-1/PD-L1 Antagonist Activity

Active

- Melanoma
- Renal cancer (clear cell and non-clear cell)
- NSCLC: Adenocarcinoma and squamous cell
- Small cell lung cancer
- Head and neck cancer
- Gastric and gastroesophageal junction cancer
- MMR-repair deficient tumors (colon, cholangiocarcinoma)
- Bladder cancer
- Triple-negative breast cancer
- Ovarian cancer
- Hepatocellular carcinoma
- Thymoma
- Mesothelioma
- Cervical cancer
- Hodgkin lymphoma
- Diffuse large cell lymphoma
- Follicular lymphoma
- T-cell lymphoma (cutaneous T-cell lymphomas, peripheral T-cell lymphoma)
- Merkel cell carcinoma

Minimal to no activity

- Prostate cancer
- MMR+ (MSS) colon cancer
- Myeloma
- Pancreatic cancer

Major PD-1/PD-L1 antagonists

- Nivolumab (anti-PD-1)
- Pembrolizumab (anti-PD-1)
- Atezolizumab (MPDL3280, anti-PD-L1)
- Durvalumab (anti-PD-L1)
- Avelumab (anti-PD-L1)



Pillars of Cancer Therapies

