Immune Checkpoint Inhibitors

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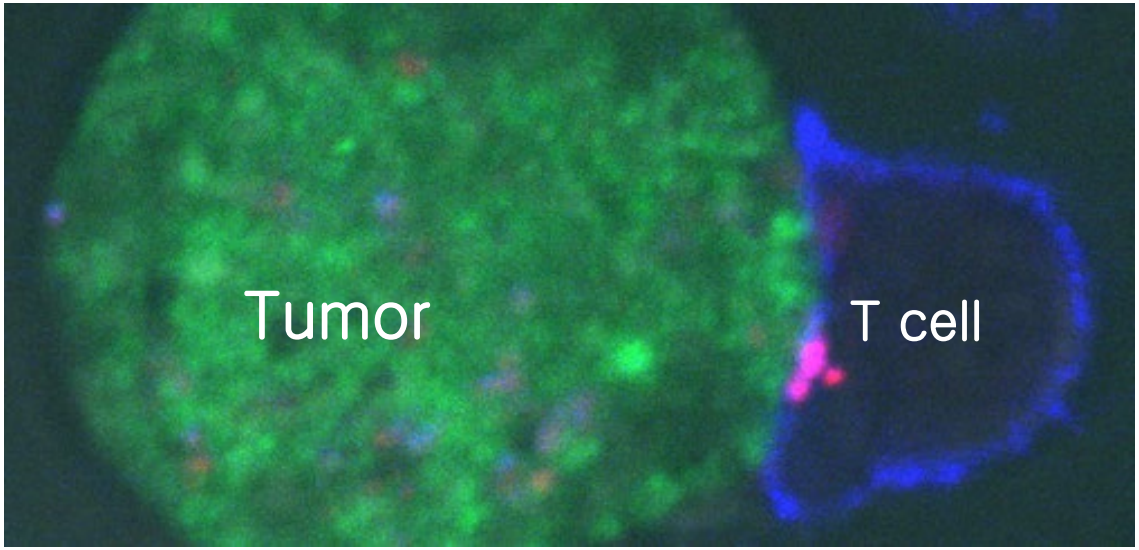
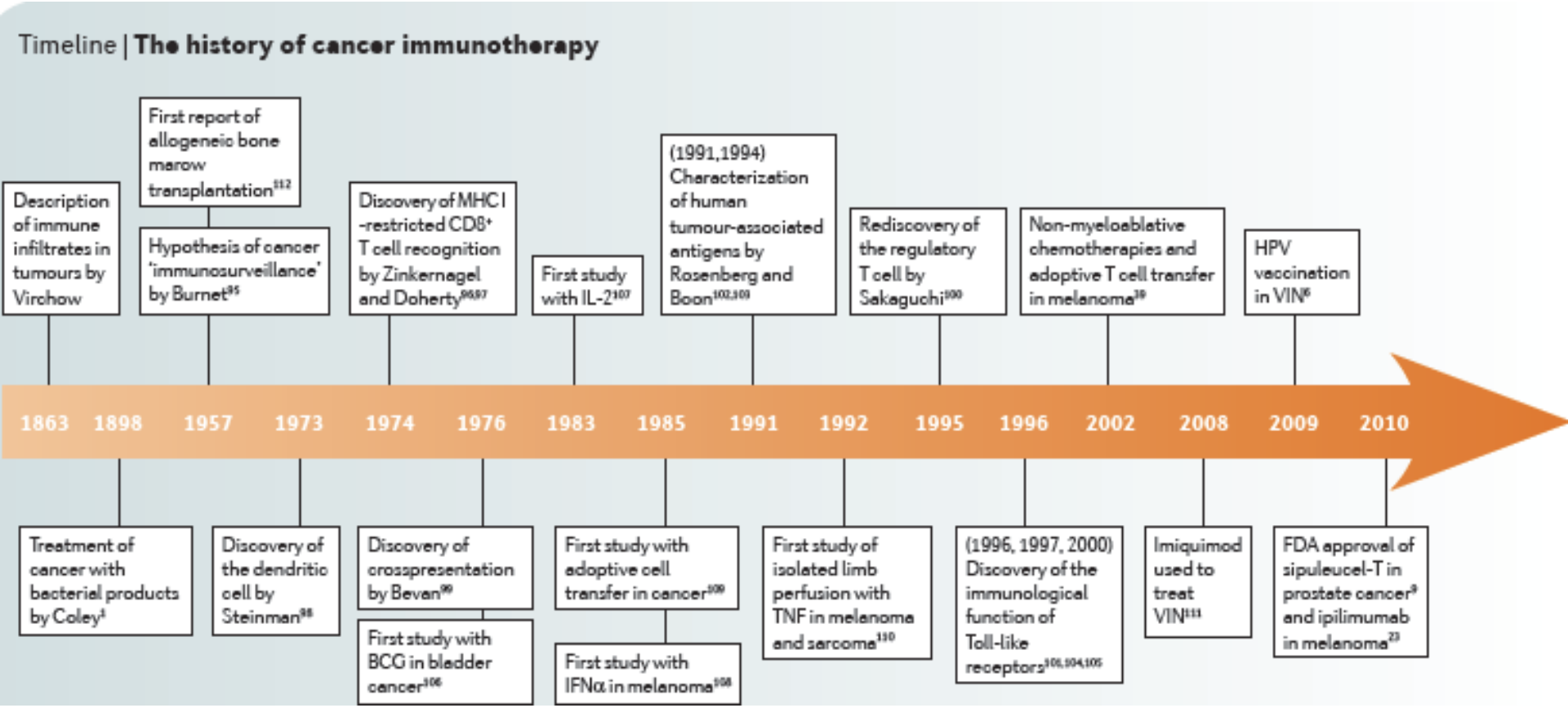


Disclosures

- Bristol Meyer Squibb – Promotional Speaker
- Astrazeneca – Promotional Speaker
- Nektar Therapeutics – Advisor/Consultant
- Xenthera - Advisor

History



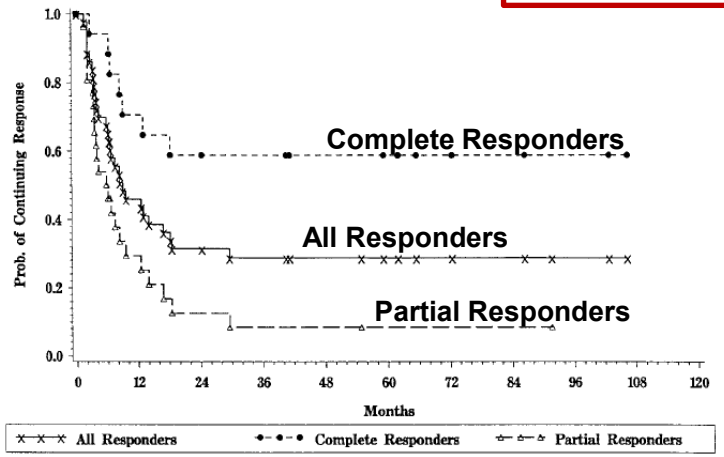
Lesterhuis et al, Nature Review, 2011

Did You Say Cure?

High Dose IL-2

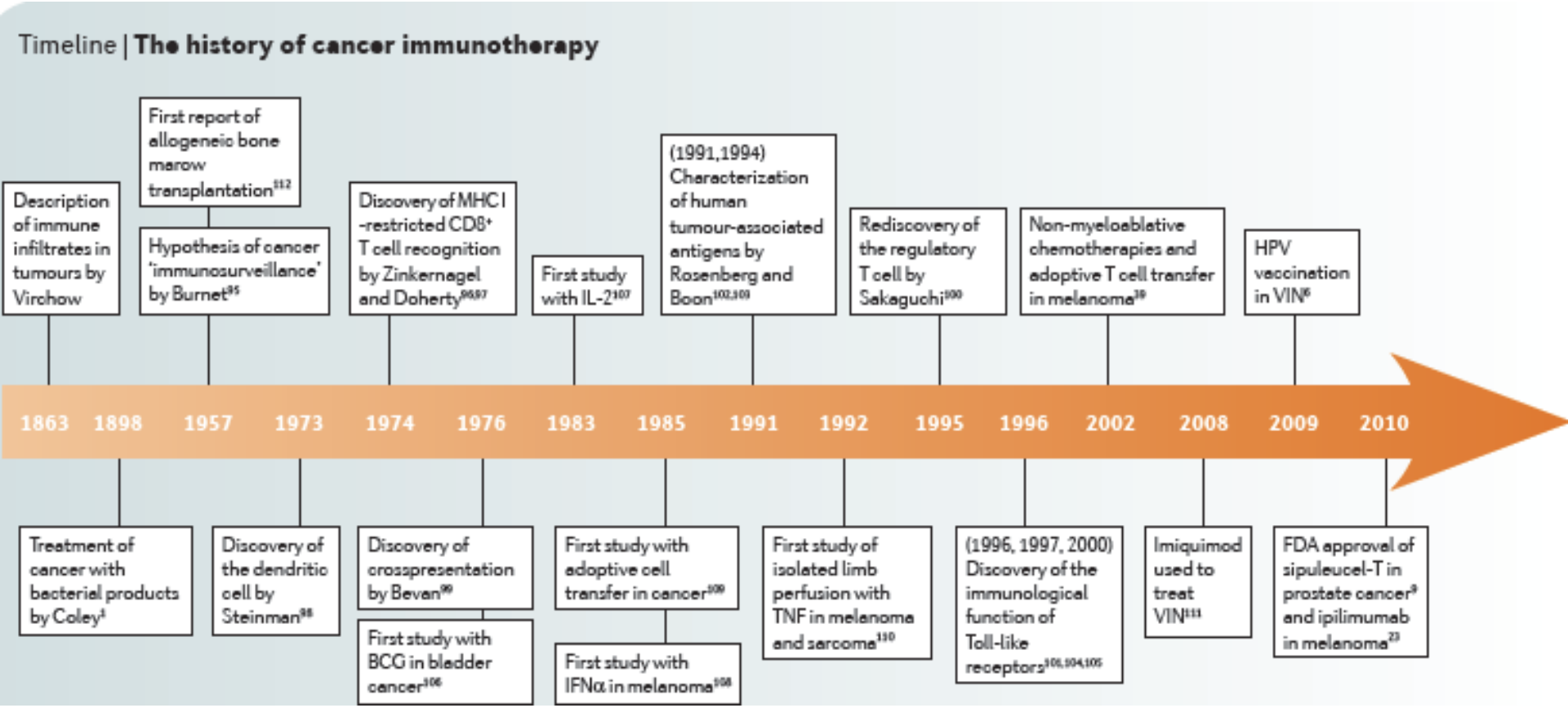
- FDA Approval for Stage IV, 1998
- Cytokine that stimulates effector T-cells
- ORR ~15%, Complete Response Rate (CR) ~6%
- Very Toxic
  - Hypotension, third spacing, renal, respiratory, psych
  - ~2% mortality in initial trials

- Strengths
  - Long-term OS in 5%
  - Proof-of-concept that stage IV melanoma pts can be cured
- Caveats
  - Low response rate
  - Can only be given in specialized centers
  - Patients must be selected carefully



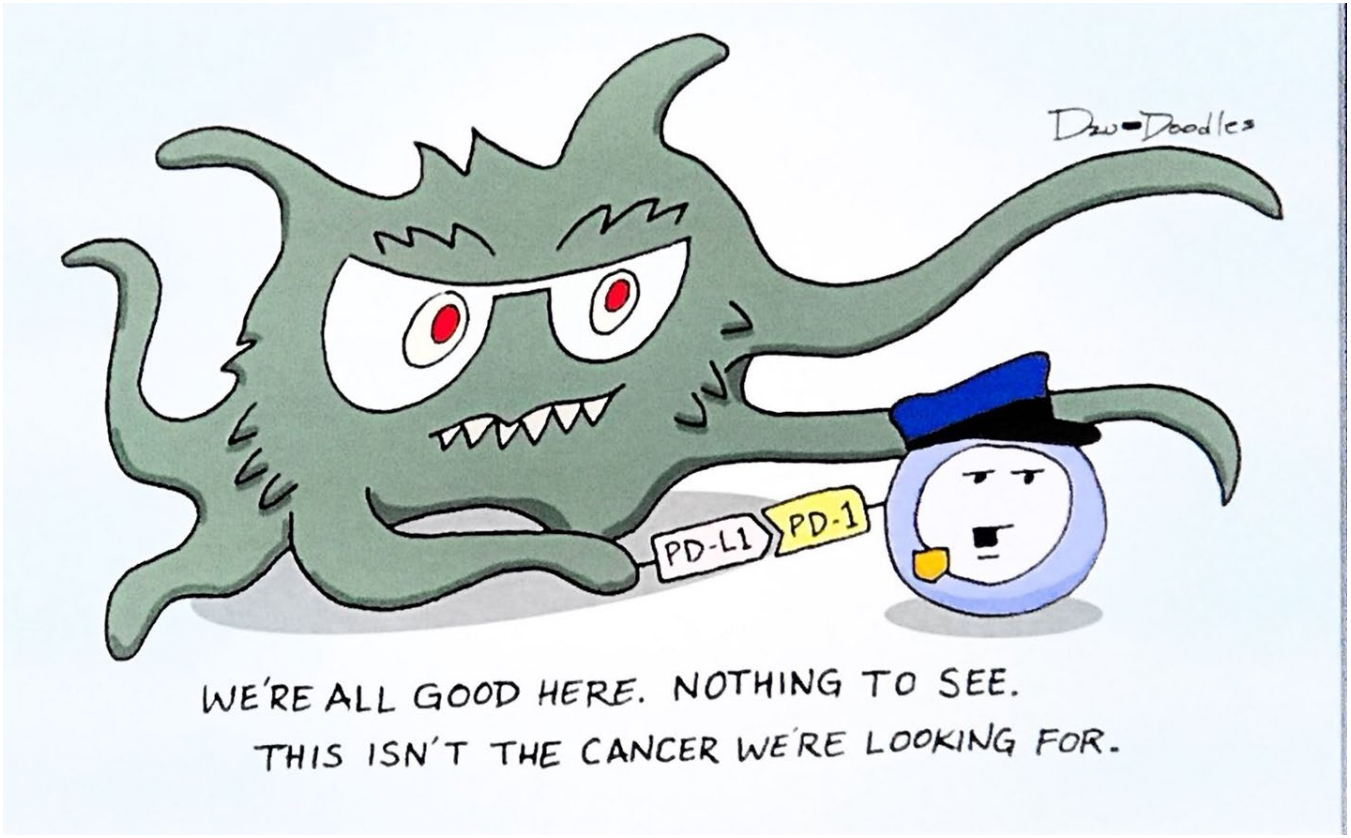
Atkins, *JCO*, 1999

History



Lesterhuis et al, Nature Review, 2011

Immune Checkpoint Blockade

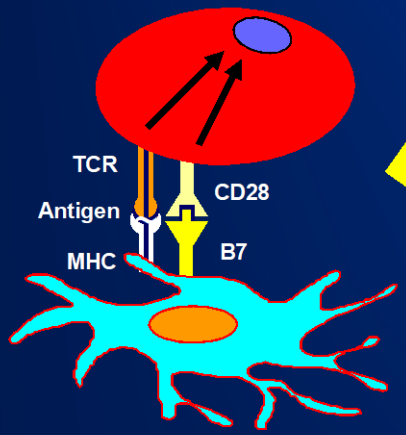


@JackWestMD

CTLA-4 Checkpoint Blockade

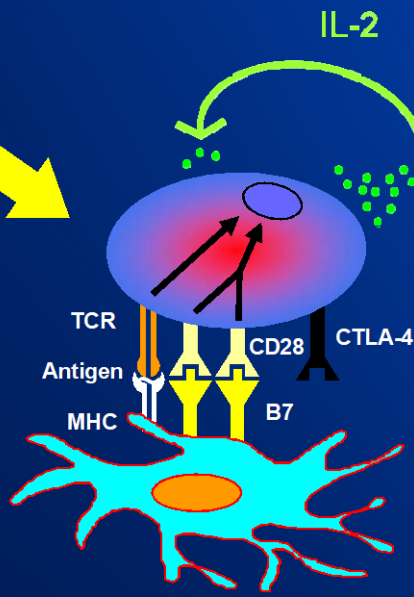
Dr. Jim Allison

Regulation of T cell activation is a Complex Process



Antigen-specific T cell Activation

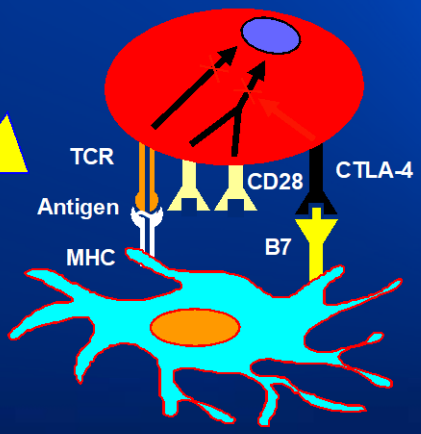
- TCR : Antigen MHC
- CD28 : B7 Co-stimulation



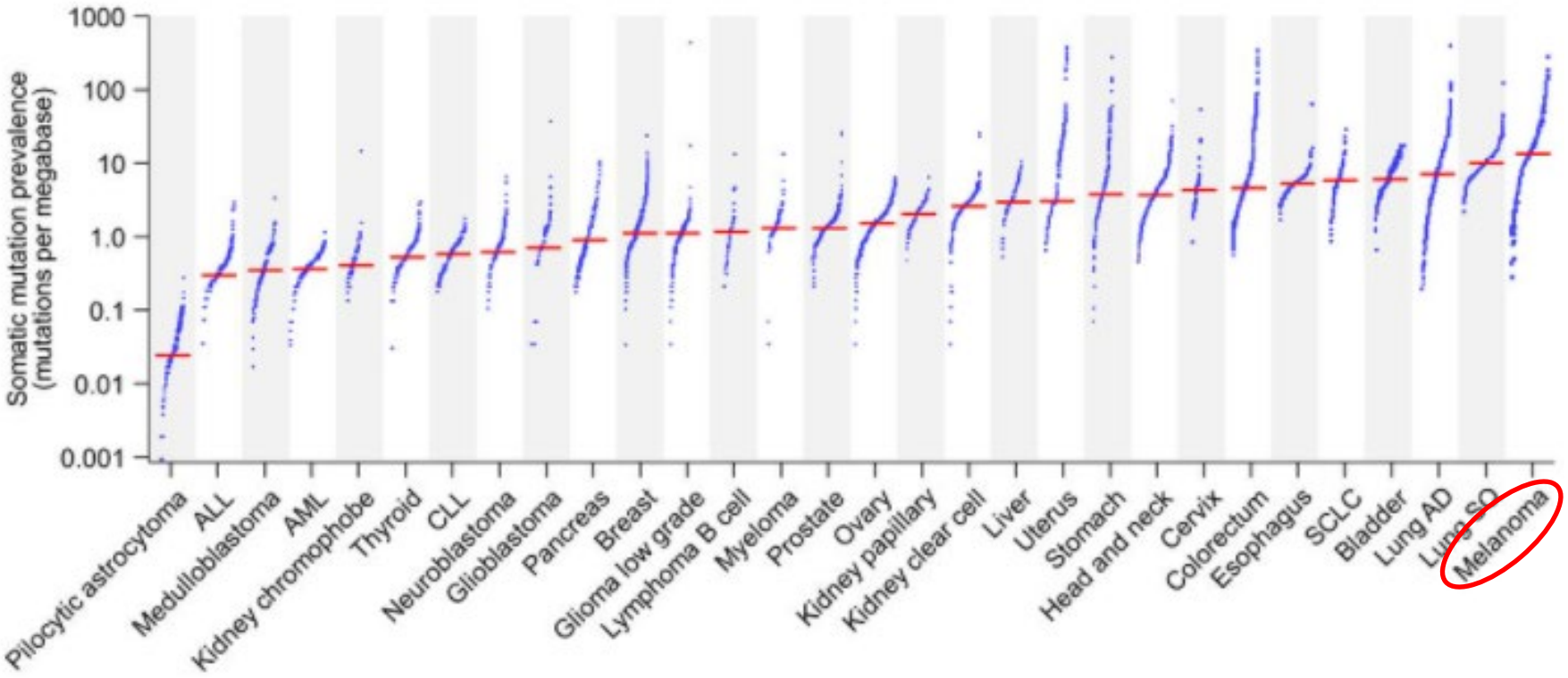
Activated T cell

- IL-2 secretion
- Proliferation
- Effector function
- Induction of CTLA-4

- CTLA-4 : B7 suppression
- Termination of response



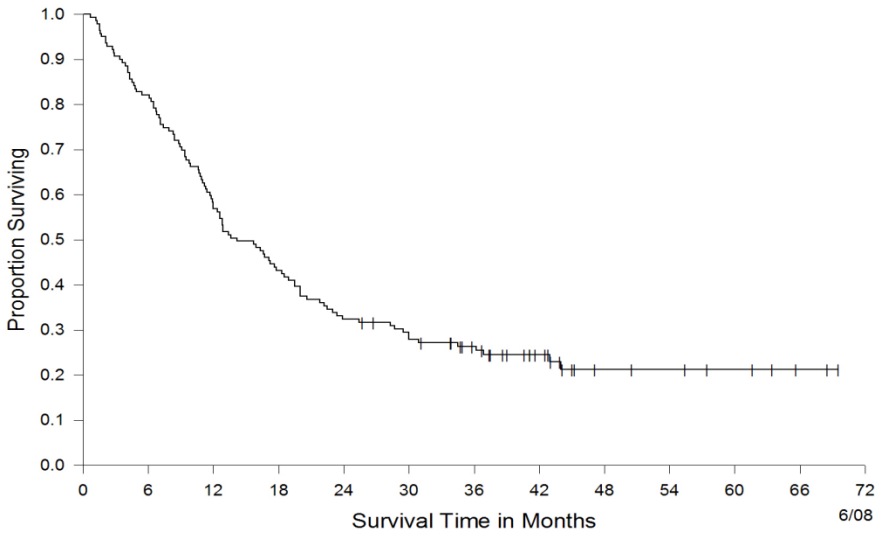
Tumor Mutational Burden



Durable responses and long term Survival

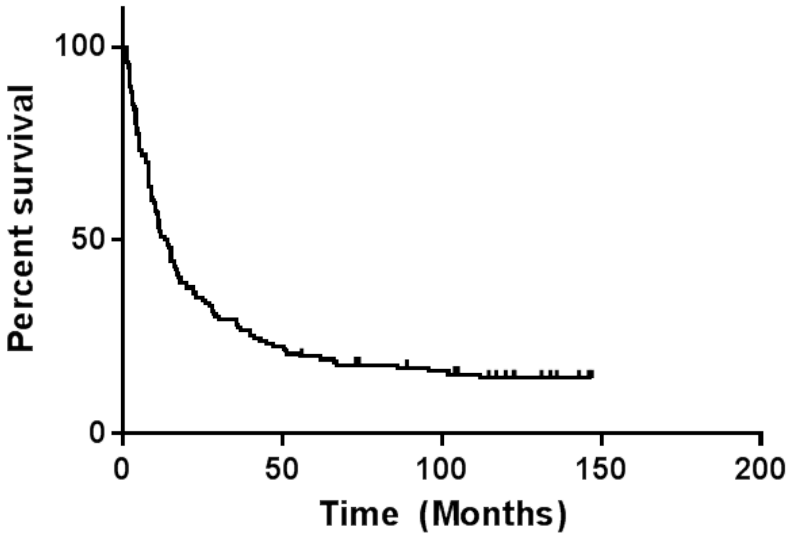
Dr. Jim Allison

Ipilimumab/Yervoy



10 yr survival rate: 22%

Tremelimumab 10 yr outcome
UCLA and MDACC



N= 147 (M1c:54%)
Median OS= 14 months
Response rate: 15%
5 yr survival rate: 19.7%
10 yr survival rate: 18.6%

Hodi et al. ESMO 2013

Prieto P A et al. Clin Cancer Res 2012;18:2039-2047

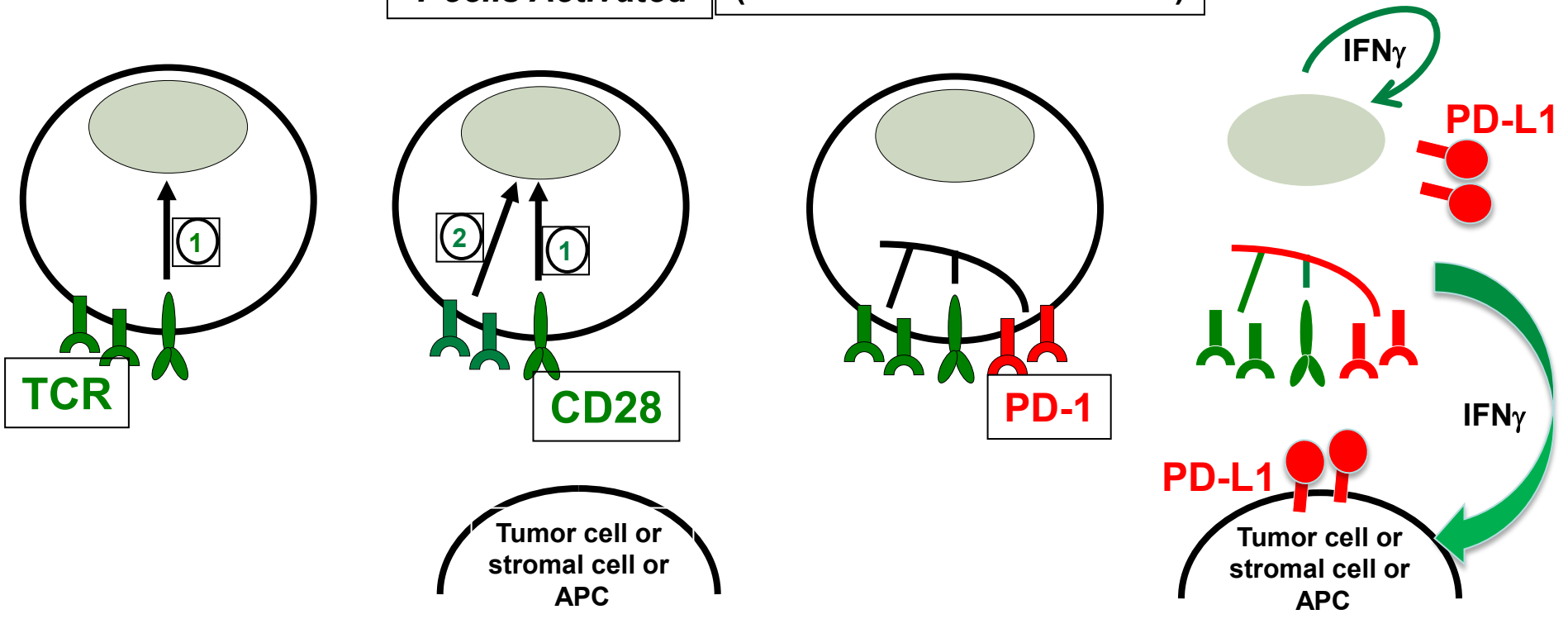
PD-(L)1 Blockade

TCR Signal Only
No Proliferation

Positive Costimulation
Proliferation and T cells Activated

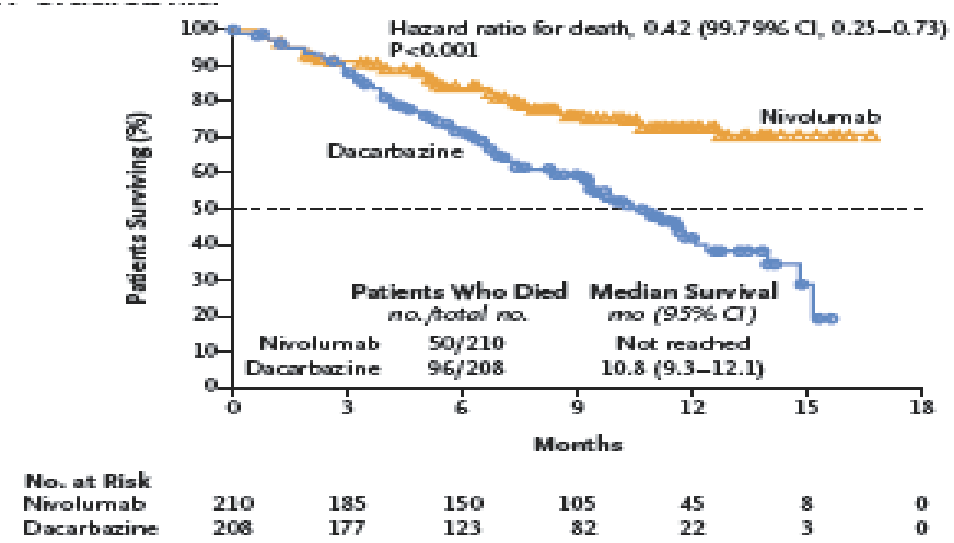
Activated T cells upregulate checkpoint molecules (such as CTLA-4 and PD-1)

Activated T cells make IFNγ, which increases PD-L1 expression

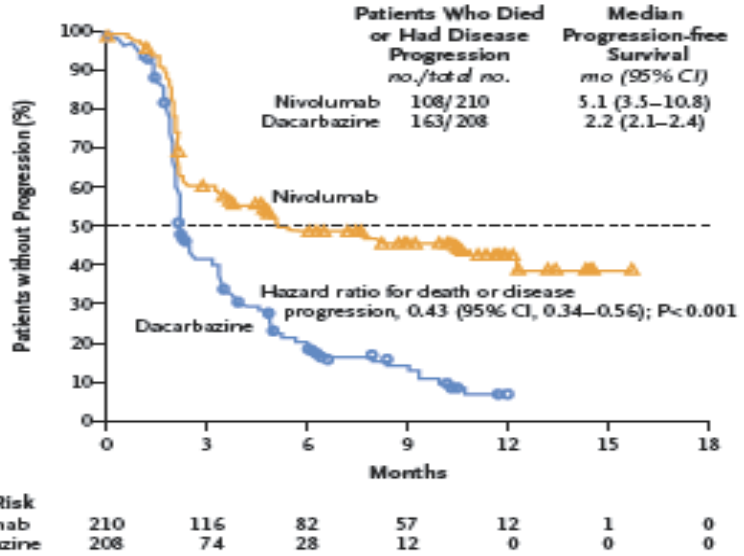


PD-(L)1 Blockade

Overall Survival: HR 0.42



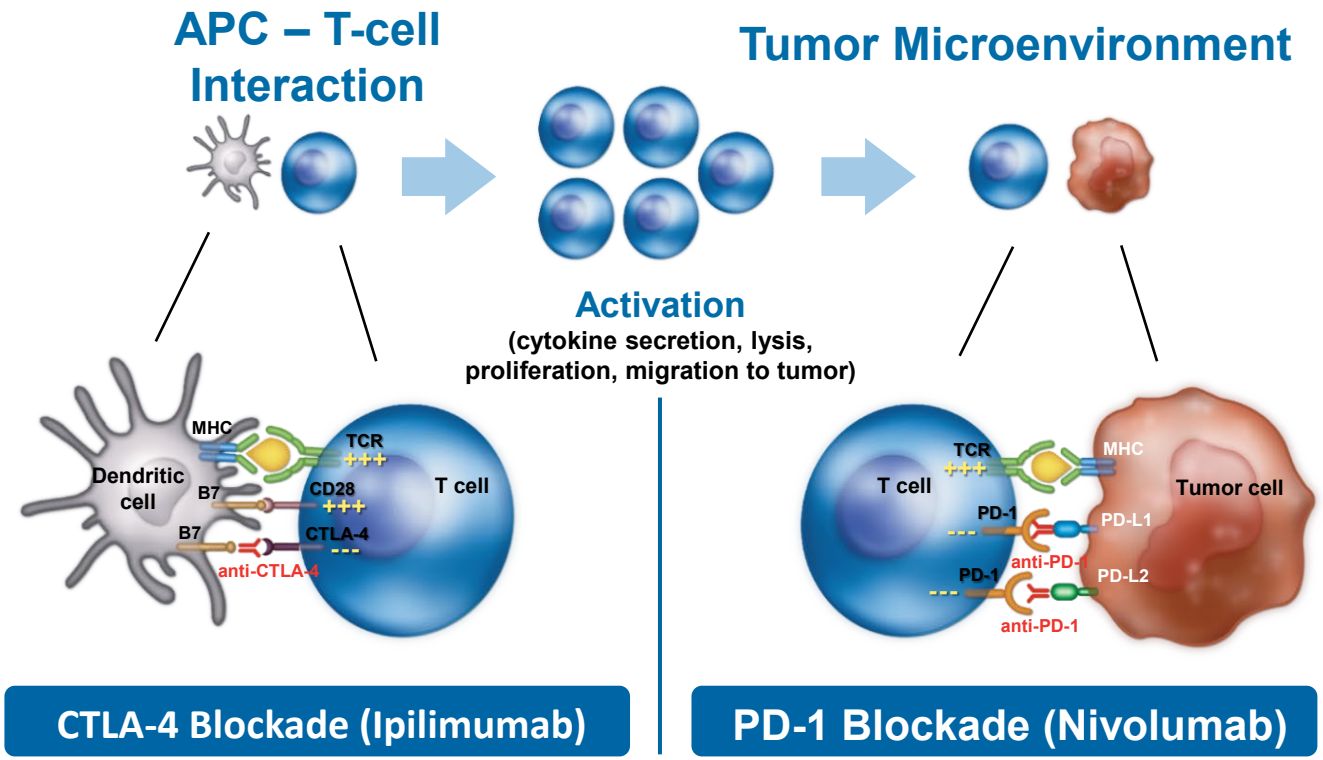
Progression-Free Survival: HR 0.43

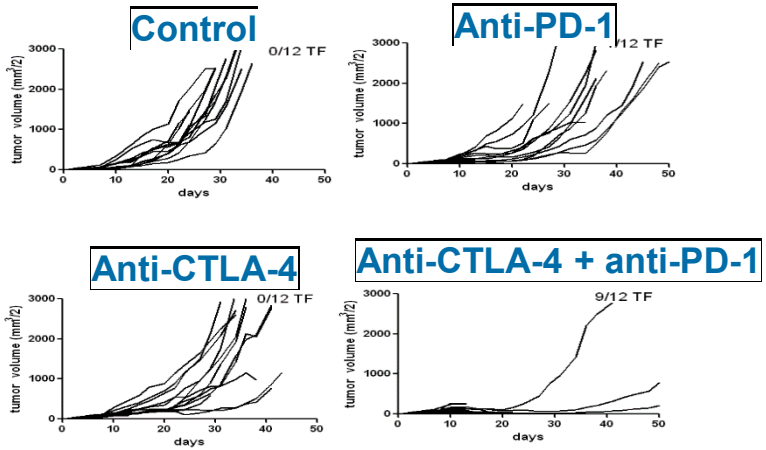


	ORR	CR	PR	SD	PD
Nivolumab/Opdivo	40%	7.6%	32.4%	16.7%	32.9%
Chemotherapy	13.9%	1.0%	13.0%	22.1%	48.6%

Long, et al SMR 2014; Robert, *NEJM,* 2014

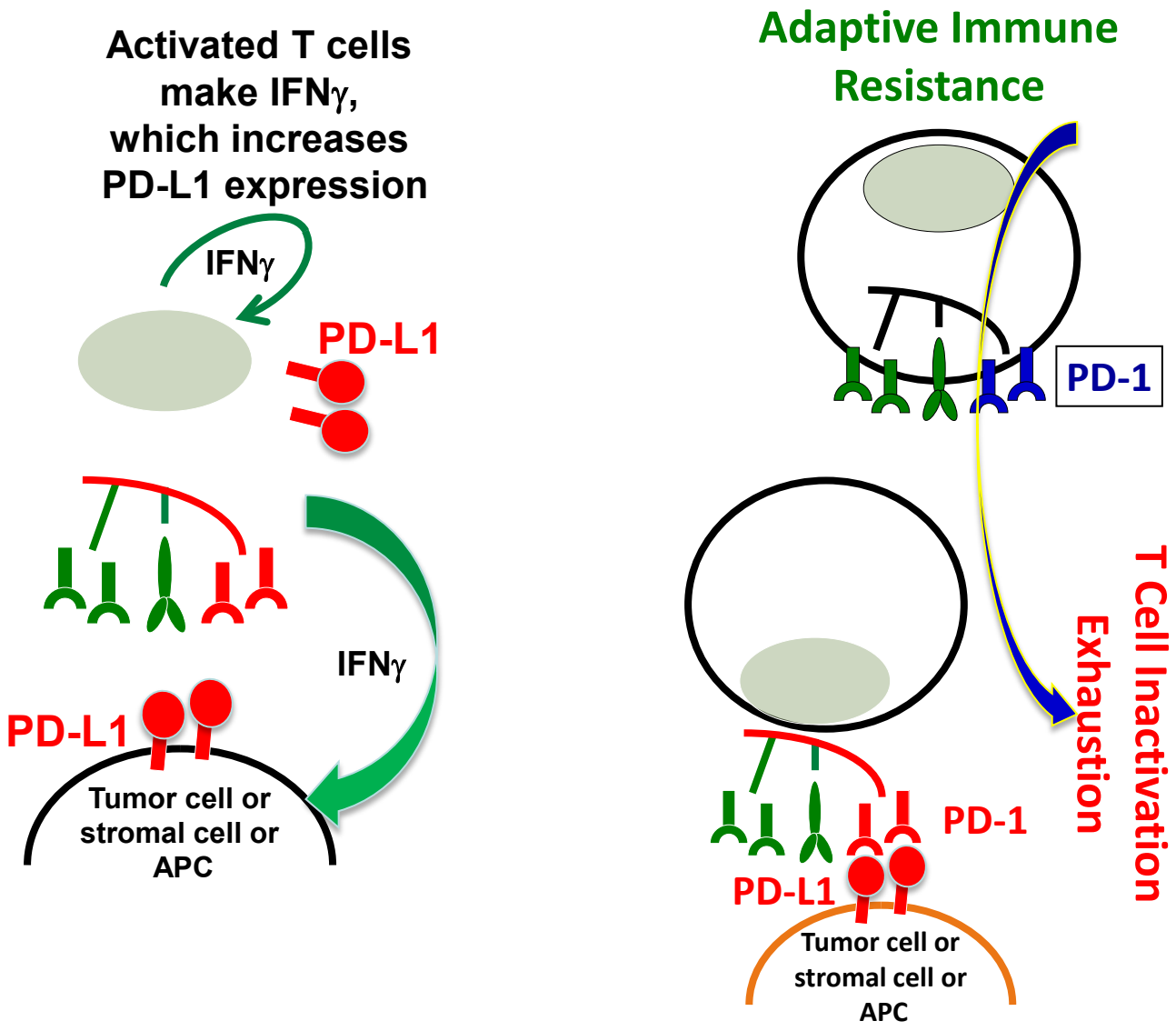
Mechanistic Differences CTLA-4 vs PD-1



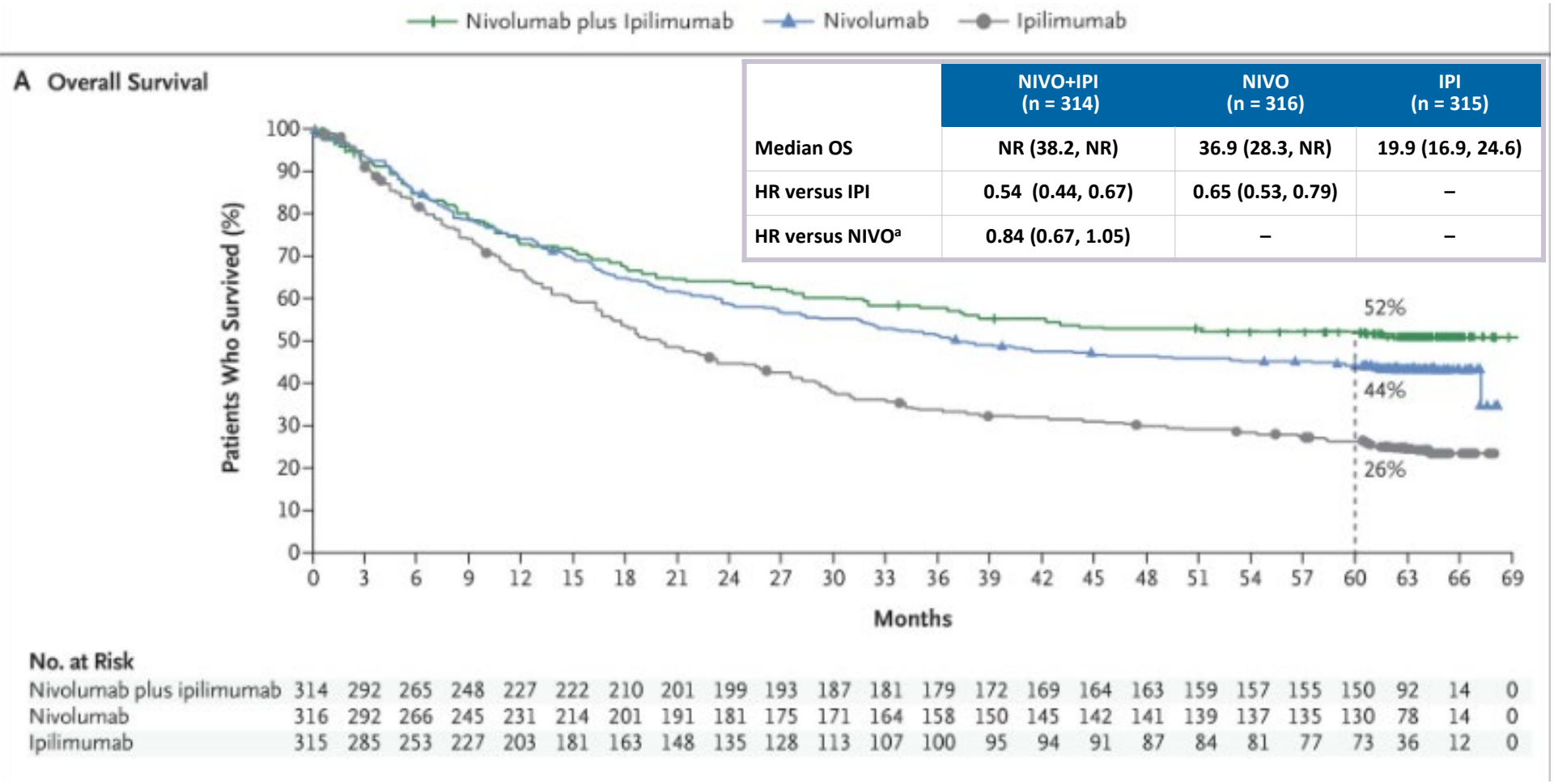


1. Korman et al. *J Immunol* 2007;178:48.37.
2. Selby et al. ASCO 2013, abs 3061.

Mechanistic Differences CTLA-4 vs PD-1



Ipilimumab + Nivolumab – Checkmate 067



	NIVO+IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median OS	NR (38.2, NR)	36.9 (28.3, NR)	19.9 (16.9, 24.6)
HR versus IPI	0.54 (0.44, 0.67)	0.65 (0.53, 0.79)	–
HR versus NIVO[a]	0.84 (0.67, 1.05)	–	–

Larkin, et. al. 2019 NEJM

Combination Ipilimumab/Nivolumab AE Data

Table 3. Adverse Events.*

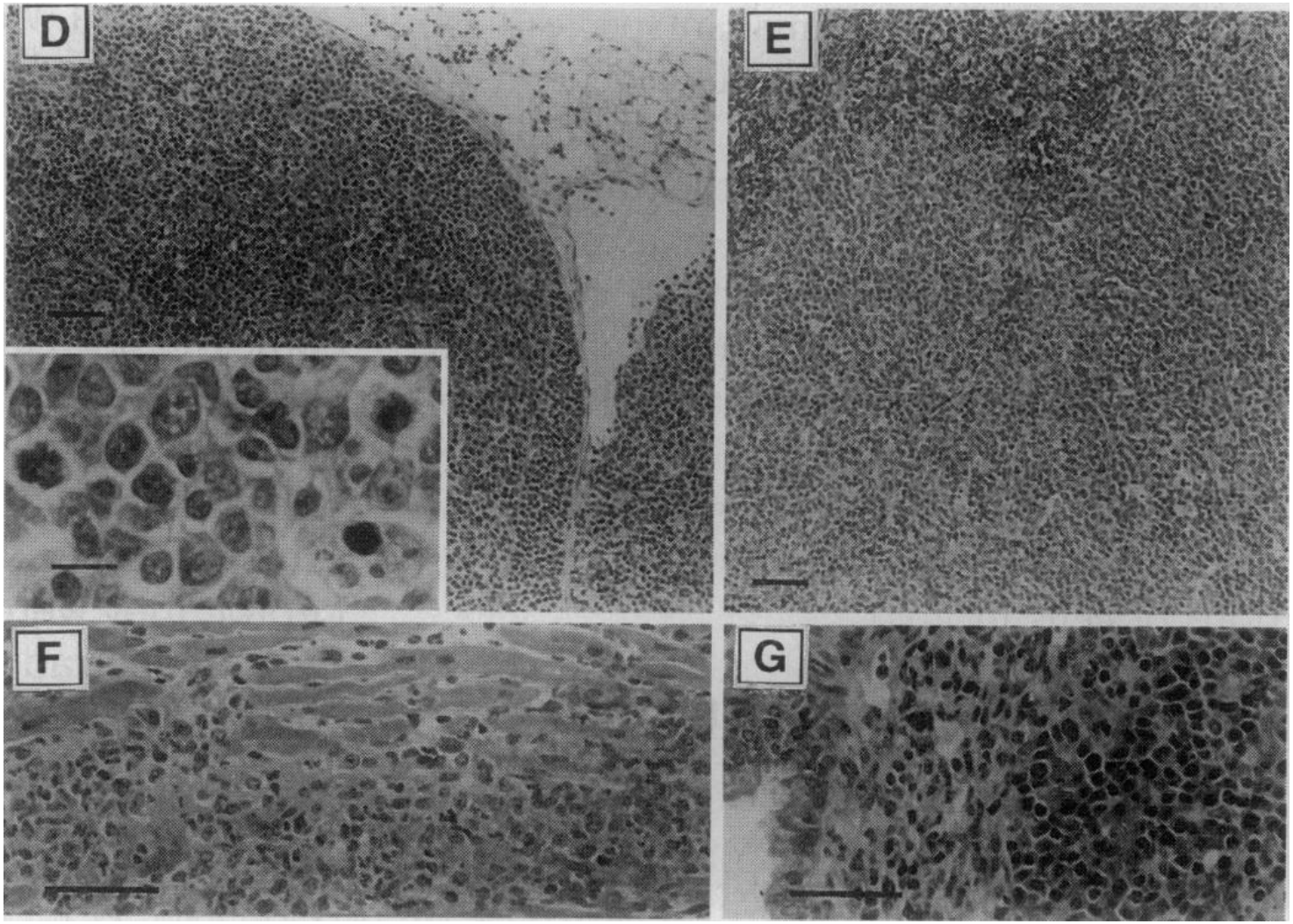
Event	Nivolumab (N=313)		Nivolumab plus Ipilimumab (N=313)		Ipilimumab (N=311)	
	Any	Grade 3 or 4	Any	Grade 3 or 4	Any	Grade 3 or 4
	number of patients with event (percent)					
Any adverse event	311 (99.4)	136 (43.5)	312 (99.7)	215 (68.7)	308 (99.0)	173 (55.6)
Treatment-related adverse event†	257 (82.1)	51 (16.3)	299 (95.5)	172 (55.0)	268 (86.2)	85 (27.3)
Diarrhea	60 (19.2)	7 (2.2)	138 (44.1)	29 (9.3)	103 (33.1)	19 (6.1)
Fatigue	107 (34.2)	4 (1.3)	110 (35.1)	13 (4.2)	87 (28.0)	3 (1.0)
Pruritus	59 (18.8)	0	104 (33.2)	6 (1.9)	110 (35.4)	1 (0.3)
Rash	81 (25.9)	2 (0.6)	126 (40.3)	15 (4.8)	102 (32.8)	6 (1.9)
Nausea	41 (13.1)	0	81 (25.9)	7 (2.2)	50 (16.1)	2 (0.6)
Pyrexia	18 (5.8)	0	58 (18.5)	2 (0.6)	21 (6.8)	1 (0.3)
Decreased appetite	34 (10.9)	0	56 (17.9)	4 (1.3)	39 (12.5)	1 (0.3)
Increase in alanine aminotransferase level	12 (3.8)	4 (1.3)	55 (17.6)	26 (8.3)	12 (3.9)	5 (1.6)
Vomiting	20 (6.4)	1 (0.3)	48 (15.3)	8 (2.6)	23 (7.4)	1 (0.3)
Increase in aspartate aminotransferase level	12 (3.8)	3 (1.0)	48 (15.3)	19 (6.1)	11 (3.5)	2 (0.6)
Hypothyroidism	27 (8.6)	0	47 (15.0)	1 (0.3)	13 (4.2)	0
Colitis	4 (1.3)	2 (0.6)	37 (11.8)	24 (7.7)	36 (11.6)	27 (8.7)
Arthralgia	24 (7.7)	0	33 (10.5)	1 (0.3)	19 (6.1)	0
Headache	23 (7.3)	0	32 (10.2)	1 (0.3)	24 (7.7)	1 (0.3)
Dyspnea	14 (4.5)	1 (0.3)	32 (10.2)	2 (0.6)	13 (4.2)	0
Treatment-related adverse event leading to discontinuation	24 (7.7)	16 (5.1)	114 (36.4)	92 (29.4)	46 (14.8)	41 (13.2)

* The safety population included all the patients who received at least one dose of study drug. The severity of adverse events was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

† The treatment-related adverse events listed here were those reported in at least 10% of the patients in any of the three study groups.

Larkin J et al. N Engl J Med 2015. DOI: 10.1056/NEJMoa1504030

Lymphoproliferative Disorders with Early Lethality in Mice Deficient in Ctla-4



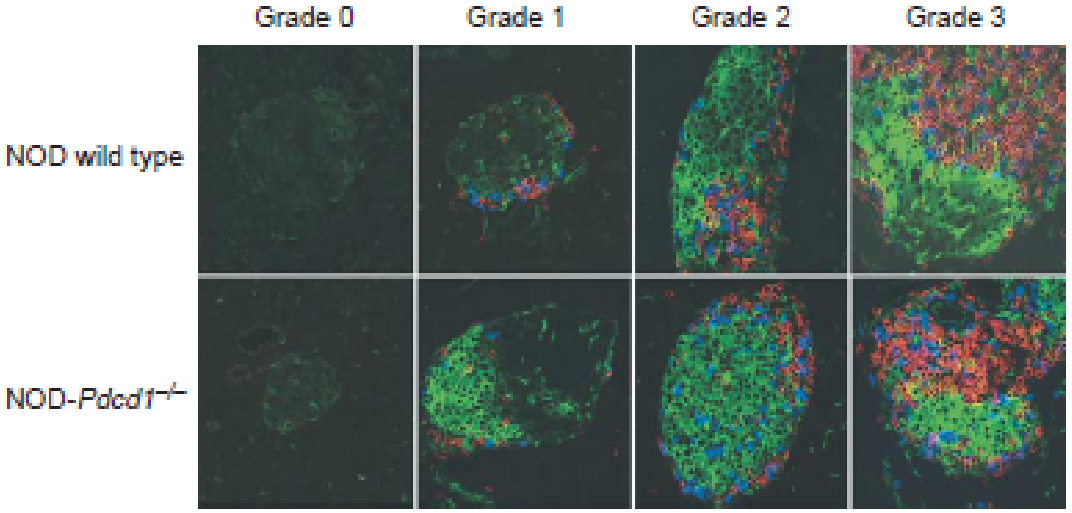
*Waterhouse P et al SCIENCE * VOL. 270 * 10 NOVEMBER 1995*

PD-1/L-1 ko mice
Higher risk for AI but compatible with life

Table 1. Autoimmune phenotypes of *Pdcd1*$^{-/-}$ mice

Genotype	Phenotype	Age at onset	Penetrance	Refs
C57BL/6-*Pdcd1*$^{-/-}$	SLE-like	>6 months	~50%	[29]
BALB/c-*Pdcd1*$^{-/-}$	DCM	5–25 weeks	10–60%[a]	[30,49]
	Gastritis	10–20 weeks	~80%	[49]
NOD-*Pdcd1*$^{-/-}$	Diabetes	4–10 weeks	100%	[33]
BALB/c-*Fcgr2b*$^{-/-}$*Pdcd1*$^{-/-}$	Hydronephrosis	10–20 weeks	35%	[49]
2C-*Pdcd1*$^{-/-}$H-2$^{b/d}$	GVH-like	5–10 weeks	25–100%[b]	[29]

[a]The penetrance of dilated cardiomyopathy (DCM) is variable among the different colonies of mice examined ([49] and our unpublished observations). [b]The penetrance of GVH-like disease is variable depending on the genetic background (our unpublished observations).



Long term Survival Stage IV Melanoma

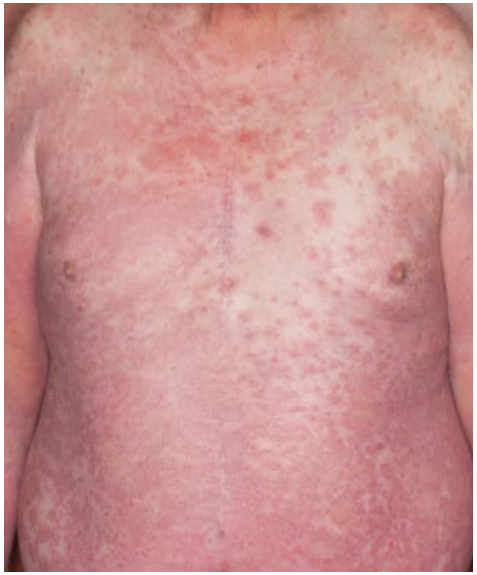
	5 Year Survival	10 Year Survival	
Before Immune Checkpoint Inhibitors	6.7-9.5%	2.5-6.0%	Balch et al. JCO 2001
Ipilimumab (Yervoy®) – approved 2011	20-26%	~ 21-22%	Hodi et al. ESMO 2013
PD-1 Inhibitors – approved 2014	34-44%	NR	Long et al. ASCO 2018 Hodi et al. AACR 2016 Larkin J. et al., NEJM 2019
CTLA-4 + PD-1 Inhibitors – approved 2015	52%	NR	Larkin J. et al., NEJM 2019

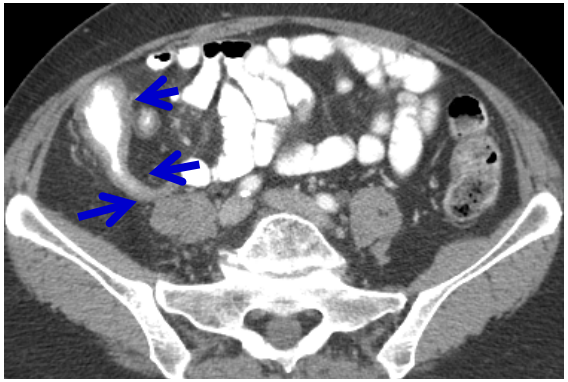
Cancers with Immune Checkpoint Inhibitors Approved

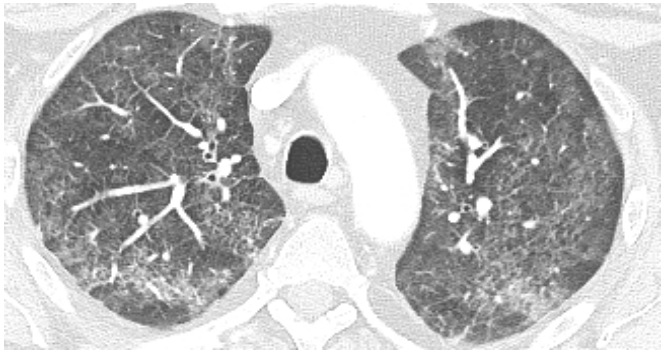
- Melanoma
- Lung Cancer
- Renal Cancer
- Head and Neck Cancer
- Bladder Cancer
- Liver Cancer
- Gastric Cancer
- Colon Cancer (Microsatellite unstable)
- Breast Cancer – Triple Negative
- Squamous Cell Carcinoma of Skin
- Merkel Cell Skin Cancer
- Cervical Cancer
- Hodgkin Lymphoma
- All cancers with Microsatellite instability

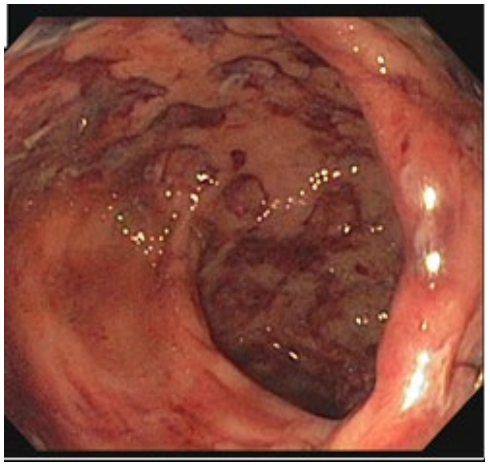
irAEs and Autoimmunity

irAEs from CPI therapies results from immune dysregulation targeting normal tissue antigens.



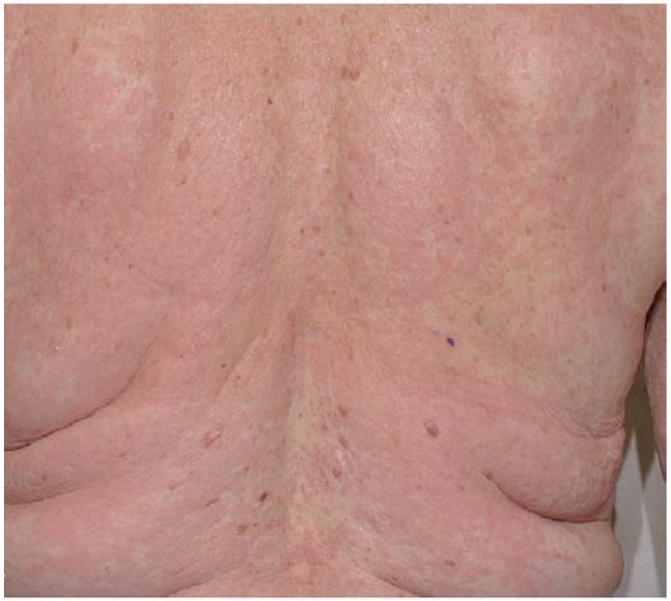


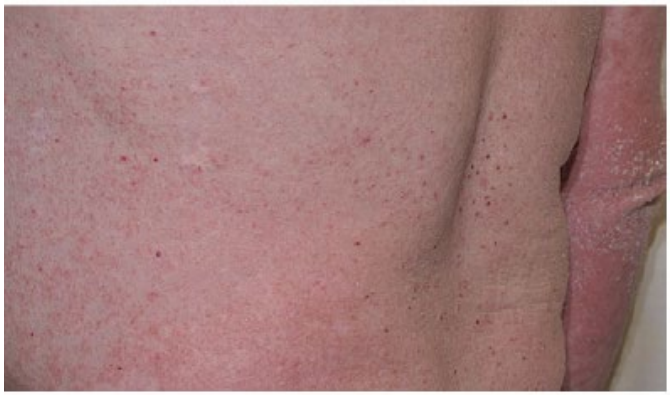




Images courtesy of Dr. Adi Diab, Melanoma Medical Oncology Department MD Anderson Cancer Center

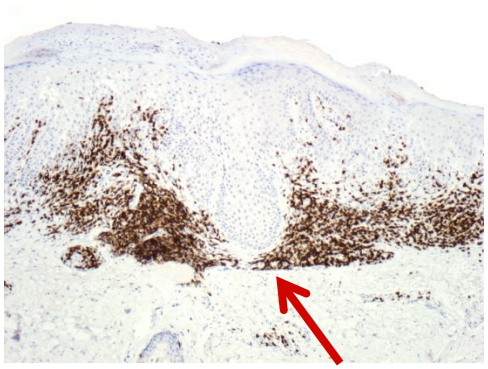
Skin Rash

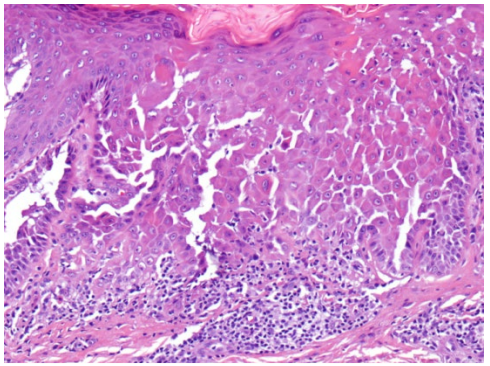




Maculopapular rash

- Lichenoid dermatitis
- Bullous Pemphigoid
- Pustular Psoriasis
- De novo Grover's disease
- Stevens-Johnson Syndrome/toxic epidermal necrolysis (SJS/TEN
- eosinophilia and systemic symptoms (DRESS),





CD3 +T cell Infiltrate

Umeura M ..Diab A JITC 2017

Dermatitis Management

DERMATOLOGIC

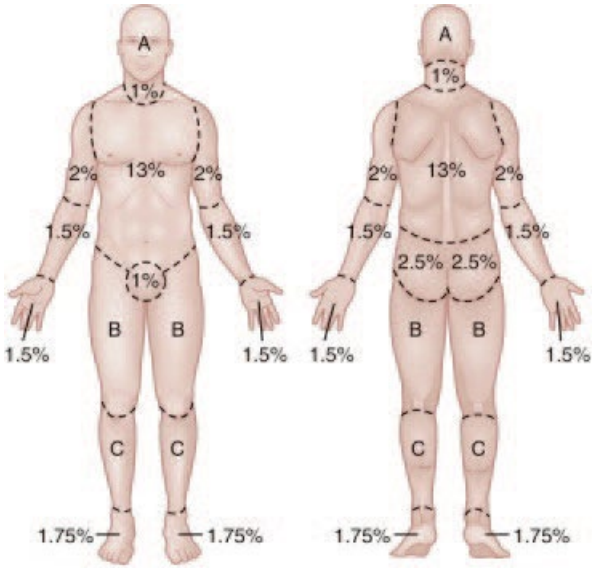
Maculopapular rash/dermatitis

Grade	Description	Management	Specialist referral?

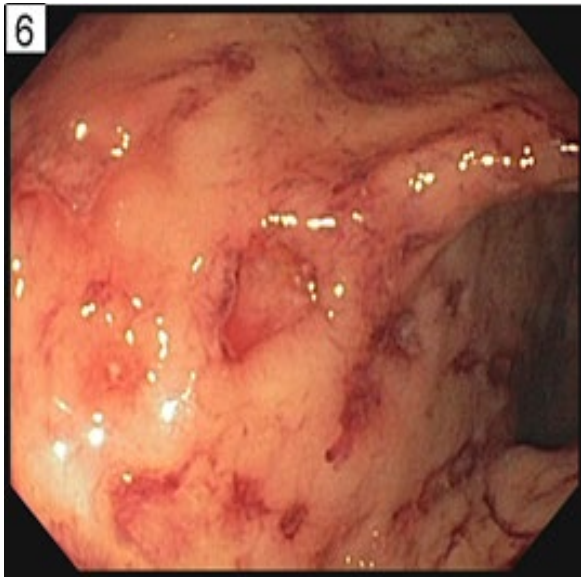
1	Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)	• Continue ICI
		• Oral antihistamines
		  ○ Cetirizine/loratidine 10 mg daily (non-sedating); hydroxyzine 10-25 mg QID, or at bedtime
		• Topical corticosteroids
		  ○ Class I topical corticosteroid (clobetasol propionate, halobetasol propionate, betamethasone dipropionate cream or ointment) for body; Class V/VI corticosteroid (aclometasone, desonide, hydrocortisone 2.5% cream) for face	

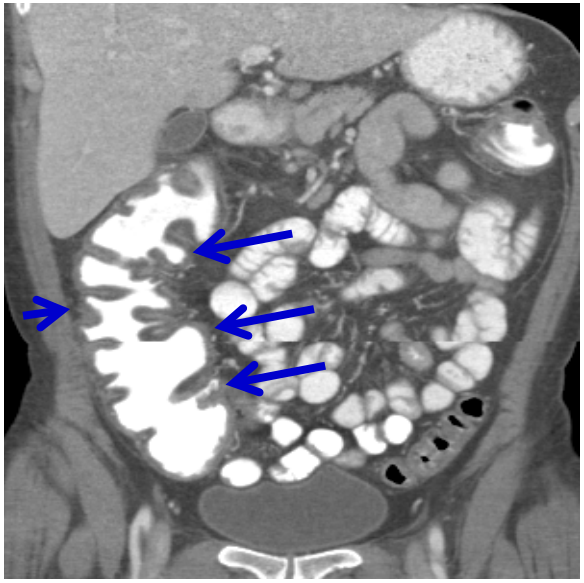
2	Macules/papules covering 10 30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL	• Continue ICI
		• Non-urgent dermatology referral
		• Oral antihistamines
		  ○ Cetirizine/loratidine 10 mg daily (non-sedating); hydroxyzine 10-25 mg QID, or at bedtime
		• Topical corticosteroids (see grade 1)
		  ○ As above
		  ○ Cetirizine/loratidine 10 mg daily (non-sedating); hydroxyzine 10-25 mg QID, or at bedtime
			✓

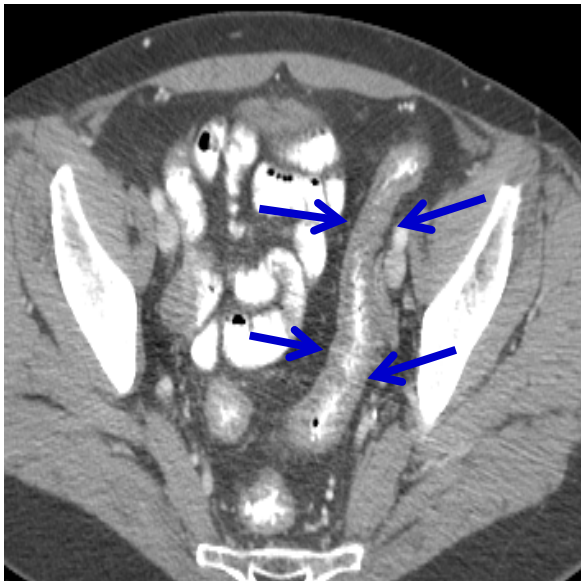
3	Macules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADL	• Hold ICI • Same day dermatology consult • Rule out systemic hypersensitivity: CBC with differential, CMP • Oral antihistamines ○ Cetirizine/loratidine 10 mg daily (non-sedating); hydroxyzine 10-25 mg QID, or at bedtime • Systemic corticosteroids • Prednisone 0.5 1 mg/kg/day (or equivalent dose of methylprednisolone) until rash resolves to ≤ grade 1	✓



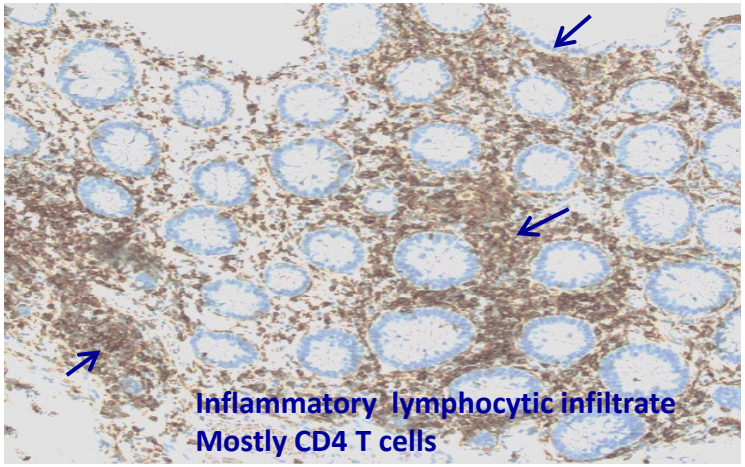
Inflammatory Colitis







3B



- Most common Grade 3/4 irAE in aCTLA4 based regimen

Dadu R… Diab A. Cancer 2016

Colitis Management

1	Asymptomatic; clinical or diagnostic observations only; intervention not indicated (Grade 1 diarrhea frequency ≤ 4/day)	- Close follow up within 24–48 h for changes or progression - Continue ICI - If symptoms persist, start routine stool and blood tests - Bland diet advisable during period of acute diarrhea - Anti-diarrheal medication is optional but not highly recommended when infectious work-up is negative.	

2	Abdominal pain; mucus or blood in stool (Grade 2 diarrhea frequency 4–6/day)	- Hold ICI
		- Outpatient stool and blood work; CRP, ESR, fecal calprotectin, lactoferrin, imaging and endoscopy are optional
		- If diarrhea only, observe for 2–3 days. If no improvement start prednisone 1 mg/kg/day (or equivalent dose of methylprednisolone); anti-diarrheal medication is not recommended
		- If diarrhea and colitis symptoms (abdominal pain +/– blood in BM), start prednisone 1 mg/kg/day (or equivalent dose of methylprednisolone)immediately
		  ○ If no improvement in 48 h, increase corticosteroid dose to prednisone 2 mg/kg/day (or equivalent dose of methylprednisolone)
		  ○ If patient improves
		  - Taper corticosteroid over 4–6 weeks may be needed
		  - Resume ICI when corticosteroid is tapered to ≤10 mg/day and patient remains symptom-free (grade ≤ 1)*
		  - Continue anti-PD-1 or anti-PD-L1 monotherapy
		  - If using combination anti-CTLA-4/anti-PD-1 immunotherapy, continue anti-PD-1 agent only
		  - ICI dose reduction is not recommended
		- If colitis returns on resuming ICI:
		  ○ Grade ≤ 2: temporarily hold ICI
		  ○ Grade ≥ 3: permanently discontinue ICI
			✓
			See note 5

3 and 4	Grade 3: Severe abdominal pain; change in bowel habits; medical intervention indicated; peritoneal signs (Grade 3 diarrhea frequency ≥ 7×/day) Grade 4: Life-threatening consequences; urgent intervention indicated	- Grade 3: withhold ICI; consider resuming ICI when corticosteroid is tapered to ≤10 mg/day and patient remains symptom-free (grade ≤ 1). Consider hospitalization - Grade 4: permanently discontinue ICI and hospitalize - Blood and stool infection work-up, inflammatory markers, imaging, endoscopy and GI consult - Start intravenous prednisone 1-2 mg/kg/day (or equivalent dose of methylprednisolone) immediately ○ If patient improves, follow instructions for 'If patient improves' for grade 2 - If refractory or no improvement on IV corticosteroid, start prednisone 2 mg/kg/day (or equivalent dose of methylprednisolone) for 3 days - Consider other anti-inflammatory agents e.g. infliximab 5 mg/kg, which can be given again after two weeks if a second dose is needed. Vedolizumab may also be used (see Note 4 below).	

Infliximab with Faster Resolution of Colitis

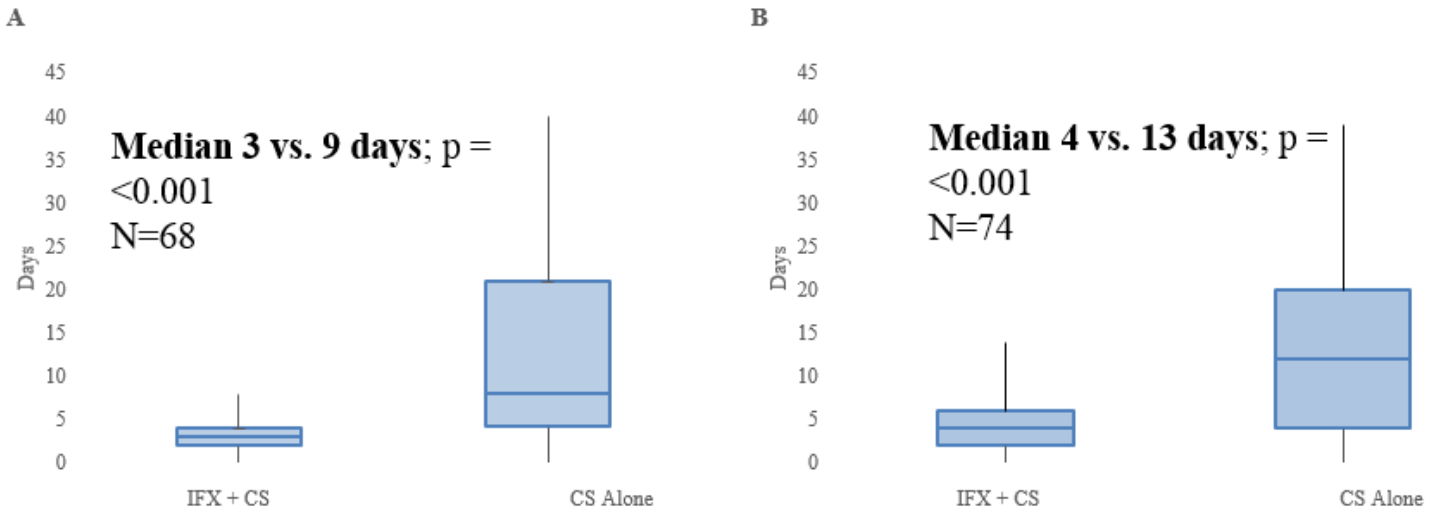


***Figure 1*: Box plots of association between treatment for irEC and time to irEC symptom resolution defined as (A) Time to diarrhea resolution and (B) Time to initiation of steroid titration.**

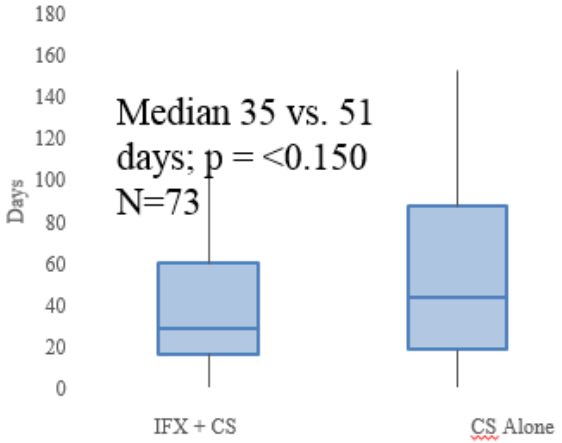
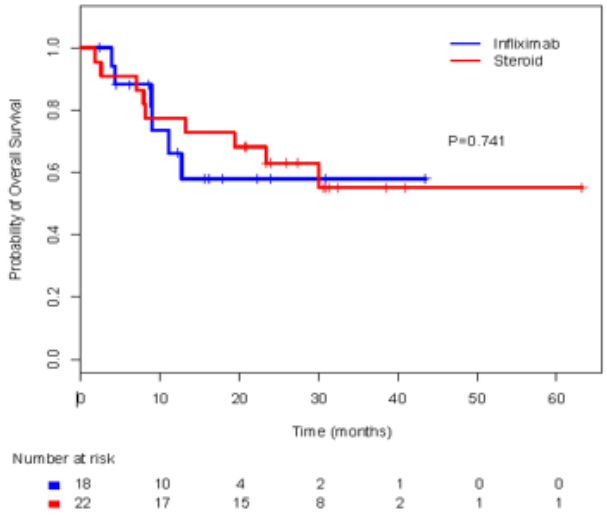


***Figure 3*: Box plot of association between treatment for irEC and total duration of corticosteroids.**



DH Johnson, et. al. JITC 2019

Hepatitis

Figure 5

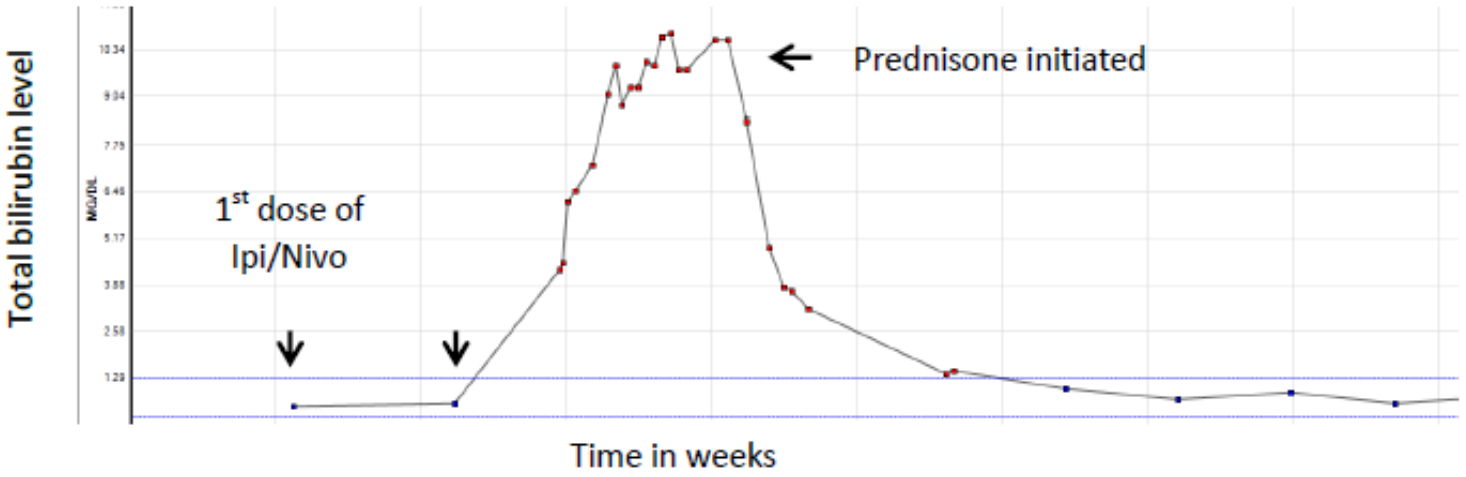


Figure Legend 5: immune mediated hepatitis manifest with elevation of LFTs including hyper-bilirubinemia occurred after the 2nd dose of combination regimen of ipilimumab and nivolumab in a patient with metastatic melanoma. his bilirubin levels and the rest of LFTs normalized very quickly in response to treatment with prednisone.

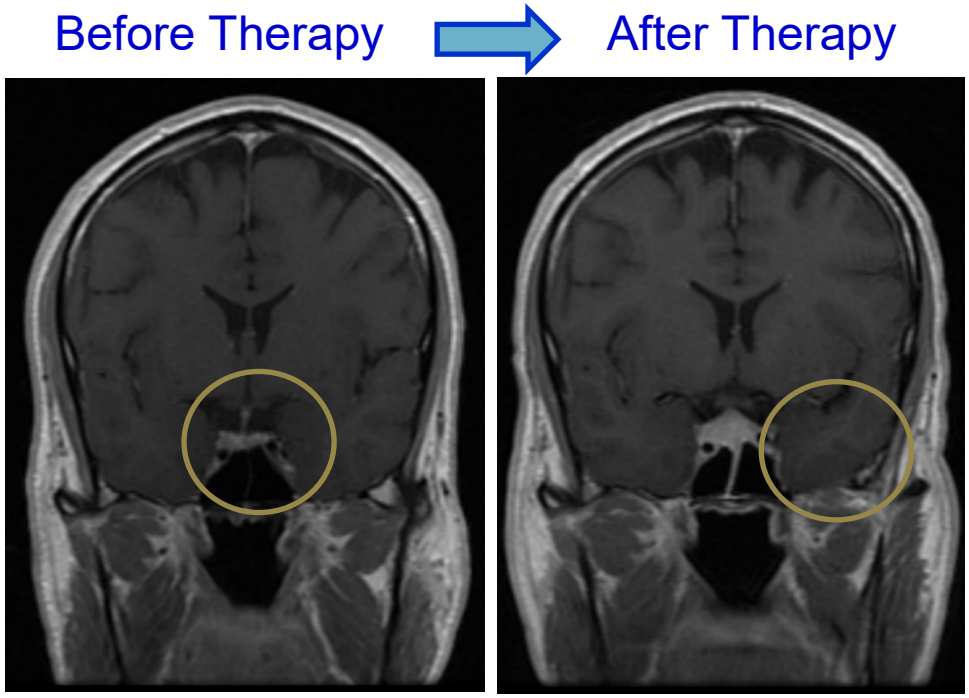
Hepatitis Management

Hepatitis

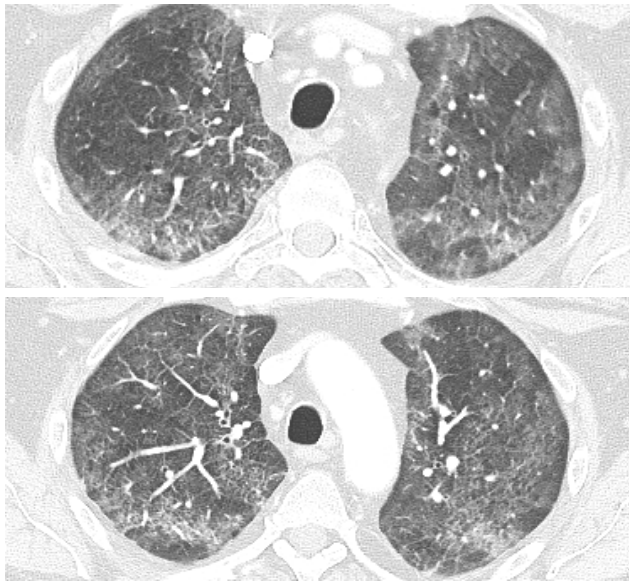
Grade	CTCAE Description (Note 1)	Management
1	AST, ALT > ULN -3xULN; total bilirubin > ULN-1.5xULN	• Continue ICI • CMP or hepatic function panel once weekly • If liver enzyme and function tests are stable, reduce frequency of blood tests
2	AST, ALT >3- ≤ 5xULN; total bilirubin > 1.5 - ≤ 3xULN	• Hold ICI • Rule out viral hepatitis, autoimmune disease, biliary obstruction, new metastasis or thrombosis
		• Start prednisone 0.5-1 mg/kg/day (or equivalent dose of methylprednisolone) with 4 week taper • Monitor CMP twice a week • Liver biopsy is optional • Resume ICI when corticosteroid taper to 10 mg/day (toxicity grade ≤ 1)
3 and 4	AST, ALT >5xULN; total bilirubin >3xULN	• Permanently discontinue ICI • Monitor CMP every 1 2 days • Start prednisone 1 2 mg/kg/day ○ If refractory after 3 days, consider mycophenolate • If liver enzymes improve, taper corticosteroid over 4 weeks • Consider liver biopsy

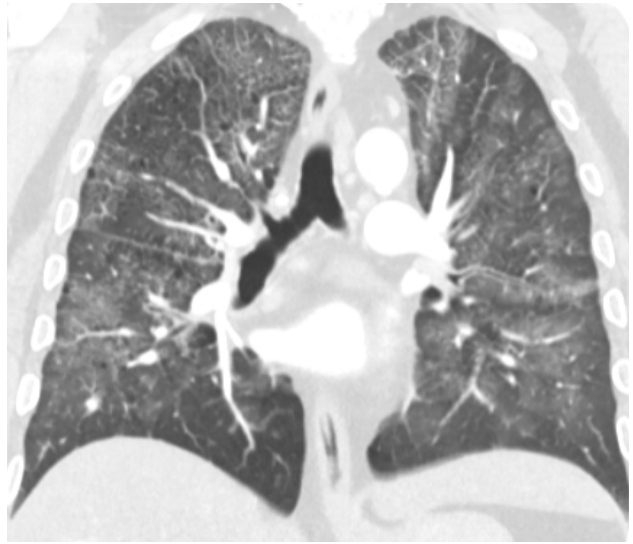
Endocrinopathies

- Thyroid abnormalities
  - Thyroiditis (hyper→ hypo)
  - Thyrotoxicosis
- Hypophysitis
- Type I Diabetes



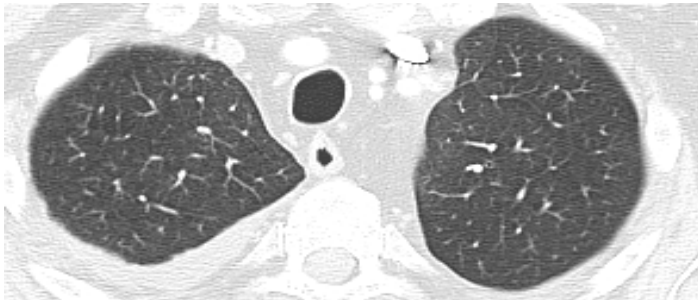
Pneumonitis

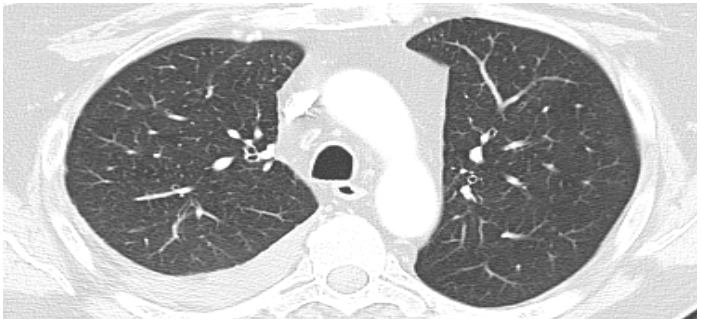


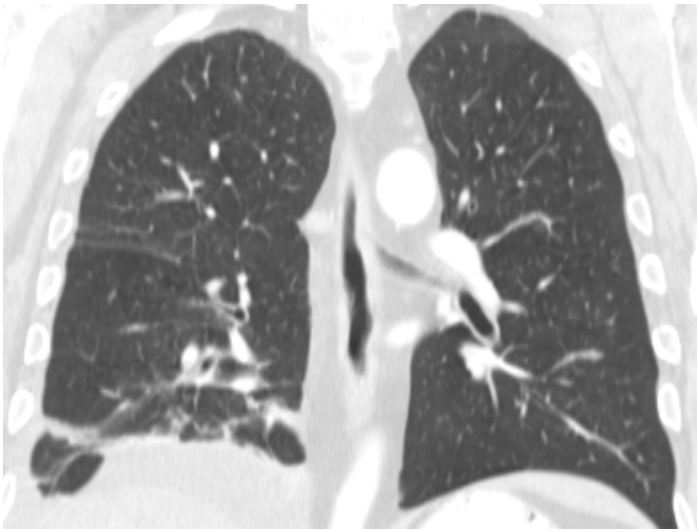


6wks Post Treatment:

Including:
hospitalization
I.V Steroid (2Mg/kg/day)
Pulmonary Consult

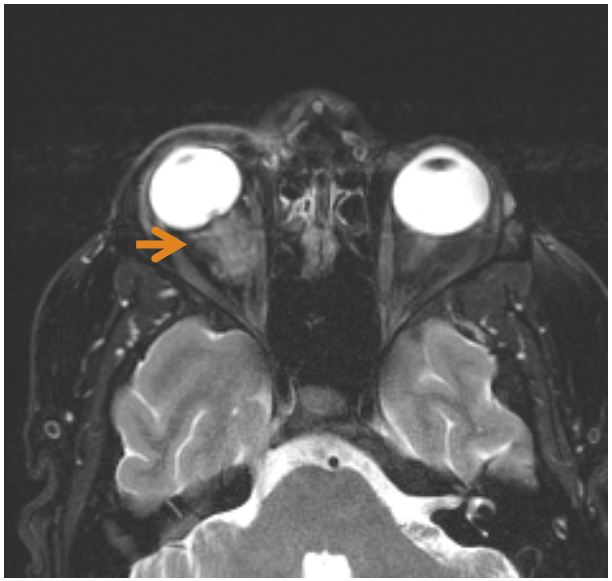




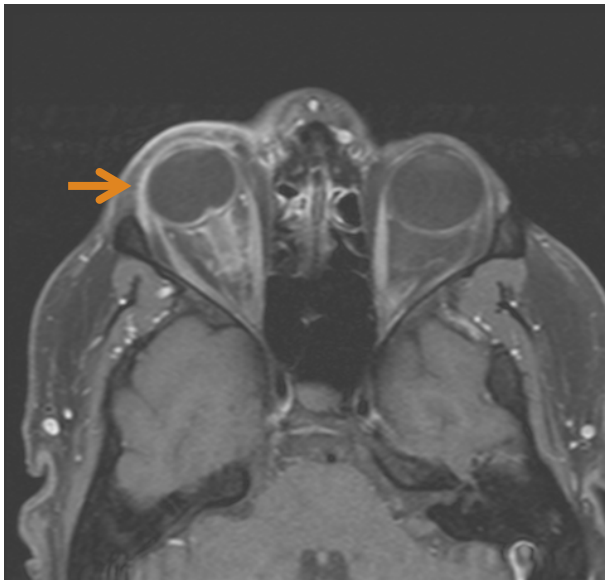


Optic neuritis

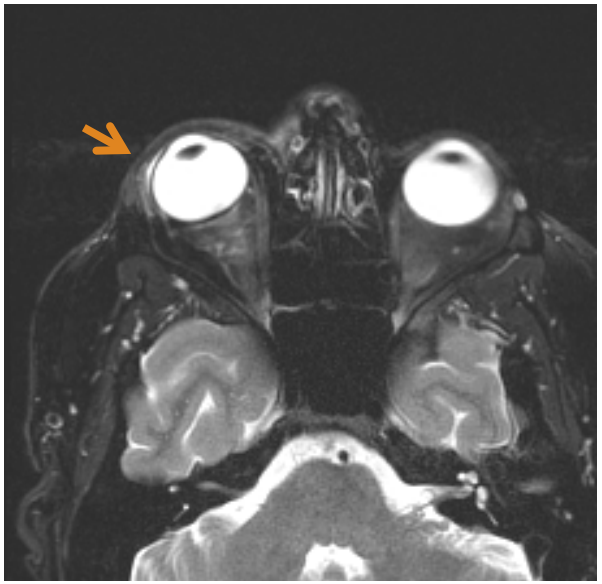
Inflammation of the R optic Nerve



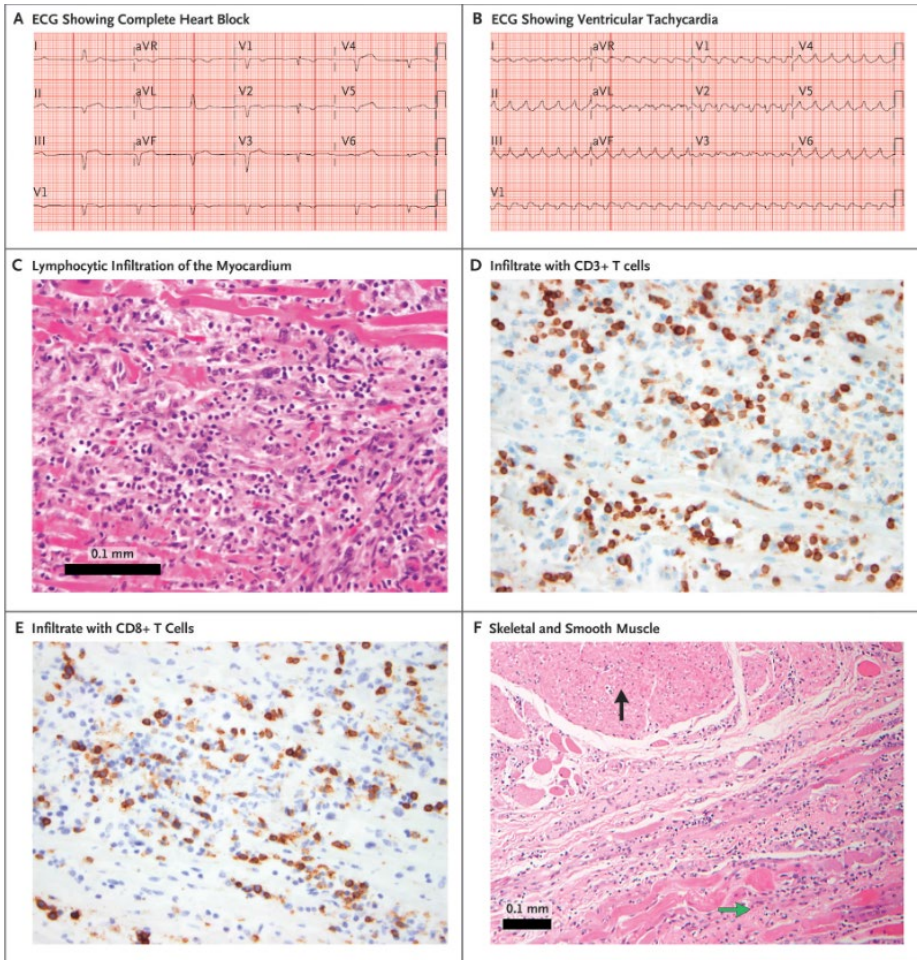
Scleral Enhancement

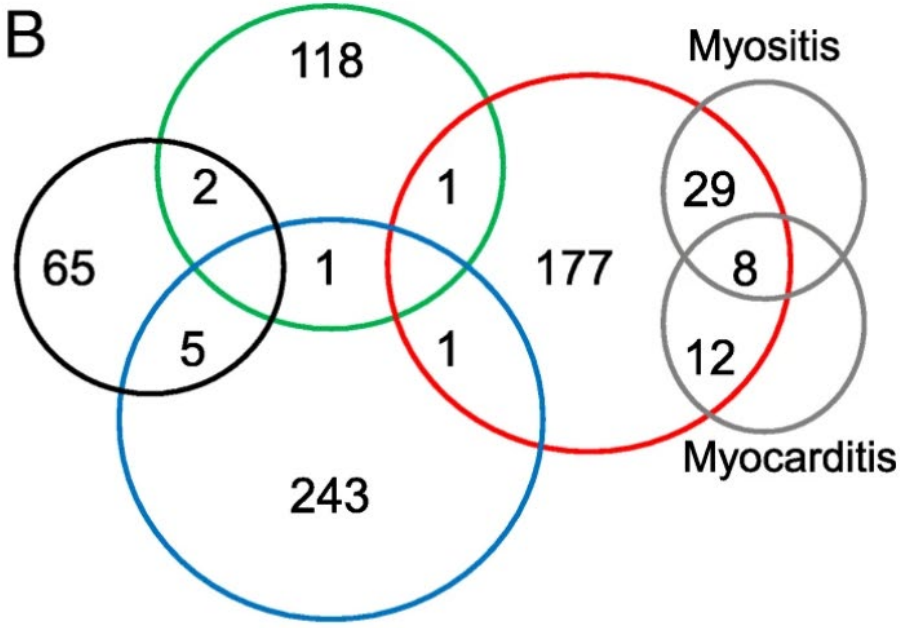


Conjunctival Edema



Myocarditis Neurologic Toxicities

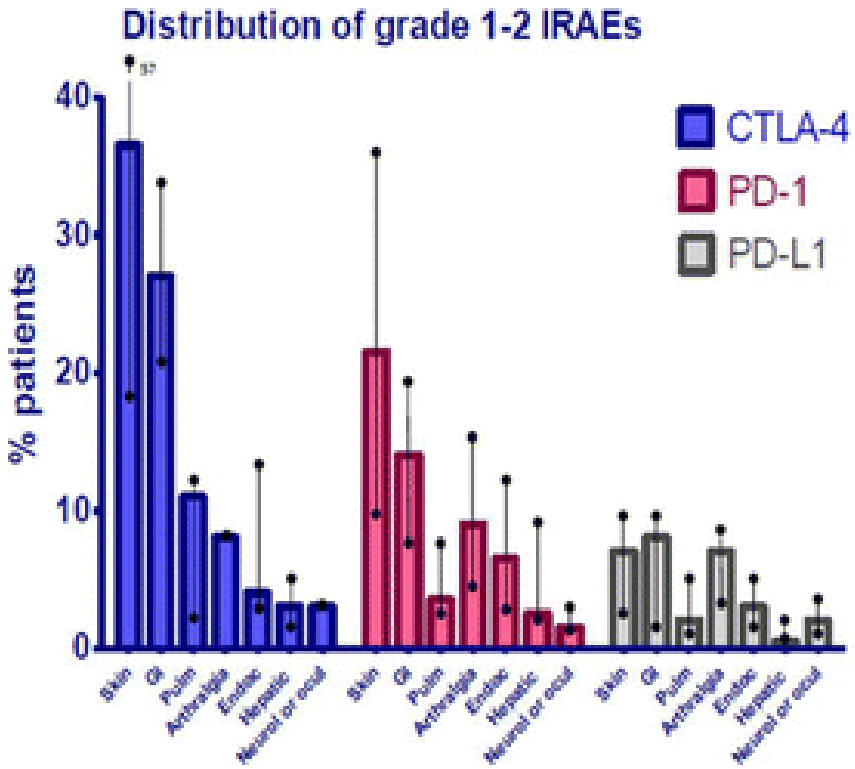


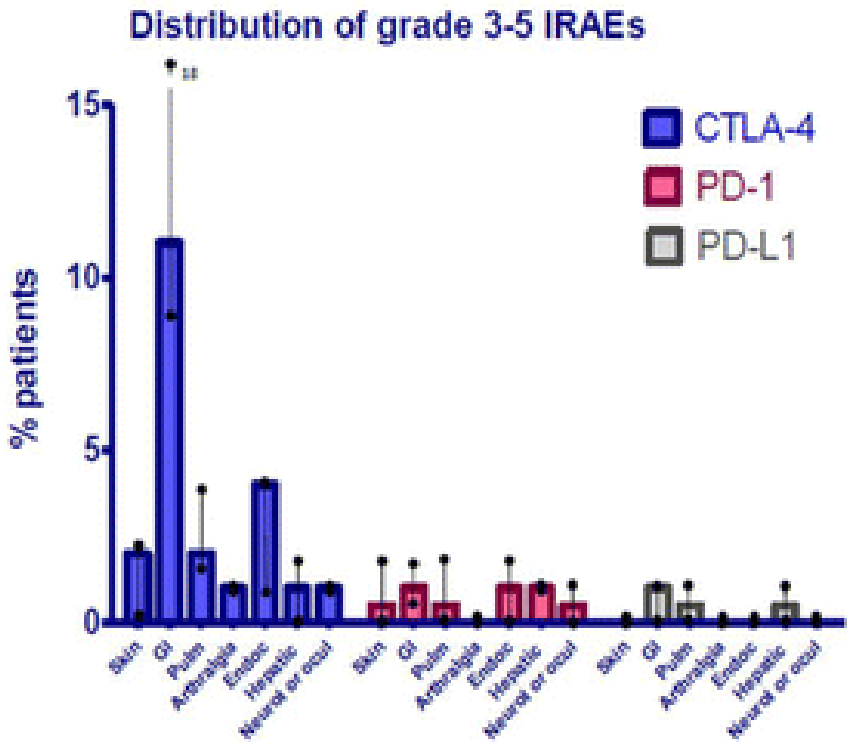


DB Johnson, et. al. JITC 2019

DB Johnson, et. al. NEJM 2016

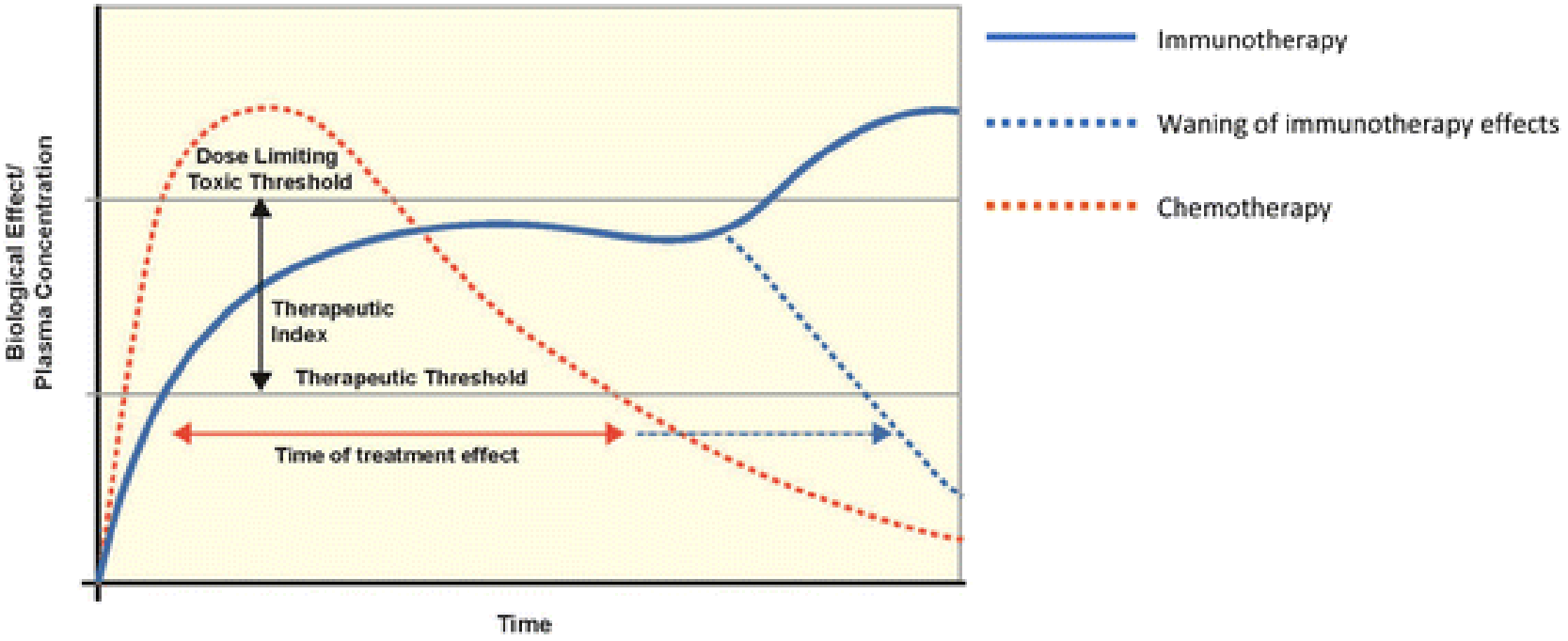
Distribution of Grades





Puzanov, Diab, et. al. SITC guidelines, JITC 2017

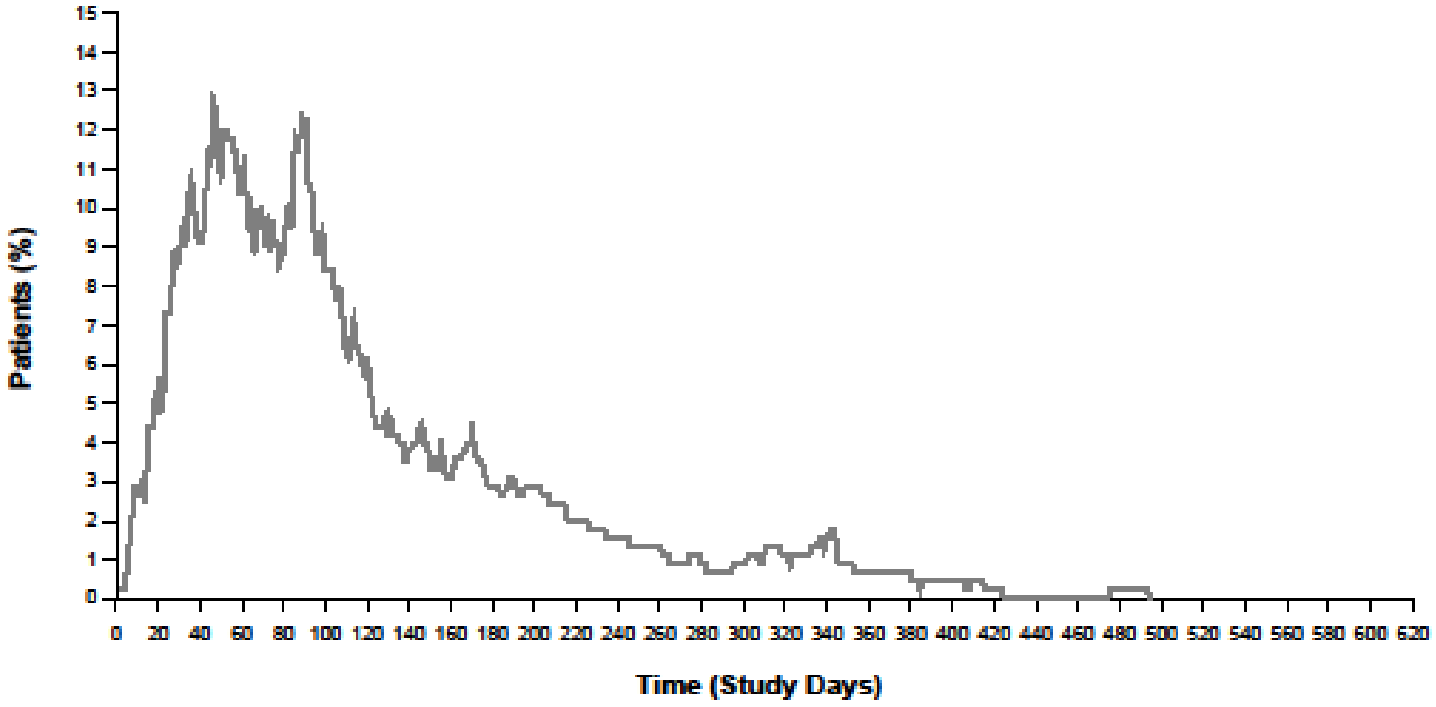
Delayed Onset



Puzanov, Diab, et. al. SITC guidelines, JITC 2017

Timing: Onset and Resolution

Figure 1. Proportion of Patients With Treatment-related Grade 3/4 AEs Over Time[a]



Sznol M ESMO 2016 : Safety Profile of **Nivolumab and Ipilimumab** Combination Therapy in Patients With Advanced Melanoma

Timing: Onset and Resolution- Anti CTLA-4

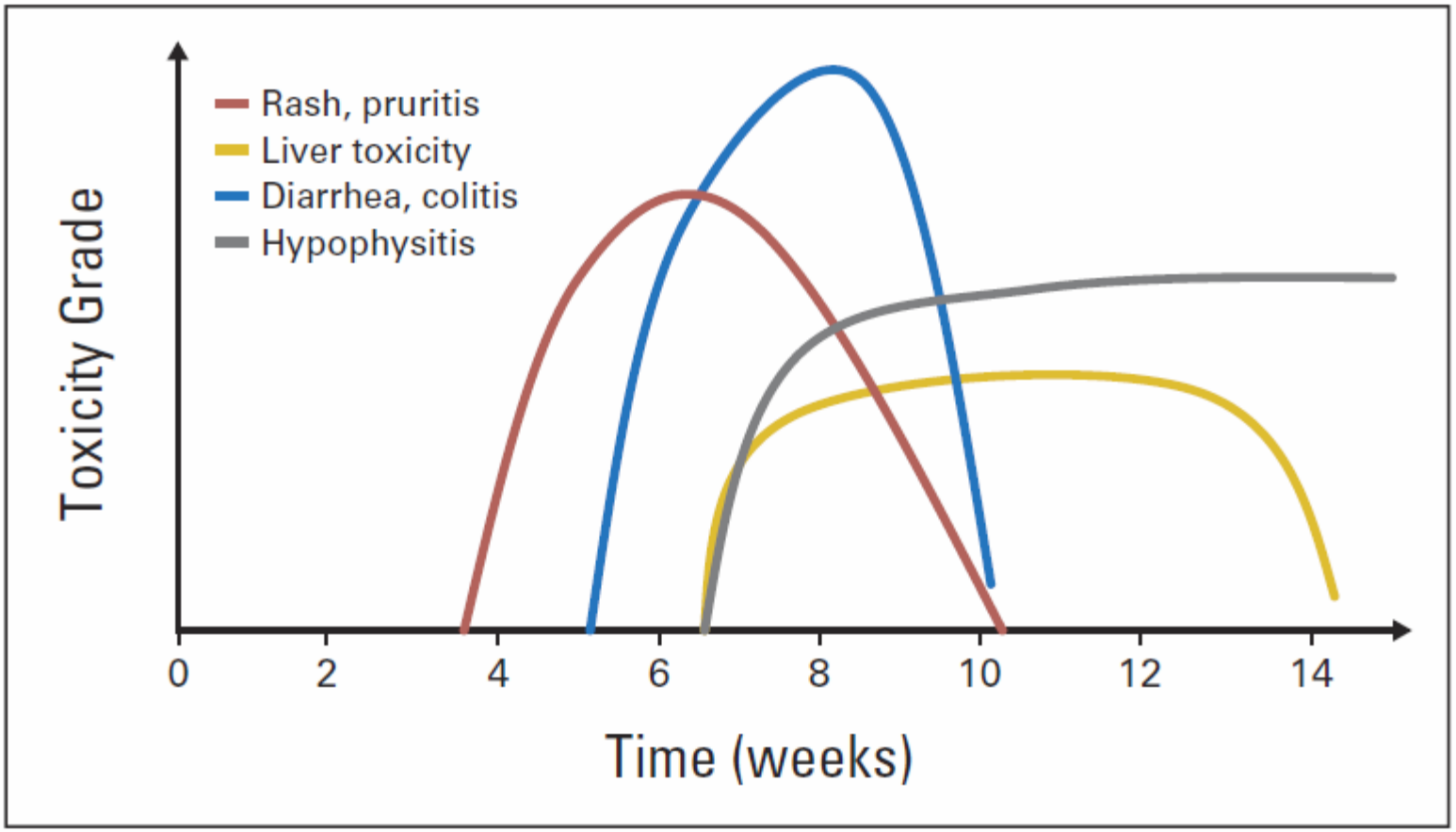
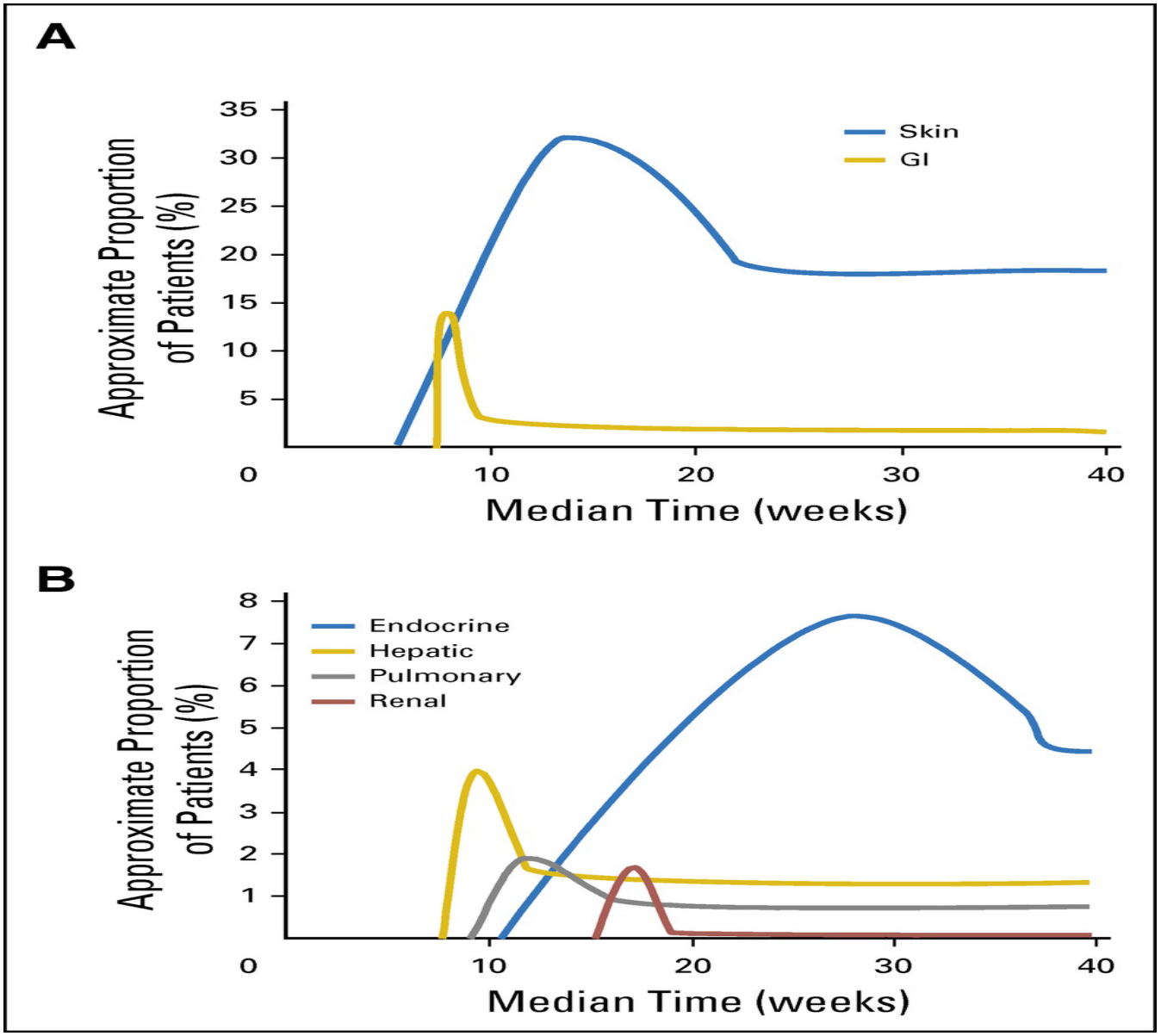


Fig 2. Kinetics of appearance of immune-related adverse event.

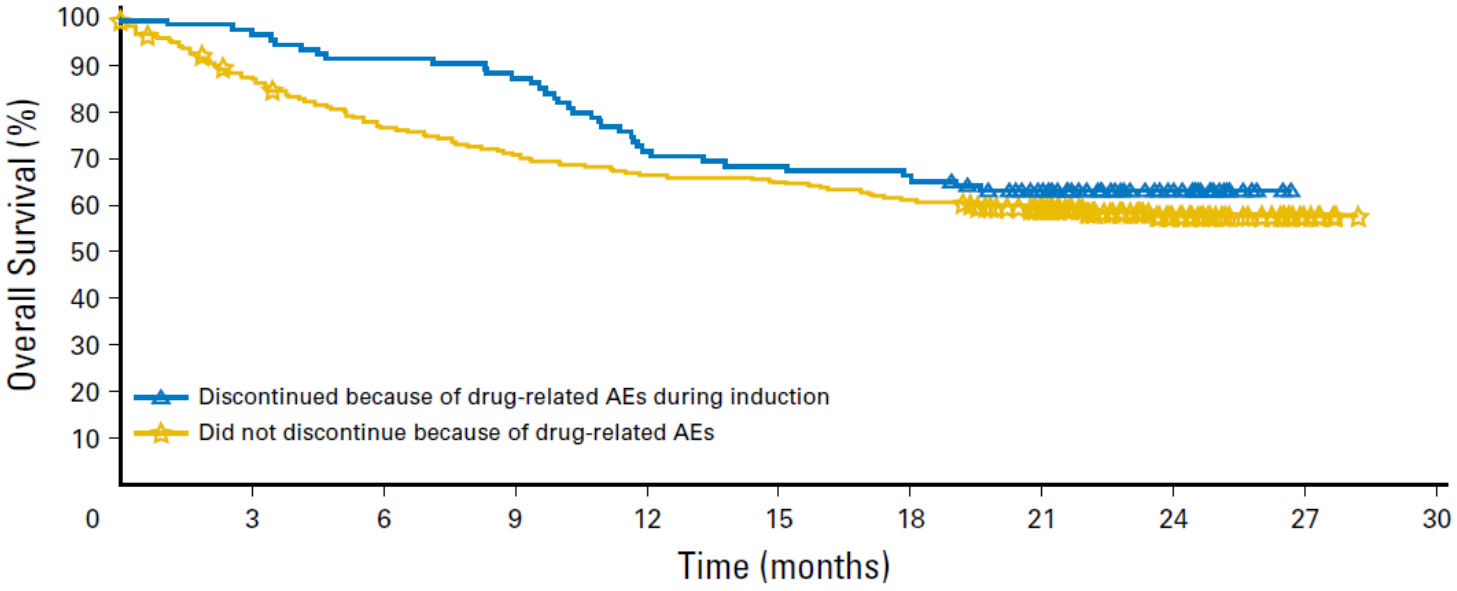
Webber J,JCO 2012

Timing: Onset and Resolution- Anti PD-1



Published in: Jeffrey S. Weber; *JCO* **2017,** 35, 785-792. DOI: 10.1200/JCO.2015.66.1389

Ipilimumab + Nivolumab Toxicity not Bad



No. at risk:											
Discontinued because of drug-related AEs during induction	98	93	88	84	69	66	64	52	23	0	0
Did not discontinue because of drug-related AEs	233	201	175	162	152	148	140	117	50	6	0

Schadendorf et al, *JCO,* 2017

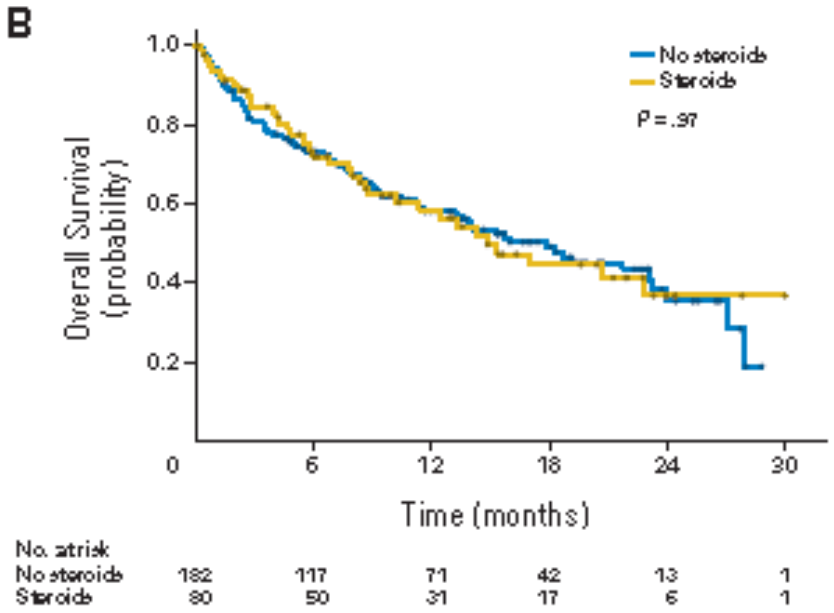
Impact of immune suppression on clinical benefit ?

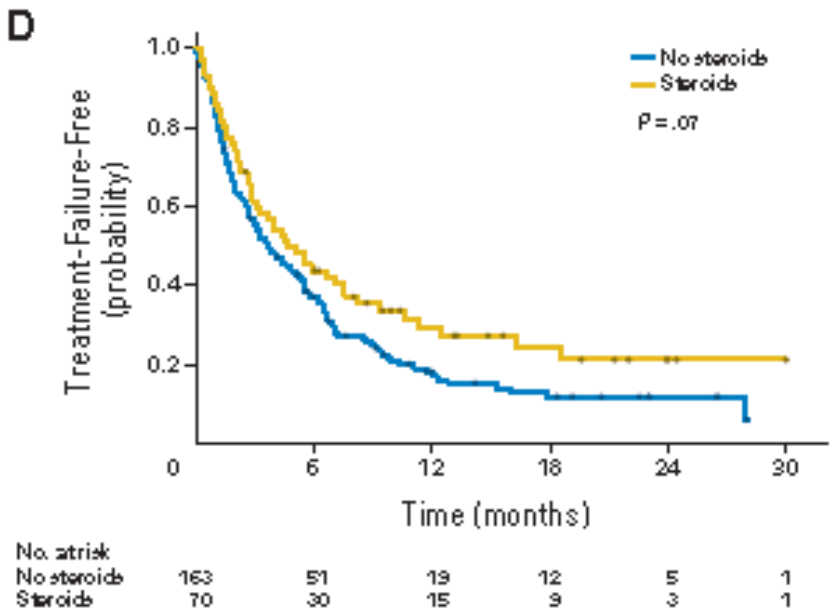
Table 2. Impact of Treatment-Related Select AEs and IM Use on Response to Nivolumab Therapy

Table 2. Impact of Treatment-Related Select AEs and IM Use on Response to Nivolumab Therapy

		Any-Grade Treatment-Related Select AEs*				Grade 3 to 4 Treatment-Related Select AEs		Patients Receiving Systemic IM	
	All Patients (N = 576)	Any (n = 255)	None (n = 321)	1-2 (n = 242)	≥ 3 (n = 13)	Yes (n = 18)	No (n = 558)	Yes (n = 114)	No (n = 462)
ORR, No. of patients (%)	181 (31.4)	124 (48.6)	57 (17.8)	113 (46.7)	11 (84.6)	5 (27.8)	176 (31.5)	34 (29.8)	147 (31.8)
95% CI	27.6 to 35.4	42.3 to 54.9	13.7 to 22.4	40.3 to 53.2	54.6 to 98.1	9.7 to 53.5	27.7 to 35.6	21.6 to 39.1	27.6 to 36.3
P		< .001		< .0001†	< .001†	1.00		.736	

Abbreviations: AE, adverse event; IM, immune-modulating agent; ORR, objective response rate.
*Data in these columns are for patients with the indicated numbers of any-grade treatment-related select AEs: any AE, no AEs, 1-2 AEs, and ≥ 3 AEs.
†Versus no treatment-related select AEs.



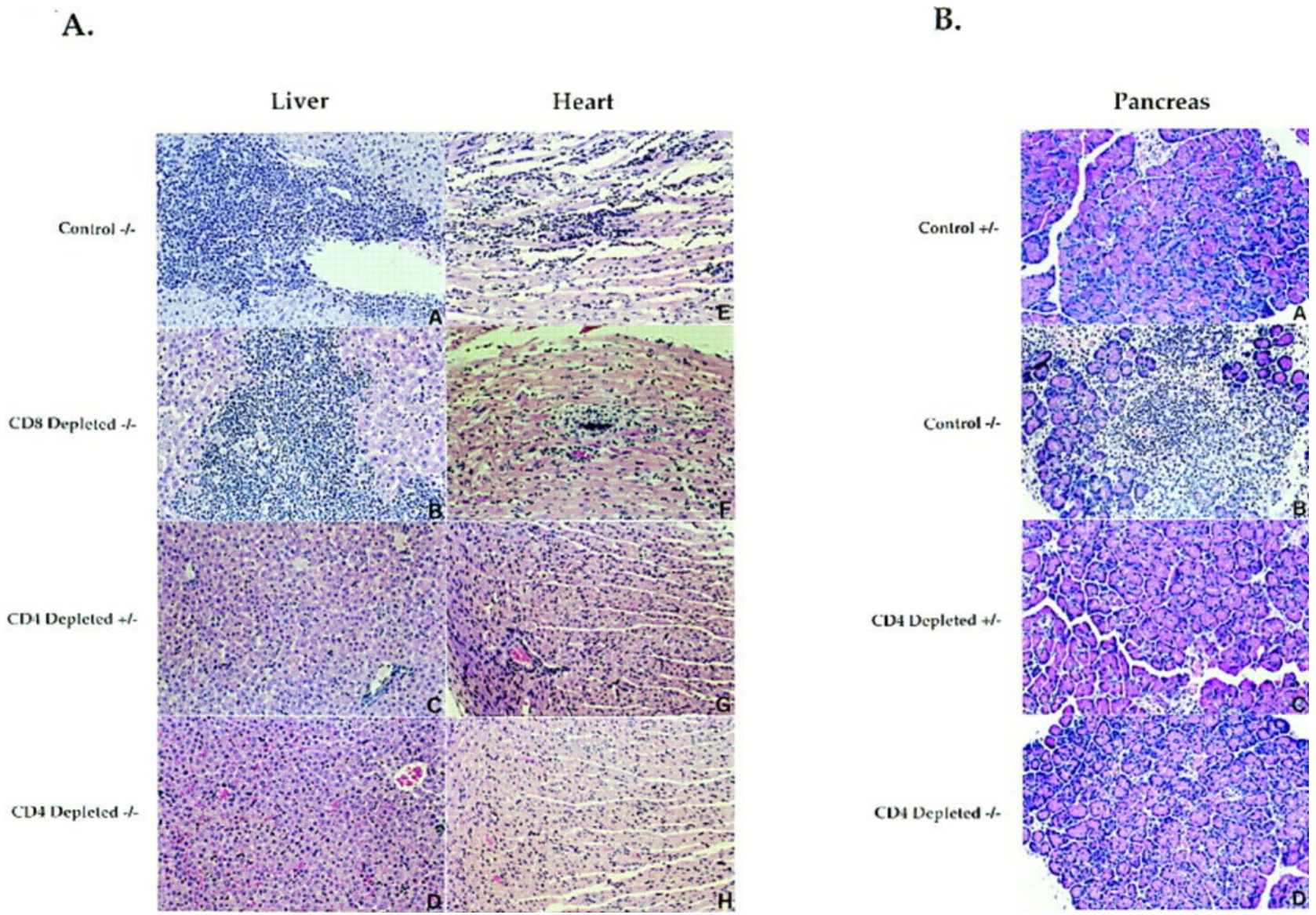


What is the solution to the irAE problem?

- Are there treatments that can target the irAE inflammation without negatively impacting anti-cancer effects?
- Are there safer combinations?
- Intra-tumorals?

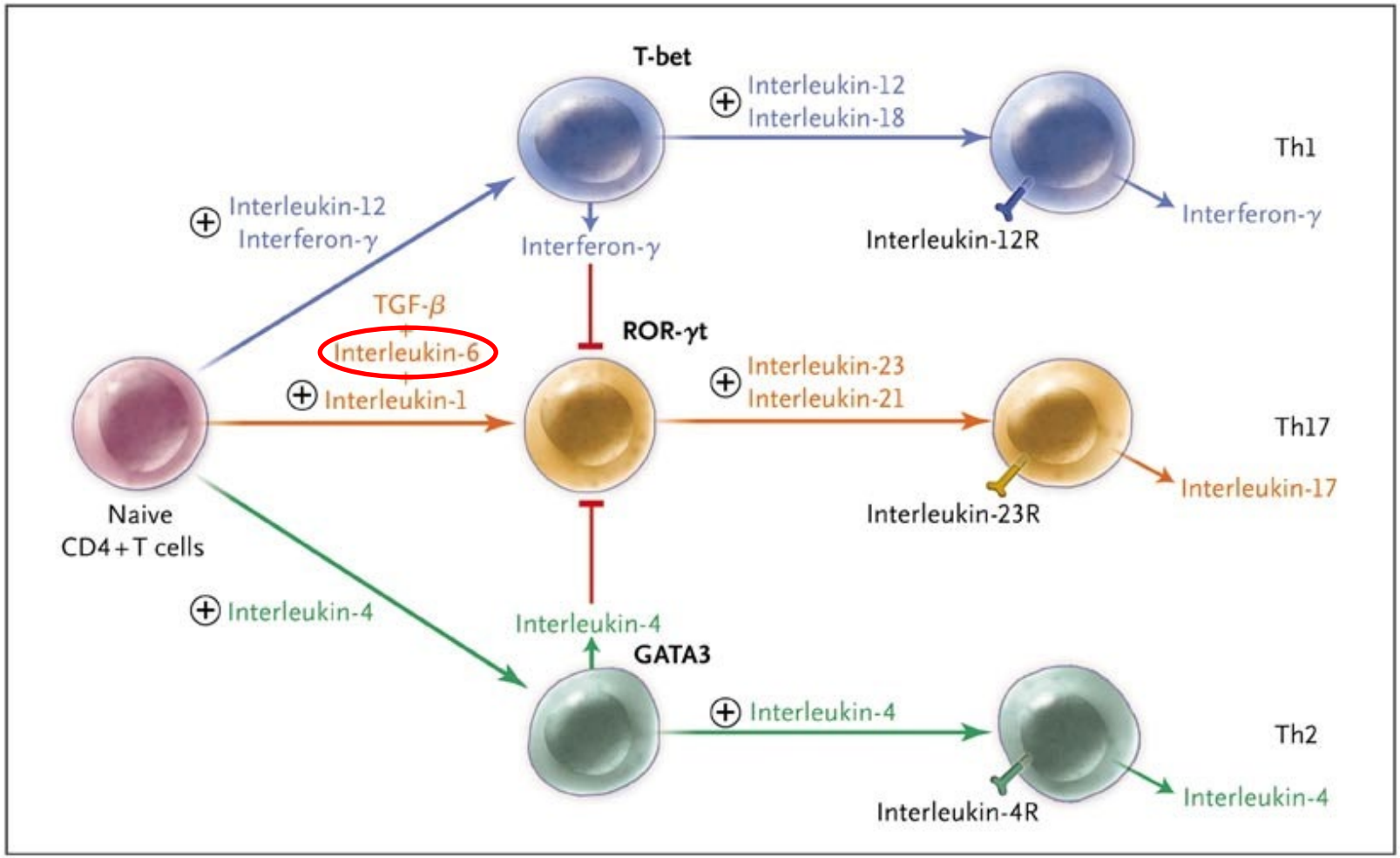
Pathophysiology of Immune Toxicities

Lymphoproliferation in CTLA-4–Deficient Mice Is Mediated by Costimulation-Dependent Activation of CD4 T Cells



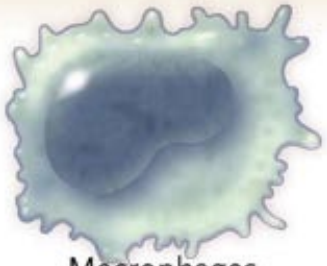
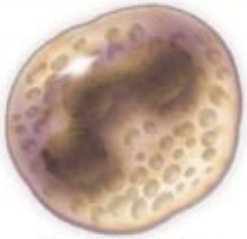
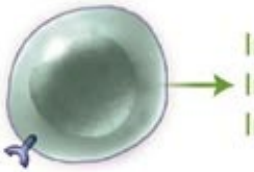
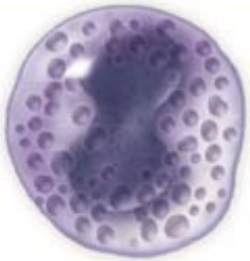
Cynthia A. Chambers, Timothy J. Sullivan, and James P. Allison* Immunity, Vol. 7, 885–895, December, 1997,

CD4 T Cells



Miossec P et al. N Engl J Med 2009;361:888-898.

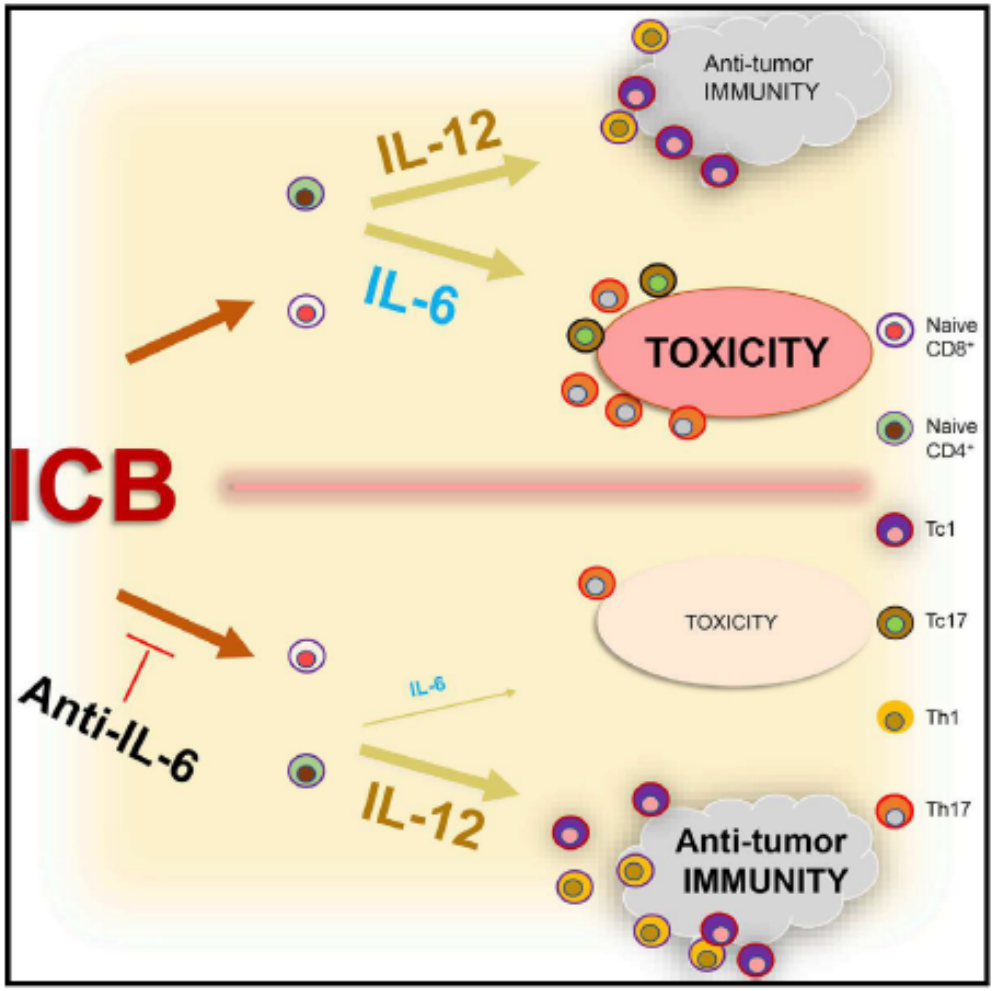
CD4 T Cells

Th Group	Cell Products	Cell Target	Infectious Agents
Th1	 Interferon-γ Interleukin-2 Interleukin-12R	 Macrophages Dendritic cells	Intracellular bacteria Fungi Viruses
Th17	 Interleukin-17A Interleukin-17F Interleukin-21 Interleukin-22 Interleukin-23R	 Neutrophils	Extracellular bacteria Fungi
Th2	 Interleukin-4 Interleukin-13 Interleukin-5 Interleukin-4R	 Eosinophils Basophils	Parasites

Miossec P et al. N Engl J Med 2009;361:888-898.

Interleukin-6 Blockade

Graphical abstract



Authors

Yared Hailemichael, Daniel H. Johnson, Noha Abdel-Wahab, ..., Patrick Hwu, Suhendan Ekmekcioglu, Adi Diab

Correspondence

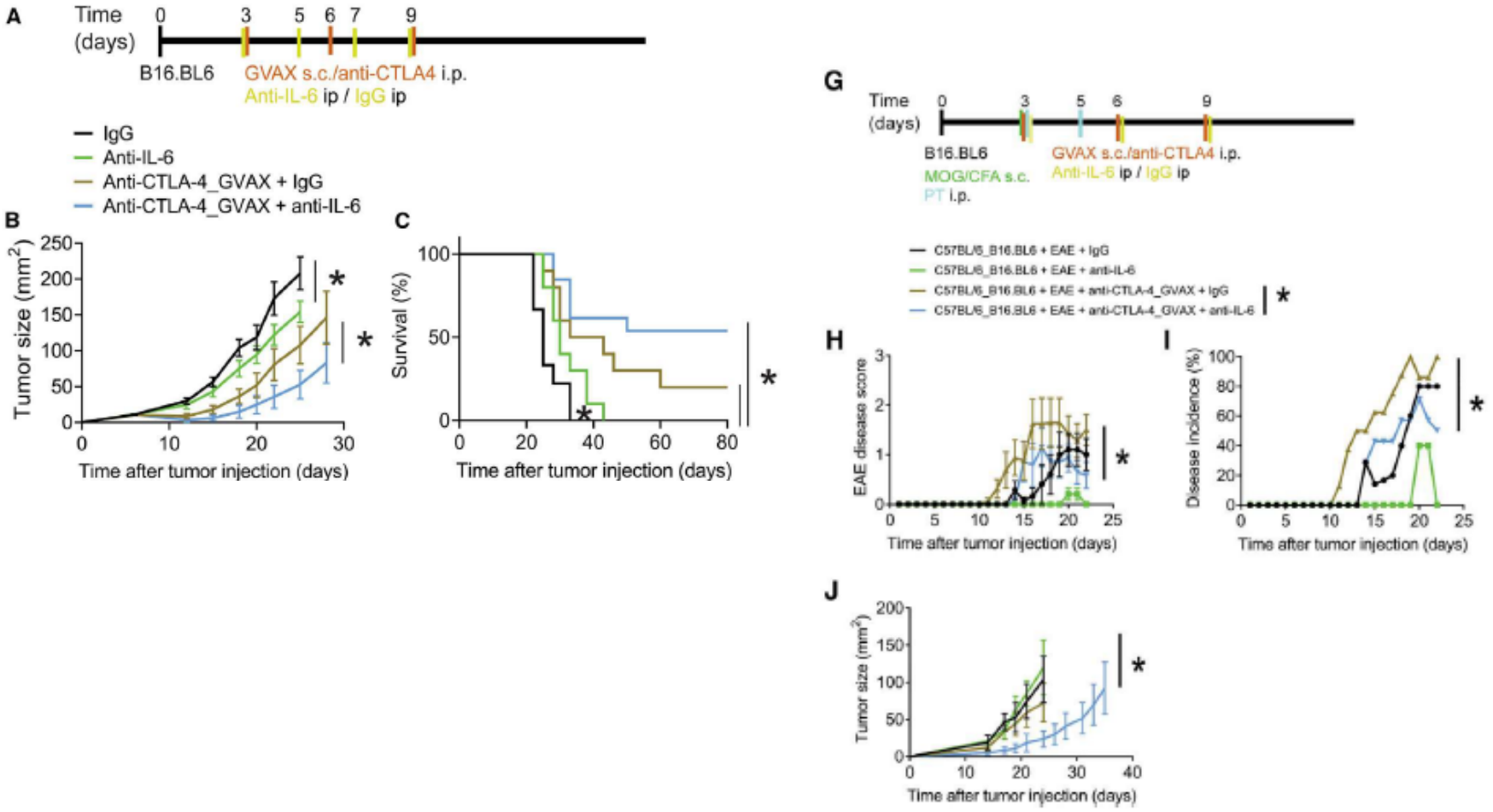
adiab@mdanderson.org

In brief

Hailemichael et al. find that expression of interleukin-6, a Th17-cell differentiation cytokine, and neutrophil and chemotactic markers increase in inflamed tissue of patients and mice receiving immuno-therapy. Blockade of IL-6 reduces Th17 and increases Th1 and $CD8^+$ T effector cell density in tumor, mitigates ICB-induced autoimmunity, and potentiates antitumor immunity.

Hailemichael Y, Johnson DH, et al., 2022, *Cancer Cell,* 40 pp 509-523

Interleukin-6 Blockade



Hailemichael Y, Johnson DH, et al., 2022, *Cancer Cell,* 40 pp 509-523

MELANOMA/SKIN CANCERS

Ipilimumab, nivolumab and tocilizumab as first-line therapy for advanced melanoma.

Check for updates

Inderjit Mehmi, Omid Hamid, F. Stephen Hodi, Melinda Vassalo, Saundra Malatyali, Swathi Krishnarajapet, ...

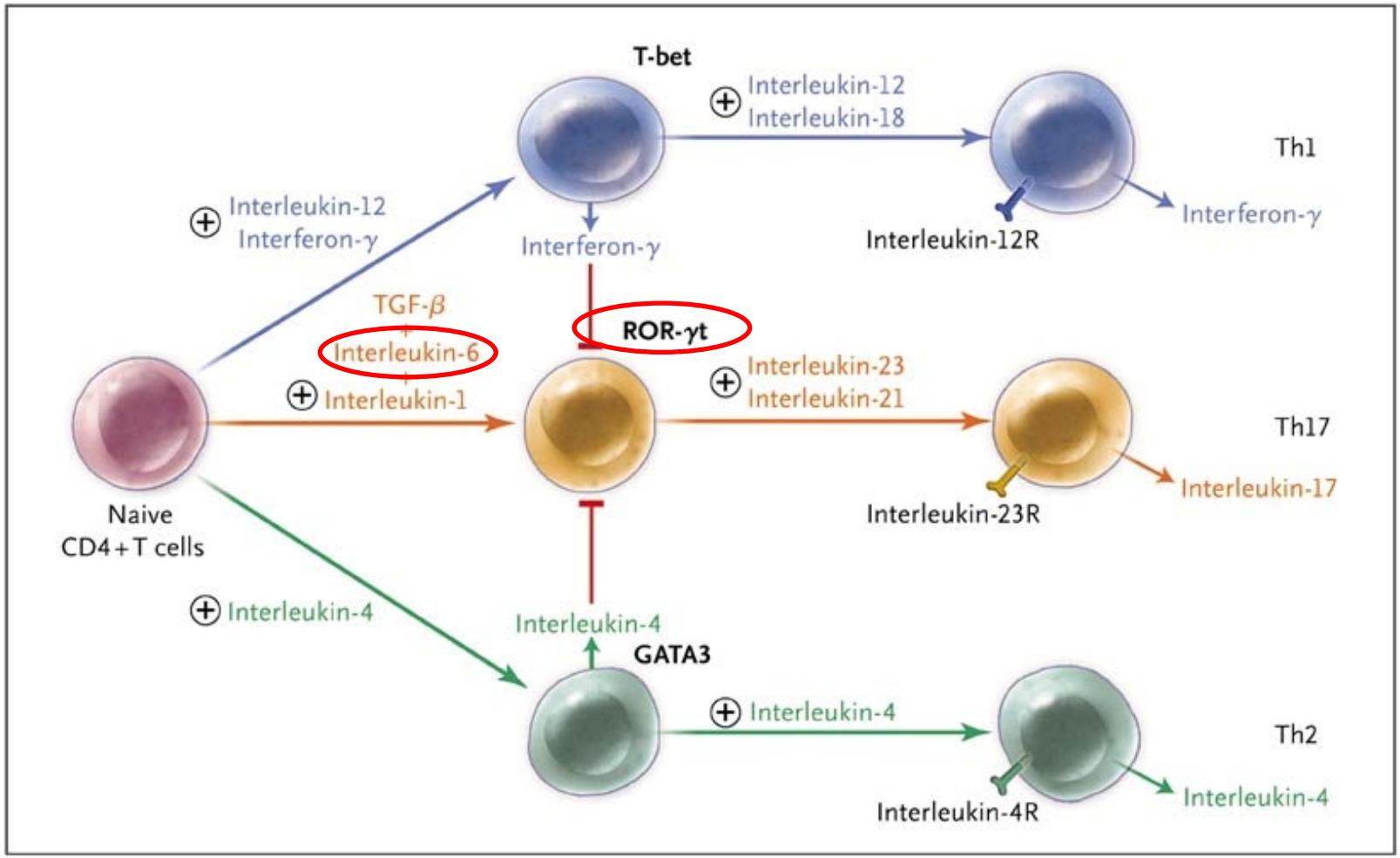
Show More

Abstract Disclosures

6 months of median follow up, there are 14 RECIST responses of 20 pts **(70% ORR)**

There were 5/24 patients **(21%)** with grade 3-4 irAEs with one each with enteritis, colitis and nephritis and two with trasaminitis.

CD4 T Cells



Miossec P et al. N Engl J Med 2009;361:888-898.

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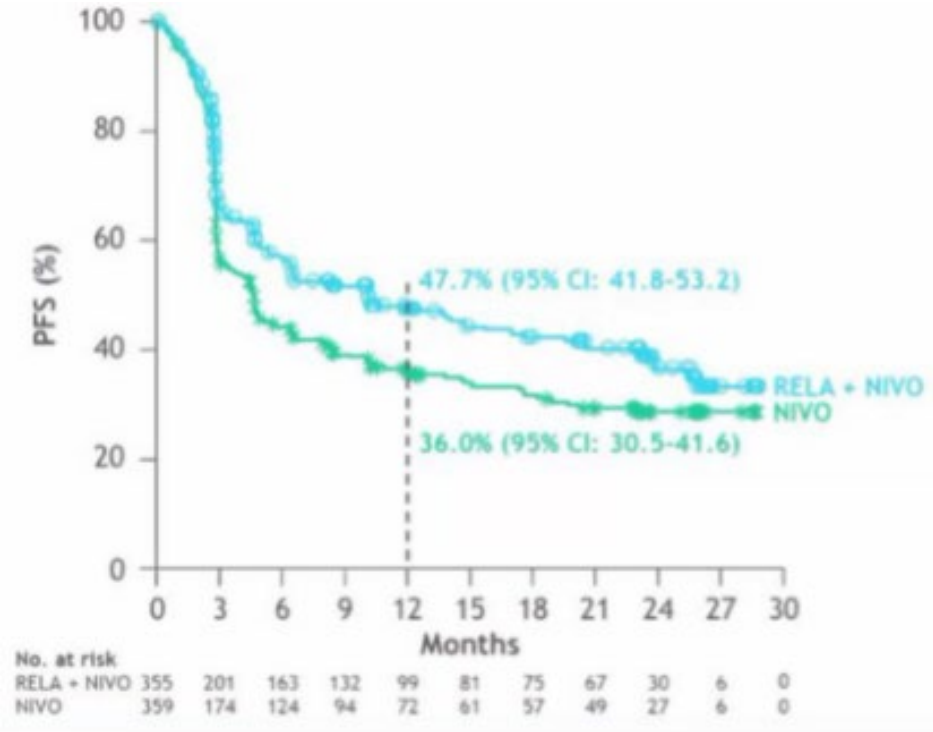
RELATIVITY-047

Relatlimab + Nivolumab Frontline Metastatic Melanoma

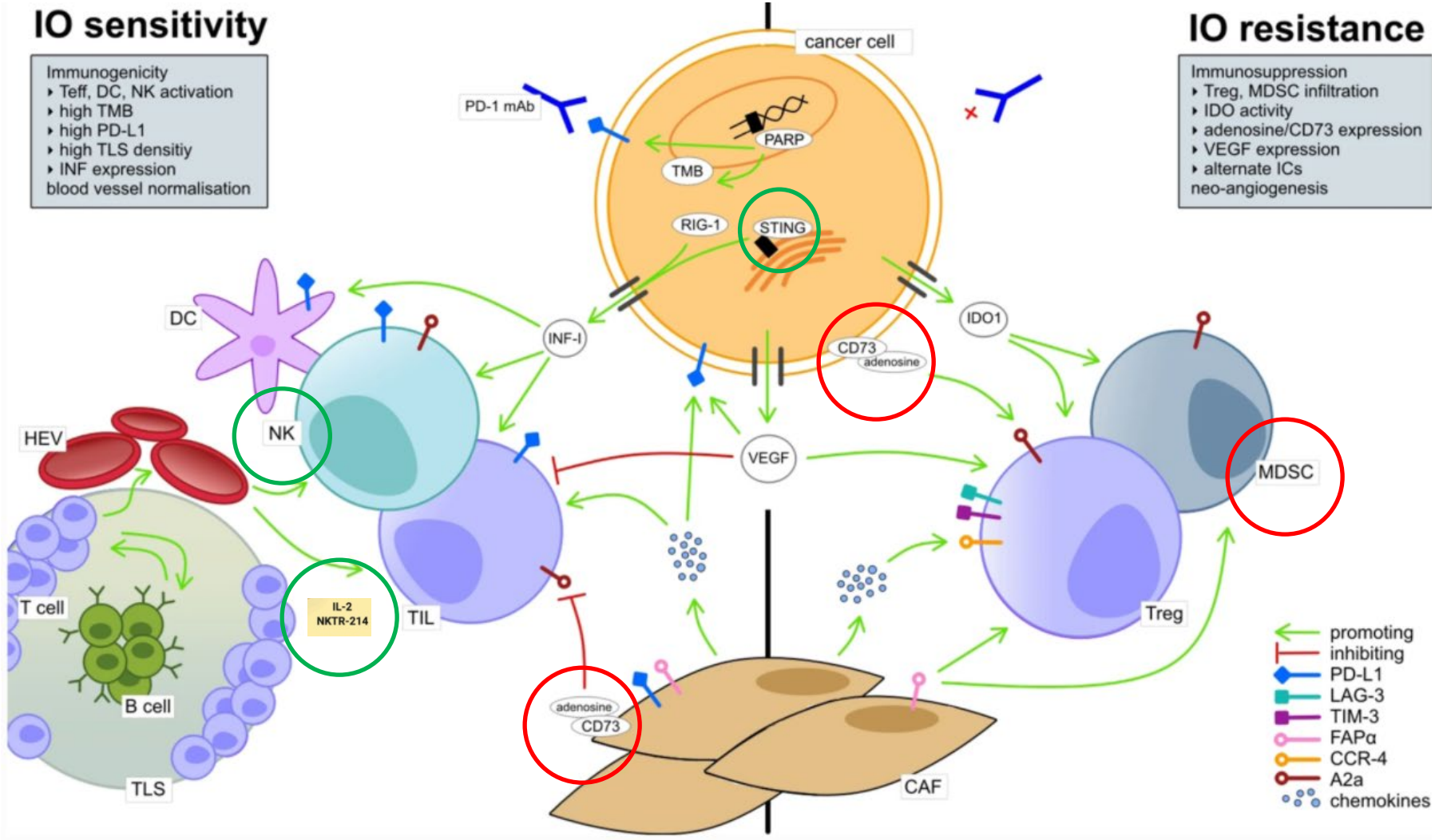


	RELA + NIVO (n = 355)	NIVO (n = 359)
Median PFS, months	10.12	4.63
(95% CI)	(6.37-15.74)	(3.38-5.62)
HR (95% CI)	0.75 (0.62-0.92)	
P value	0.0055	

CI, confidence interval; HR, hazard ratio.
All randomized patients. Statistical model for HR and *P* value: stratified Cox proportional hazard model and stratified log-rank test. Stratified by LAG-3 (≥ 1% vs < 1%), BRAF (mutation positive vs mutation wild-type), AJCC M stage (M0/M1any[0] vs M1any[1]). PD-L1 was removed from stratification because it led to subgroups with < 10 patients.

- Relatlimab + Nivolumab significantly improved PFS verus Nivo
- Grade 3/4 treatment-related adverse events 18.9% in RELA + NIVO versus NIVO (9.7%). Discontinuation due to toxicity 14.6% versus 6.7%

Next Generation of Immunotherapies



Horvath et. al. Molecular Cancer. 2020

What is the solution to the irAE problem?

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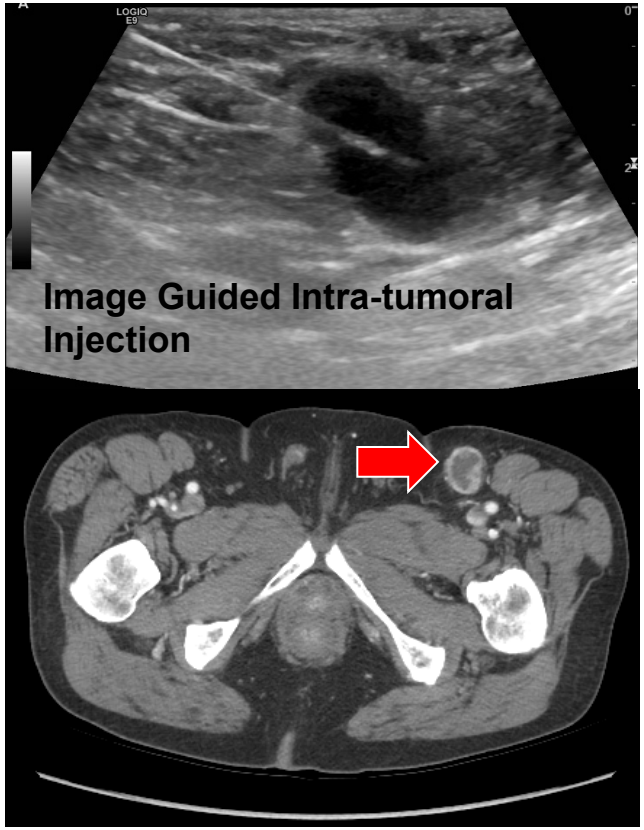
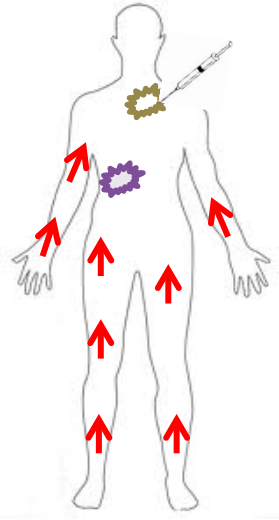
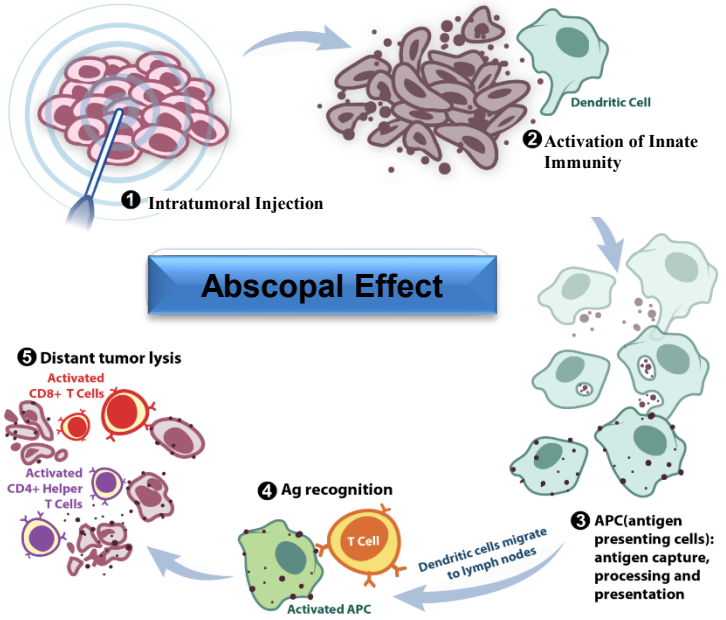
Intra-Tumoral Immunotherapy







Conclusions

- Immune Checkpoint Inhibitors (CPIs) have durable responses that can even cure some patients with advanced cancers.
- Indications for CPIs in cancer are expanding
- Though usually well tolerated, CPIs can cause severe immune related adverse events.
- These toxicities can be life-threatening if not treated promptly.
- More targeted treatments for irAEs and safer combinations are needed