Immunotherapy Case Studies

Weighing risks and benefits when risks are difficult to predict

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September 23, 2016

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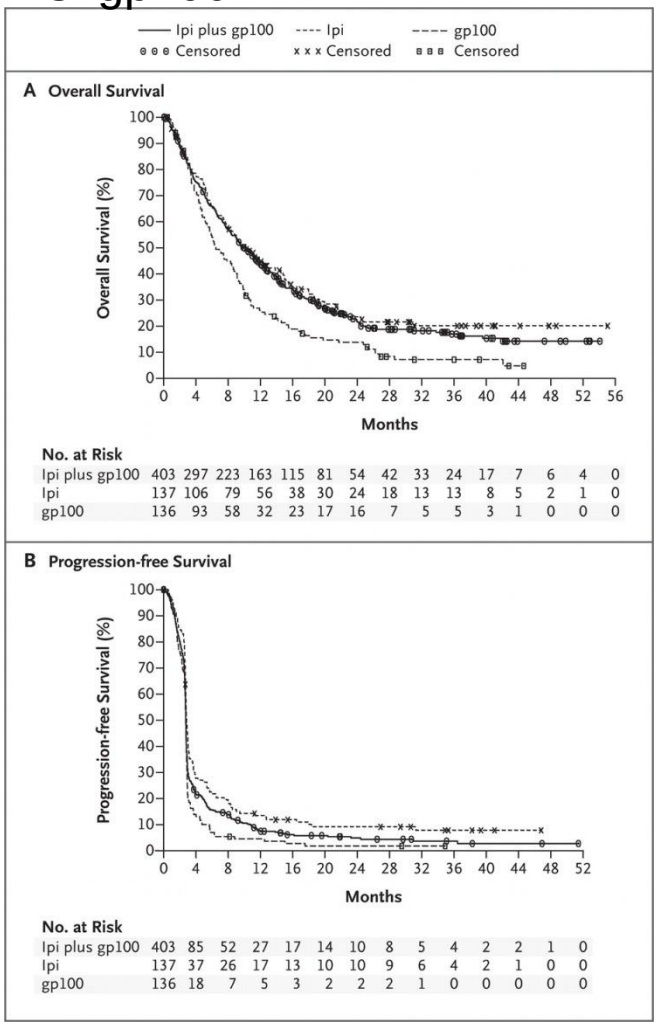
Melanoma: Ipilimumab (Yervoy)

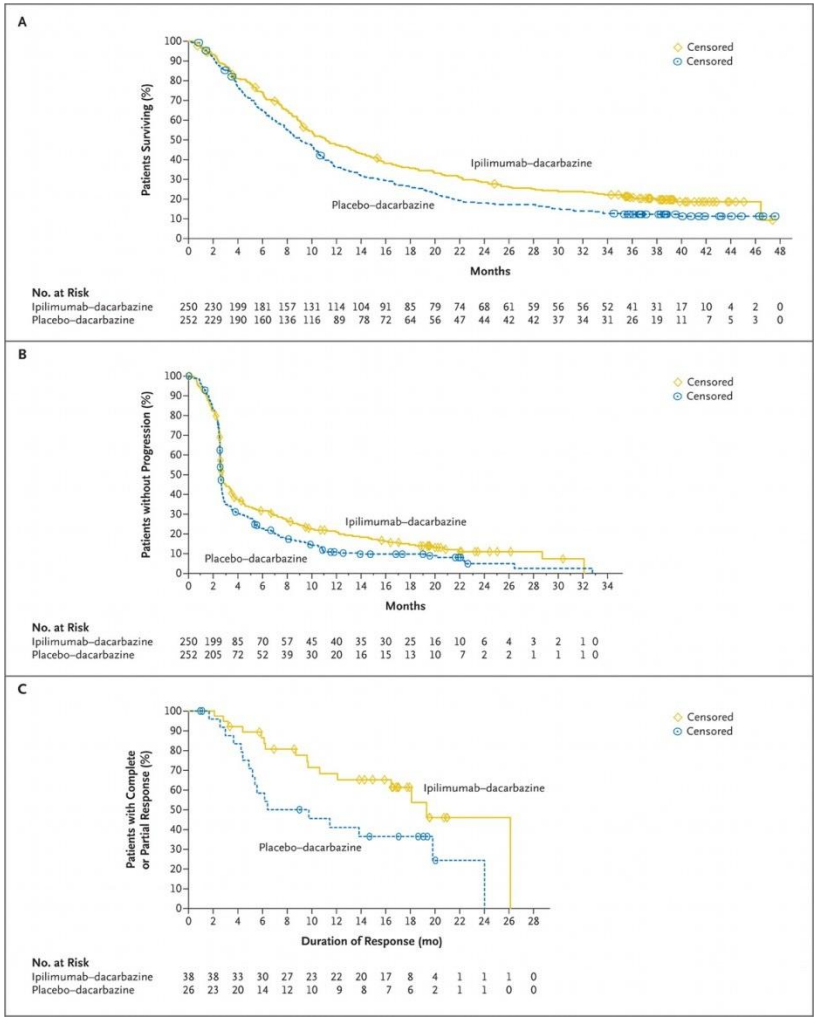
vs. gp100



OS: 10.1 vs 6.4 mo
PFS: 2.8 vs 2.8 mo

Hodi FS et al. N Engl J Med 2010;363:711-723.

Ipi +DTIC vs DTIC alone

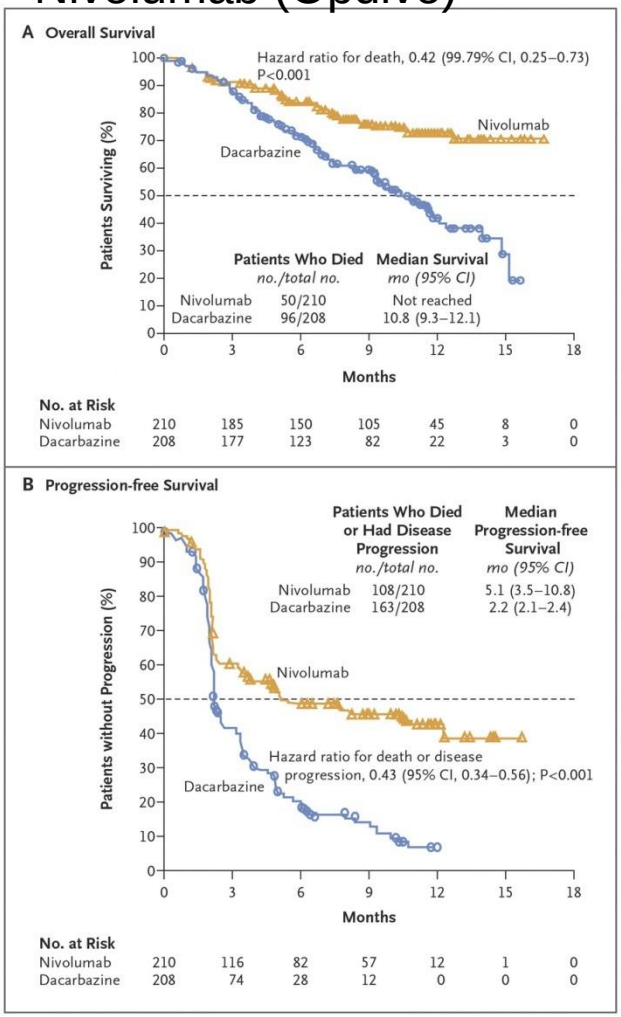


OS: 11.2 vs. 9.1 mo
PFS: No median diff
DoR: 19.2 vs 8.1 mo

Robert C et al. N Engl J Med 2011;364:2517-2526.

Melanoma: PD-1 Blockade

Nivolumab (Opdivo)

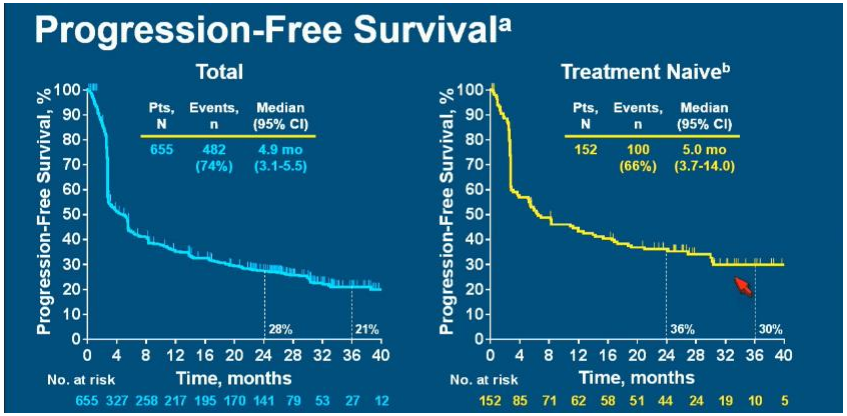


OS: HR 0.42 vs DTIC

PFS: median 5.1 vs. 2.2 months

Robert C et al. N Engl J Med 2015;372:320-330.

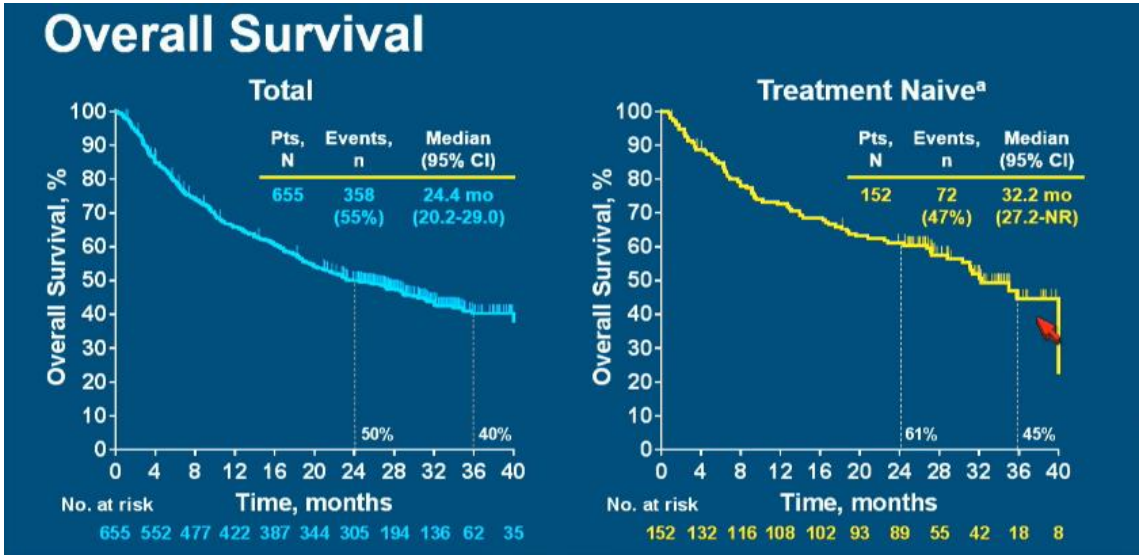
Pembrolizumab (Keytruda) (KEYNOTE-001)



CRR 10%

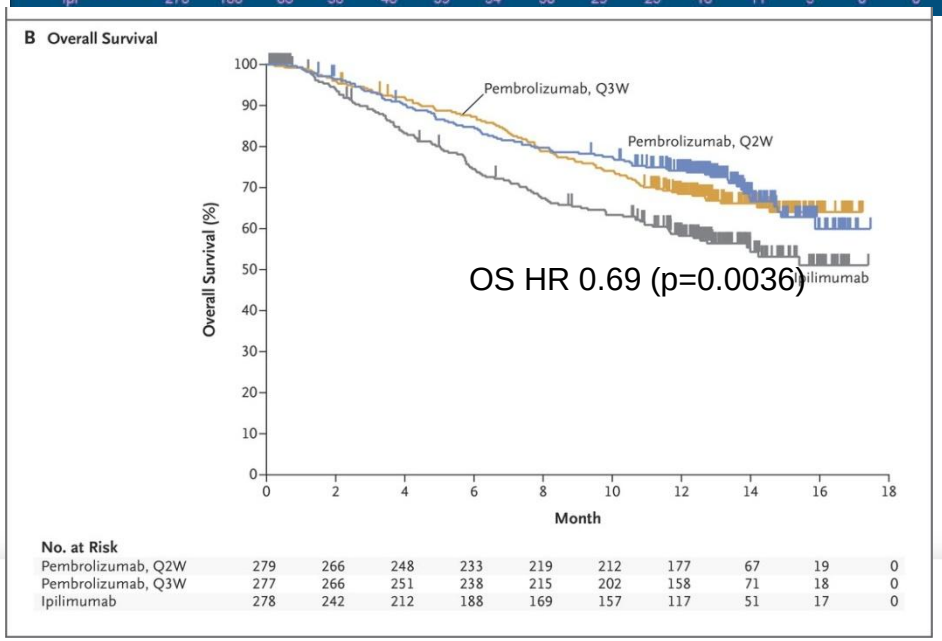
ORR 33%

DCR 51%



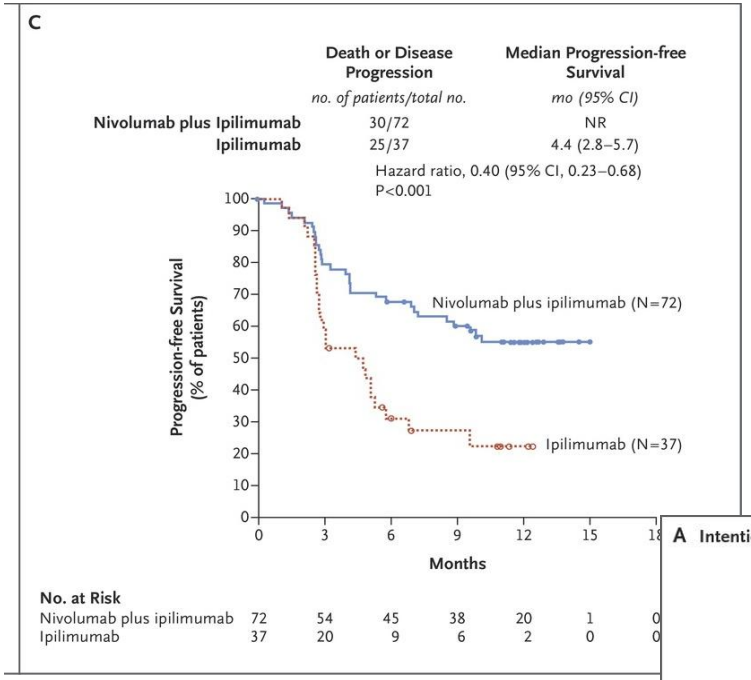
Robert et al. ASCO 2016

Melanoma: Pembrolizumab vs. Ipilimumab

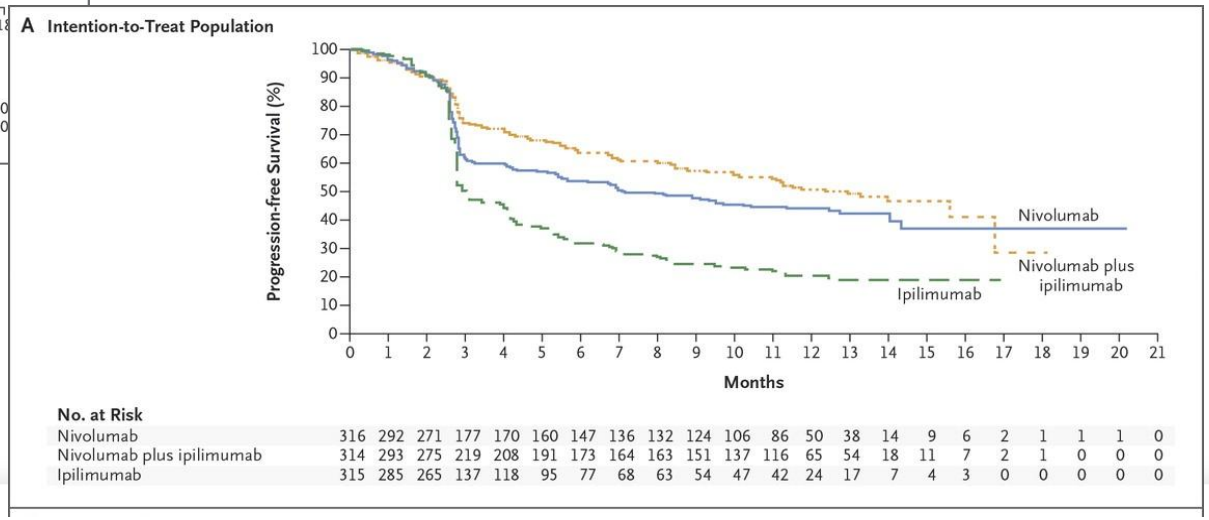


Robert C et al. N Engl J Med 2015. DOI: 10.1056/NEJMoa1503093

Melanoma: Dual Checkpoint Blockade



Postow MA et al. N Engl J Med 2015. DOI: 10.1056/NEJMoa1414428



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

Case #1: Shortness of breath

- 61 year old man with melanoma, recently treated with ipilimumab and nivolumab
- Following 4th cycle, developed chills and low-grade temp to 100.1° which resolved
- Subsequently increased fatigue and insidiously progressive shortness of breath, eventually progressing to dyspnea on mild exertion and conversational dyspnea
- CXR revealed lower lobe pneumonia
- Received ceftriaxone injection and Rx for Augmentin and Flagyl
- Symptoms continued to worsen, went to primary MD. PO2 at 89% on room air
- Additionally complains of dry cough. No nausea/vomiting. On exam dry rales in middle/lower lung fields
- New CXR revealed bilateral pulmonary infiltrates
- CT revealed chronic appearing interstitial thickening and bronchiectasis in LUL, scattered ground glass, and more confluent airspace opacities predominantly in lower lobe suggesting diffuse pneumonitis, favor infectious etiology

Case #1: Shortness of breath (cont)

Oncologic history:

- 61 yo man with hyperlipidemia, BPH, melanoma
- Noticed left axillary LAD in 2012. Size increase in 2014. LNBx showing melanoma in 2015. ALND
- Brain metastases in 5/2015, treated with gamma knife
- Received dabrafenib/trametinib x8 months with good response but had high fever, rigors, and rash resulting in stopping drugs in 2015
- Disease remaining well controlled with possible recurrence in brain in 5/2016

Relevant Pathology:

- 2015. Lymph node totally replaced by atypical melanocytes
- BRAF V600E mutation
- PD-L1 50% positive

Clinical course:

- Admitted to hospital. Started on vancomycin, pip/tazo, and cipro. Blood cultures and urine cultures performed. DuoNeb started.
- In 48 hours, no clinical improvement. Repeat CXR revealed continued opacities
- At that time, began prednisone 100mg (1mg/kg) with improvement of symptoms within 1 day
- All antibiotics d/c'ed at d/c
- Put on slow taper of steroids over 4 weeks
- Nivolumab held indefinitely

Case #1: Shortness of breath

1. What is the likelihood of autoimmune pneumonitis in patients treated with combination immunotherapy?

Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma

The NEW ENGLAND JOURNAL of MEDICINE

James Larkin, M.D., Ph.D., Vanna Chiarion-Sileni, M.D., Rene Gonzalez, M.D., Jean Jacques Grob, M.D., C. Lance Cowey,

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.

JAMA Oncology | Original Investigation

Incidence of Programmed Cell Death 1 Inhibitor–Related Pneumonitis in Patients With Advanced Cancer

A Systematic Review and Meta-analysis

Mizuki Nishino, MD, MPH; Anita Giobbie-Hurder, MS; Hiroto Hatabu, MD, PhD; Nikhil H. Ramai

Table 1. Incidence of PD-1 Inhibitor–Related Pneumonitis in All Studies Included in the Systematic Review

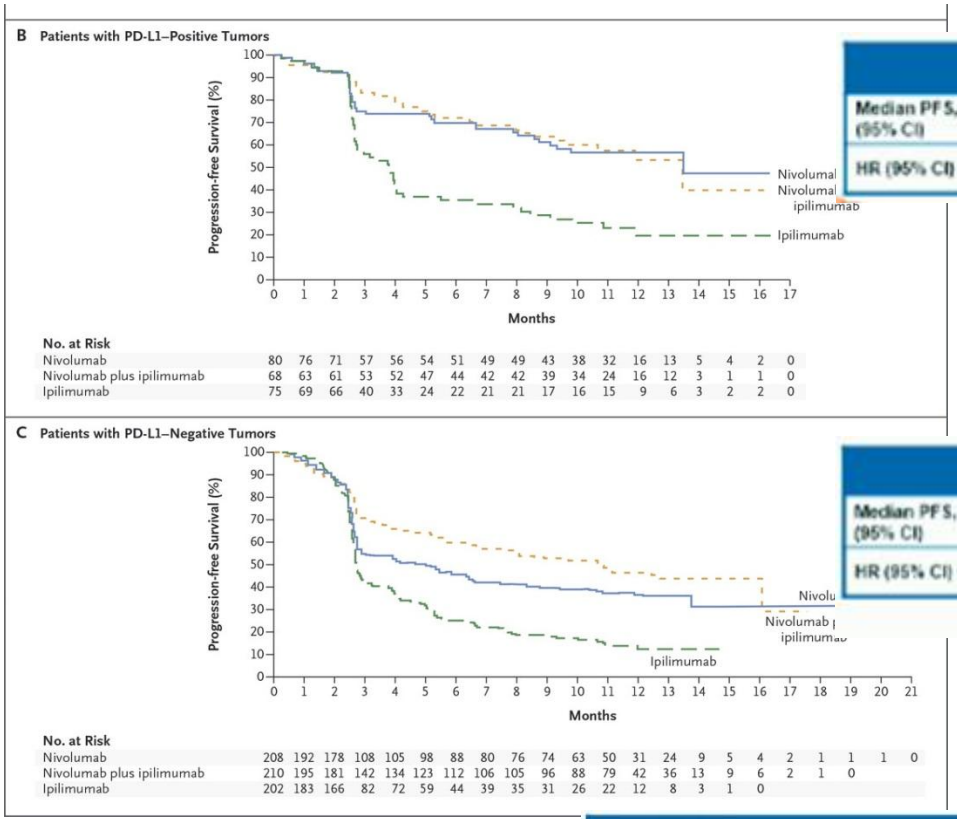
Source	Drug	Tumor Type	Phase	No. of Treated Patients[a]	No. (%) of Patients		
					All-Grade Pneumonitis	Grade ≥3 Pneumonitis	Pneumonitis-Related Death
Brahmer et al,[1] 2010[b]	Nivolumab	Advanced solid tumors	1	39	NA	0	0
Topalian et al,[2] 2012[b]	Nivolumab	Advanced solid tumors	1	296	9 (3.0)	3 (1.0)	3 (1.0)
Hamid et al,[3] 2013	Pembrolizumab	Melanoma	1	135	6 (4.4)	0	0
Wolchok et al,[5] 2013[c]	Nivolumab and ipilimumab (concurrent)	Melanoma	1	53	3 (5.7)	1 (1.9)	0
	Nivolumab and ipilimumab (sequential)	Melanoma	1	33	1 (3.0)	0	0
Weber et al,[37] 2013[c]	Nivolumab	Melanoma	1	41	0	0	0
	Nivolumab and peptide vaccine	Melanoma	1	49	3 (6.1)	2 (4.1)	0
Topalian et al,[4] 2014	Nivolumab	Melanoma	1	107	2 (1.9)	0	0
Robert et al,[24] 2014	Pembrolizumab	Melanoma	1	173	3 (1.7)	1 (0.6)	0
Robert et al,[20] 2015	Nivolumab	Melanoma	3	206	3 (1.5)	0	0
Motzer et al,[22] 2015	Nivolumab	RCC	2	167	8 (4.8)	0	0
Ansell et al,[35] 2015[b]	Nivolumab	Lymphoma	1	23	NA	1 (4.3)	0
Gibney et al,[32] 2015	Nivolumab and peptide vaccine	Melanoma	1	33	1 (3.0)	0	0
Rizvi et al,[21] 2015	Nivolumab	NSCLC	2	117	6 (5.1)	4 (3.4)	0
Weber et al,[19] 2015	Nivolumab	Melanoma	3	268	5 (1.9)	0	0
McDermott et al,[23] 2015	Nivolumab	RCC	1	34	1 (2.9)	0	0
Robert et al,[34] 2015	Pembrolizumab	Melanoma	3	555	6 (1.1)	1 (0.2)	0
Garon et al,[12] 2015	Pembrolizumab	NSCLC	1	495	18 (3.6)	9 (1.8)	1 (0.2)
Postow et al,[33] 2015	Nivolumab and ipilimumab	Melanoma	1	94	10 (10.6)	3 (3.2)	1 (1.1)
Gettinger et al,[11] 2015	Nivolumab	NSCLC	1	129	11 (8.5)	4 (3.1)	3 (2.3)
Patnaik et al,[27] 2015[b]	Pembrolizumab	Advanced solid tumors	1	30	1 (3.3)	0	0
Larkin et al,[6] 2015[c]	Nivolumab	Melanoma	3	313	4 (1.3)	1 (0.3)	0
	Nivolumab and ipilimumab	Melanoma	3	313	20 (6.4)	3 (1.0)	0
Le et al,[28] 2015[b]	Pembrolizumab	Advanced solid tumors[d]	2	41	1 (2.4)	0	0
Brahmer et al,[30] 2015	Nivolumab	NSCLC	3	131	6 (4.6)	0	0
Ribas et al,[26] 2015	Pembrolizumab	Melanoma	2	357	6 (1.7)	2 (0.6)	0
Hamanishi et al,[29] 2015[b]	Nivolumab	Ovarian	2	20	0	0	0
Motzer et al,[36] 2015	Nivolumab	RCC	3	406	16 (3.9)	6 (1.5)	0
Borghaei et al,[31] 2015	Nivolumab	NSCLC	3	287	4 (1.4)	3 (1.0)	0

Case #1: Shortness of breath

Should the patient have received combination immunotherapy?

How can we stratify based on risk versus benefit?

Melanoma: Role of PD-L1 Status



	NIVO + IPI (N=212)	NIVO (N=218)	IPI (N=215)
Median PFS, months (95% CI)	NR (9.7–NR)	22.0 (8.9–NR)	3.9 (2.8–4.2)
HR (95% CI) vs. NIVO	0.87 (0.54–1.41)*	–	–

	NIVO + IPI (N=210)	NIVO (N=208)	IPI (N=202)
Median PFS, months (95% CI)	11.1 (9.0–22.2)	5.3 (2.8–7.1)	2.8 (2.8–3.1)
HR (95% CI) vs NIVO	0.74 (0.56–0.98)*	–	–

*Exploratory endpoint

		NIVO+IPI	NIVO	IPI
PD-L1 (≥5%)	ORR, % (95% CI)	**72.1** (59.9–82.3)	**57.5** (45.9–68.5)	**21.3** (12.7–32.3)
	Median Duration of Response (months)	NR	20.7	NR
PD-L1 (<5%)	ORR, % (95% CI)	**54.8** (47.8–61.6)	**41.3** (34.6–48.4)	**17.8** (12.8–23.8)
	Median Duration of Response (months)	NR	22.3	18.2

Larkin J et al. N Engl J Med 2015. DOI: 10.1056/NEJMoa1504030
Wolchok et al. ASCO 2016

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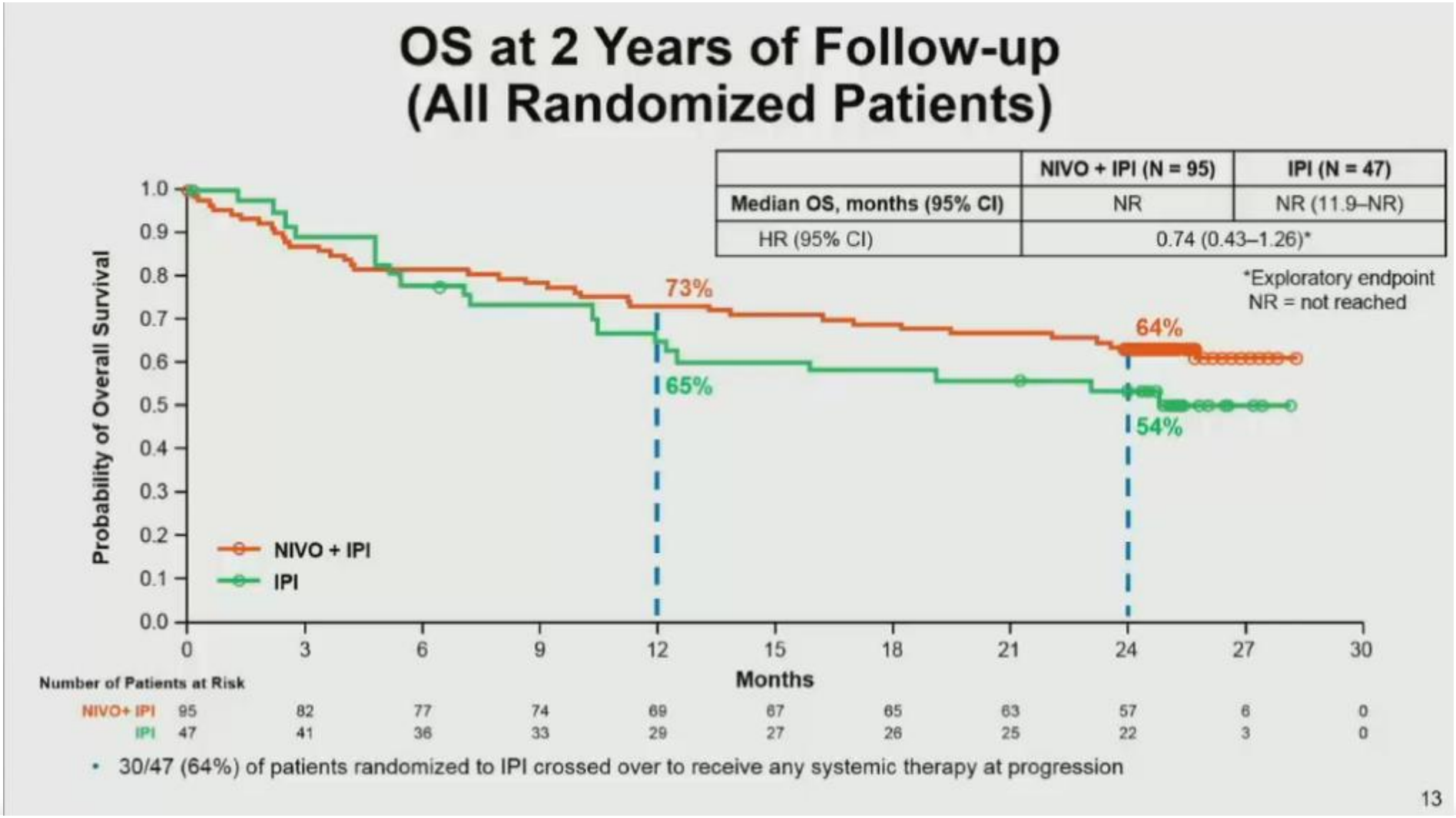
Melanoma: Benefit of Combination



Postow et al. AACR Annual Meeting, 2016.

Toxicity associated with nivolumab and ipilimumab (Nivo+Ipi) combination therapy in melanoma patients (pts) treated at a single-institution under an expanded-access program (EAP).

Claire F. Friedman, Pedram Navid-Azarbaijani, Alexander N. Shoushtari, Shonnette C. Campbell, Margaret K. Callahan, Parisa Momtaz, Nana A. Prempeh-Keteku, Michael A. Postow, Yelena Shames, Jedd D. Wolchok, Paul B. Chapman

DEMOGRAPHICS

- 64 pts: Median age 56 , range 22 – 82.
- Male to female ratio: 1:1
- 31% of patients had an elevated LDH
- 81% o f patients were ECOG 0, 19% ECOG 1
- 50% stage IV, 17% stage III

RESULTS

- 58 pts (91%) had ≥ 1 clinically significant irAE (median=2, range 0-6)
- 38 pts (59%) had a grade 3-4 irAE
- 46 pts (72%) required ≥ 1 course of steroids.
- 14 pts (22%) required infliximab for steroid-refractory diarrhea
- 2 pts (3%) required mycophenolate for steroid-refractory transaminitis

- 40 pts (63%) had ≥1 visit to the ED (range 0-5); 61% of those visits were related to irAEs
- 30 pts (48%) had ≥1 hospitalization; 70% of those hospitalizations were related to irAEs

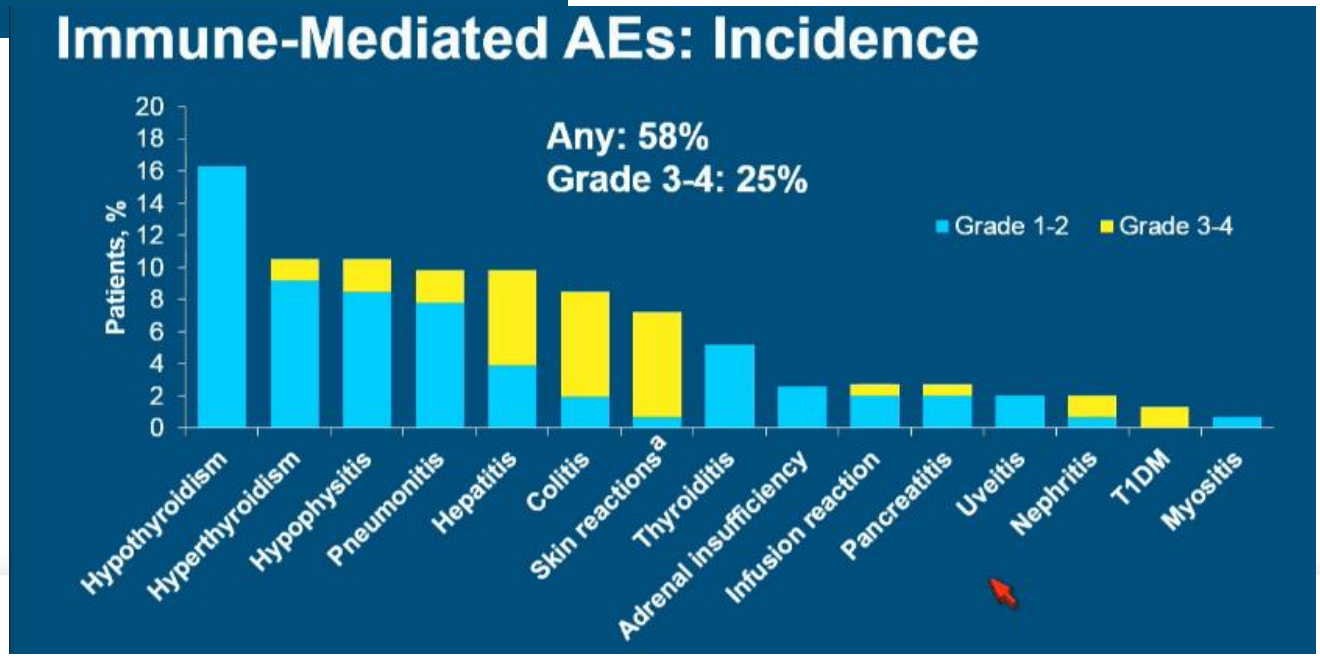
- Nivo+Ipi irAEs did recur after transition to anti-PD-1 monotherapy, including colitis (2 pts), amylase/lipase elevation (3 pts) and pneumonitis (1 pt)
- Colitis recurrences required re-treatment with infliximab

Adverse events with Ipilimumab + Pembrolizumab

AE Summary

Category	Treatment Related N = 153	Immune Mediated[a] N = 153
Any grade	145 (95%)	89 (58%)
Grade 3-4	64 (42%)	38 (25%)
Led to death	0	0
Led to ipilimumab discontinuation only	16 (10%)	12 (8%)
Led to pembrolizumab discontinuation[b]	11 (7%)	6 (4%)
Led to ipilimumab and pembrolizumab discontinuation[c]	16 (10%)	11 (7%)

Immune-Mediated AEs: Incidence



Case #1: Shortness of breath

1. What are common causes of delays in starting steroids?
    1. Low index of suspicion
    2. Delay in development of symptoms
    3. Concern for steroids dampening effect of immunotherapy

Toxicity associated with nivolumab and ipilimumab (Nivo+Ipi) combination therapy in melanoma patients (pts) treated at a single-institution under an expanded-access program (EAP).

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- 61% of pts discontinued Nivo+Ipi before receiving all 4 cycles
- 79% of those who discontinued stopped for toxicity
- 47% of pts did not receive any anti-PD-1 monotherapy, including 54% of patients who stopped Nivo+Ipi early

Figure 1: Early Discontinuation of Nivo+Ipi

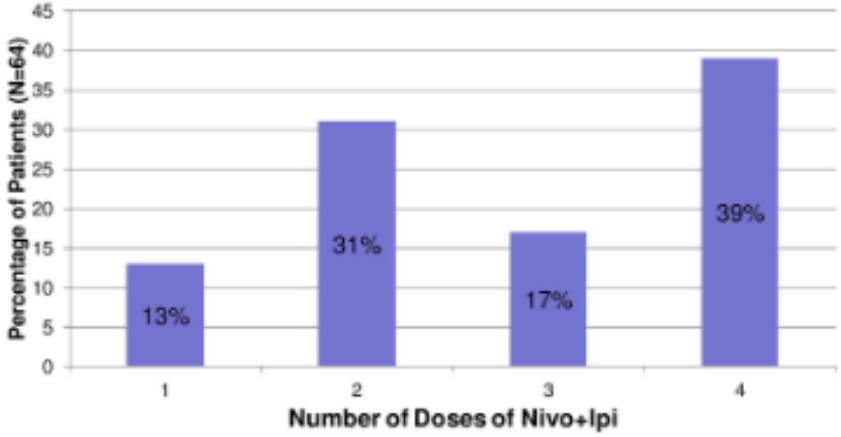
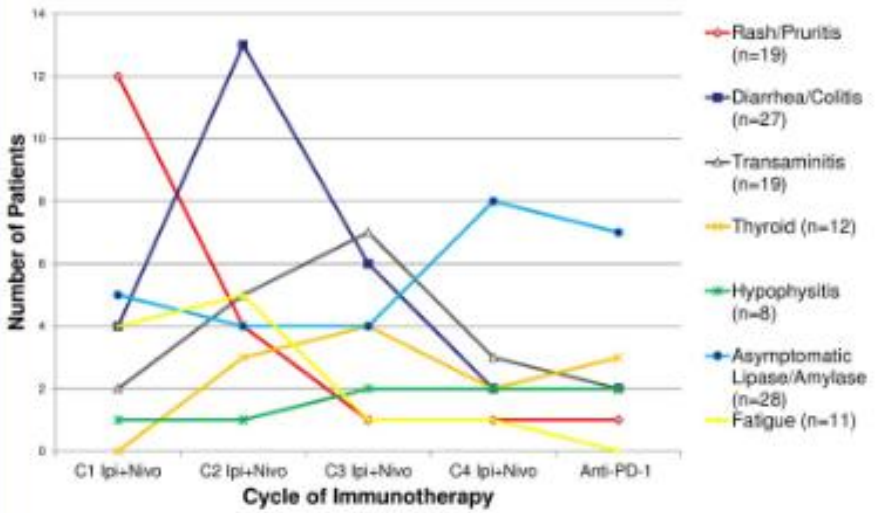


Figure 2: Timing of diagnosis of irAEs



Overall Survival in Patients With Advanced Melanoma (MEL) Who Discontinued Treatment With Nivolumab (NIVO) Plus Ipilimumab (IPI) Due to Toxicity in a Phase II Trial (CheckMate 069)

F. Stephen Hodi,[1] Michael A. Postow,[2] Jason Chesney,[3] Anna C. Pavlick,[4] Caroline Robert,[5] Kenneth Grossmann,[6] David McDermott,[7] Gerald Linette,[8] Nicolas Meyer,[9] Jeffrey Giguere,[10] Sanjiv S. Agarwala,[11] Montaser Shaheen,[12] Marc S. Ernstoff,[13] David R. Minor,[14] April Salama,[15] Matthew H. Taylor,[16] Patrick A. Ott,[1] Joel Jiang,[17] Paul Gagnier,[17] Jedd D. Wolchok[2]

Table 3. Response to treatment (NIVO+IPI patients)

	All randomized (N = 95)	Discontinued due to AEs (n = 35)
ORR, % (95% CI)	59 (48-69)	66 (48-81)
Best overall response, %		
Complete response	22	20
Partial response	37	46
Stable disease	13	17
Progressive disease	16	9
Could not be determined	13	9

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Figure 4B. Progression-free survival at 2 years of follow-up

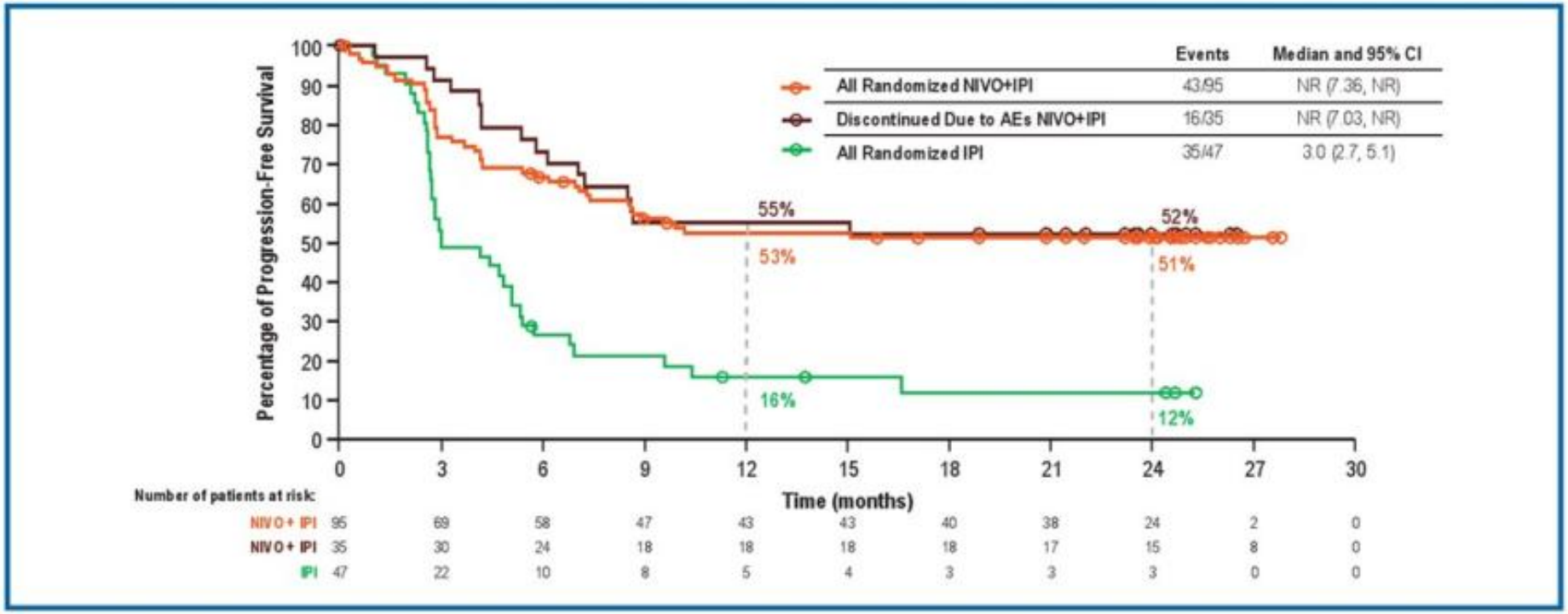

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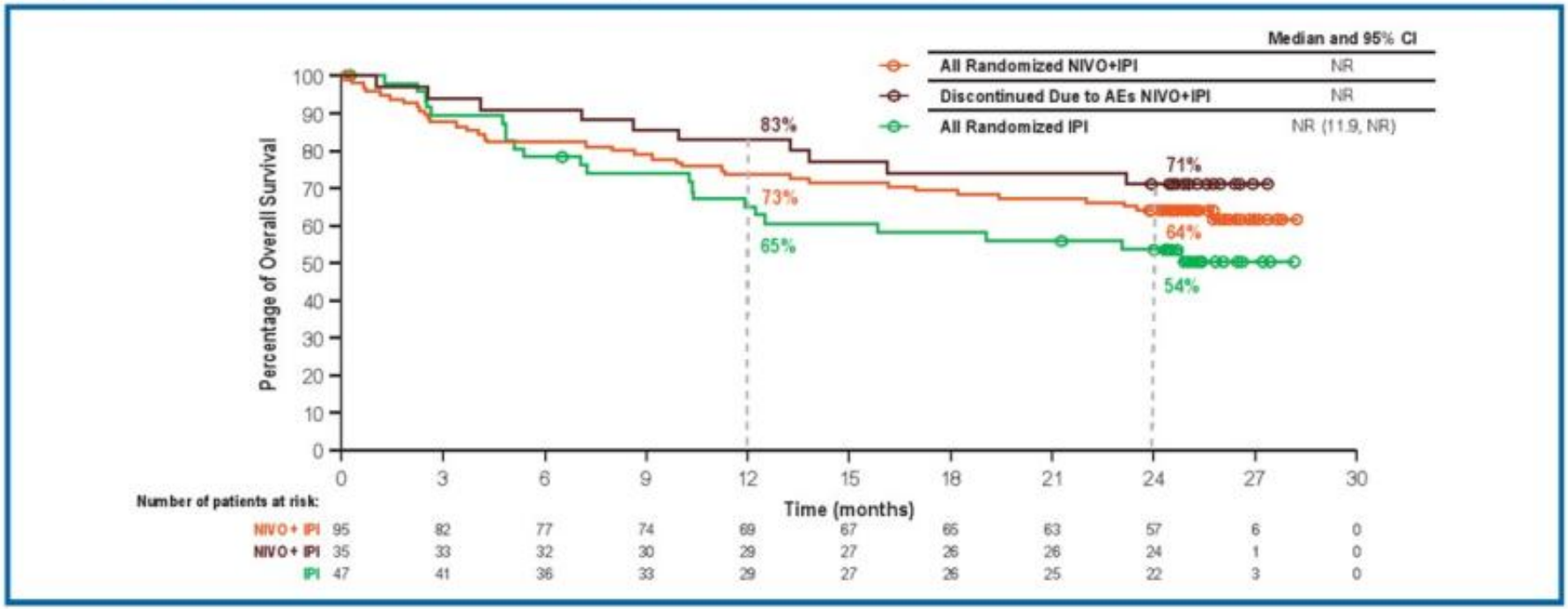
Figure 4A. Overall survival at 2 years of follow-up



Case #2: Blurry Vision

- 63 year old man with melanoma and brain metastasis
- Received gamma-knife treatment 6 weeks ago
- Started on single-agent pembrolizumab 2 weeks ago
- 6 days prior to admission, developed blurry vision accompanied with headache and shortness of breath
- Within last 3 days, had dyspnea and fatigue even on a few steps
- Exam shows mild lid lag in both eyes, respiratory exam normal
- CT chest shows 1cm RLL nodule. No evidence of other abnormalities
- MRI brain shows improved brain metastasis. No other intracranial abnormalities

Case #2: Blurry Vision

PMH:

- Presented in 2014 with cutaneous ulcerated melanoma of scalp
- Received wide local excision and neck dissection.
- Started on clinical trial with vemurafenib vs. placebo
- Eight months following trial initiation, developed asymptomatic brain metastasis

Relevant pathology:

- Initial pathology revealed ulcerated nodular melanoma (Breslow thickness 18mm), 5 mitoses/mm^2
- SLNBx showed positive cervical node with extracapsular extension. No additional nodal involvement on neck dissection- T4bN1aM0
- BRAF V600K mutation

Clinical Course:

- Admitted, neurology consulted. Pyridostigmine started. Concern for pneumonia so steroids held. Myasthenia panel ordered
- Day 3: Prednisone 60mg qday and IVIG started on Day 3
- Day 6: Acetylcholine receptor Ab returned positive. Switched to 1000mg methylprednisolone
- Day 7: Started plasmapheresis
- Day 9: Worsening shortness of breath. Intubated
- Day 12: Patient opted to withdraw care. Terminally extubated.

Case #2: Blurry Vision

What are potential causes of blurry vision?

Is it autoimmune?

Neurological, respiratory, musculoskeletal, cardiac and ocular side-effects of anti-PD-1 therapy

European Journal of Cancer
Volume 60, June 2016, Pages 210–225

Lisa Zimmer [a], Simone M. Goldinger [b], Lars Hofmann [c],

- 496 patients treated with PD-1 inhibitors in 15 centers in Germany and Switzerland
- 242 autoimmune side effects in 138 patients
- 77 of 138 patients had neurologic, respiratory, musculoskeletal, cardiac, hematologic, ocular toxicities
- 1.6% of patients developed ocular adverse events

Table 5
Miscellaneous side-effects of anti-PD-1 therapy (infectious, ocular, blood).

Type of side-effect	Grade CTCAE	Anti-PD-1 antibody	Occurrence in week(s) after initiation of anti-PD-1	Treatment of side-effect	Outcome of side-effect	Clinical tumour response to anti-PD-1	Gender (female/male)	Age	Pre-treatments
Iritis	3	p	3	Mydriatics; dexamethasone eye drops	Resolved	PR	f	53	Vemurafenib; ipilimumab
Anterior uveitis, both eyes	1	n	7	Topical corticosteroids	Resolved	PR	f	62	Interferon-alpha; ipilimumab
Uveitis	2	p	4	Topical corticosteroids	Resolved	PR	m	71	Dabrafenib; ipilimumab; radiotherapy
Inflammation ear	2	p	65	Ciprofloxacin	Resolved	PR	m	79	No prior treatment
Conjunctivitis	2	n	60	Topical corticosteroids	Not resolved	PD	m	78	Interferon-alpha
Uveitis with oedema of the macula	2	p	11	Topical therapy	Resolved	PR	m	74	Vemurafenib; ipilimumab; BRAF inhibitor/MEK inhibitor/CDK4/6 inhibitor

Neurological side-effects of anti-PD-1 therapy.

Type of side-effect	Grade CTCAE	Anti-PD-1 antibody	Occurrence in week(s) after initiation of anti-PD-1	Treatment of side-effect	Outcome of side-effect	Clinical tumour response to anti-PD-1	Gender (female/ male)	Age	Pre-treatments
Polyneuropathy	2	n	6	Prednisolone 1 mg/kg/d p.o.; methylprednisolone 1 g/d; immunoglobulins i.v.; physiotherapy; pause of nivolumab	Improved	SD	f	81	Chemotherapy (unknown); ipilimumab
Seizure	2	p	7	Levetiracetam 500 mg 2×/d	Resolved; intracerebral bleeding 3 weeks later	SD	m	30	Interferon-alpha; intranodal vaccine; ipilimumab; radiotherapy
Polyneuropathy	2	p	4	Pregabalin 75 mg 2×/d	Not resolved	PD	m	68	Temozolomide; cisplatin; sorafenib; irinotecan; ipilimumab
Seizure (probably due to SIRS)	2	p	20	Lorazepam	Resolved	PD	m	79	No prior treatment
Recurring seizures; parkinsonoid/ bradykinesia	2	p	68	Levetiracetam; stop of pembrolizumab	Improved	CR	f	63	Dacarbazine; ipilimumab
Polyneuropathy worsening	2	p	6	Magnesium	Not resolved	PR	f	65	Dacarbazine; ipilimumab
Paresis, neuritis (oculomotor nerve)	2	p	13	Prednisolone 100 mg/d; pause of pembrolizumab	Resolved	PR	m	84	Interferon-alpha; dacarbazine; ipilimumab
Paresis (abducens nerve, facial nerve)	3	n	6	Methylprednisolone 1 mg/kg/d; pause of nivolumab	Resolved	SD	m	83	Interferon-alpha; fotemustine; ipilimumab
Guillian-Barré syndrome	3	n	15	immunoglobulins i.v.; prednisolone 1 mg/kg/d i.v.; stop of nivolumab	Resolved with sequelae	SD	m	51	Interferon-alpha
Paraesthesia	1	p	1, 4	No treatment	Resolved	PD	m	45	Interferon-alpha; dacarbazine; carboplatin/paclitaxel; carboplatin; vaccine; radiotherapy; ipilimumab (including reinduction)
Paraesthesia	1	p	40	No treatment	Not resolved	PR	m	64	Radiotherapy; dacarbazine; carboplatin/paclitaxel; ipilimumab
Paraesthesia	1	p	1	No treatment	Not resolved	PR	m	68	Radiotherapy; dacarbazine; dabrafenib; dabrafenib/ trametinib; carboplatin/paclitaxel; ipilimumab
(Meningo)-radiculitis	3	n	9	Dexamethasone 4 mg 4×/d p.o.; stop of nivolumab	Improved	PD	m	76	Radiotherapy
Paralysis (eyelids/hands)/ myasthenia gravis	4	p	10	Methylprednisolone 1000 mg i.v.3 d; pyridostigmine 30 mg p.o.3 d; plasmaphaeresis	Not resolved; death	PR	f	69	Ipilimumab
Changes in taste	1	n	10	No treatment	Not resolved	PR	m	76	Ipilimumab (including reinduction); radiotherapy
Polyradiculitis	3	p	35	Prednisolone 1 g i.v., following prednisolone p.o., tapering; pause of pembrolizumab	Improved	PR	m	38	Radiotherapy; ipilimumab; dabrafenib/trametinib; interleukin-2

p, Pembrolizumab; n, Nivolumab; CTCAE, Common Terminology Criteria for Adverse Events; SD, Stable disease; PR, Partial response; CR, Complete response; PD, Progressive disease; SIRS, Systemic inflammatory response syndrome; i.v., Intravenous; p.o., Oral.

Case #2: Blurry Vision

How do we treat extremely rare side effects?

What are the sequelae?

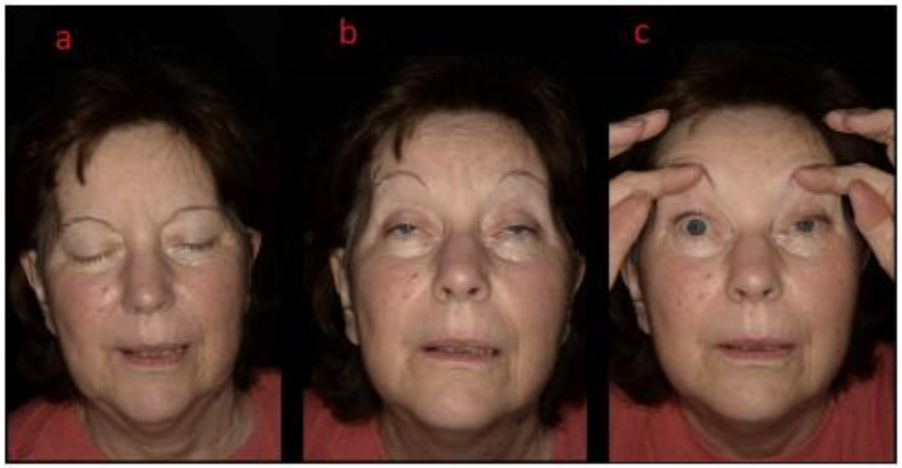


Fig. 1. Paralysis/myasthenia gravis: 69-year-old female patient with a movement disorder of her eyes and ptosis of her eyelids. Relaxed (a), forced (b) and supported (c), shortly after the third infusion of pembrolizumab.

Case #3: Pain and Weakness

- 62 year old man with non-small cell lung cancer with vertebral mets being treated with pembrolizumab since 9/2015
- Progressive lower back pain starting in 2/2016. Pain worse at night. Pain begins in lower back, legs go numb for 20 seconds, then sensation returns with throbbing pain in back and legs
- Assumed due to vertebral mets, referred to XRT with no relief
- By 4/2016, developed lower extremity weakness and inability to walk

Case #3: Pain and Weakness

PMH:

- T4N3M1 lung cancer diagnosed in 2015
- Excellent response to first-line pembrolizumab, with 90% resolution of RUL and pleural lesions
- Known vertebral metastases remained stable throughout course
- No history of autoimmune disease, arthritis, radiculopathy

Relevant pathology:

- Right upper lobe lesion with poorly differentiated NSCLC.
- PD-L1>50%. EGFR wt, ALK negative

Clinical Course:

- After completion of RT, increased pain. Diaphoretic, tachycardic. No PE on imaging. Pembro held.
- Hospitalization with extensive neuro workup: LP showed high protein, low glucose, negative cytology.
- Developed encephalopathy. Presumed carcinomatous meningtis, started depocyte. Has received 8 doses to date
- Several days later, empiric high dose steroids started. Slow taper. Slight improvement of symptoms, but continued pain
- Repeat LP in 7/2016 showed cytology positive for malignant cells

Case #3: SP

1. Is this immunotherapy related?
2. How can we tell?
3. How do we treat?
4. What do we do when we don’t know?

Questions?

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