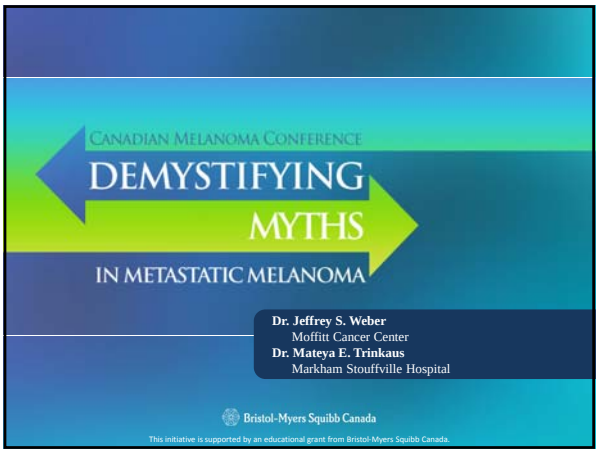


Learning Objectives

- Review recent developments in the management of melanoma
- Involve the multidisciplinary team in the management of patients with metastatic melanoma
- Optimize treatment of metastatic melanoma to maximize long-term overall survival

Agenda

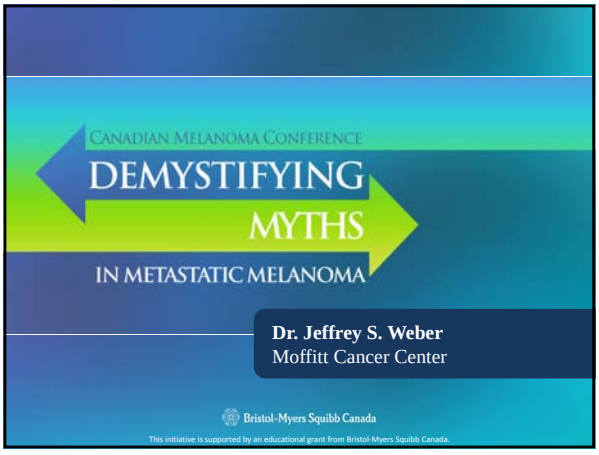
10:45 am – 11:00 am	Recent Developments in the Management of Melanoma	Dr. Jeffrey Weber
11:00 am – 11:10 am	Building a Multidisciplinary Team to Manage Metastatic Melanoma	Dr. Jeffrey Weber
11:10 am – 11:35 am	Treating Metastatic Melanoma in the Community Setting	Dr. Mateya Trinkaus
11:35 am – 11:45 am	Question-and-Answer Period	All

Disclosures – Dr. Weber

- Participated in advisory boards and received honoraria for:
  - Amgen
  - AstraZeneca
  - Bristol-Myers Squibb
  - Genetech
  - GlaxoSmithKline
  - Novartis

Disclosures – Dr. Trinkaus

- Participated in advisory boards and received honoraria for:
  - Amgen
  - AstraZeneca
  - Bristol-Myers Squibb
  - Novartis
  - Roche

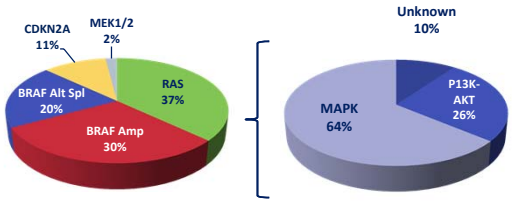


Latest ASCO/ECCO Data: Overcoming BRAF Resistance

- FDA-approved BRAF inhibitors vemurafenib and dabrafenib have PFS of 5–7 months
- A major clinical issue in melanoma treatment is resistance to BRAF inhibition
- What do we know about the mechanisms of BRAF resistance, and how to overcome it?

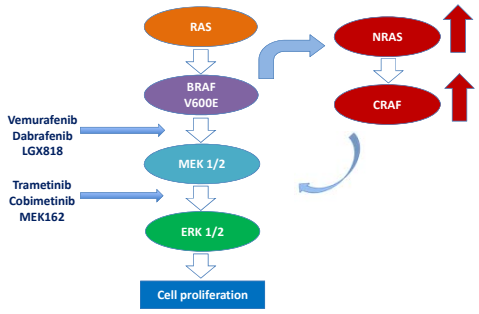
ASCO: American Society of Clinical Oncology; ECCO: European CanCer Organisation; PFS: progression-free survival

Frequency of Acquired Resistant Mechanisms to BRAF Inhibitors

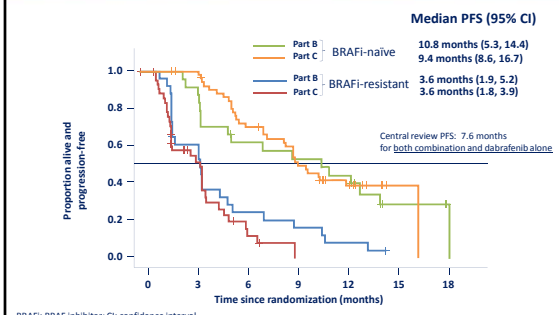


Shi H *et al.* Submitted manuscript.

Frequency of Acquired Resistant Mechanisms to BRAF Inhibitors

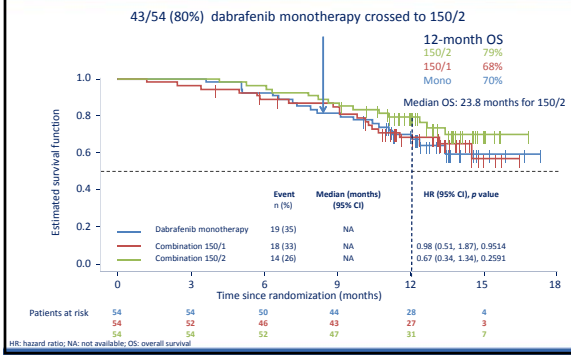


Dabrafenib + Trametinib: PFS in BRAFi-Naïve vs. BRAFi-Resistant Patients



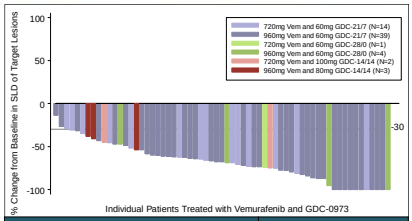
BRAFi: BRAF inhibitor; CI: confidence interval
Sosman J *et al.* ASCO 2013. Abstract 9005.

OS: BRAF + MEK



HR: hazard ratio; NA: not available; OS: overall survival

BRIM7: Response Rate and Best Response in BRAFi-Naïve Patients

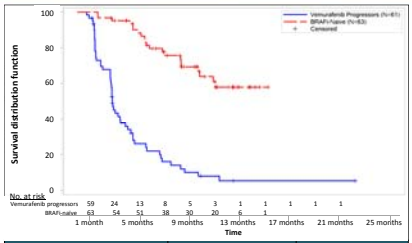


RECIST 1.1 Confirmed Responses	(n = 63)
Objective responses	**53 (85%)**
Complete response	6 (10%)
Partial response	47 (75%)
Stable disease	8 (13%)
Progressive disease	2 (3%)

SLD: sum of longest diameters

Data cut: June 21, 2013

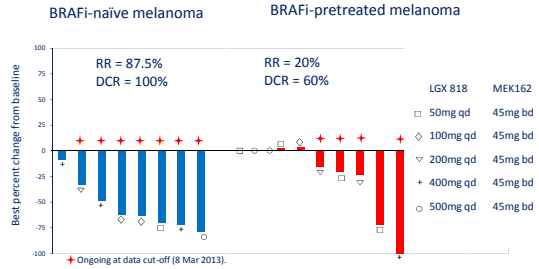
BRIM7: PFS



	Vem-Progressors (n = 61)	BRAFi–naïve (n = 63)
Patients with events	52 (85.2%)	21 (33.3%)
Median time to PFS events (months)	**2.8**	**Not reached**
95% CI for median	2.6, 3.8	9.8, –

Data cut: June 21, 2013

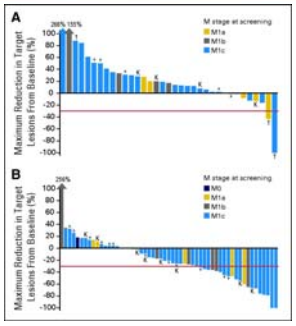
LGX818 + MEK162: Best Confirmed Response



Pretreated ≠ Progressed

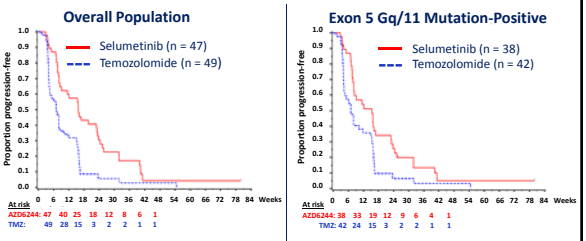
Kefford R *et al.* ASCO 2013. Abstract 9029.

MEK Inhibitor (Trametinib) Response



Kim KB *et al. J Clin Oncol* 2013; 31(4):482-9.

MEK Inhibition Improves PFS in Uveal Melanoma Regardless of Mutation Status



15.9 weeks (95% CI: 8.4, 23.1) vs.
7.0 weeks (95% CI: 4.3, 8.4)

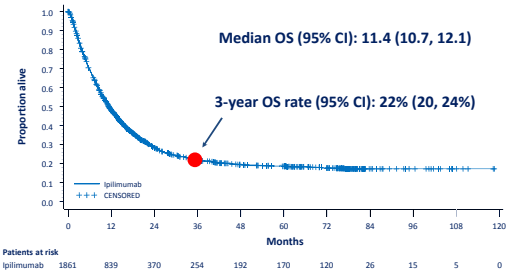
HR = 0.46 (95% CI: 0.30, 0.71)
***p* = 0.0005**

15.4 weeks (95% CI: 8.1, 16.9) vs.
7.0 weeks (95% CI: 4.3, 11.9)

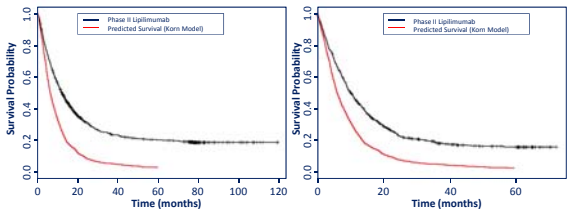
HR = 0.55 (95% CI: 0.34, 0.87)
***p* = 0.011**

Carvajal R *et al.* ASCO 2013. Abstract 9003.

Primary Analysis of Pooled OS Data: 1861 Patients that Received Ipilimumab

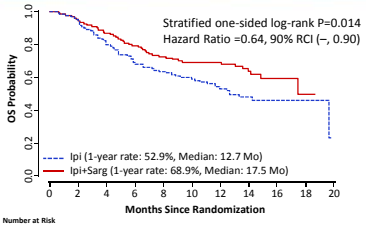


OS for Ipilimumab Relative to Historical Data



- Historical controls
  - Phase II: 1278 patients in 42 cooperative group trials from 1975–2005
  - Phase III: 3739 patients in 10 trials from 1999–2011

Phase II Trial of GM-CSF + Ipilimumab vs. Ipilimumab Alone: OS



Number at Risk

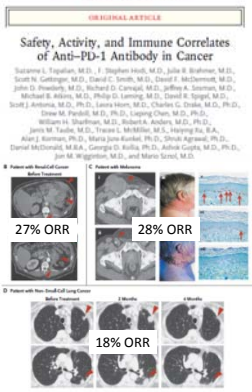
122	114	94	80	72	64	49	28	14	6	0	trt=Ipi
123	115	104	94	84	75	63	39	11	2	0	trt=Ipi+Sarg

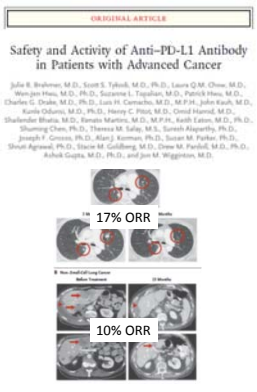
	Arm A: Ipilimumab + GM-CSF (n = 123)	Arm B: Ipilimumab alone (n = 122)	Comparisons
- Median OS (95% CI)	17.5 months (14.9, NR)	12.7 mo (10.0, NR)	*P1** = 0.014 (stratified log-rank test)
- 1-year OS rate, (95% CI)	68.9% (60.6, 85.5)	52.9% (43.6, 62.2)	
- HR (90% RCI for HR)	0.64 (-, 0.90)	Reference	*P1** = 0.014 (stratified Cox model)

Hodi FS *et al.* ASCO 2013. Abstract CRA9007.

NR: not releasable; RCI: repeated confidence interval

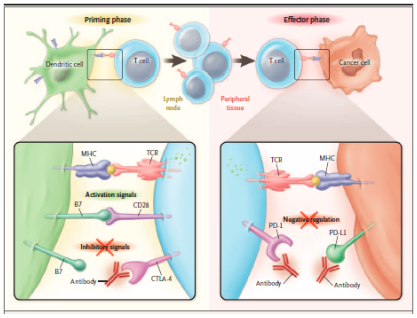
ASCO 2012





N Engl J Med 2012.

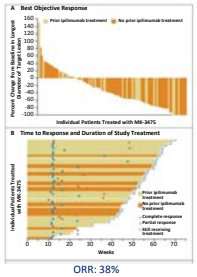
Mechanism of Action of Checkpoint Protein Inhibition



Ribas A. *N Engl J Med* 2012; 366(26):2517-9.

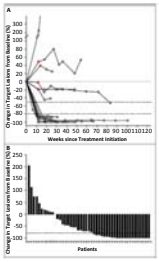
ASCO/NEJM 2013: MK-3475 and Nivolumab + Ipilimumab Show High Response Rates in Melanoma

MK-3475



ORR: 38%
Highest dose ORR: 52%
(by RECIST 1.1 with confirmation assessed by ICR)

Nivolumab + Ipilimumab



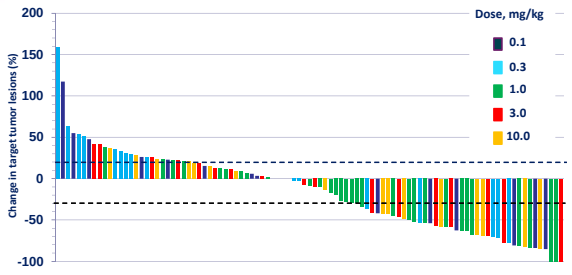
ORR: 40%
Highest dose ORR: 53%
(by investigator-assessed irRC with confirmation)

ICR: independent central review; irRC: immune-related response criteria; ORR: objective response rate; RECIST: Response Evaluation Criteria In Solid Tumors

PD-1/PD-L1-Inhibiting Agents in Clinical Development

Target	Agent	Class	K_D
PD-1	Nivolumab (MDX1106, BMS936558, BMS-ONO)	IgG4 fully human antibody	3 nM
	MK-3475 (Merck)	IgG4 engineered humanized antibody	29 pM
	Pidilizumab (CT-011, CureTech-Teva)	IgG1 humanized antibody	-
	AMP-224 (Amplimmune-GSK)	Fc-PD-L2 fusion protein	-
PD-L1	BMS935559 (MDX-1105, BMS-ONO)	IgG4 fully human antibody	-
	MPDL3280A (Genentech)	IgG1 engineered fully human antibody	-
	MEDI4736 (MedImmune, AZ)	IgG1 engineered fully human antibody	-

Nivolumab Single-Agent Therapy: ASCO 2013 Update – Best Change in Target Lesions to First RECIST Progression



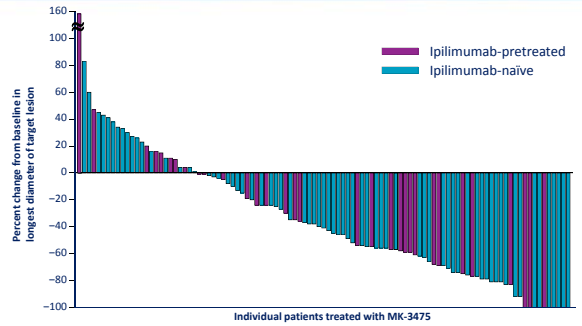
***Non-conventional responders**

Horizontal line at −30% = threshold for defining objective response (partial tumor regression) in absence of new lesions or non-target disease according to RECIST. Horizontal line at +20% indicates the threshold for determination of progressive disease according to RECIST.

Sznol M *et al.* ASCO 2013. Abstract CRA9006.

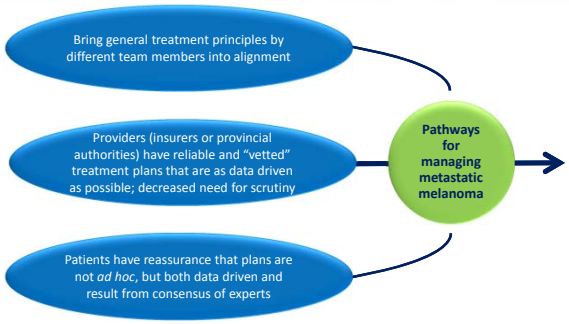
MK-3475 Single-Agent Therapy: Maximum Change from Baseline in Tumor Size

(ICR per RECIST 1.1)



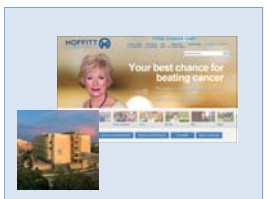
Ribas A *et al*. ASCO 2013. Abstract 9009.

Pathways for Managing Metastatic Melanoma



Pathways for Managing Metastatic Melanoma

- Relevant team members from each specialty across disciplines come to a consensus over the proper pathway for each stage of disease



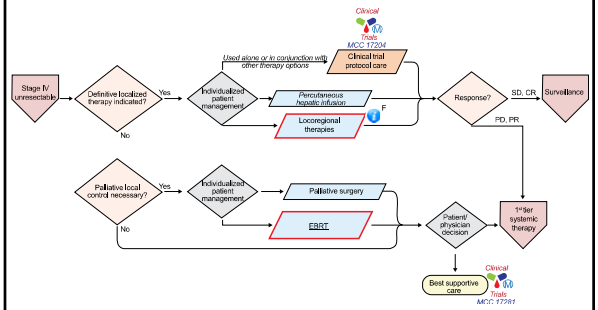
At Moffitt, we use the existence of the pathways to negotiate preferential rates for care from insurers.

In Canada, provincial authorities may be assured pathway care is state of the art, economical and best practice.

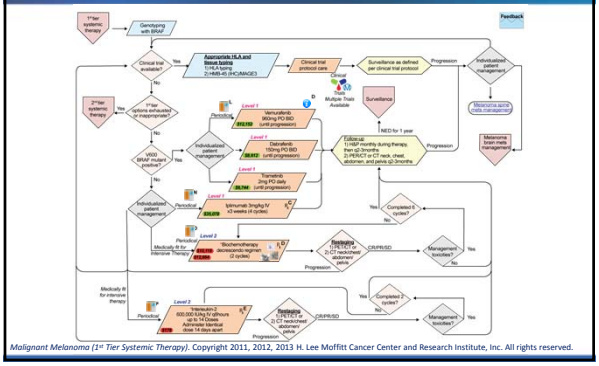
Pathways for Managing Metastatic Melanoma

- Process brings the control of care back to the physician, where it belongs
- It allows clinical trials to be front and center
- Reduces unnecessary use of scans for surveillance
- Can be updated at reasonable intervals and reflect current best practices
- Does reduce autonomy for some physicians, but can have inbuilt flexibility

Overall Pathway: Stage IV Disease



Detailed Stage IV Pathway



Building a Multidisciplinary Team to Manage Immunotherapeutic Toxicity

- A team of specialists needs to be created at any center specializing in immunotherapy to act as consultants for toxicity management
- They are:
  - Gastroenterologist
  - Endocrinologist
  - Dermatologist
  - Pulmonologist
  - Ophthalmologist

Building a Multidisciplinary Team to Manage Immunotherapeutic Toxicity

- Major side effects of ipilimumab, IL-2 and PD-1/PD-L1 antibodies that are unfamiliar to oncologists are colitis, pneumonitis and hypophysitis
- The spectrum of immune-related adverse events is becoming consistent across different agents
- The unusual side effects are neurologic, so have a reliable neurologist available

Building a Multidisciplinary Team to Manage Immunotherapeutic Toxicity

- Having a gastroenterologist to be able to colonoscope patients on short notice is crucial when the results will determine outcome of management
- Being able to refer to an endocrinologist in a timely manner for the borderline cases of hypopituitarism is also critical for proper care
- Very useful to have an ophthalmologist for urgent referrals in case of uveitis

Building a Multidisciplinary Team to Manage Immunotherapeutic Toxicity

The more cases of side effects are seen by the experts, the better and quicker they will be at managing them properly.

Patient care will improve with expert management.

Opportunity for publications and an academic interest by the specialist consultant.

CANADIAN MELANOMA CONFERENCE

DEMYSTIFYING MYTHS IN METASTATIC MELANOMA

Dr. Mateya E. Trinkaus
Markham Stouffville Hospital

Bristol-Myers Squibb Canada
This initiative is supported by an educational grant from Bristol-Myers Squibb Canada.

How Does this Translate to the Community Setting?

MARKHAM STOUFFVILLE HOSPITAL
MARKHAM SITE

- Mid-sized community hospital serving ~300,000 people
- One of first community cancer centers in Ontario to use immune checkpoint inhibitors

- Small team of 3 medical oncologists
- Supportive staff and multidisciplinary team

Myth or Reality?

- Discuss several concerns raised by oncologists regarding treatment of melanoma related to:
  - Safety of immune checkpoint inhibitor (i.e., ipilimumab, PD-1 inhibitors) use in the community
  - Sequencing of immune checkpoint inhibitors with BRAF inhibitors
  - Role of immune checkpoint inhibitors and BRAF inhibitors with metastasectomy
  - Safety of immune checkpoint inhibitors and BRAF inhibitors in the elderly population

The Treatment of Metastatic Melanoma Is Becoming More Complicated

- Targeting mutations
- Optimizing clinical trial participation
- New medications with new toxicities:
  - BRAF inhibitors (dabrafenib, vemurafenib)
  - Monoclonal antibodies targeting CTLA-4 (ipilimumab)
  - Monoclonal antibodies targeting PD-1 (nivolumab, MK-3475) and PD-L1 (MPDL-3280A)
- Increased consideration for metastasectomy
- Increased consideration for stereotactic radiation

Immune checkpoint inhibitors (i.e., monoclonal antibodies targeting CTLA-4, PD-1 or PD-L1) are too unsafe to be used in the community.

A. Agree	5%
B. Disagree	36%
C. It depends	58%

Concerns about Safe Use in the Community *re:* Immune Checkpoint Inhibitors in Melanoma

"We do not have the expertise"

"This will be too onerous for my already overwhelmed practice"

"We do not have the support to sustain this program" (i.e., nursing care to contact patients regularly, multidisciplinary team, on-call MD support, etc.)

"Melanoma is best treated in an academic center"

Medscape Medical News > Oncology

Ipilimumab Is for Community-Based Oncologists Too, Says Expert

Nick Mulcahy
April 07, 2011

Because of the potential severity and relative novelty of these immune-mediated reactions, one melanoma expert has suggested that ipilimumab should only be administered by oncologists who are trained to use the drug and who work in medical center settings.

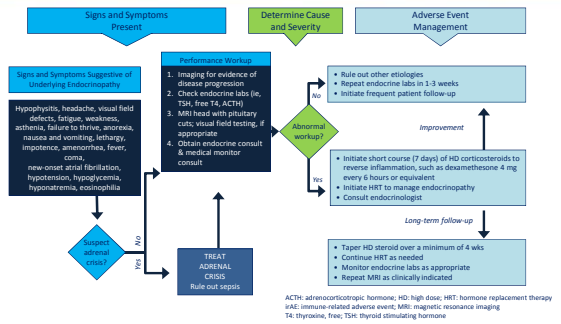
However, another expert disagrees. Ipilimumab is for use by community-based clinicians too, said Jedd Wolchok, MD, PhD, from Memorial Sloan-Kettering Cancer Center in New York City, who is one of the drug's investigators.

"I don't think using ipilimumab is beyond any oncologist," Dr. Wolchok told *Medscape Medical News*.

"Formal training" is not necessary, he noted, "but you must become familiar with the side effects and how they have been successfully managed."

The newly issued REMS is a good starting point for clinicians, suggested Dr. Wolchok.

Guidelines Are Available to Assist with irAEs



ACTH: adrenocorticotropic hormone; HD: high dose; HRT: hormone replacement therapy
irAE: immune-related adverse event; MRI: magnetic resonance imaging
T4: thyroxine, free; TSH: thyroid stimulating hormone

irAE: immune-related adverse event

Recommendations for the Diagnosis, Prevention and Management of Cutaneous Adverse Events Associated with Vemurafenib

August 2012

Adverse event	Presentation and symptoms	Management
Erythema nodosum-type rash	Nodular, indurated painful widespread subcutaneous nodules (hot, red swellings often starting on the shins) May also be associated with macular/papular or perifollicular eruption	• Refer to dermatologist for advice on treatment and diagnosis plus biopsy and bloods • Analgesia: paracetamol, non-steroidal anti-inflammatories • Emollients: topical steroids • Consider oral steroids: prednisolone 0–5 mg/kg once daily (maximum 60 mg/day) for 5–7 days, then reduced by 5 mg every 3 days • Consider interrupting vemurafenib
Photosensitivity	Red skin typical of sunburn after minimal sun exposure, + blistering	• Soap substitutes • Emollients: water-based first • Topical steroids • Sunscreen SFP ≥30 (UVB) plus 5* (UVA) rating; cover up
Squamous papillomas/warts	Non-inflamed warty lesions	• If symptomatic or unsure of diagnosis, refer to dermatologist for treatment with cryotherapy or curettage, if indicated
Keratoacanthoma/ SCC	Rapidly growing warty lesions, often with erythematous base	• Refer to dermatologist
Dry skin	Generalized dry flaky skin + scalp	• Soap substitutes • Emollients: water-based first • Therapeutic shampoos
Folliculitis or cysts	Localized or widespread lesions	• Soap substitutes • Antibiotics: topical or systemic • For symptomatic but uninfected cysts, consider excision

SCC: squamous cell carcinoma

Sinha R *et al. Br J Dermatol* 2012; 167(5):987-94.

Immune checkpoint inhibitors (i.e., monoclonal antibodies targeting CTLA-4, PD-1 or PD-L1) are highly toxic drugs.

A. Agree 30%

B. Disagree 23%

C. It depends 47%

The Reality of Toxicity Associated with Monoclonal Antibodies Targeting CTLA-4, PD-1 or PD-L1

- Diarrhea is common but severe diarrhea and/or colitis are not common with ipilimumab
- Rash is common, but severe dermatitis is not common
- Endocrinopathies are uncommon
- Hepatitis is not common
- Infusion reactions are very rare

irAEs: Ipilimumab 10 mg/kg Pivotal Phase III Trial

CA184-024

Adverse events*	Ipilimumab + dacarbazine (n = 247)			Placebo + dacarbazine (n = 251)		
	Total, %	Grade 3, %	Grade 4, %	Total, %	Grade 3, %	Grade 4, %
Any irAE	77.7	31.6	10.1	38.2*	3.2*	2.8*
Dermatologic						
Pruritus	26.7	2.0	0	6.0	0	0
Rash	22.3	1.2	0	4.8	0	0
Gastrointestinal						
Diarrhea	32.8	4.0	0	15.9	0	0
Colitis	4.5	1.6	0.4	0	0	0
Hepatic						
↑ in ALT	29.1	15.0	5.7	4.4	0.8	0
↑ in AST	26.7	13.8	3.6	3.2	0.4	0
Hepatitis	1.6	1.2	0	0	0	0

*Adverse events judged to be associated with inflammation
↑: increase; ALT: alanine aminotransferase; AST: aspartate aminotransferase
Robert C *et al. N Engl J Med* 2011; 364(26):2517-26.

Selected Toxicity Profile of Ipilimumab 3 mg/kg: Trial of Ipilimumab Alone or with gp100

Toxicity (N = 131)	Total, n (%)	Grade 3, n (%)	Grade, 4 n (%)
Any drug event	127 (96.9)	49 (37.4)	11 (8.4)
Diarrhea	43 (33)	7 (5)	0
Colitis	10 (7.6)	7 (5.3)	0
Hypophysitis	2 (1.5)	2 (1.5)	0
Fatigue	55 (42)	9 (7)	0
Dermatologic	57 (43)	2 (1.5)	0

Note: safety profile of ipilimumab + gp100 is similar.
Hodi FS *et al. N Engl J Med* 2010; 363(8):711-23.

Selected Toxicity Profile of Nivolumab + Ipilimumab: Phase I Data

Toxicity (combined cohort, N = 53)	All grades, n (%)	Grades 3–4, n (%)
Drug toxicity	50 (93)	20 (53)
Diarrhea	18 (34)	3 (6)
Colitis	5 (9)	2 (4)
Endocrinopathy	7 (13)	1 (2)
Hepatic disorder	12 (23)	8 (15)
Rash	29 (55)	2 (4)

Wolchok JD *et al. N Engl J Med* 2013; 369(2):122-33.

Selected Toxicity Profile of MK-3475: Phase I Data

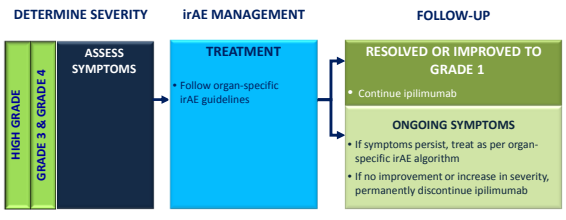
Toxicity (N = 135; varying dose cohorts)	All grades, n (%)	Grades 3–4, n (%)
Drug toxicity	107 (79)	17 (13)
Diarrhea	27 (20)	1 (1)
Hypothyroidism	11 (8)	1 (1)
Increase in liver enzymes (AST)	10 (13)	2 (1)
Rash	28 (21)	3 (2)
Fatigue	41 (30)	2 (1)

Hamid *O et al. N Engl J Med* 2013; 369(2):134-44.

Patients with grade 3 toxicity cannot receive further therapy with an immune checkpoint inhibitor.

- A. Agree 8%
- B. Disagree 34%
- C. It depends 58%

"Patients with Grade 3 Toxicity Cannot Receive Further Immune Checkpoint Inhibitor Treatment"



irAE: immune-related adverse event

Grade 3 Toxicities Related to CTLA-4 and PD-1 or PD-L1 Inhibitors

Toxicities that can be re-challenged with immune checkpoint inhibitors once ≤ grade 1	Toxicities that should not be re-challenged
Endocrinopathies	Grade 3–4 diarrhea
Asymptomatic rise in biochemical parameters (Liver enzymes, lipase, amylase)	Grade 3–4 colitis
Rash (pending severity)	Grade 3–4 neurologic toxicity
	Grade 3–4 renal dysfunction
	Grade 3–4 pneumonitis

Immune checkpoint inhibitors cannot be used after BRAF inhibitors.

A. Agree	0%
B. Disagree	77%
C. It depends	23%

Ipilimumab Use after BRAF Agents

- ASCO 2013: EAP experience in Italy
  - 855 Italian patients received ipilimumab from June 2010–January 2012
  - 93 of 173 found to have BRAF mutation treated sequentially with ipilimumab and BRAF inhibitor
  - 48 received BRAF inhibitor after PD with ipilimumab
  - 45 received ipilimumab after PD with BRAF inhibitor

BRAF inhibitor post-ipilimumab (n=48)	Ipilimumab post-BRAF inhibitor (n=45)
Median OS = 14.5 months (11.1–17.9)	Median OS = 9.7 months (4.6–14.9)
	18 patients (40%) had rapid PD and could not complete 4 cycles of ipilimumab (median OS = 5.8 months)
	27 patients (60%) were able to complete ipilimumab cycles (median OS = 19.7 months)

EAP: expanded access program; PD: progressive disease
Ascierto PAA *et al. J Clin Oncol* 2013; 31(Suppl):abstract 9035.

Ongoing Challenges in Treating Metastatic Melanoma

- Deciding how to sequence BRAF agents with immune checkpoint inhibitors
- In general, we should consider immune checkpoint inhibitors prior to using BRAF inhibitors with patients who have more indolent disease progression

Surgery is not indicated for patients after treatment with CTLA-4, PD-1 or BRAF agents.

A. Agree	0%
B. Disagree	64%
C. It depends	36%

Surgery May Be Appropriate for Patients after Treatment with CTLA-4, PD1 or BRAF Agents

- Single-center retrospective review
  - N = 44 with stage 4 melanoma
    - 20 had metastasectomy first
    - 24 had ipilimumab first
  - 5-year disease-specific survival 61% in the surgery upfront group and 42% in the ipilimumab upfront group ($p = 0.27$)
  - Median OS = 60 months, with 51% 5-year disease-specific survival

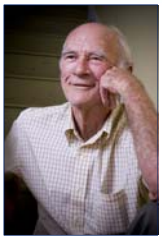
Ozao-Choy J *et al.* Society of Surgical Oncology Symposium 2013; abstract #45.

Patients >80 years should not be considered for treatment with immune checkpoint inhibitors.

A. Agree	15%
B. Disagree	25%
C. It depends	60%

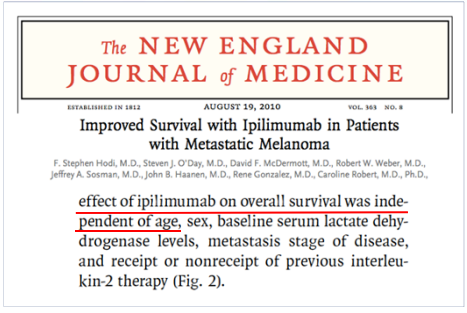
Concerns with Treating the Elderly with Immune Checkpoint Inhibitors

- After all, older patients are more frail:
  - Socially isolated
  - Physiologic changes
    - Decreased renal function
    - Increased body fat
    - Decreased marrow reserve



  - Decreased stamina
  - Already reduced life expectancy
  - Comorbidities
  - Polypharmacy

Improved Survival with Ipilimumab in Patients with Metastatic Melanoma



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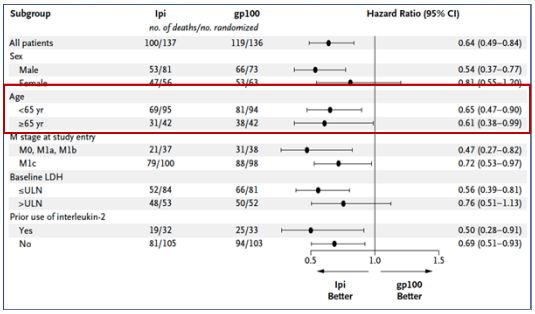
Improved Survival with Ipilimumab in Patients with Metastatic Melanoma

F. Stephen Hodi, M.D., Steven J. O'Day, M.D., David F. McDermott, M.D., Robert W. Weber, M.D., Jeffrey A. Sosman, M.D., John B. Haanen, M.D., Rene Gonzalez, M.D., Caroline Robert, M.D., Ph.D.,

effect of ipilimumab on overall survival was independent of age, sex, baseline serum lactate dehydrogenase levels, metastasis stage of disease, and receipt or nonreceipt of previous interleukin-2 therapy (Fig. 2).

Hodi FS *et al. N Engl J Med* 2010; 363(8):711-23.

Phase 3 Trial of Ipilimumab and gp100: Subgroup Anaysis for OS



Subgroup	Ipi	gp100	Hazard Ratio (95% CI)
	no. of deaths/no. randomized		
All patients	100/137	119/136	0.64 (0.49–0.84)
Sex			
Male	53/81	66/73	0.54 (0.37–0.77)
Female	47/56	53/63	0.81 (0.55–1.20)
Age			
<65 yr	69/95	81/94	0.65 (0.47–0.90)
≥65 yr	31/42	38/42	0.61 (0.38–0.99)
M stage at study entry			
M0, M1a, M1b	21/37	31/38	0.47 (0.27–0.82)
M1c	79/100	88/98	0.72 (0.53–0.97)
Baseline LDH			
≤ULN	52/84	66/81	0.56 (0.39–0.81)
>ULN	48/53	50/52	0.76 (0.51–1.13)
Prior use of interleukin-2			
Yes	19/32	25/33	0.50 (0.28–0.91)
No	81/105	94/103	0.69 (0.51–0.93)

Hodi FS *et al. N Engl J Med* 2010; 363(8):711-23.

LDH: lactate dehydrogenase; ULN: upper limit of normal

Phase I Trial of Nivolumab + Ipilimumab: Baseline Characteristics of All Treated Patients

Characteristic	Concurrent treatment (N = 53)	Sequenced treatment (N = 33)
Age, years		
Median	58	64
Range	22-79	23-89
Sex, n (%)		
Male	32 (60)	18 (55)
Female	21 (40)	15 (45)
ECOG performance status, n (%)		
0	44 (83)	22 (67)
1	8 (15)	11 (33)
Unknown	1 (2)	0

Wolchok JD *et al. N Engl J Med* 2013; 369(2):122-33.

Comprehensive Geriatric Assessment for Older Patients with Cancer

IADL vs. ECOG Performance Status as Independent Predictors of Outcome in Multivariate Analyses

	Predictors of outcome					
Reference	IADL	ECOG	Other	Outcome(s)	Cancer types	Comments
Extermann	No	No	MAX2 index, diastolic BP, marrow invasion, LDH	Chemo toxicity	All	Small series
Maione	Yes	Yes	QOL, no. of sites of disease	OS	NSCLC	Miles study
Audisio	Yes	Yes	No. of comorbidities, GDS, ADL, IADL	30-day postoperative morbidity	All	Preliminary results: ASA score not predictive
Ramesh	Yes	Yes	BFI	30-day postoperative morbidity	All	Multicenter study
	Yes	No	BFI	Length of hospital length		
Wedding	Yes	Yes	Comorbidity	OS	All	
Soubeyran	No	No	MNA, advanced disease	Early death	All	Chemotherapy treated
Robb	Yes	Yes	MMSE	OS	All	
Freyer	Yes*	Yes	Depression	Chemo toxicity	Ovary	Multicenter study
	No	No	Depression, FIGO stage IV, initial non-optimal surgery	PFS		
	No	No	Depression, FIGO stage IV, >6 meds/day	OS		

ADL: activities of daily Living; ASA: American Society of Anesthesiologists; BFI: Brief Fatigue Inventory; BP: blood pressure; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; GDS: Geriatric Depression Scale; IADL: instrumental activities of daily living; LDH: lactate dehydrogenase; MILES: Multicenter Italian Lung Cancer in the Elderly Study; MMSE: Mini-Mental Status Exam; MNA: Mini-Nutritional Assessment; NSCLC: non-small-cell lung cancer; QOL: quality of life
*Fully independent vs. at home with assistance, or nursing home
Extermann M, Hurria A. *J Clin Oncol* 2007; 25(14):1824-31.

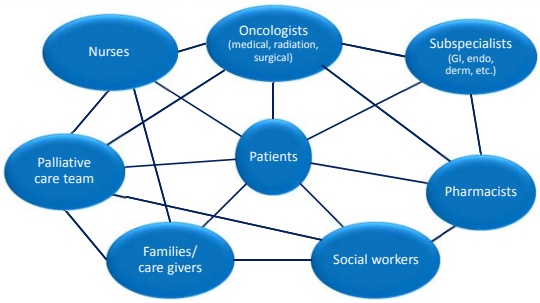
Impact of Social Isolation

- Social isolation has been linked with increased mortality[1]
- Need to ensure that if the patient cannot consistently monitor his/her symptoms, a reliable caregiver is doing so

- Importance of multidisciplinary team
  - Community nursing, early palliative care referral, Meals on Wheels, etc.
- Regular telephone calls
  - Associated with less distress, anxiety and more timely referral to appropriate follow up and specialist referrals[2]

1. Kroenke CH *et al. J Clin Oncol* 2006; 24(7):1105-11.
2. Kornblith AB *et al. Cancer* 2006; 107(11):2706-14.

Multidisciplinary Approach



derm: dermatology; endo: endocrinology; GI: gastroenterology

Suggestions for a Community Melanoma Program

- Acknowledge that you will need to be available for advice for your colleagues (i.e., emergency room physicians) who are treating complications of these new medications
- Create a network of other melanoma experts that you can turn to for support
- Start or join (i.e., teleconference) a melanoma multidisciplinary cancer conference
- Enroll your colleagues from other subspecialties to assist with complications (i.e., GI, endo, derm, etc.)
- Consider doing grand rounds, lunch-and-learn sessions, dinner talks, etc. for your colleagues involved in melanoma care – nurses, pharmacists, surgeons, pathologists, radiologists

New Era of Melanoma Care

MYTH

There are many myths about the safe use of immune checkpoint inhibitors and BRAF inhibitors in the community.

They are now an integral part and standard of care for metastatic melanoma.

REALITY

These agents work.
They are safe when given to informed patients and when support for complications is available.
There is a network of support to help you.