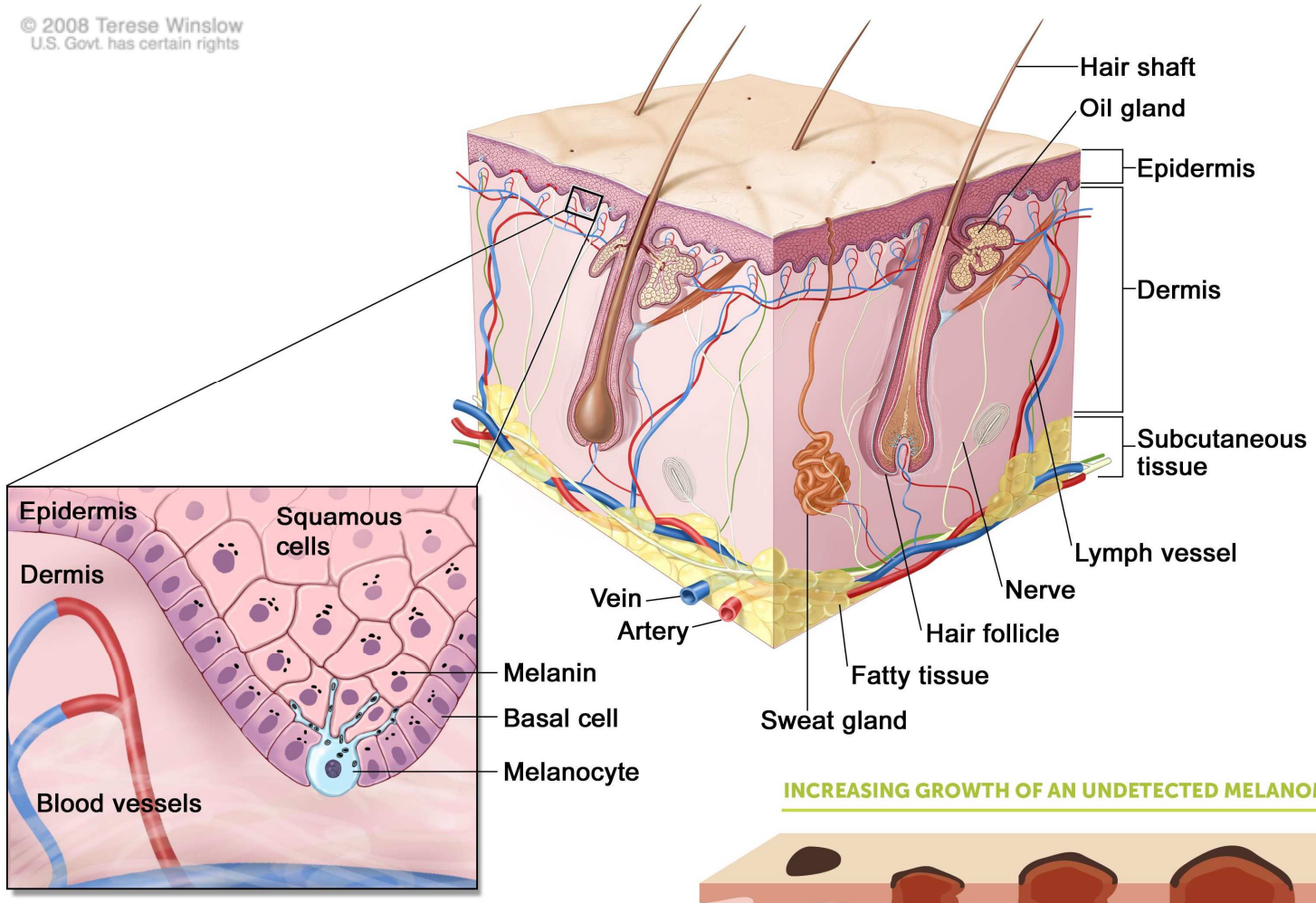
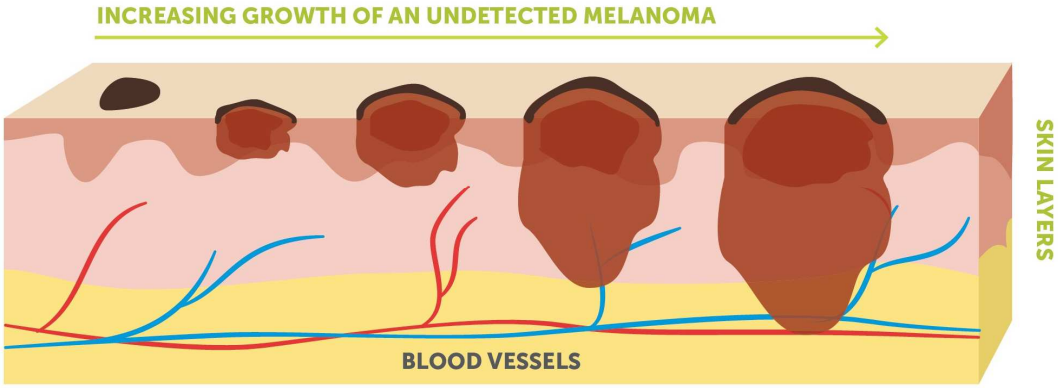
Latvian Biomedical
Research and Study Centre
research and education in biomedicine from genes to human

Immunotherapy of Melanoma

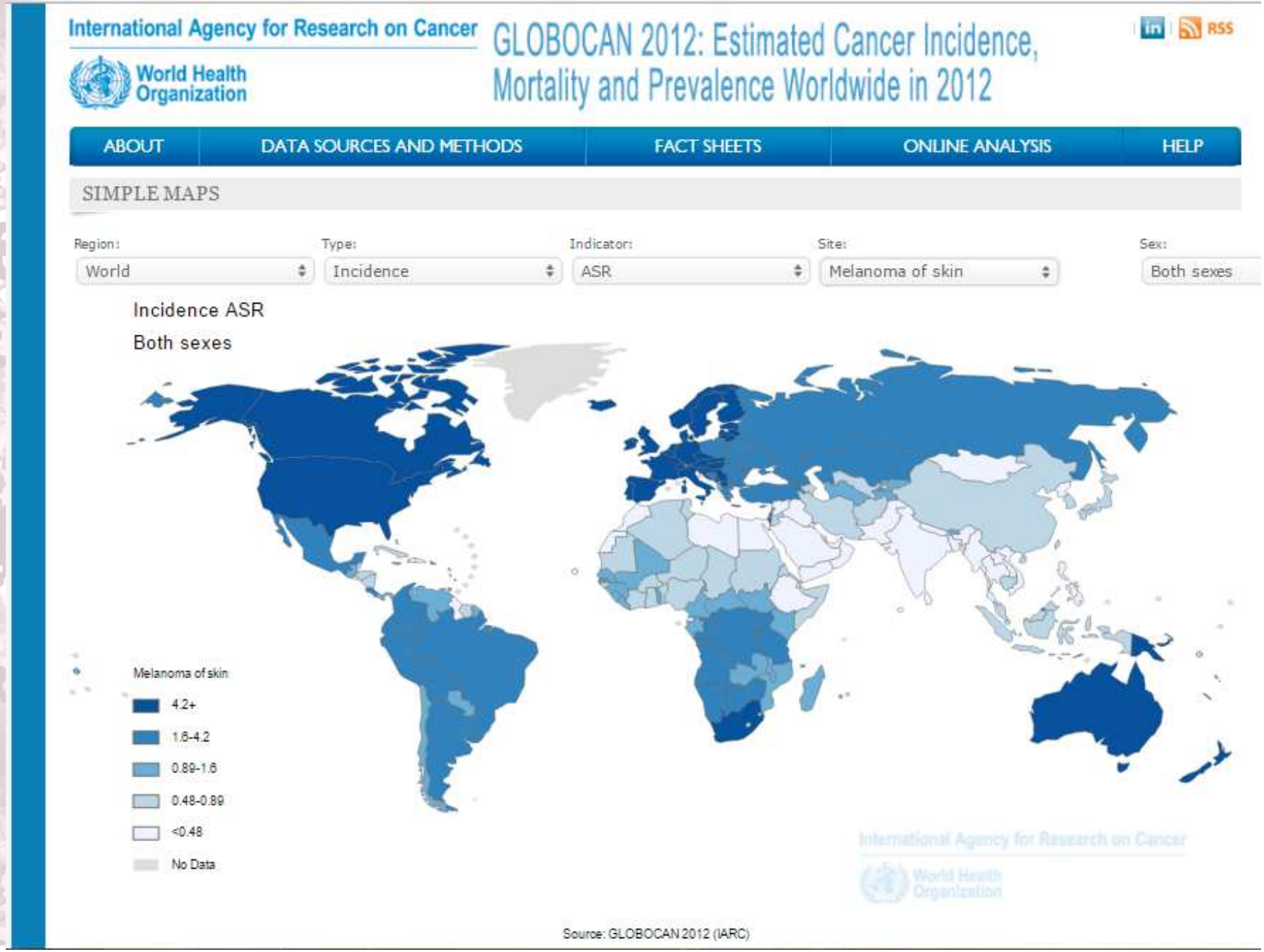
Dace Pjanova, PhD

Skin Melanoma

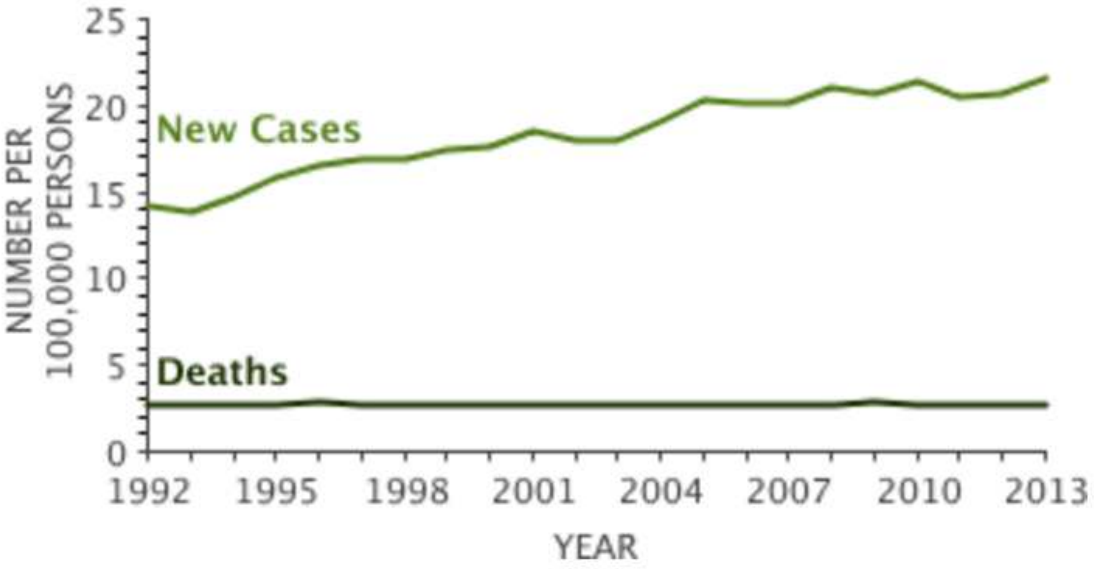




Melanoma Incidence



Increasing Melanoma Incidence and Decreasing Mortality

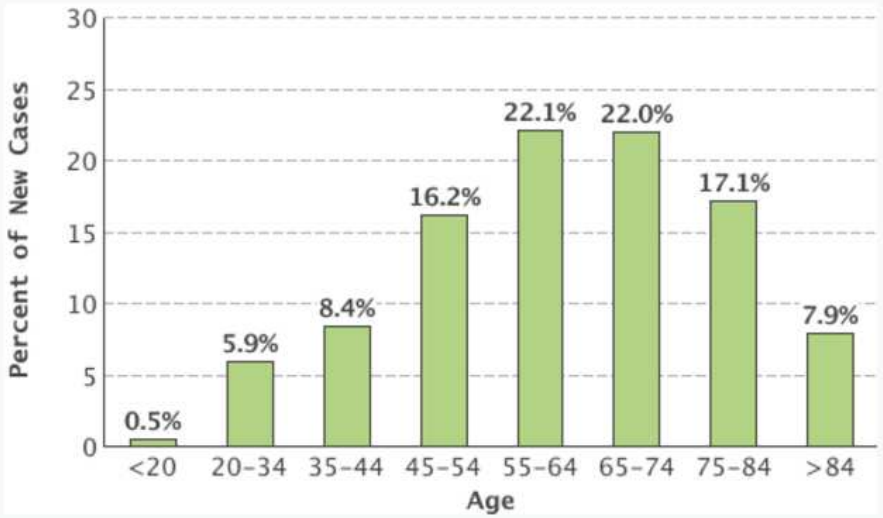


Percent Surviving 5 Years
91.5%
2006-2012

- **New melanoma cases almost tripled between 1975 and 2012 (from 7.9/100 000 to 22.9/100 000)**
- **Death rate per 100 000: no changes (2.1/100 000 in 1975 and 2.7/100 000 in 2012)**

http://seer.cancer.gov/statfacts

Percent of New Cases and Deaths by Age Groups

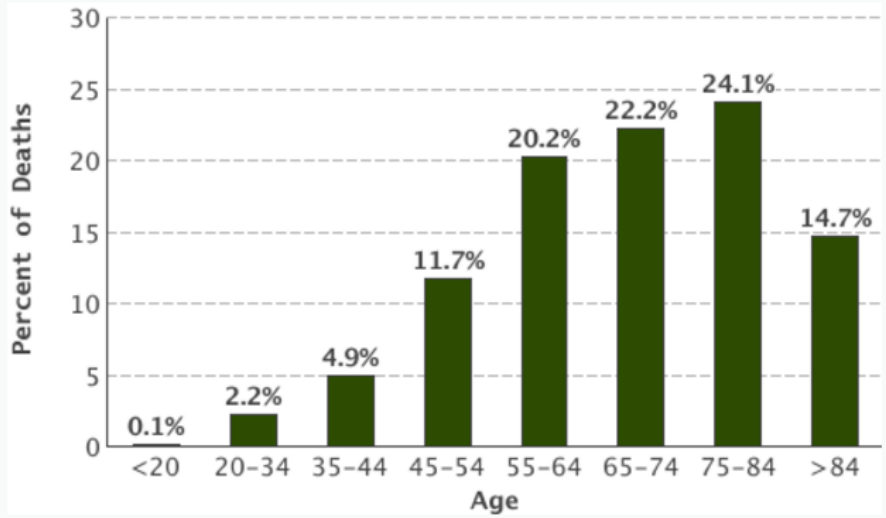


Melanoma of the skin is most frequently diagnosed among people aged 55-64.

Median Age At Diagnosis

63

SEER 18 2009-2013, All Races, Both Sexes



The percent of melanoma of the skin deaths is highest among people aged 75-84.

Median Age At Death

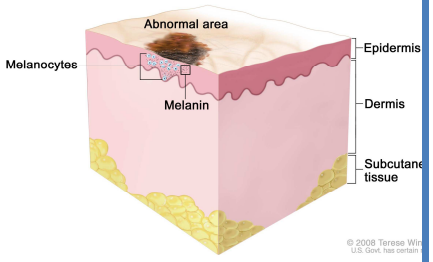
69

U.S. 2009-2013, All Races, Both Sexes

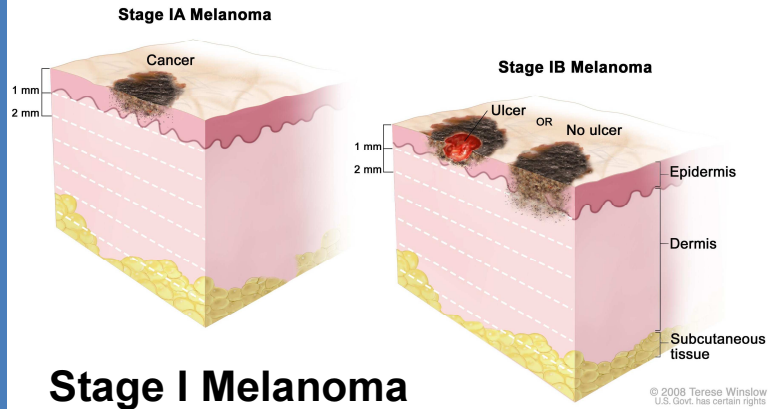
http://seer.cancer.gov/statfacts

Melanoma Stages

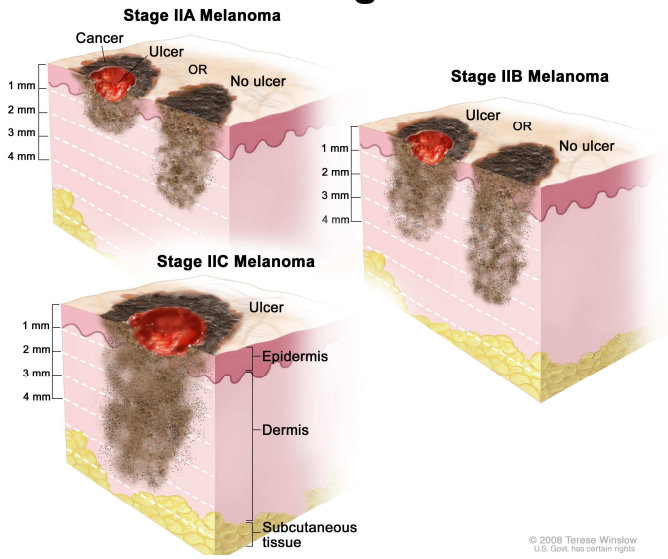
In situ Melanoma



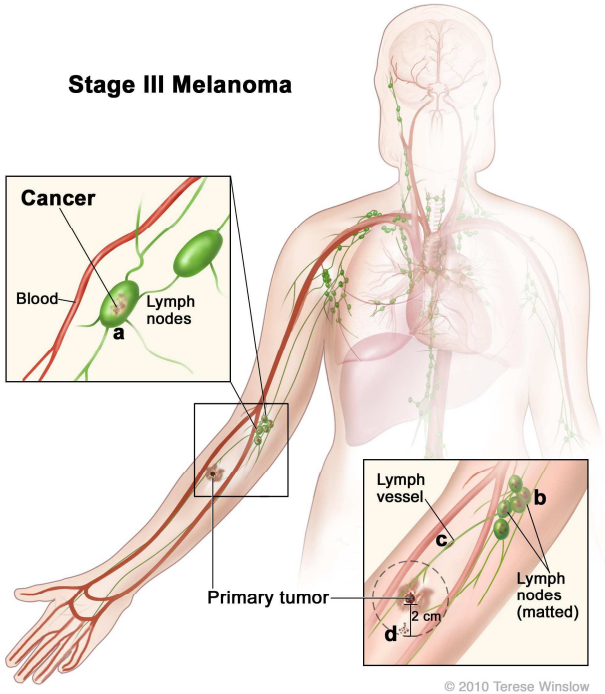
Stage I Melanoma



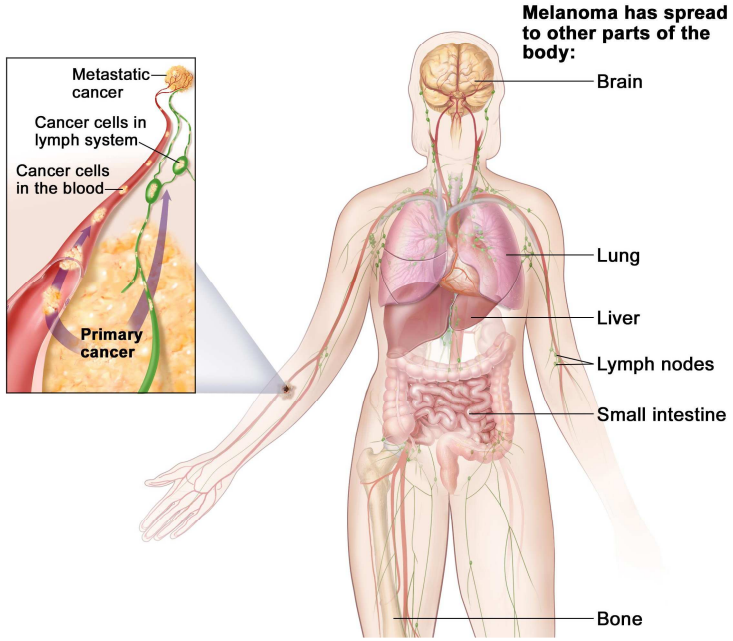
Stage II Melanoma



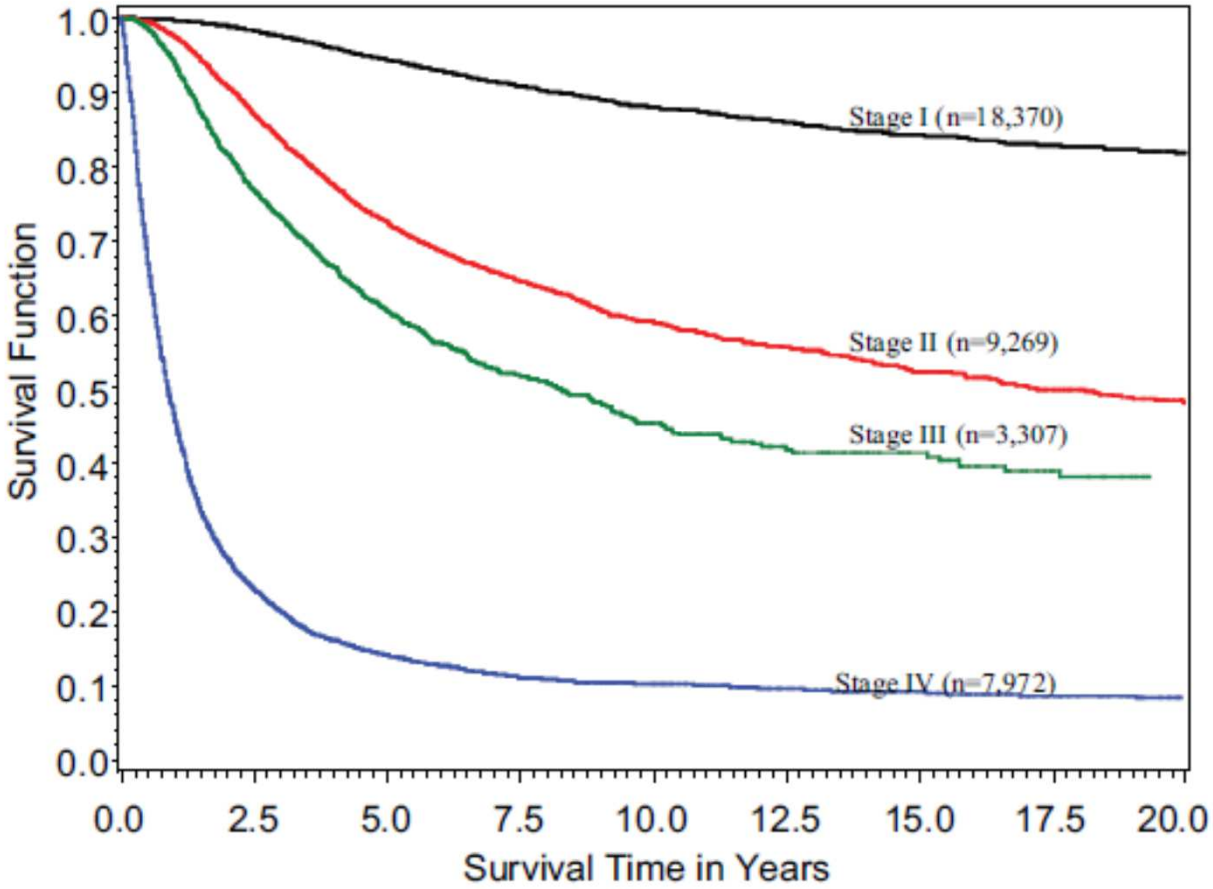
Stage III Melanoma



Stage IV Melanoma



Overal survival by Stage



Lymph node involvement most significant prognostic factor for survival

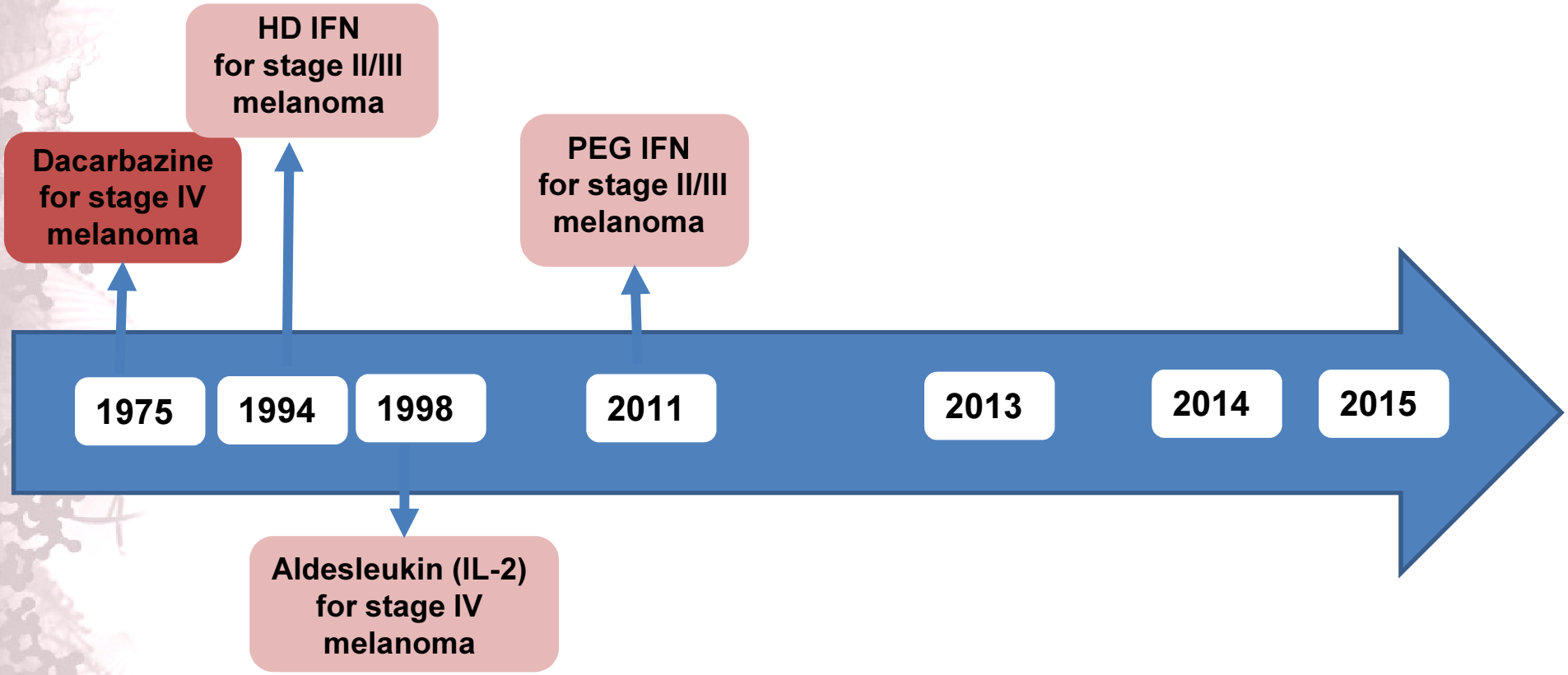
Balch CM, et al. 2009, *J Clin Oncol.* 2009; *27:6199-6206.*

Treatment Options by Stage

Melanoma Stage	Treatment option	Challenges
Stage 0 (in situ)	• Surgery	• Early diagnosis
Stage I	• Surgery (lymph node mapping, removal of lymph nodes)	• New ways to find melanoma cells in the lymph nodes
Stage II	• Surgery (lymph node mapping, sentinel lymph node biopsy) • Biologic therapy	• New treatment to be used after surgery
Stage III (can remove by surgery)	• Surgery (lymph node mapping, sentinel lymph node biopsy) • Biologic therapy	• New treatment to be used after surgery • Trials oncolytic virus therapy
Stage III (can't remove by surgery), **Stage IV** **Recurrent Melanoma**	• Targeted therapy • Biologic therapy • Immunotherapy • Chemotherapy • Palliative therapy	• New types of immunotherapy • Combinations of therapies • Targeted therapies • Angiogenesis inhibitors • Oncolytic virus therapy • Regional chemotherapy • Systemic chemotherapy, etc.

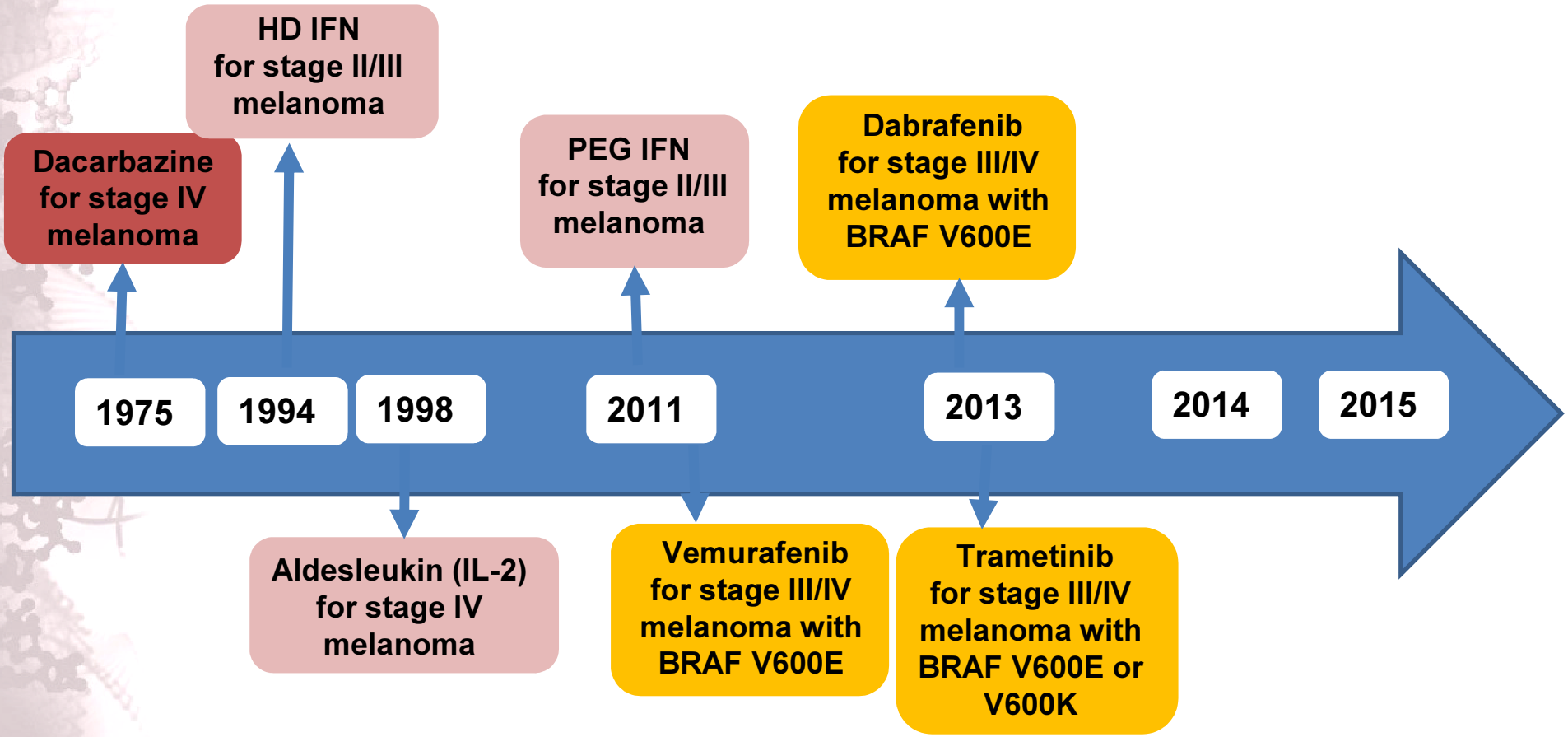
http://www.cancer.gov/types/skin/patient/melanoma-treatment

Timeline for FDA Approved Drugs for melanoma



FDA – U.S. Food and Drug Administration

Timeline for FDA Approved Drugs for melanoma



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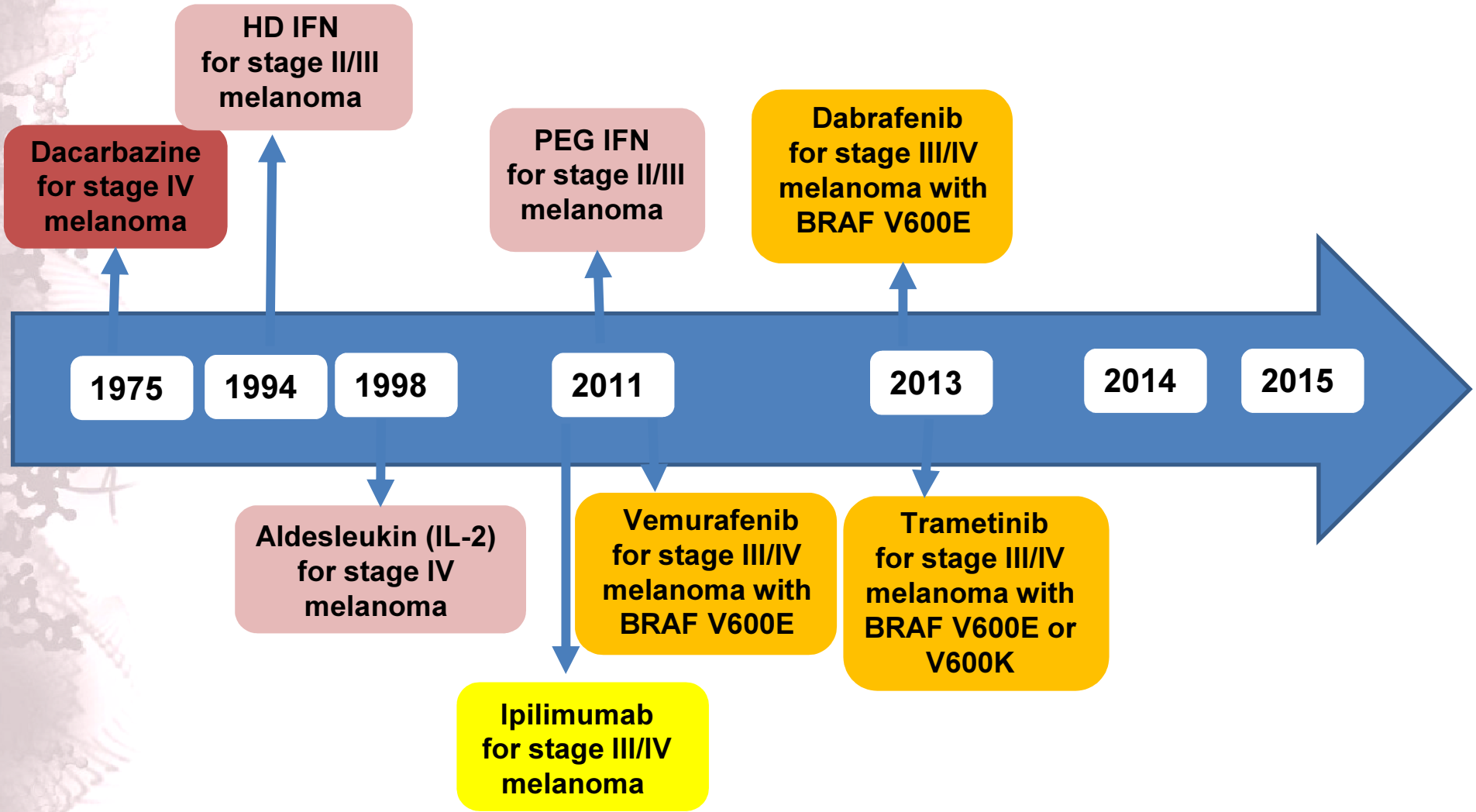
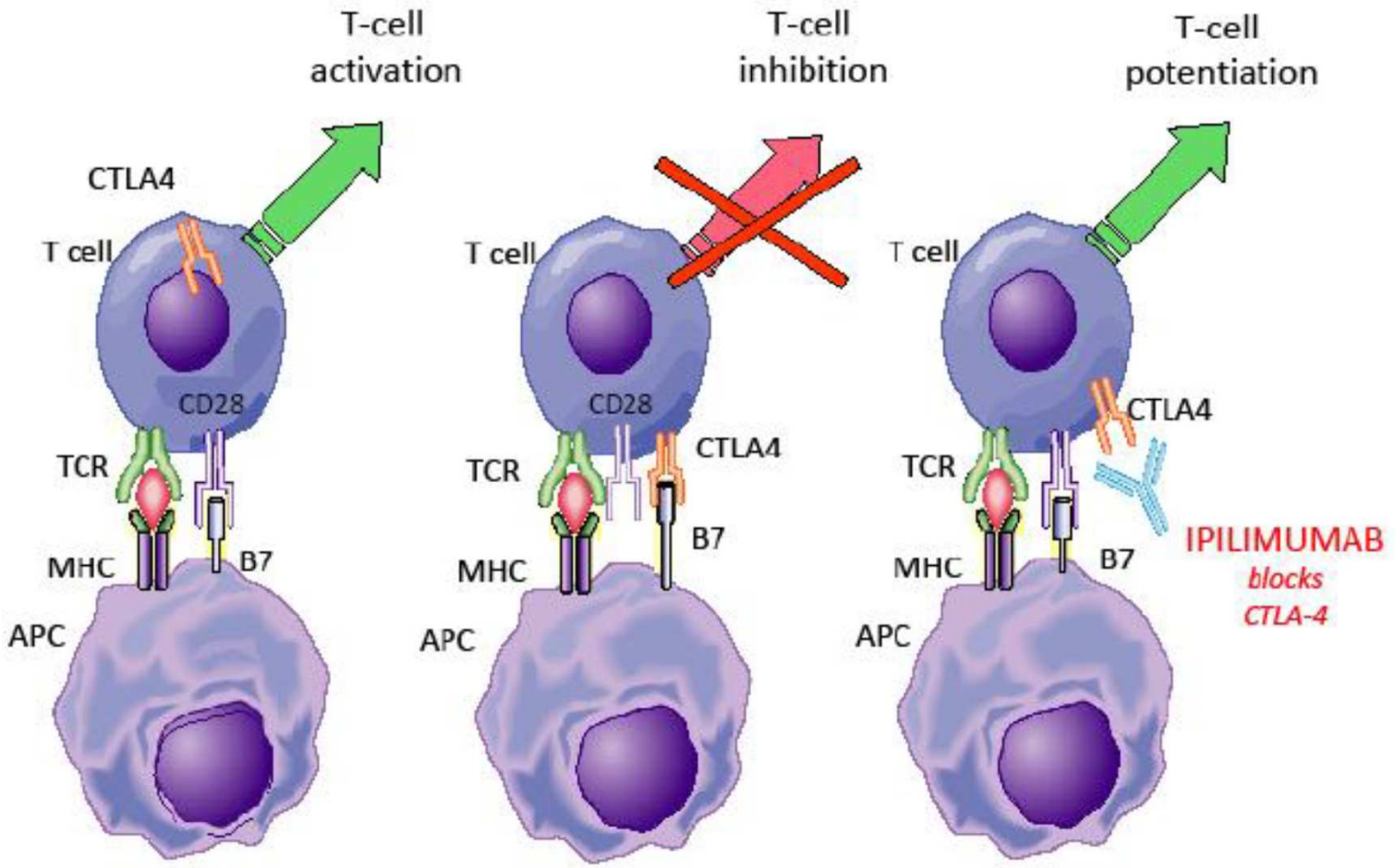
Timeline for FDA Approved Drugs for melanoma



FDA – U.S. Food and Drug Administration

Ipilimumab mode of action



O'Day S et al. ASCO 2010

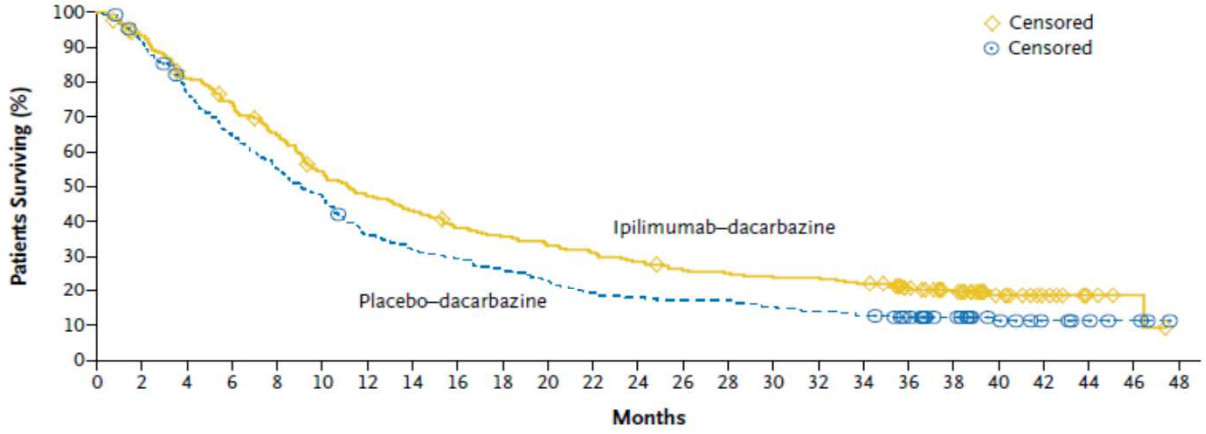
Activation is initiated by binding of B7 molecule on the APC to CD28 receptorson the T cell

Inhibition results from CTLA-4 expression on the T-cell surface where it competes with CD28 for binding to B7 on APCs

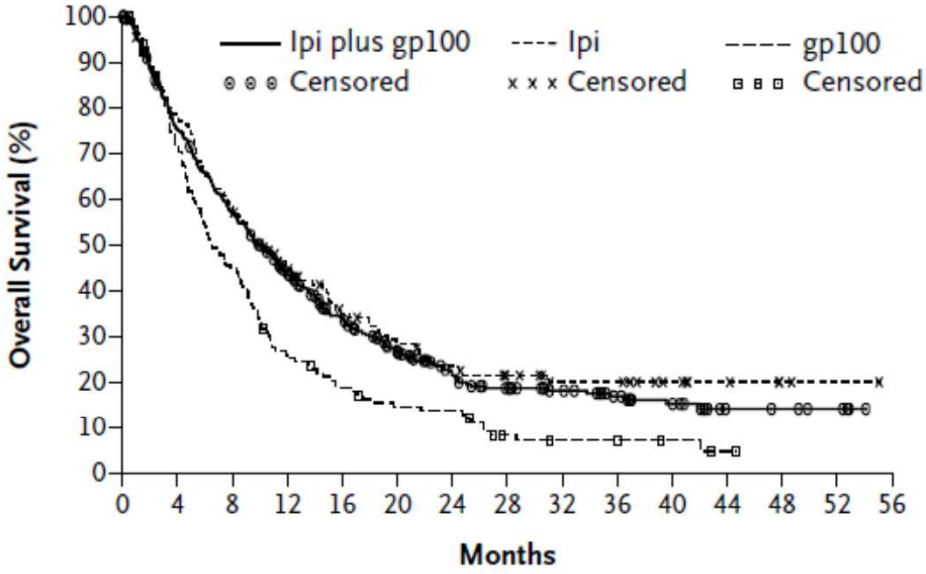
Potentiation of T-cell proliferation achieved by CTLA-4 inhibition using ipilimumab, an anti-CTLA-4 monoclonal antibody

Ipilimumab in Metastatic Melanoma (I)

Overal survival



No. at Risk																								
Ipilimumab–dacarbazine	250	230	199	181	157	131	114	104	91	85	79	74	68	61	59	56	56	52	41	31	17	10	4	2	0
Placebo–dacarbazine	252	229	190	160	136	116	89	78	72	64	56	47	44	42	42	37	34	31	26	19	11	7	5	3	0



No. at Risk															
Ipi plus gp100	403	297	223	163	115	81	54	42	33	24	17	7	6	4	0
Ipi	137	106	79	56	38	30	24	18	13	13	8	5	2	1	0
gp100	136	93	58	32	23	17	16	7	5	5	3	1	0	0	0

Robert C, et al. N Engl J Med. 2011;364:2517-2526;
Hodi FS, et al. N Engl J Med. 2010

Ipilimumab in Metastatic Melanoma (II)

Table 2. Efficacy Results.

End Point	Ipilimumab plus Dacarbazine (N=250)	Placebo plus Dacarbazine (N=252)	Hazard Ratio with Ipilimumab plus Dacarbazine (95% CI)	P Value
Secondary end points				
Disease progression — no. of events	203	223	0.76 (0.63–0.93)	0.006
Best overall response — no. (%)*	38 (15.2)	26 (10.3)		
Complete response	4 (1.6)	2 (0.8)		
Partial response	34 (13.6)	24 (9.5)		
Stable disease — no. (%)*	45 (18.0)	50 (19.8)		
Progressive disease — no. (%)	111 (44.4)	131 (52.0)		
Response not evaluated — no. (%)†	56 (22.4)	45 (17.9)		

	Ipilimumab plus gp100 (N=403)	Ipilimumab Alone (N=137)	gp100 Alone (N=136)
Evaluation of therapy			
Induction			
Best overall response — no. (%)			
Complete response	1 (0.2)	2 (1.5)	0
Partial response	22 (5.5)	13 (9.5)	2 (1.5)
Stable disease	58 (14.4)	24 (17.5)	13 (9.6)
Progressive disease	239 (59.3)	70 (51.1)	89 (65.4)
Not evaluated	83 (20.6)	28 (20.4)	32 (23.5)

Robert C, et al. N Engl J Med. 2011;364:2517-2526; Hodi FS, et al. N Engl J Med. 2010

Ipilimumab in Metastatic Melanoma (III)

Table 3. Adverse Events and Immune-Related Adverse Events.*

Adverse Event	Ipilimumab plus Dacarbazine (N = 247)			Placebo plus Dacarbazine (N = 251)		
	Total	Grade 3	Grade 4	Total	Grade 3	Grade 4
	number of patients (percent)					
All adverse events, regardless of cause†						
Any event	244 (98.8)	99 (40.1)	40 (16.2)	236 (94.0)	45 (17.9)	24 (9.6)
Gastrointestinal: diarrhea	90 (36.4)	10 (4.0)	0	62 (24.7)	0	0
Dermatologic						
Pruritus	73 (29.6)	5 (2.0)	0	22 (8.8)	0	0
Rash	61 (24.7)	3 (1.2)	0	17 (6.8)	0	0
Hepatic						
Increase in alanine aminotransferase	82 (33.2)	40 (16.2)	14 (5.7)	14 (5.6)	2 (0.8)	0
Increase in aspartate aminotransferase	72 (29.1)	36 (14.6)	9 (3.6)	14 (5.6)	3 (1.2)	0
Other						
Pyrexia	91 (36.8)	0	0	23 (9.2)	0	0
Chills	28 (11.3)	0	0	10 (4.0)	0	0
Weight loss	27 (10.9)	1 (0.4)	0	13 (5.2)	1 (0.4)	0
Immune-related adverse events						
Any event	192 (77.7)	78 (31.6)	25 (10.1)	96 (38.2)	8 (3.2)	7 (2.8)
Dermatologic						
Pruritus	66 (26.7)	5 (2.0)	0	15 (6.0)	0	0
Rash	55 (22.3)	3 (1.2)	0	12 (4.8)	0	0
Gastrointestinal						
Diarrhea	81 (32.8)	10 (4.0)	0	40 (15.9)	0	0
Colitis	11 (4.5)	4 (1.6)	1 (0.4)	0	0	0
Hepatic‡						
Increase in alanine aminotransferase	72 (29.1)	37 (15.0)	14 (5.7)	11 (4.4)	2 (0.8)	0
Increase in aspartate aminotransferase	66 (26.7)	34 (13.8)	9 (3.6)	8 (3.2)	1 (0.4)	0
Hepatitis	4 (1.6)	3 (1.2)	0	0	0	0

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

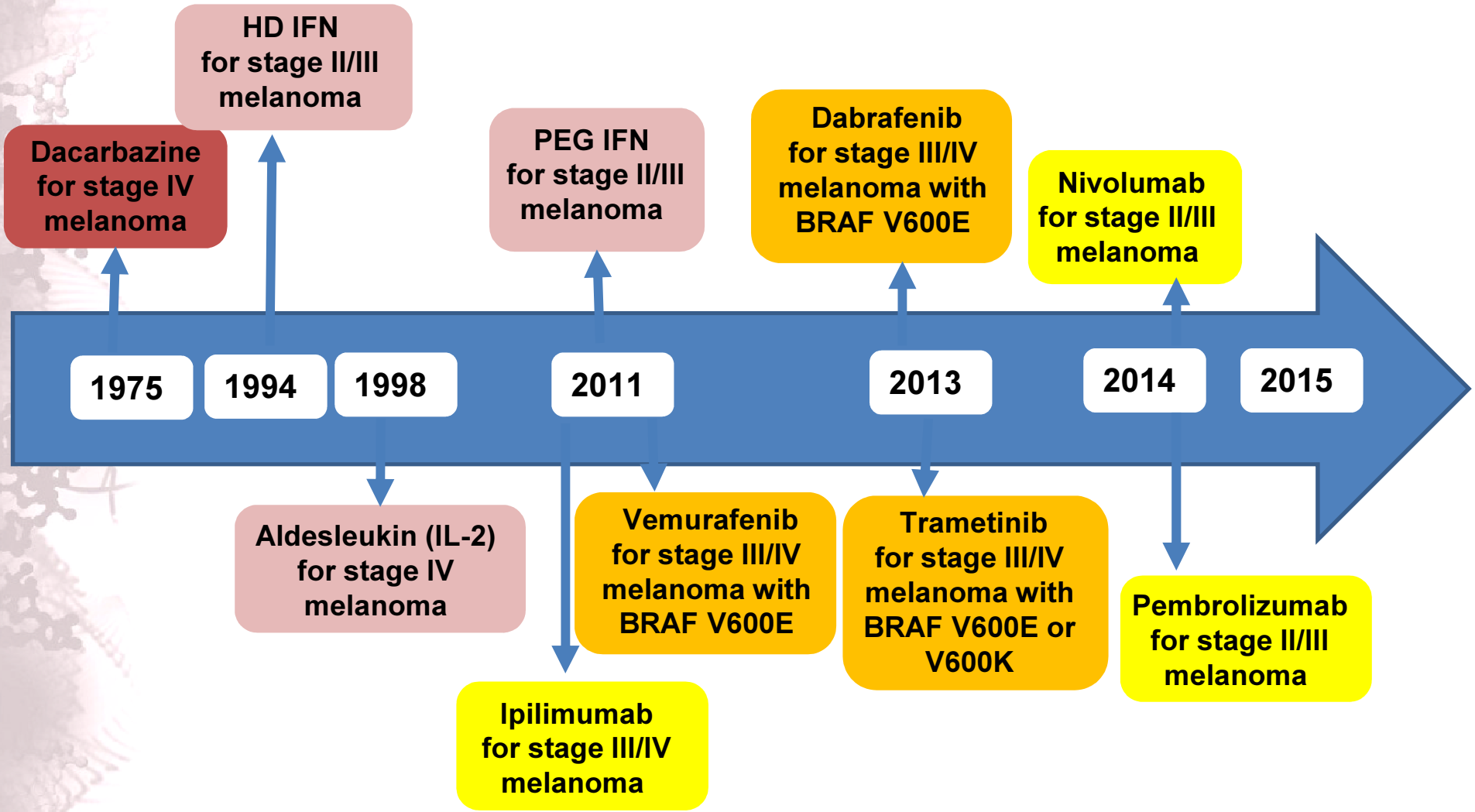
Ipilimumab in Metastatic Melanoma (IV)

Table 3. Adverse Events in the Safety Population.*

Adverse Event	Ipilimumab plus gp100 (N=380)			Ipilimumab Alone (N=131)			gp100 Alone (N=132)		
	Total	Grade 3	Grade 4	Total	Grade 3	Grade 4	Total	Grade 3	Grade 4
	number of patients (percent)								
Any event	374 (98.4)	147 (38.7)	26 (6.8)	127 (96.9)	49 (37.4)	11 (8.4)	128 (97.0)	54 (40.9)	8 (6.1)
Any drug-related event	338 (88.9)	62 (16.3)	4 (1.1)	105 (80.2)	25 (19.1)	5 (3.8)	104 (78.8)	15 (11.4)	0
Gastrointestinal disorders									
Diarrhea	146 (38.4)	16 (4.2)	1 (0.3)	43 (32.8)	7 (5.3)	0	26 (19.7)	1 (0.8)	0
Nausea	129 (33.9)	5 (1.3)	1 (0.3)	46 (35.1)	3 (2.3)	0	52 (39.4)	3 (2.3)	0
Constipation	81 (21.3)	3 (0.8)	0	27 (20.6)	3 (2.3)	0	34 (25.8)	1 (0.8)	0
Vomiting	75 (19.7)	6 (1.6)	1 (0.3)	31 (23.7)	3 (2.3)	0	29 (22.0)	3 (2.3)	0
Abdominal pain	67 (17.6)	6 (1.6)	0	20 (15.3)	2 (1.5)	0	22 (16.7)	6 (4.5)	1 (0.8)
Other									
Fatigue	137 (36.1)	19 (5.0)	0	55 (42.0)	9 (6.9)	0	41 (31.1)	4 (3.0)	0
Decreased appetite	88 (23.2)	5 (1.3)	1 (0.3)	35 (26.7)	2 (1.5)	0	29 (22.0)	3 (2.3)	1 (0.8)
Pyrexia	78 (20.5)	2 (0.5)	0	16 (12.2)	0	0	23 (17.4)	2 (1.5)	0
Headache	65 (17.1)	4 (1.1)	0	19 (14.5)	3 (2.3)	0	19 (14.4)	3 (2.3)	0
Cough	55 (14.5)	1 (0.3)	0	21 (16.0)	0	0	18 (13.6)	0	0
Dyspnea	46 (12.1)	12 (3.2)	2 (0.5)	19 (14.5)	4 (3.1)	1 (0.8)	25 (18.9)	6 (4.5)	0
Anemia	41 (10.8)	11 (2.9)	0	15 (11.5)	4 (3.1)	0	23 (17.4)	11 (8.3)	0
Any immune-related event	221 (58.2)	37 (9.7)	2 (0.5)	80 (61.1)	16 (12.2)	3 (2.3)	42 (31.8)	4 (3.0)	0
Dermatologic	152 (40.0)	8 (2.1)	1 (0.3)	57 (43.5)	2 (1.5)	0	22 (16.7)	0	0
Pruritus	67 (17.6)	1 (0.3)	0	32 (24.4)	0	0	14 (10.6)	0	0
Rash	67 (17.6)	5 (1.3)	0	25 (19.1)	1 (0.8)	0	6 (4.5)	0	0
Vitiligo	14 (3.7)	0	0	3 (2.3)	0	0	1 (0.8)	0	0
Gastrointestinal	122 (32.1)	20 (5.3)	2 (0.5)	38 (29.0)	10 (7.6)	0	19 (14.4)	1 (0.8)	0
Diarrhea	115 (30.3)	14 (3.7)	0	36 (27.5)	6 (4.6)	0	18 (13.6)	1 (0.8)	0
Colitis	20 (5.3)	11 (2.9)	1 (0.3)	10 (7.6)	7 (5.3)	0	1 (0.8)	0	0
Endocrine	15 (3.9)	4 (1.1)	0	10 (7.6)	3 (2.3)	2 (1.5)	2 (1.5)	0	0
Hypothyroidism	6 (1.6)	1 (0.3)	0	2 (1.5)	0	0	2 (1.5)	0	0
Hypopituitarism	3 (0.8)	2 (0.5)	0	3 (2.3)	1 (0.8)	1 (0.8)	0	0	0
Hypophysitis	2 (0.5)	2 (0.5)	0	2 (1.5)	2 (1.5)	0	0	0	0
Adrenal insufficiency	3 (0.8)	2 (0.5)	0	2 (1.5)	0	0	0	0	0
Increase in serum thyrotropin level	2 (0.5)	0	0	1 (0.8)	0	0	0	0	0
Decrease in serum corticotropin level	0	0	0	2 (1.5)	0	1 (0.8)	0	0	0
Hepatic	8 (2.1)	4 (1.1)	0	5 (3.8)	0	0	6 (4.5)	3 (2.3)	0
Increase in alanine aminotransferase	3 (0.8)	2 (0.5)	0	2 (1.5)	0	0	3 (2.3)	0	0
Increase in aspartate aminotransferase	4 (1.1)	1 (0.3)	0	1 (0.8)	0	0	2 (1.5)	0	0
Hepatitis	2 (0.5)	1 (0.3)	0	1 (0.8)	0	0	0	0	0
Other	12 (3.2)	5 (1.3)	0	6 (4.6)	2 (1.5)	1 (0.8)	3 (2.3)	1 (0.8)	0

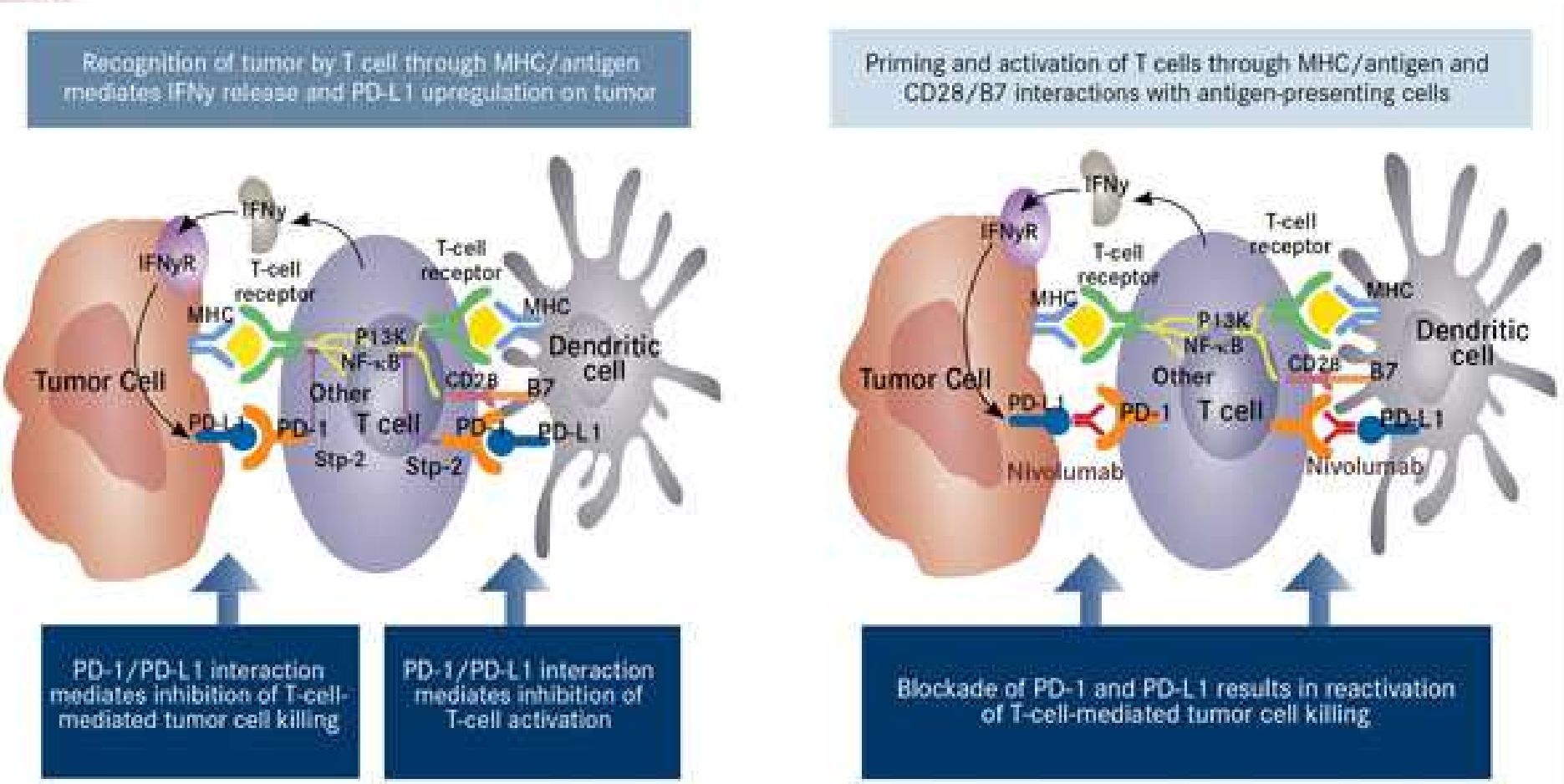
Hodi FS, et al. N Engl J Med. 2010

Timeline for FDA Approved Drugs for melanoma



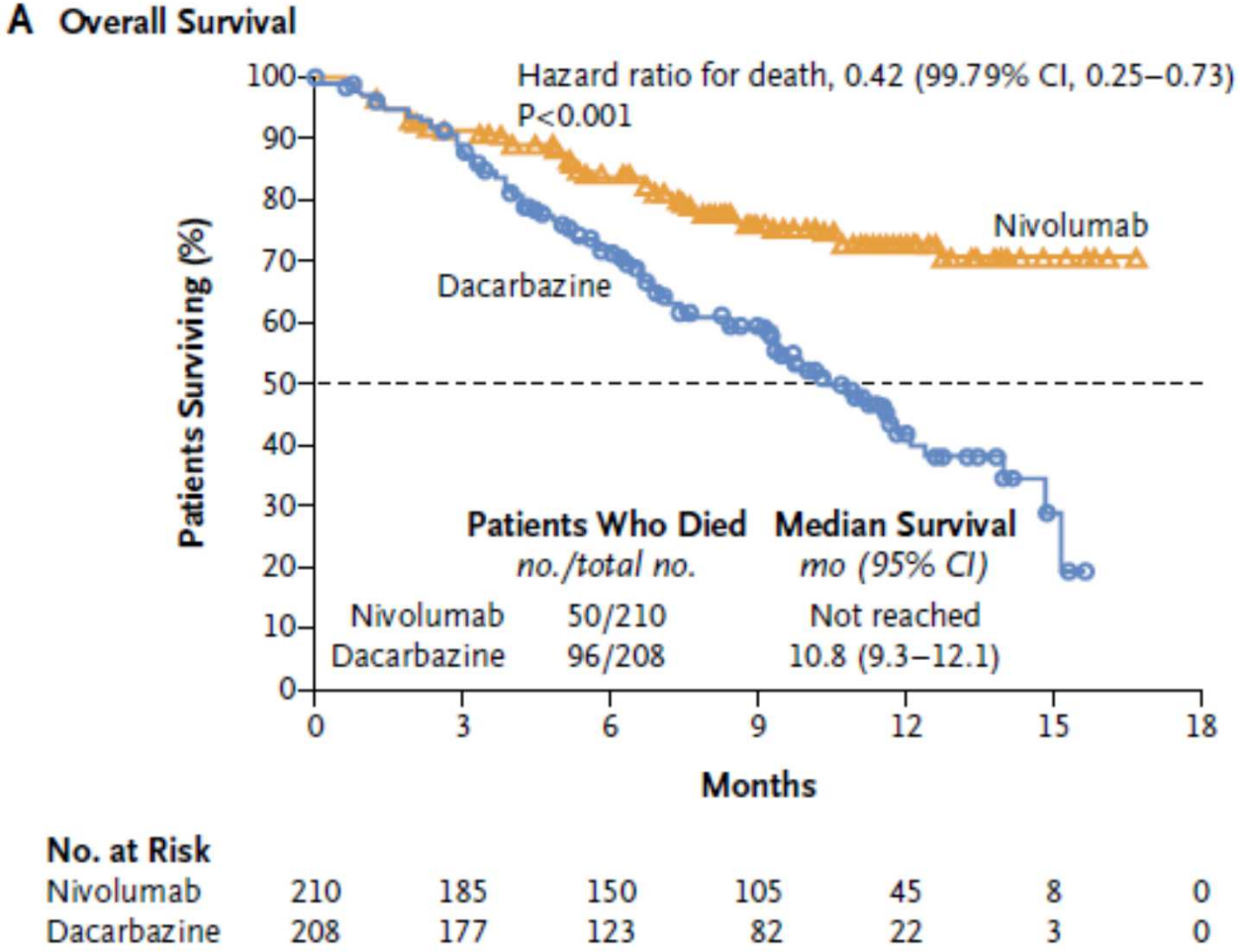
FDA – U.S. Food and Drug Administration

Nivolumab mode of action



Adapted from Nourkeyhani H, George S. J Targeted Ther Cancer. 2014;3(5):46-50

Nivolumab in treatment-naïve patients with unresectable stage III or IV Melanoma without BRAF mutation (I)



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

Nivolumab in treatment-naïve patients with unresectable stage III or IV Melanoma without BRAF mutation (II)

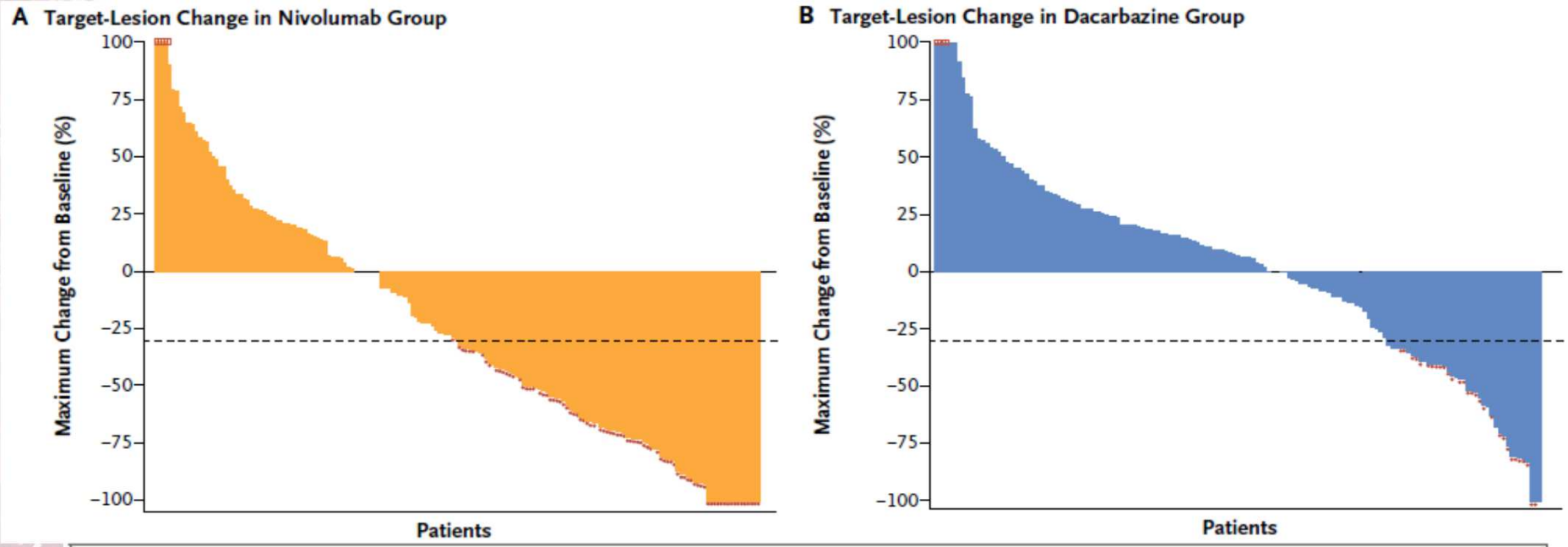


Table 2. Response to Treatment.*

Response	Nivolumab (N=210)	Dacarbazine (N=208)
Best overall response — no. (%)†		
Complete response	16 (7.6)	2 (1.0)
Partial response	68 (32.4)	27 (13.0)
Stable disease	35 (16.7)	46 (22.1)
Progressive disease	69 (32.9)	101 (48.6)
Could not be determined	22 (10.5)	32 (15.4)

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

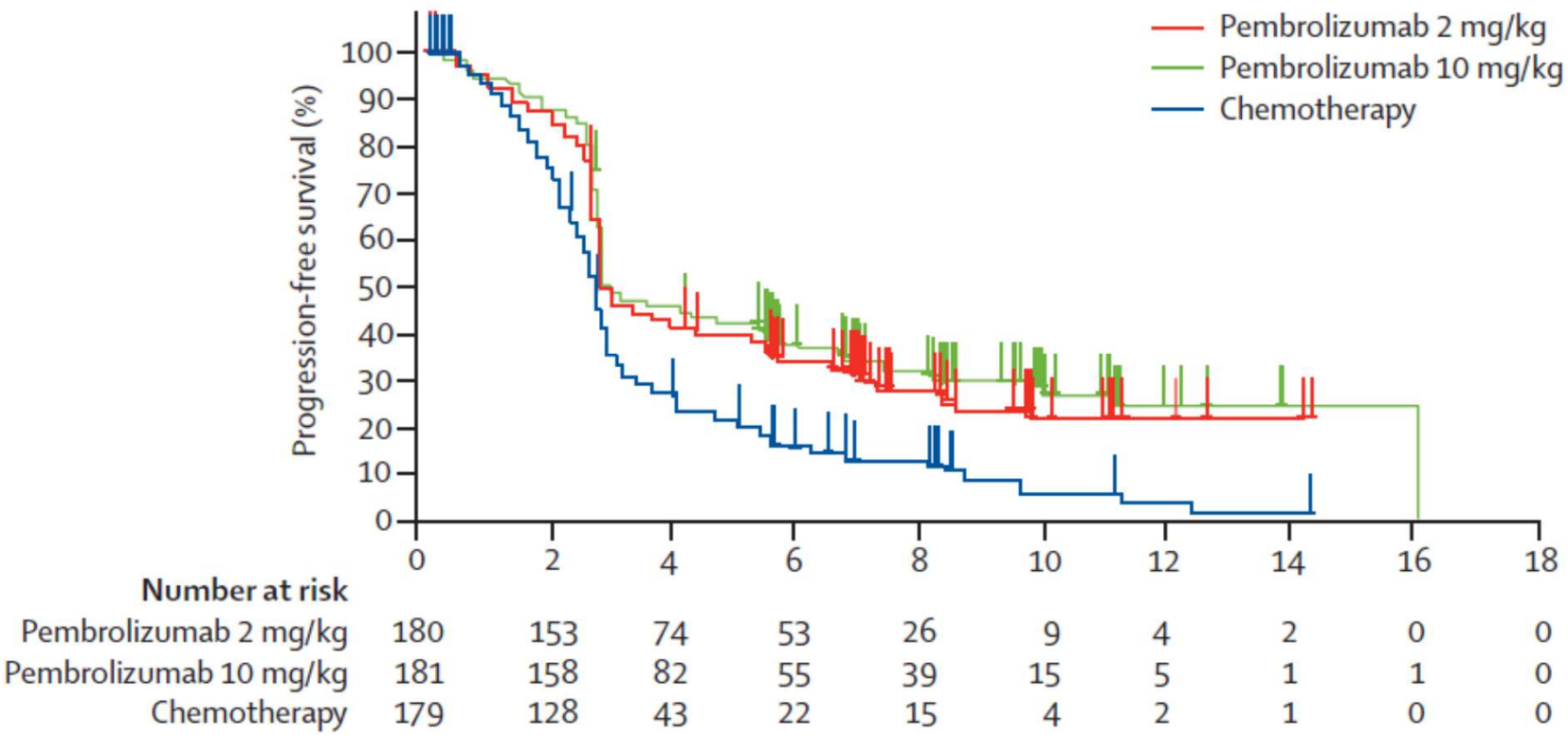
Nivolumab in treatment-naïve patients with unresectable stage III or IV Melanoma without BRAF mutation (III)

Table 3. Adverse Events.*

Event	Nivolumab (N=206)		Dacarbazine (N=205)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	no. of patients with event (%)			
Any adverse event	192 (93.2)	70 (34.0)	194 (94.6)	78 (38.0)
Treatment-related adverse event†	153 (74.3)	24 (11.7)	155 (75.6)	36 (17.6)
Fatigue	41 (19.9)	0	30 (14.6)	2 (1.0)
Pruritus	35 (17.0)	1 (0.5)	11 (5.4)	0
Nausea	34 (16.5)	0	85 (41.5)	0
Diarrhea	33 (16.0)	2 (1.0)	32 (15.6)	1 (0.5)
Rash	31 (15.0)	1 (0.5)	6 (2.9)	0
Vitiligo	22 (10.7)	0	1 (0.5)	0
Constipation	22 (10.7)	0	25 (12.2)	0
Asthenia	21 (10.2)	0	25 (12.2)	1 (0.5)
Vomiting	13 (6.3)	1 (0.5)	43 (21.0)	1 (0.5)
Neutropenia	0	0	23 (11.2)	9 (4.4)
Thrombocytopenia	0	0	21 (10.2)	10 (4.9)
Adverse event leading to discontinuation of treatment	14 (6.8)	12 (5.8)	24 (11.7)	19 (9.3)
Serious adverse event				
Any event	64 (31.1)	43 (20.9)	78 (38.0)	54 (26.3)
Treatment-related event	19 (9.2)	12 (5.8)	18 (8.8)	12 (5.9)

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

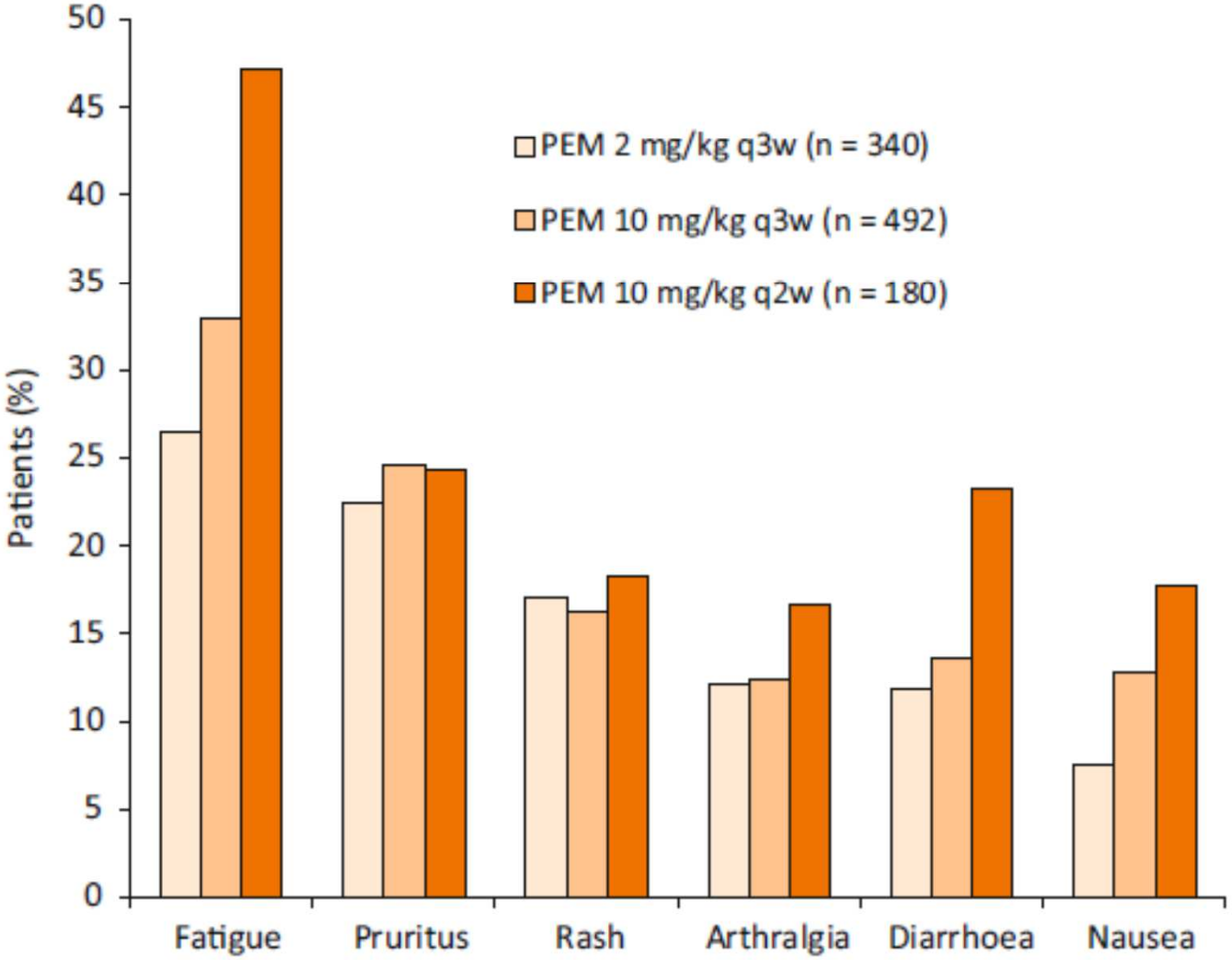
Pembrolizumab versus investigator-choice chemotherapy



	Pembrolizumab 2 mg/kg (n=180)	Pembrolizumab 10 mg/kg (n=181)	Chemotherapy control (n=179)
Best overall response assessed per RECIST v1.1, by independent central review			
Complete response	4 (2%)	5 (3%)	0
Partial response	34 (19%)	41 (23%)	8 (4%)
Stable disease	32 (18%)	31 (17%)	33 (18%)
Progressive disease	84 (47%)	86 (48%)	111 (62%)
Not evaluable‖	26**(14%)	18 (10%)	27 (15%)

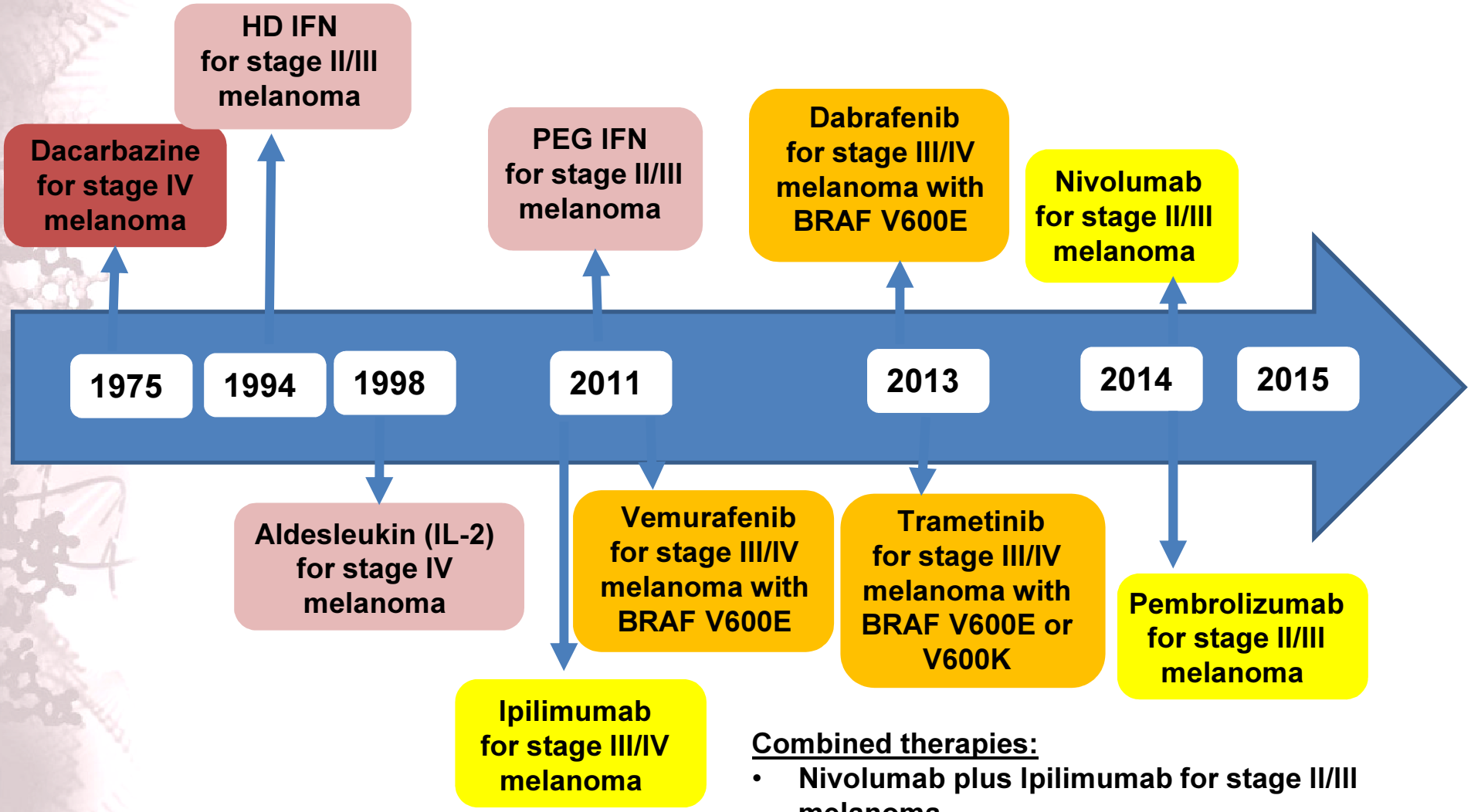
Ribas A, et al. *Lancet*. 2015; 16:908-18.

Pembrolizumab treatment-related adverse events



Deeks ED, 2016,76:375-386

Timeline for FDA Approved Drugs for melanoma



Combined therapies:

- Nivolumab plus Ipilimumab for stage II/III melanoma
- Dabrafenib plus trametinib stage III/IV melanoma with BRAF V600E or V600K
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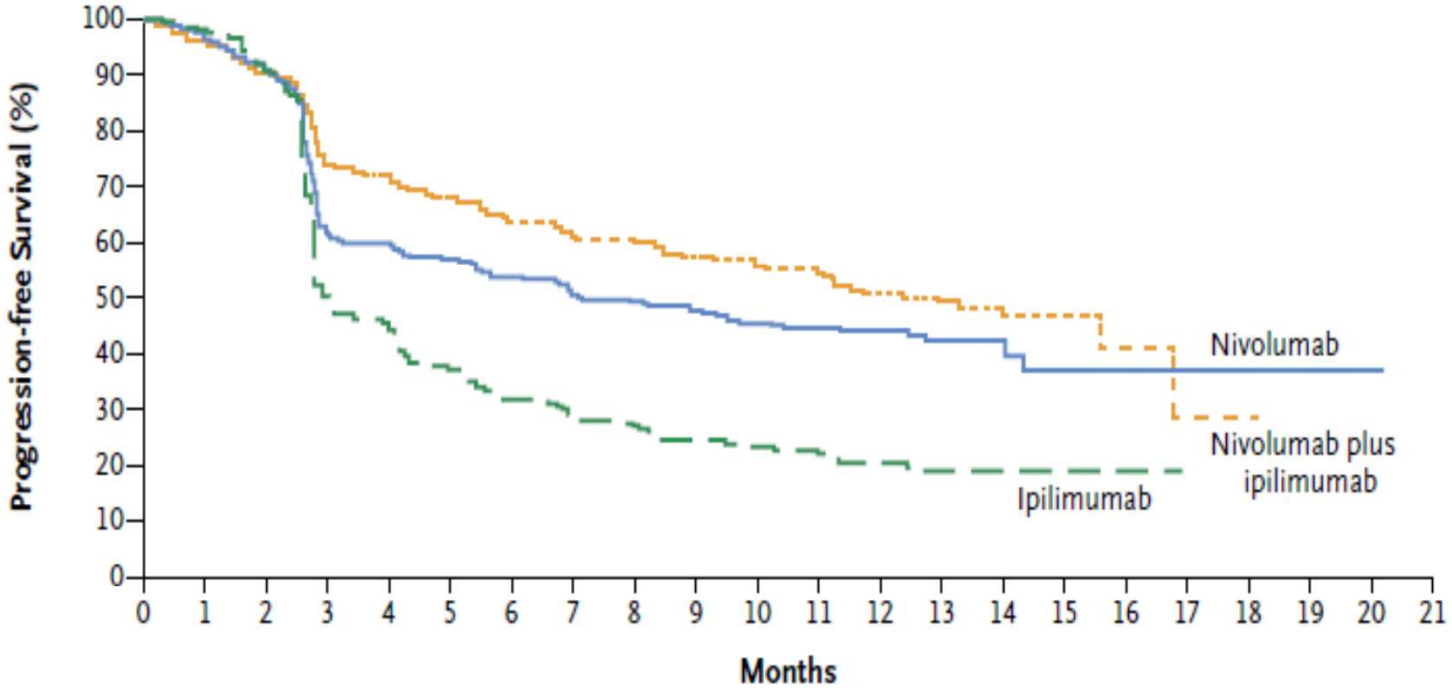
FDA – U.S. Food and Drug Administration

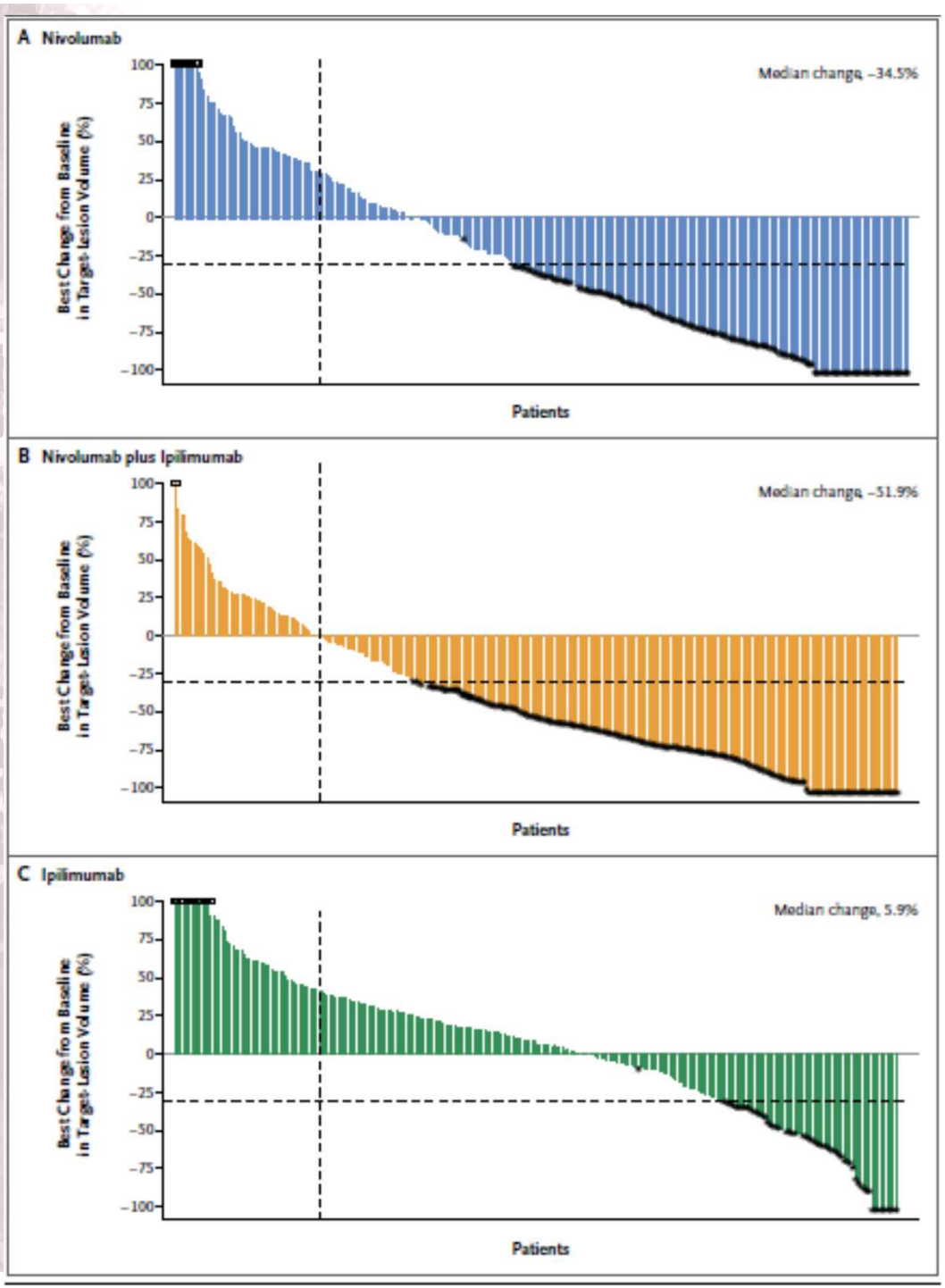
Combined Nivolumab and Ipilimumab or Monotherapy (I)



No. at Risk																						
Nivolumab	316	292	271	177	170	160	147	136	132	124	106	86	50	38	14	9	6	2	1	1	1	0
Nivolumab plus ipilimumab	314	293	275	219	208	191	173	164	163	151	137	116	65	54	18	11	7	2	1	0	0	0
Ipilimumab	315	285	265	137	118	95	77	68	63	54	47	42	24	17	7	4	3	0	0	0	0	0

Larkin J et al. N Engl J Med 2015

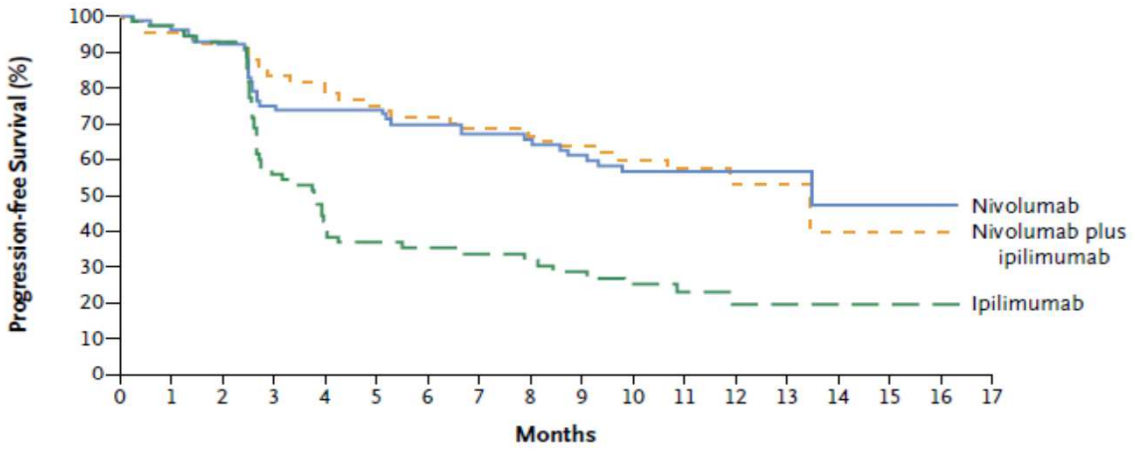
Combined Nivolumab and Ipilimumab or Monotherapy (II)



Larkin J et al. N Engl J Med 2015

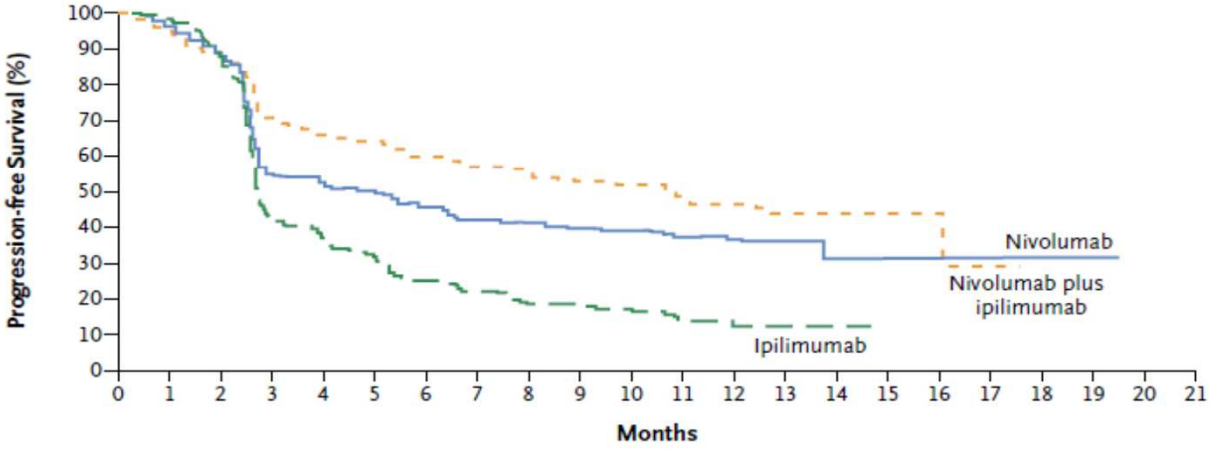
Combined Nivolumab and Ipilimumab or Monotherapy (III)

B **Patients with PD-L1–Positive Tumors**



No. at Risk																		
Nivolumab	80	76	71	57	56	54	51	49	49	43	38	32	16	13	5	4	2	0
Nivolumab plus ipilimumab	68	63	61	53	52	47	44	42	42	39	34	24	16	12	3	1	1	0
Ipilimumab	75	69	66	40	33	24	22	21	21	17	16	15	9	6	3	2	2	0

C **Patients with PD-L1–Negative Tumors**



No. at Risk																					
Nivolumab	208	192	178	108	105	98	88	80	76	74	63	50	31	24	9	5	4	2	1	1	1	0
Nivolumab plus ipilimumab	210	195	181	142	134	123	112	106	105	96	88	79	42	36	13	9	6	2	1	0		
Ipilimumab	202	183	166	82	72	59	44	39	35	31	26	22	12	8	3	1	0					

Larkin J et al. N Engl J Med 2015

Combined Nivolumab and Ipilimumab or Monotherapy (IV)

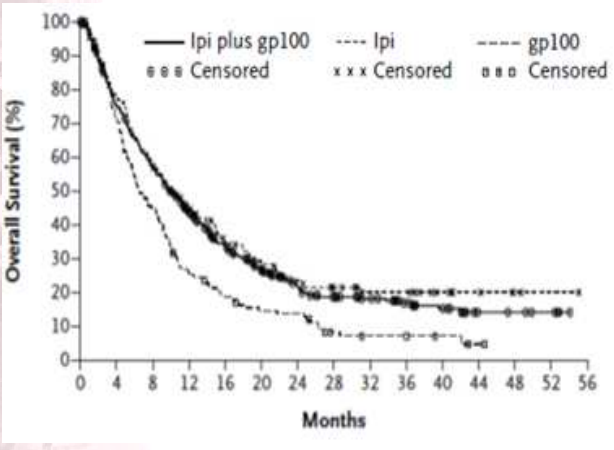
Table 3. Adverse Events.*

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 amino-transferase 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 amino-transferase 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)

Larkin J et al. N Engl J Med 2015

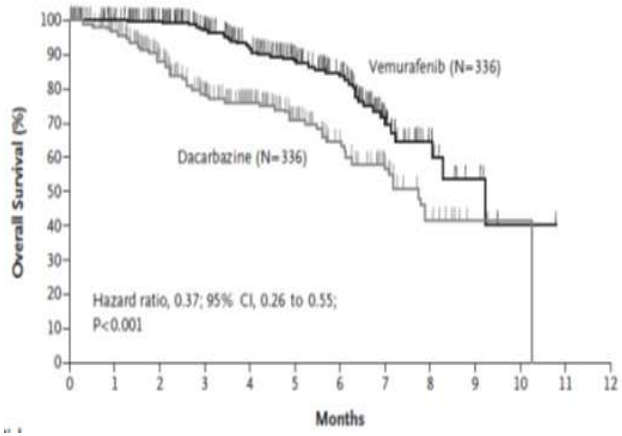
Combining Immunotherapy and Targeted Therapy

Immunotherapy



Hodi FS, et al. N Engl J Med. 2010

Targeted therapy

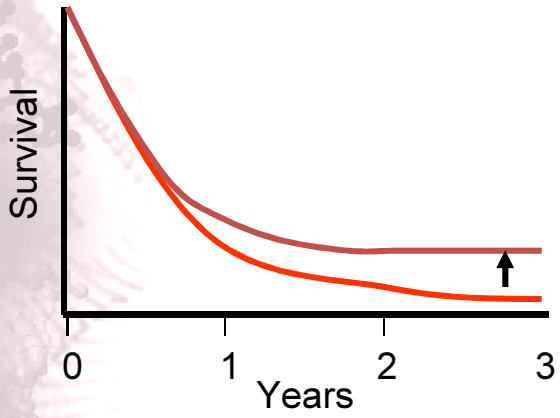


Chapman PB, et al. N Engl J Med. 2011

Combination

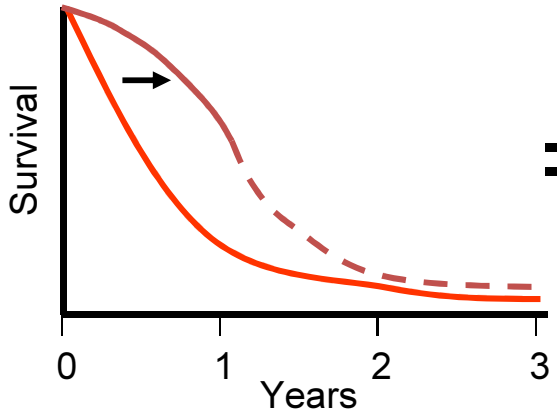
?

Immunotherapy



+

Targeted therapy



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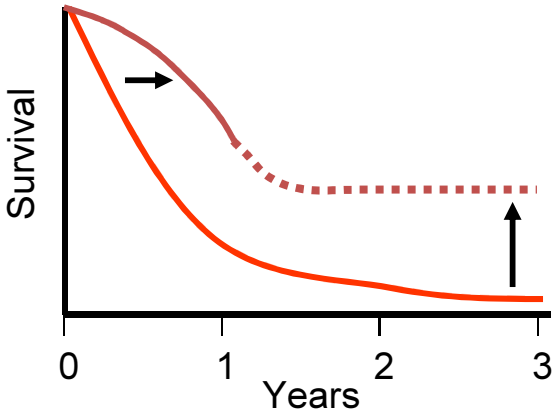
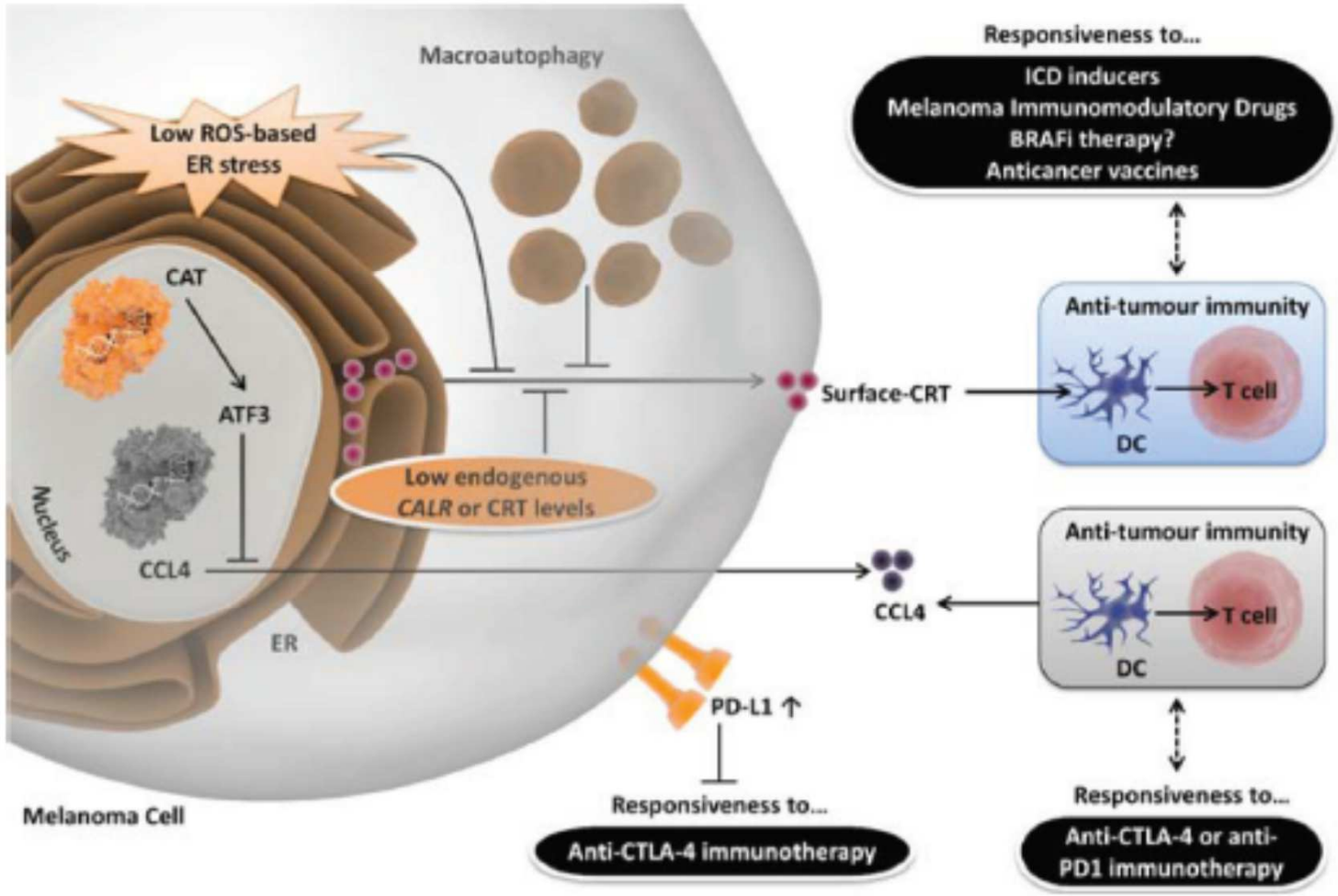
Combination



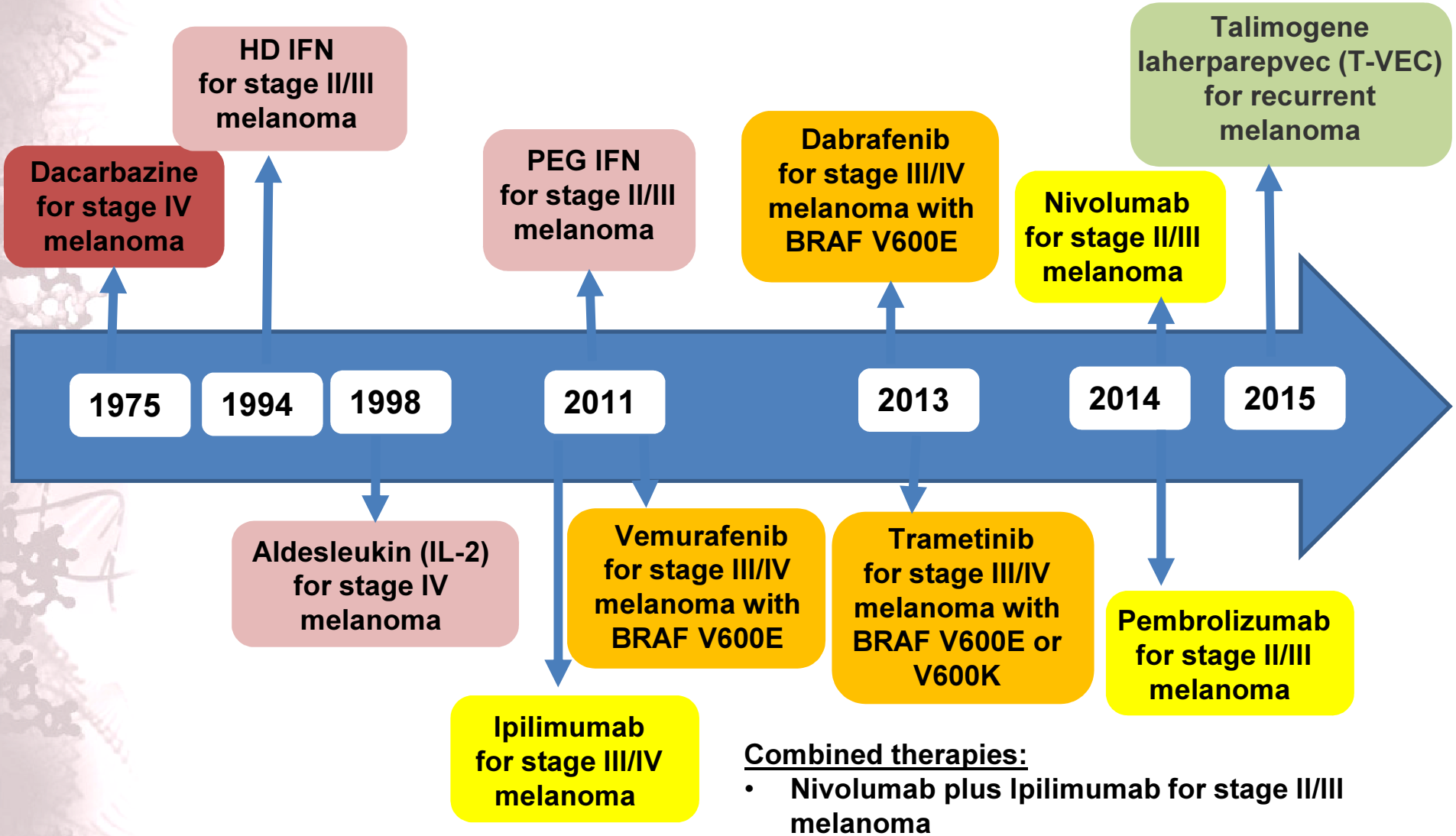
Ribas A, et al., Clin Cancer Res. 2012 Jan 15; 18(2): 336–341.

Melanoma Resistance Mechanisms Against Immunotherapeutic Paradigms



Abhishek DG, Oncoscience 2015, Vol.2, No.10

Timeline for FDA Approved Drugs for melanoma



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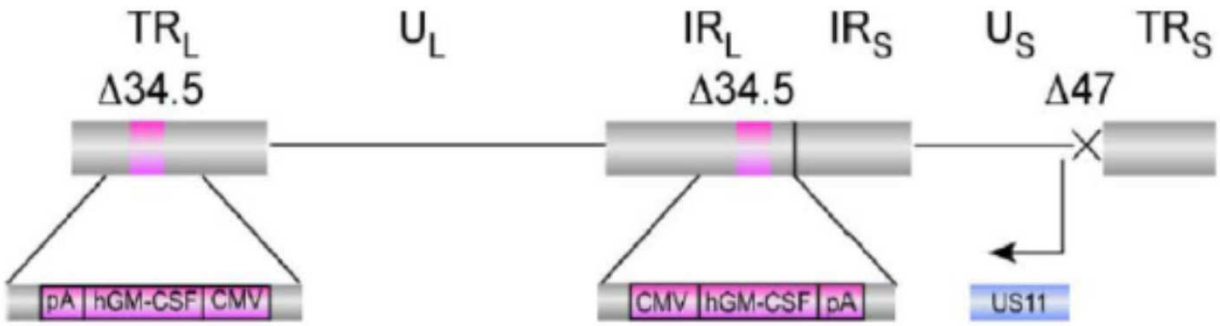
FDA – U.S. Food and Drug Administration

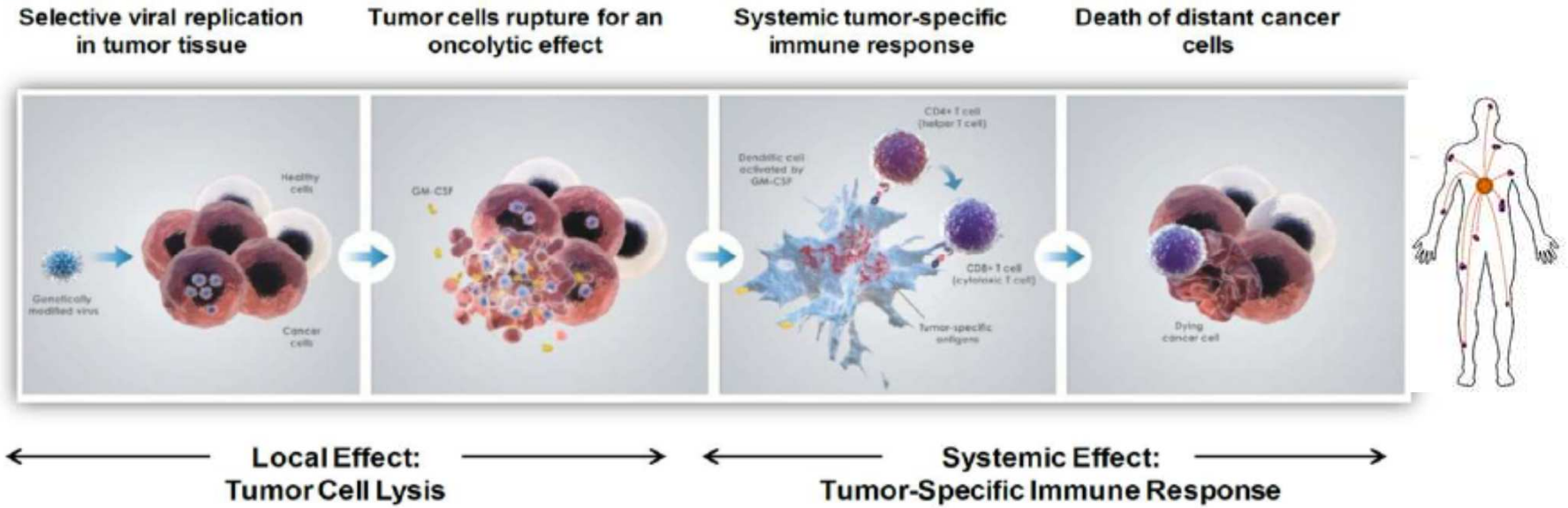
T-VEC: An HSV-1 Derived Oncolytic Immunotherapy

Genomic structure of T-VEC:



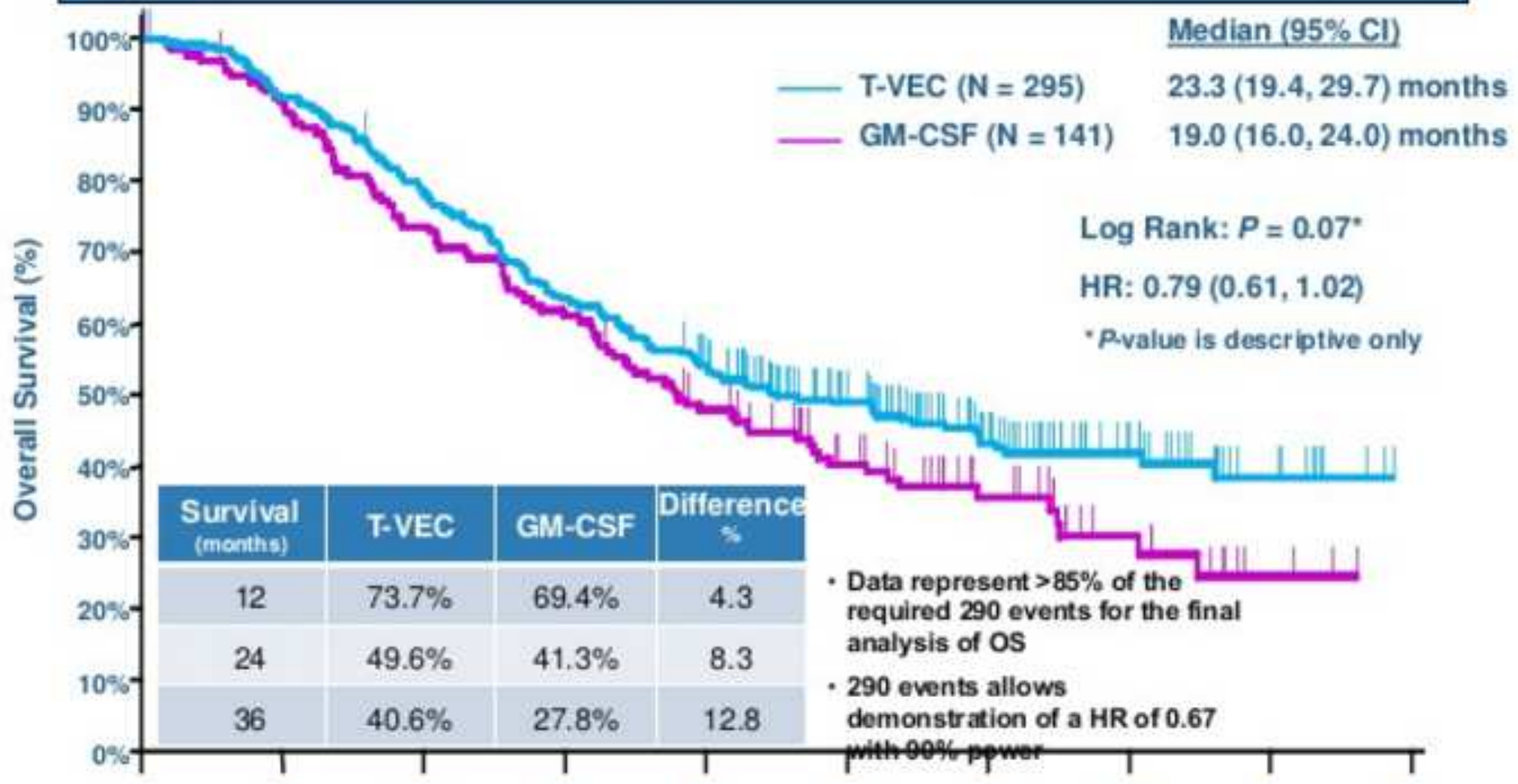
Mode of action:

Produce Both Local and Systemic Effects



U.S. Food and Drug Administration

Interim Overall Survival (ITT)



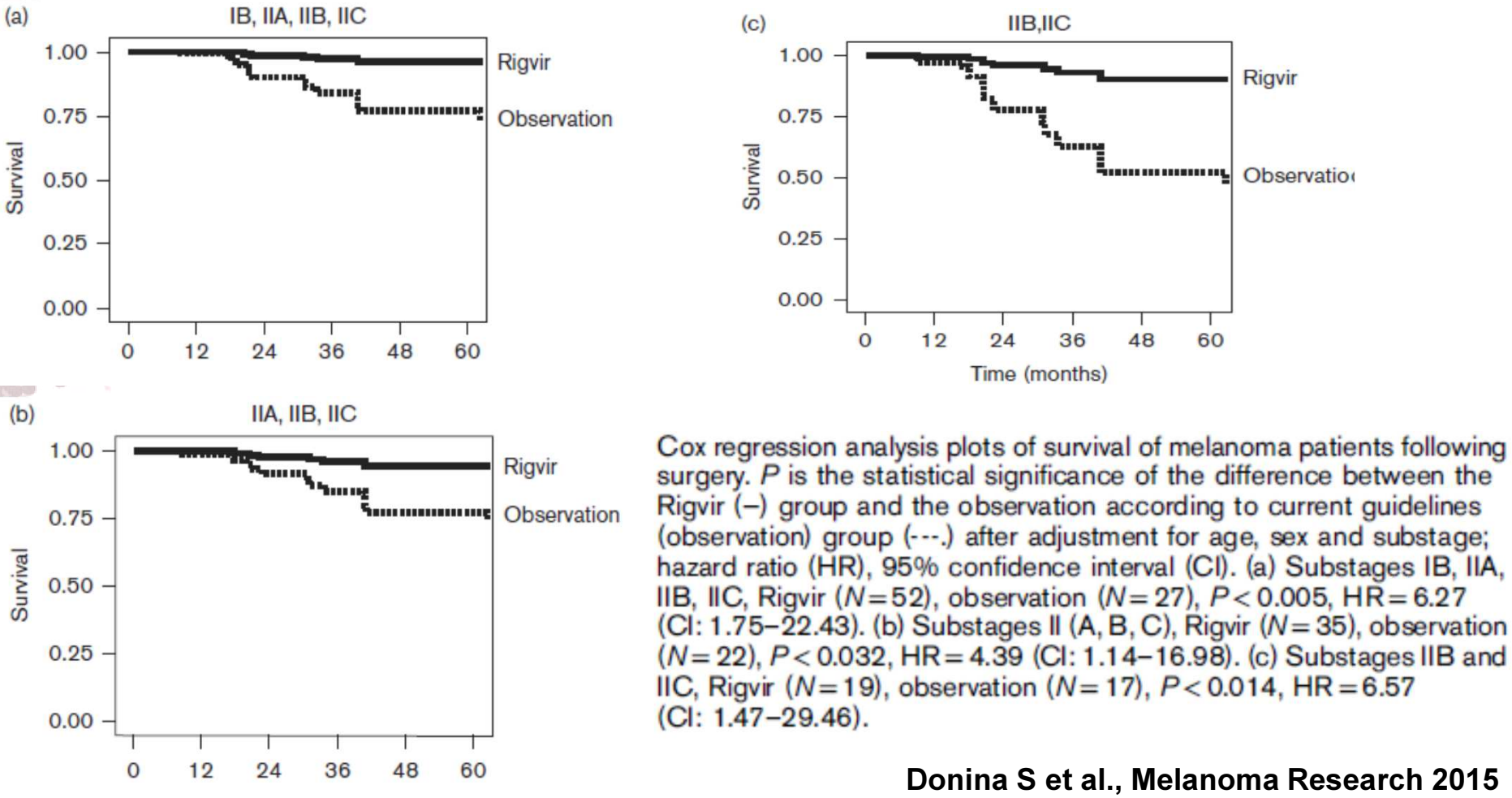
Survival (months)	T-VEC	GM-CSF	Difference %
12	73.7%	69.4%	4.3
24	49.6%	41.3%	8.3
36	40.6%	27.8%	12.8

- Data represent >85% of the required 290 events for the final analysis of OS
- 290 events allows demonstration of a HR of 0.67 with 90% power

ASCO & SMR 2013 data summary

Oncolytic Immunotherapy with Echo-7 virus (Rigvir)

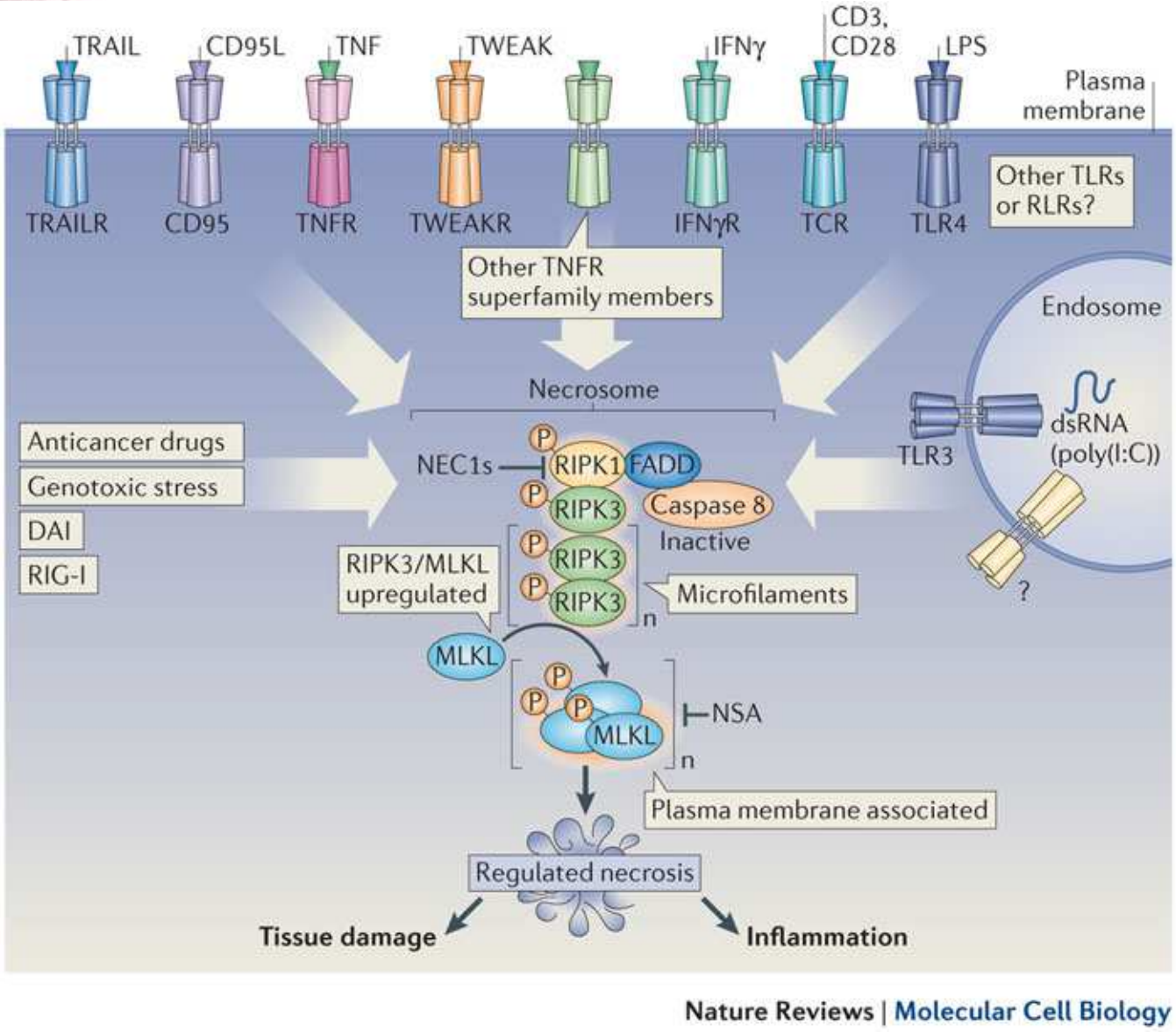
Registered in Latvia for melanoma, melanoma cutaneous and subcutaneous metastasis treatment, prevention of relapse and metastasis after radical surgery.



Cox regression analysis plots of survival of melanoma patients following surgery. *P* is the statistical significance of the difference between the Rigvir (–) group and the observation according to current guidelines (observation) group (---.) after adjustment for age, sex and substage; hazard ratio (HR), 95% confidence interval (CI). (a) Substages IB, IIA, IIB, IIC, Rigvir ($N=52$), observation ($N=27$), $P<0.005$, HR = 6.27 (CI: 1.75–22.43). (b) Substages II (A, B, C), Rigvir ($N=35$), observation ($N=22$), $P<0.032$, HR = 4.39 (CI: 1.14–16.98). (c) Substages IIB and IIC, Rigvir ($N=19$), observation ($N=17$), $P<0.014$, HR = 6.57 (CI: 1.47–29.46).

Donina S et al., Melanoma Research 2015

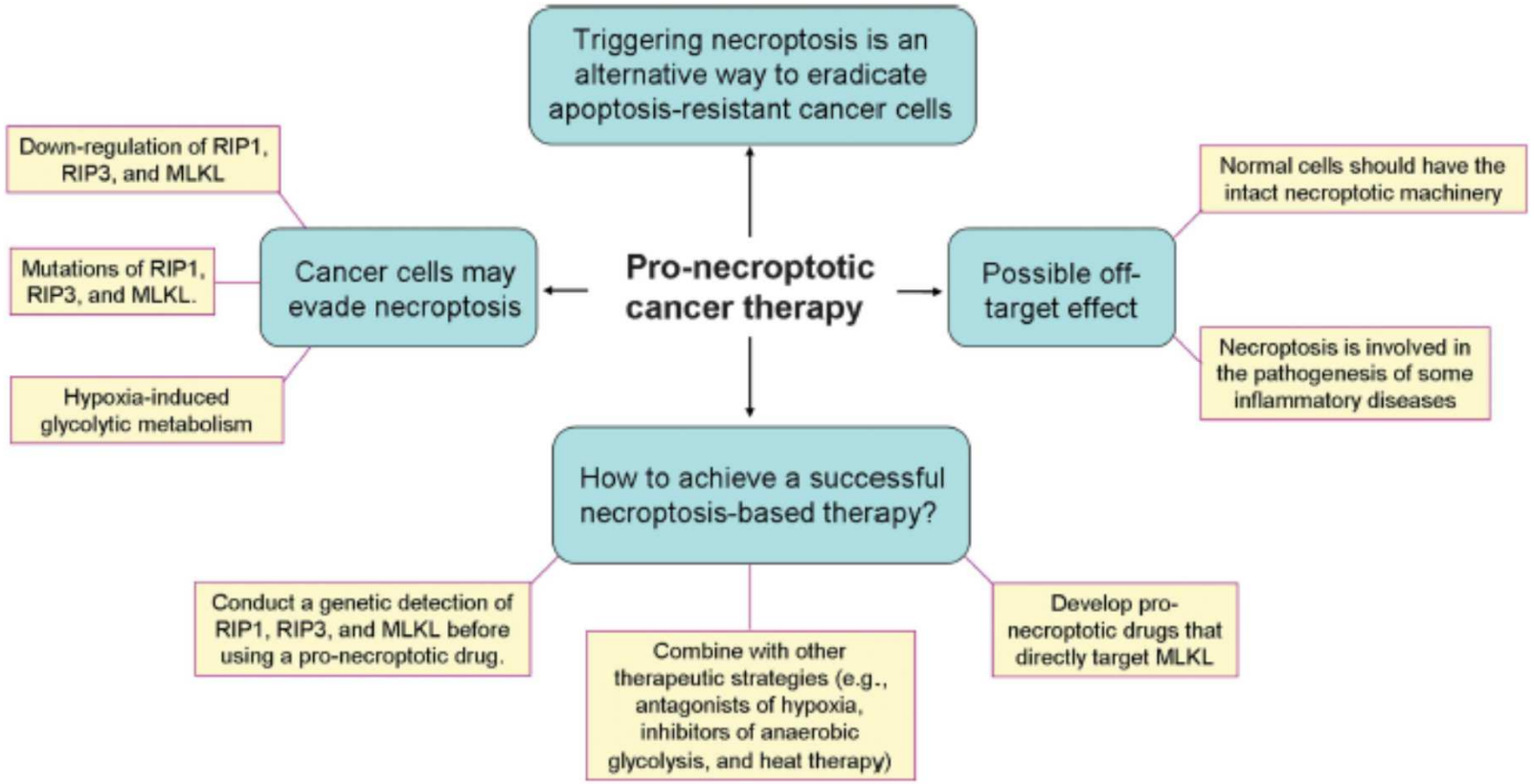
Therapeutic exploitation of regulated necrosis (necroptosis) for cancer therapy



Necroptosis induction by activation:

- **TNF receptor superfamily**
- **T cell receptors**
- **interferon receptors Toll-like receptors**
- **cellular metabolic and genotoxic stresses**
- **various anti-cancer agents**

Pro-necroptotic cancer therapy



Su Z et al., Cell Death and Differentiation (2016) 23, 748–756

MELANOMA THERAPY:

IMMUNOTHERAPY
TARGETED THERAPIES
COMBINATIONS
NEW TARGETS
……
ENDLESS WORK


Thank you!