

Czerniak złośliwy – wyzwania współczesnej terapii

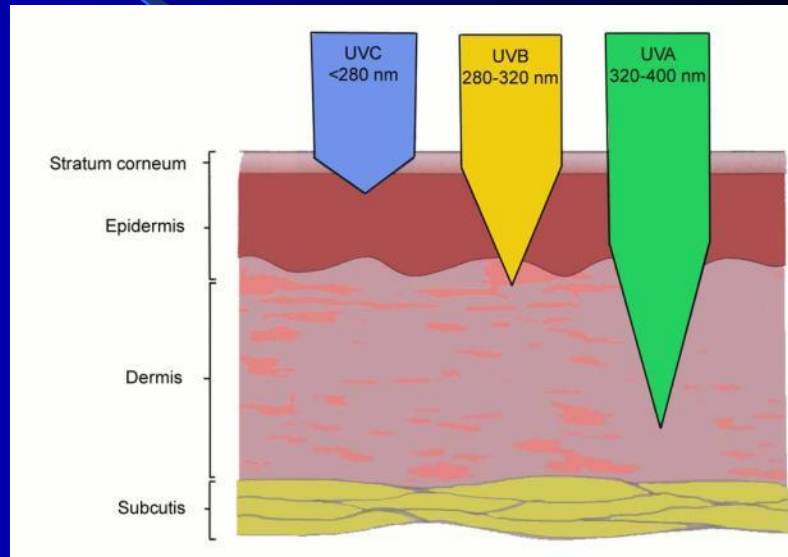
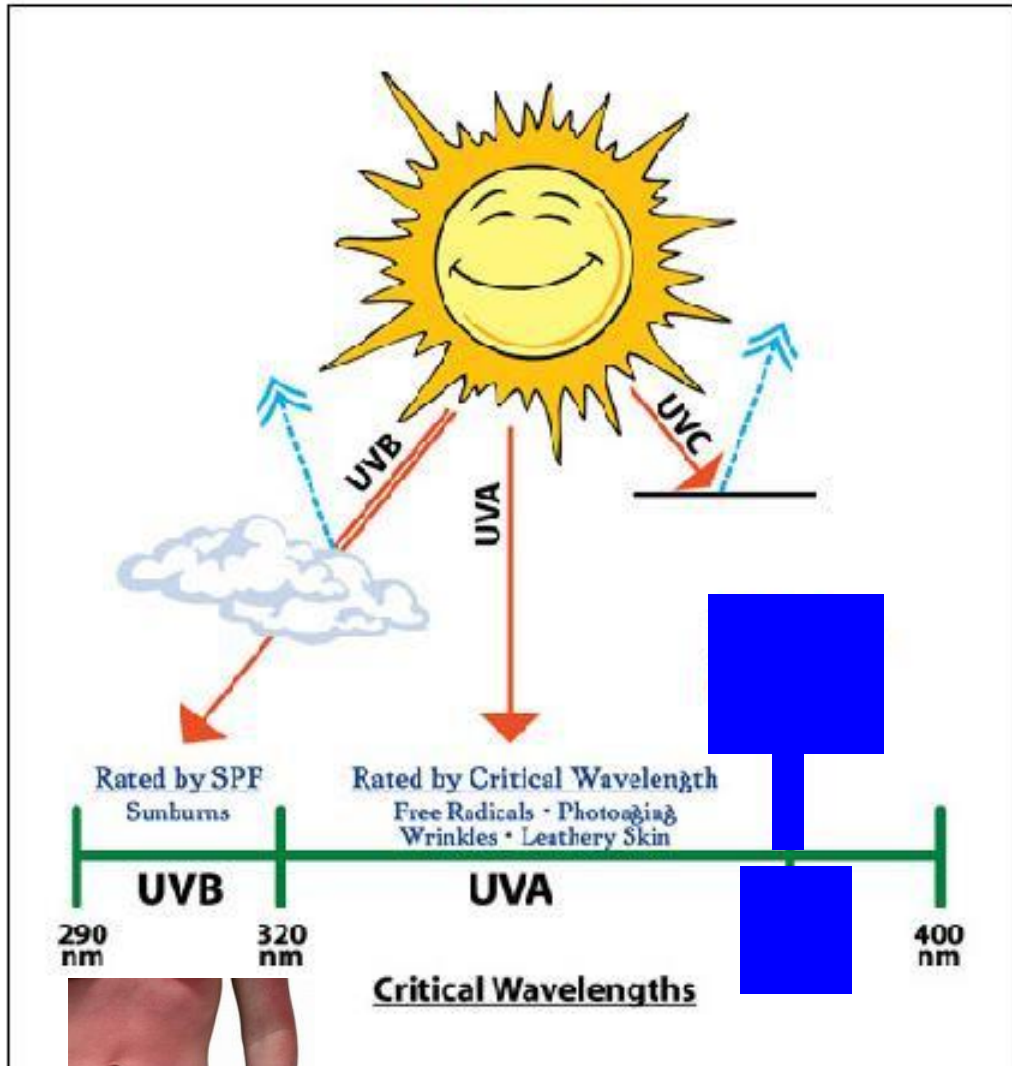
Prof. dr hab. Adam Reich







UVA Protection



Czerniak złośliwy

- Epidemiologia

- 70 tys. zachorowań na świecie każdego roku

- $1,5/10^5$ osób na rok na świecie

- $0,2-0,3/10^5$ - Azja

- $6,2 /10^5$ - Ameryka Północna

- $40/10^5$ - Australia

- $2,7/10^5$ - Polska

Czerniak złośliwy

Związek z intensywnymi, krótkotrwałymi ekspozycjami na słońce (oparzenia słoneczne)

Oparzenia słoneczne szczególnie istotne w wieku <15 lat

2-5 oparzenia <15 lat – 1,5-2x wzrost ryzyka czerniaka

>5 oparzeń <15 lat – 2,7x wzrost ryzyka czerniaka

Czerniak złośliwy

- **Korzystanie z solariów:**
 - 1,5 – 1,8 wzrost ryzyka czerniaka
 - Rozwój czerniaka okolicy anogenitalnej

The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review

The International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer

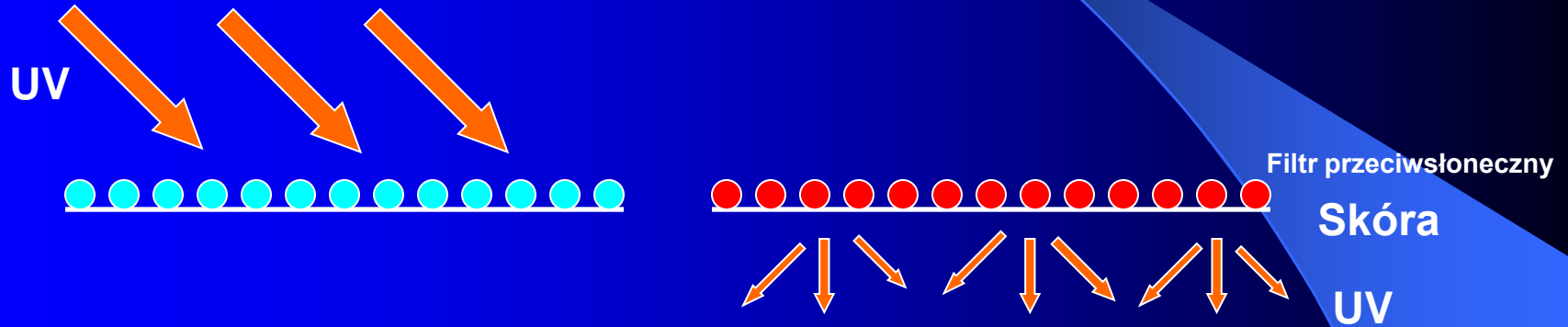
Exposure	Number of studies	Summary relative risk ¹
Melanoma		
Ever use of indoor tanning equipment	19	1.15 (1.00–1.31)
First exposure in youth	7	1.75 (1.35–2.26)
Exposure distant in time	5	1.49 (0.93–2.38)
Exposure recent in time	5	1.10 (0.76–1.60)
Squamous cell carcinoma		
Ever use of indoor tanning equipment	3	2.25 (1.08–4.70)
Basal cell carcinoma		
Ever use of indoor tanning equipment	4	1.03 (0.56–1.90)



Zapobieganie – filtry przeciwsłoneczne

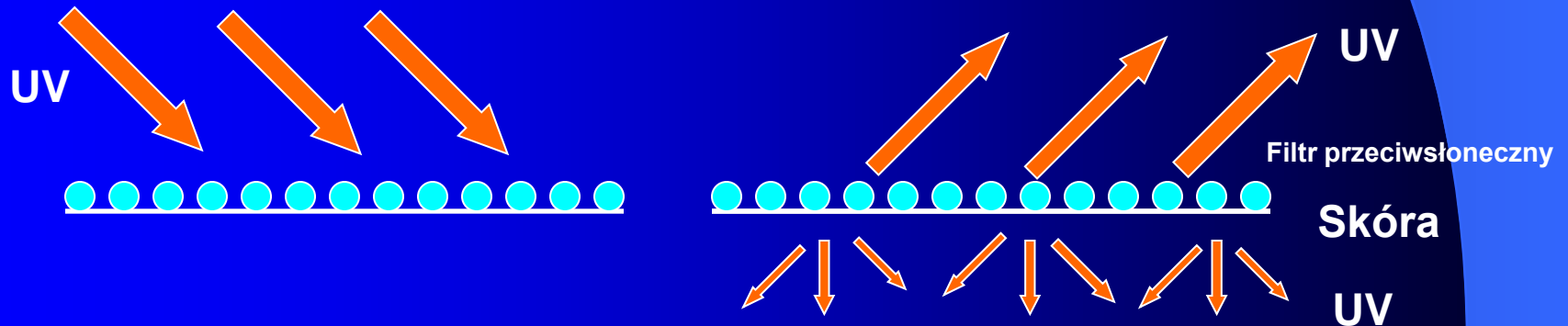
Filtry chemiczne

absorbpcja, rozpraszanie UV



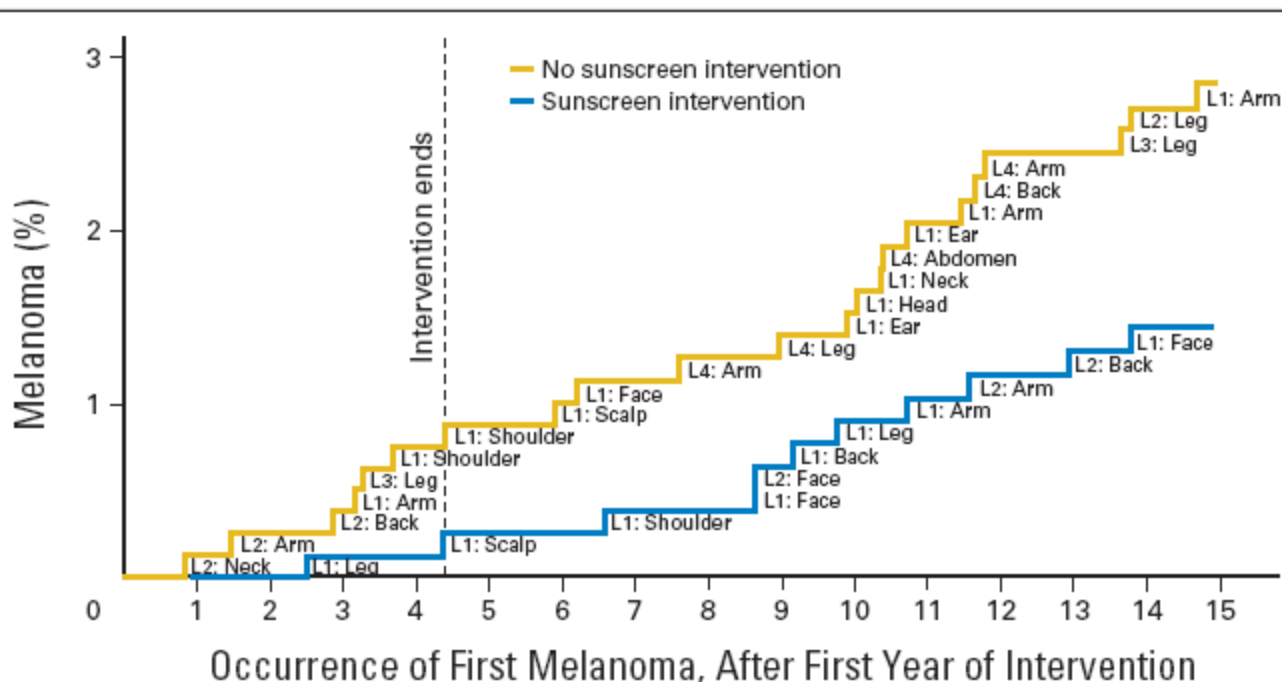
Filtry fizyczne (mineralne)

odbicie, rozproszenie UV



Reduced Melanoma After Regular Sunscreen Use: Randomized Trial Follow-Up

Adèle C. Green, Gail M. Williams, Valerie Logan, and Geoffrey M. Strutton



Persons at risk

No sunscreen intervention	809	806	804	803	798	792	789	784	780	773	764	752	745	740	738
Sunscreen intervention	812	808	804	800	795	788	782	780	773	769	763	754	747	744	741





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Czerniak złośliwy

- **Profilaktyka i wczesna diagnostyka**
 - 1. uwrażliwienie na unikanie poparzeń słonecznych, szczególnie w dzieciństwie - stosowanie filtrów ochronnych**
 - 2. Diagnostyka dermatoskopowa zmian barwnikowych – wczesne wykrywanie znamion atypowych i czerniaka**

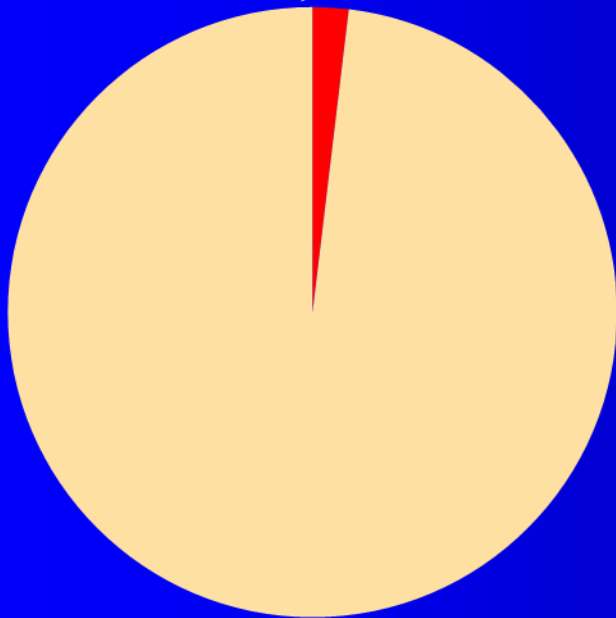
Czerniak złośliwy – częstość zachorowań



KRAJOWY REJESTR
NOWOTWORÓW

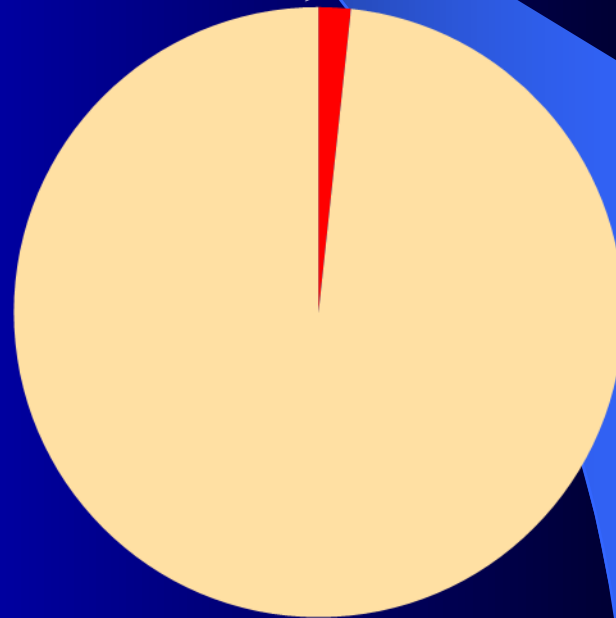
Kobiety

1,9%

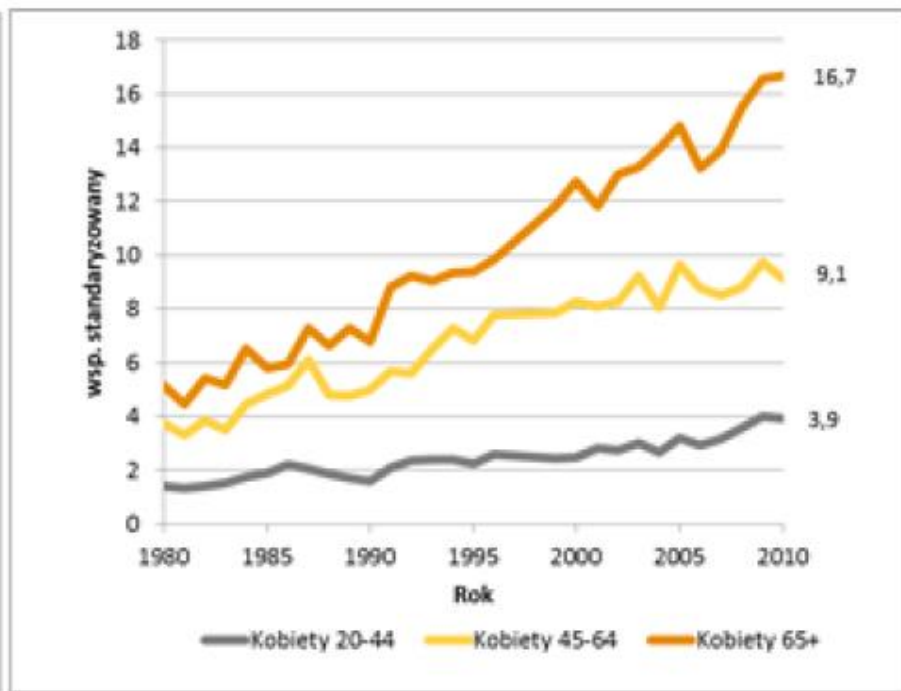
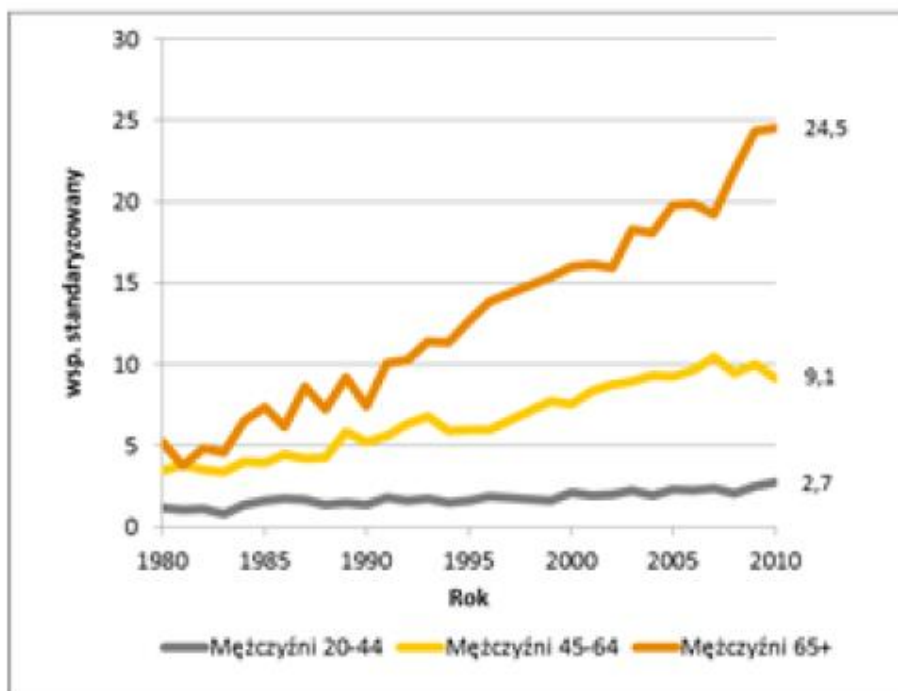


Mężczyźni

1,7%



Czerniak złośliwy – częstość zachorowań



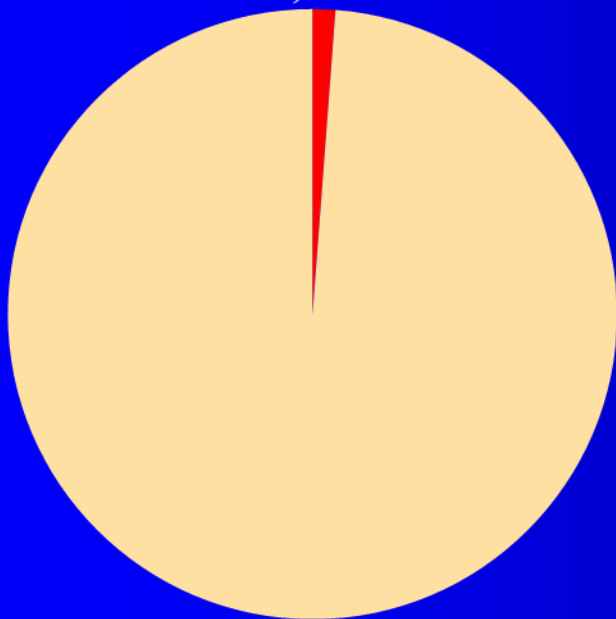
Czerniak złośliwy – częstość zgonów



KRAJOWY REJESTR
NOWOTWORÓW

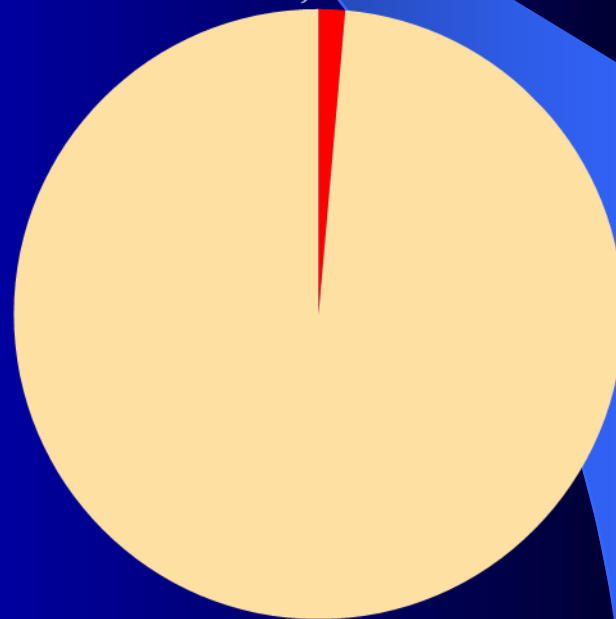
Kobiety

1,2%



Mężczyźni

1,4%

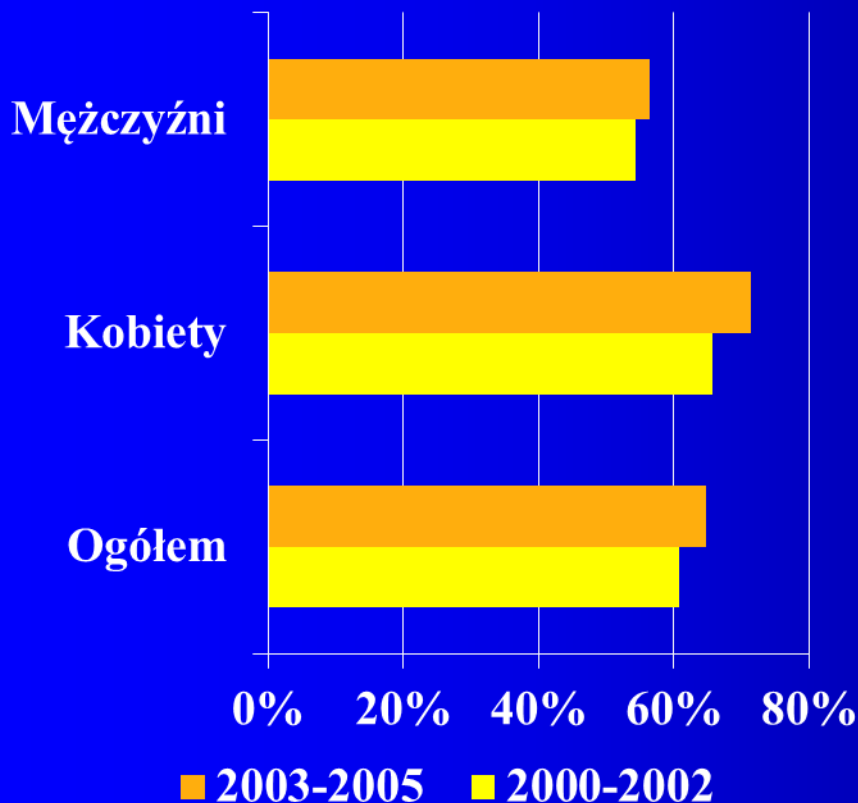


Liczba zgonów z powodu Czerniaka skóry wynosiła w 2010 roku prawie 1200

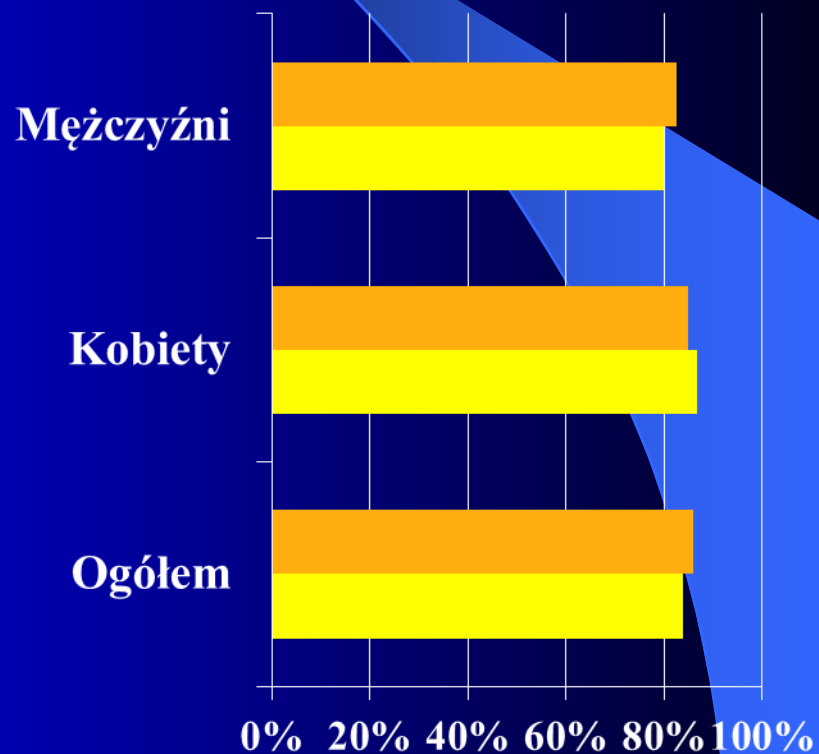
Czerniak złośliwy – częstość zgonów



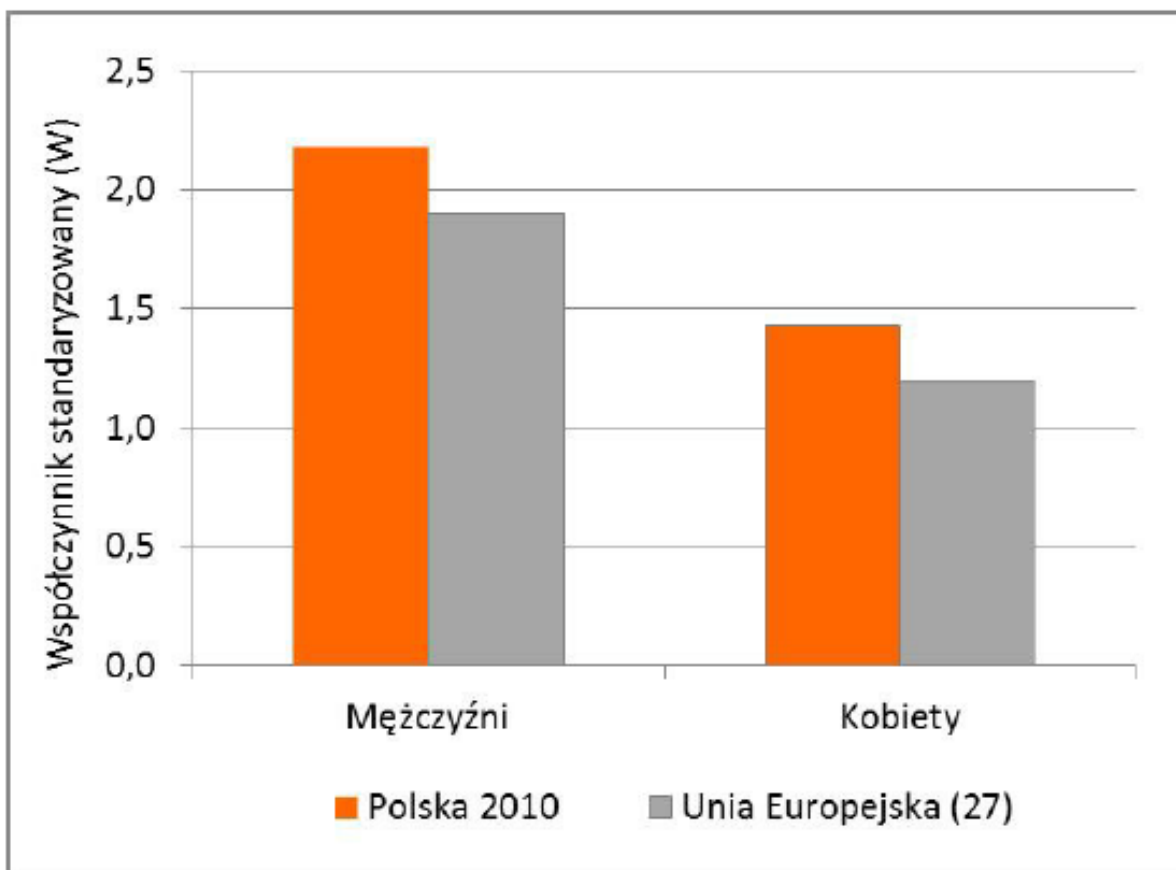
Przeżycie 5-letnie



Przeżycie roczne



Czerniak złośliwy – częstość zgonów



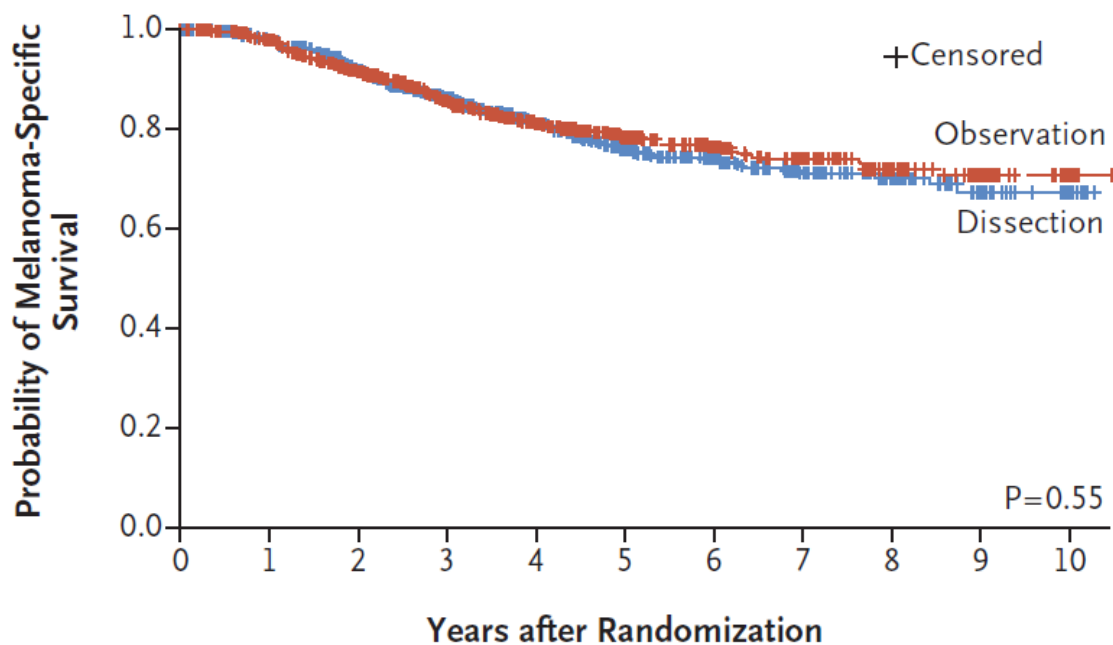
Czerniak złośliwy

- **Leczenie**
 - **usuwanie chirurgiczne nowotworu**
 - **usuwanie węzłów chłonnych**
 - **chemioterapia** (dakarbazyna, cisplatyna, karboplatyna, winkrystyna, lomustyna)
 - **immunoterapia**
 - **genoterapia**
 - **wiroterapia**

Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

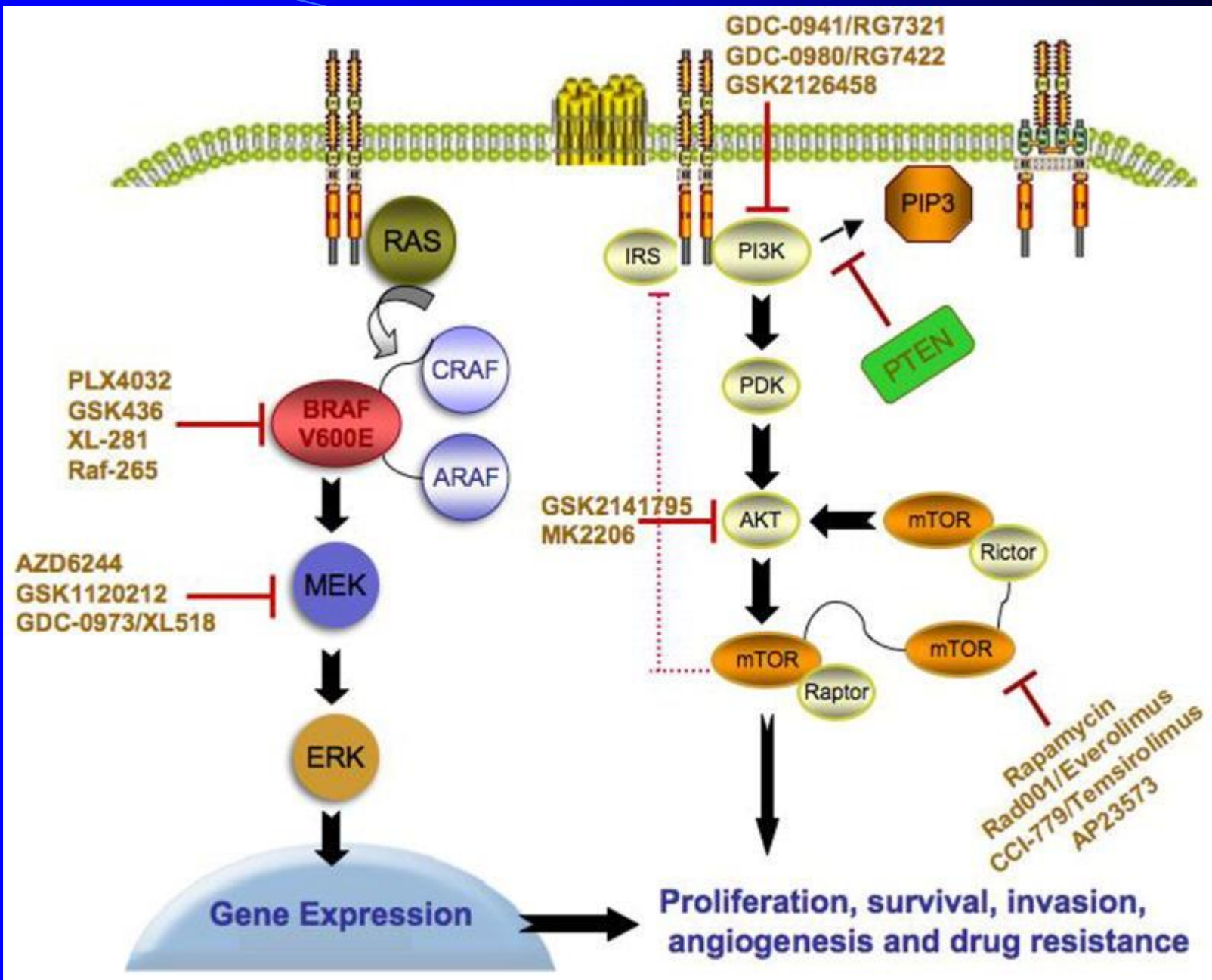
M.B. Faries, J.F. Thompson, A.J. Cochran, R.H. Andtbacka, N. Mozzillo, J.S. Zager, T. Jahkola, T.L. Bowles, A. Testori, P.D. Beitsch, H.J. Hoekstra, M. Moncrieff, C. Ingvar, M.W.J.M. Wouters, M.S. Sabel, E.A. Levine, D. Agnese, M. Henderson, R. Dummer, C.R. Rossi, R.I. Neves, S.D. Trocha, F. Wright, D.R. Byrd, M. Matter, E. Hsueh, A. MacKenzie-Ross, D.B. Johnson, P. Terheyden, A.C. Berger, T.L. Huston, J.D. Wayne, B.M. Smithers, H.B. Neuman, S. Schneebaum, J.E. Gershenwald, C.E. Ariyan, D.C. Desai, L. Jacobs, K.M. McMasters, A. Gesierich, P. Hersey, S.D. Bines, J.M. Kane, R.J. Barth, G. McKinnon, J.M. Farma, E. Schultz, S. Vidal-Sicart, R.A. Hofer, J.M. Lewis, R. Scheri, M.C. Kelley, O.E. Nieweg, R.D. Noyes, D.S.B. Hoon, H.-J. Wang, D.A. Elashoff, and R.M. Elashoff

A

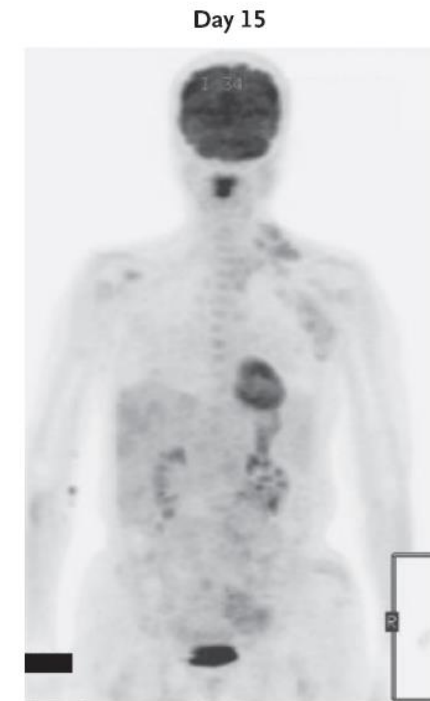
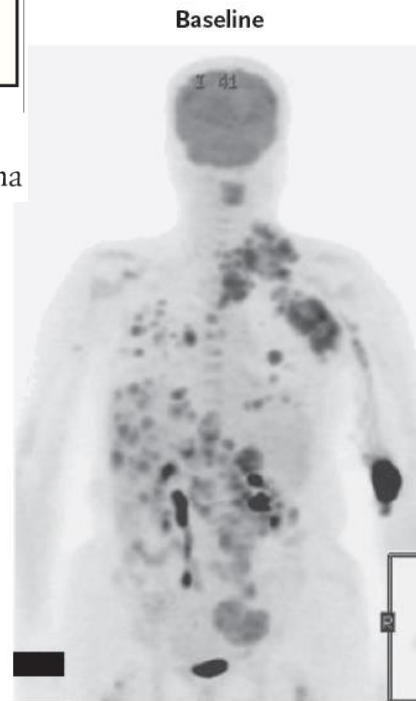


No. at Risk

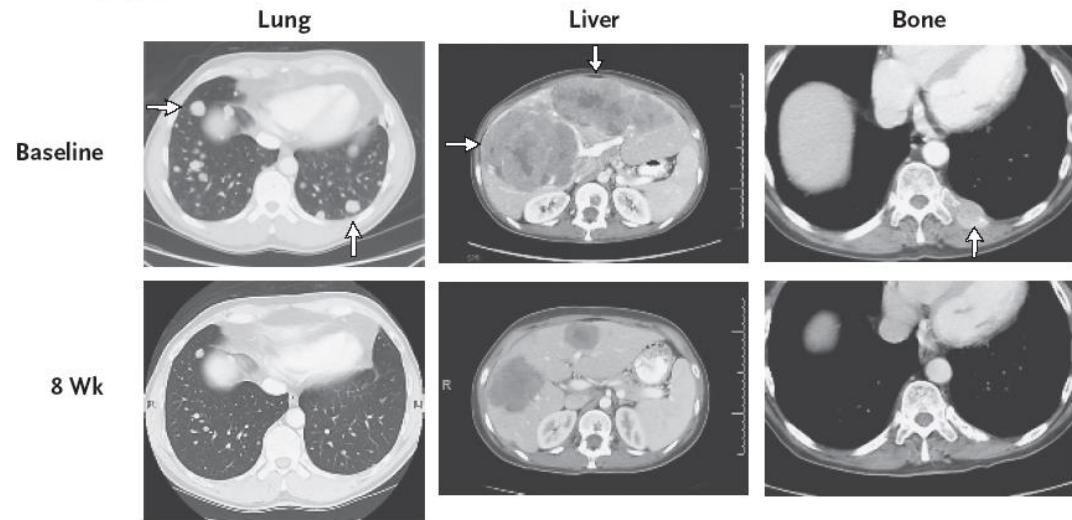
Dissection	824	759	654	510	389	275	191	128	83	39	13
Observation	931	856	734	564	425	304	217	151	95	55	13



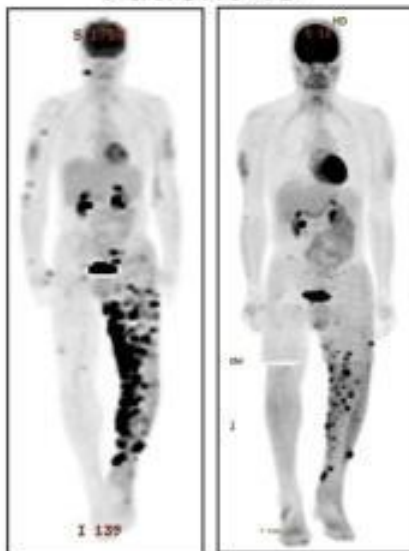
Inhibition of Mutated, Activated BRAF in Metastatic Melanoma



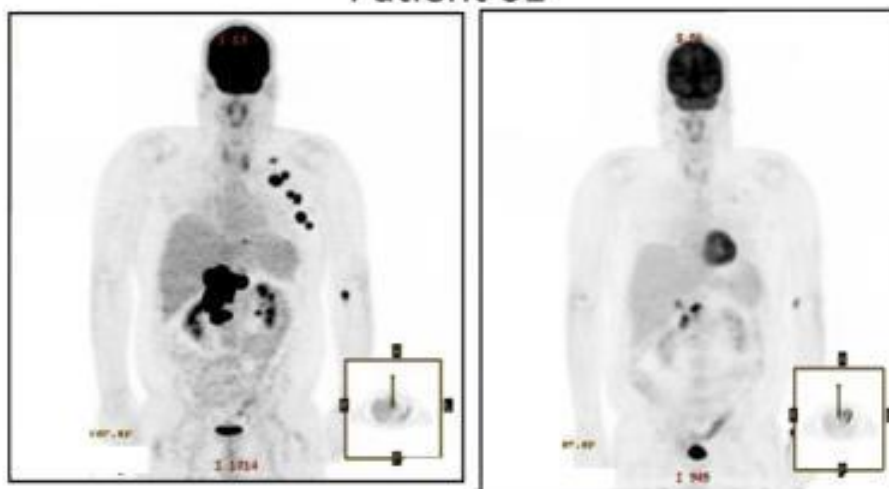
C Computed Tomography



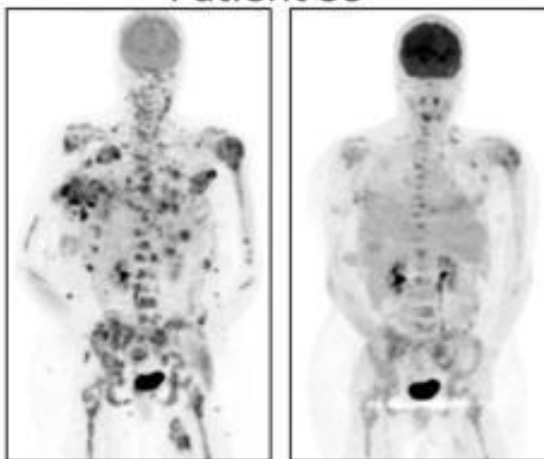
Patient 45



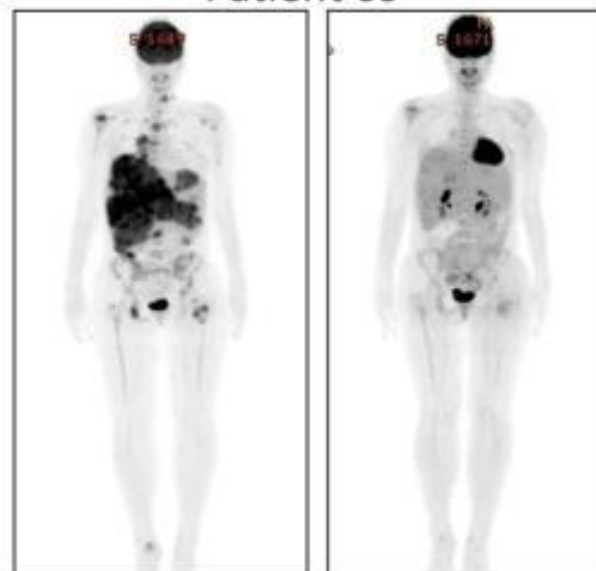
Patient 61

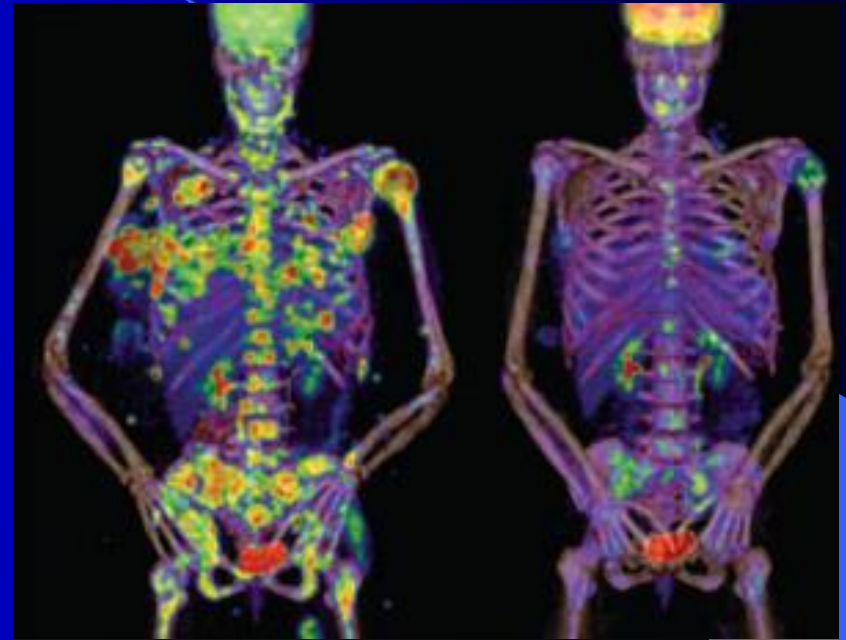
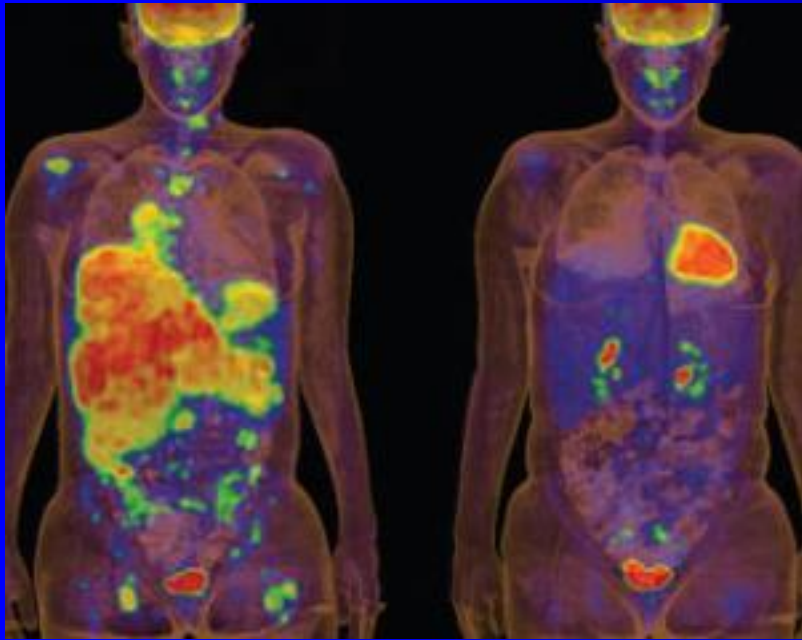


Patient 59



Patient 69

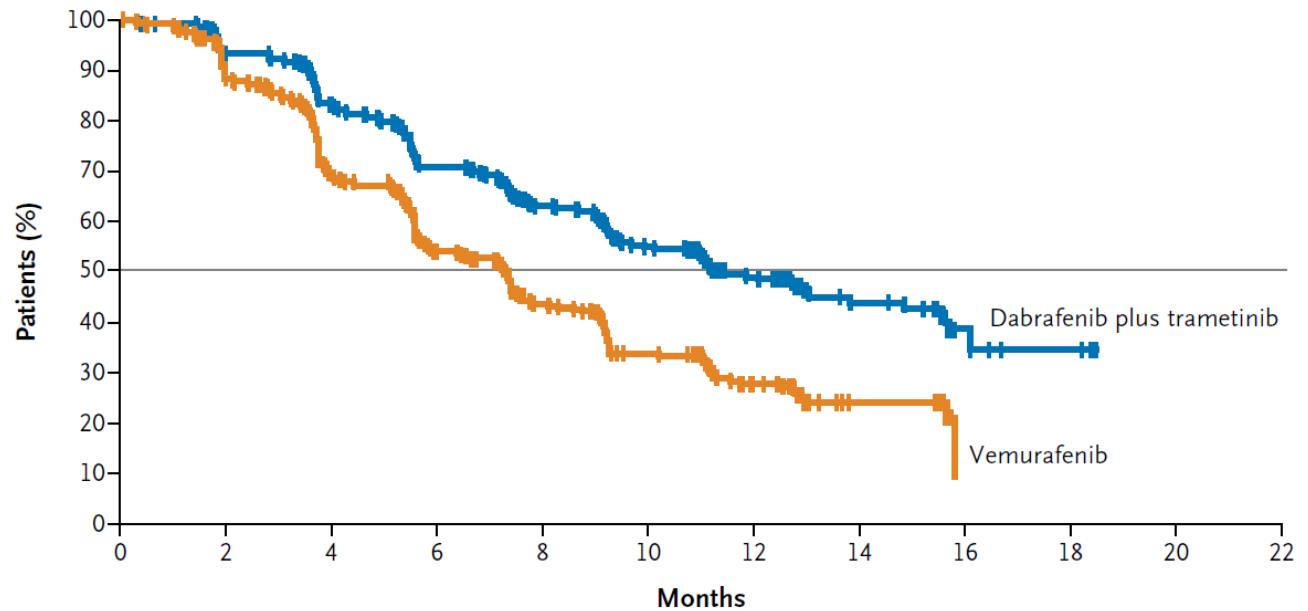




Improved Overall Survival in Melanoma with Combined Dabrafenib and Trametinib

Caroline Robert, M.D., Ph.D., Boguslawa Karaszewska, M.D., Jacob Schachter, M.D., Piotr Rutkowski, M.D., Ph.D., Andrzej Mackiewicz, M.D., Ph.D., Daniil Stroiakovski, M.D., Michael Lichinitser, M.D., Reinhard Dummer, M.D., Florent Grange, M.D., Ph.D., Laurent Mortier, M.D., Vanna Chiarion-Sileni, M.D., Kamil Drucis, M.D., Ph.D., Ivana Krajsova, M.D., Axel Hauschild, M.D., Ph.D., Paul Lorigan, M.D., Pascal Wolter, M.D., Georgina V. Long, M.D., Ph.D., Keith Flaherty, M.D., Paul Nathan, M.D., Ph.D., Antoni Ribas, M.D., Ph.D., Anne-Marie Martin, Ph.D., Peng Sun, Ph.D., Wendy Crist, B.A., Jeff Legos, Ph.D., Stephen D. Rubin, M.D., Shonda M. Little, M.P.H., and Dirk Schadendorf, M.D.

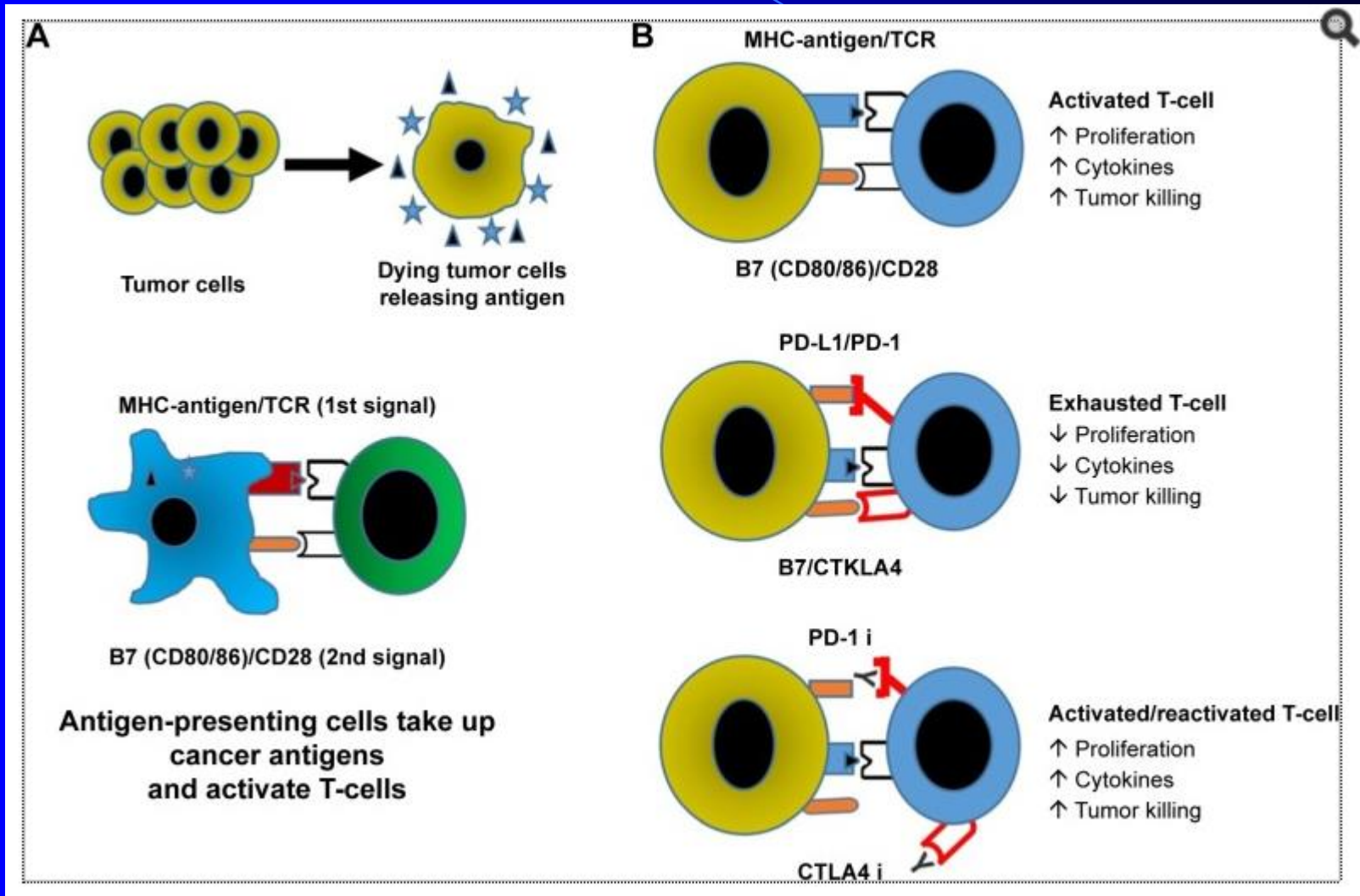
A Progression-free Survival



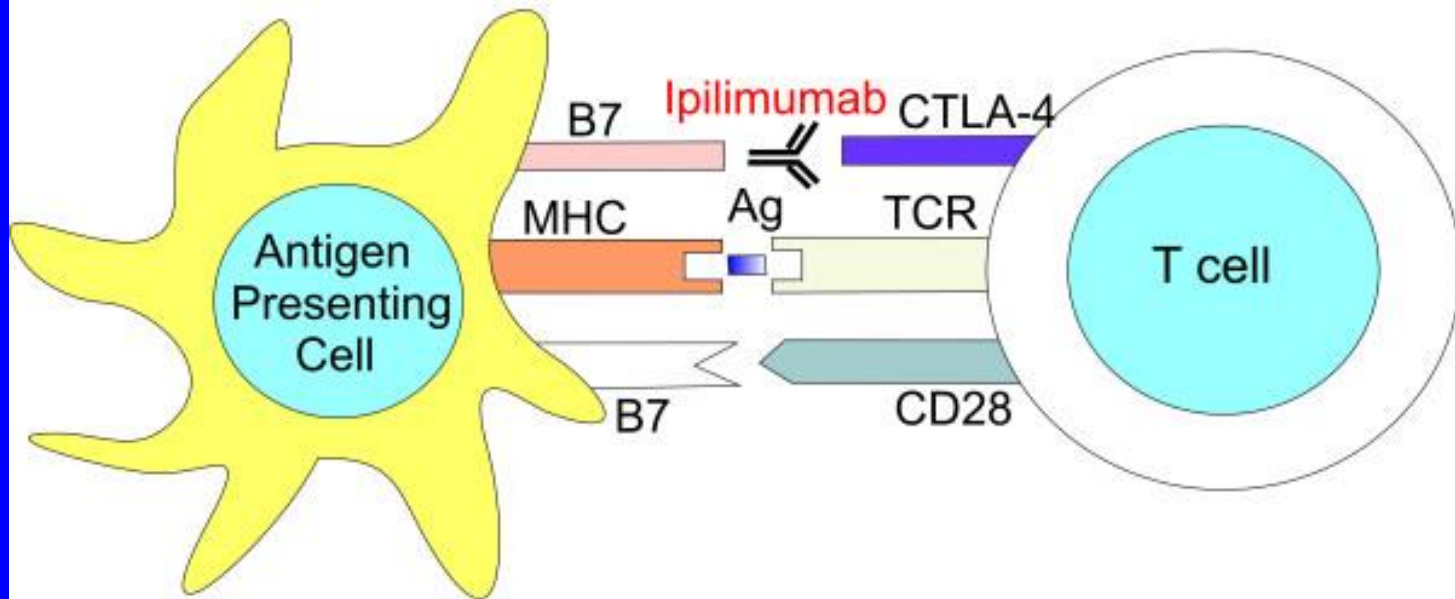
No. at Risk

Dabrafenib plus trametinib	352	310	270	228	194	142	83	39	10	7	0	0
Vemurafenib	352	279	214	161	121	83	45	11	0	0	0	0

Immunoterapia czerniaka



CTLA-4, inhibitory receptor
blocks T cell activation.
Ipilimumab blocks CTLA-4 and
augments T cell activation

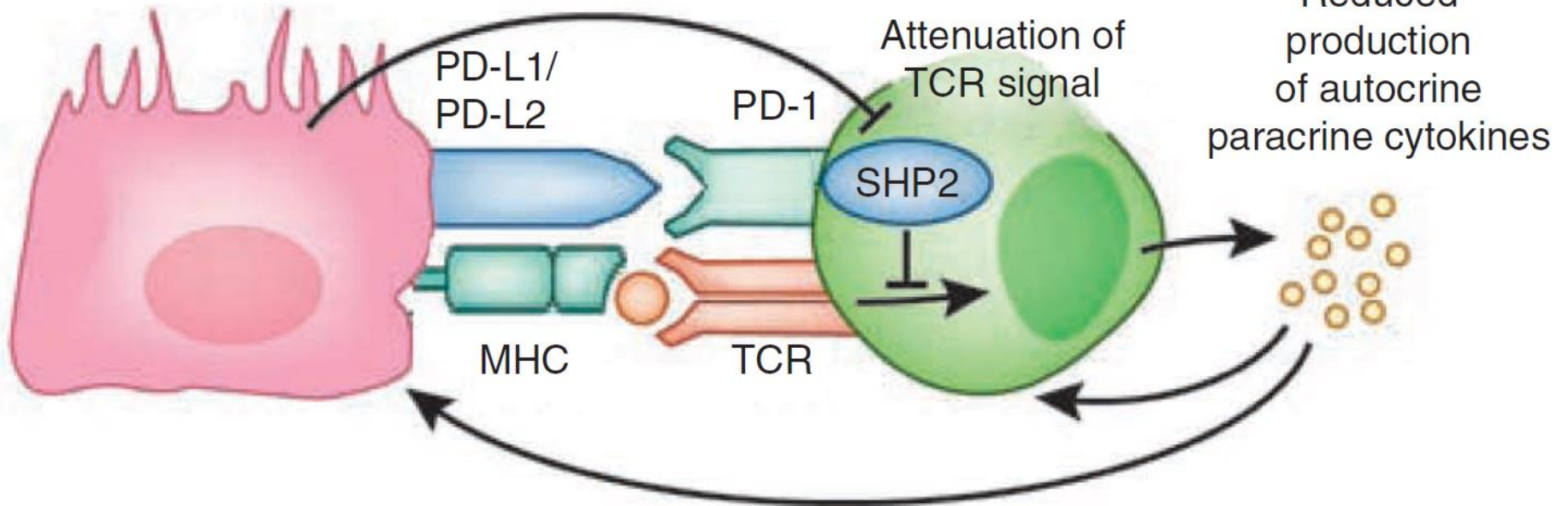


B7, co-stimulatory "ligand"
activates co-stimulatory
receptor Cd28 and stimulates
T cell

a

Infected cells/tumor

Effector T cell (CD8⁺)

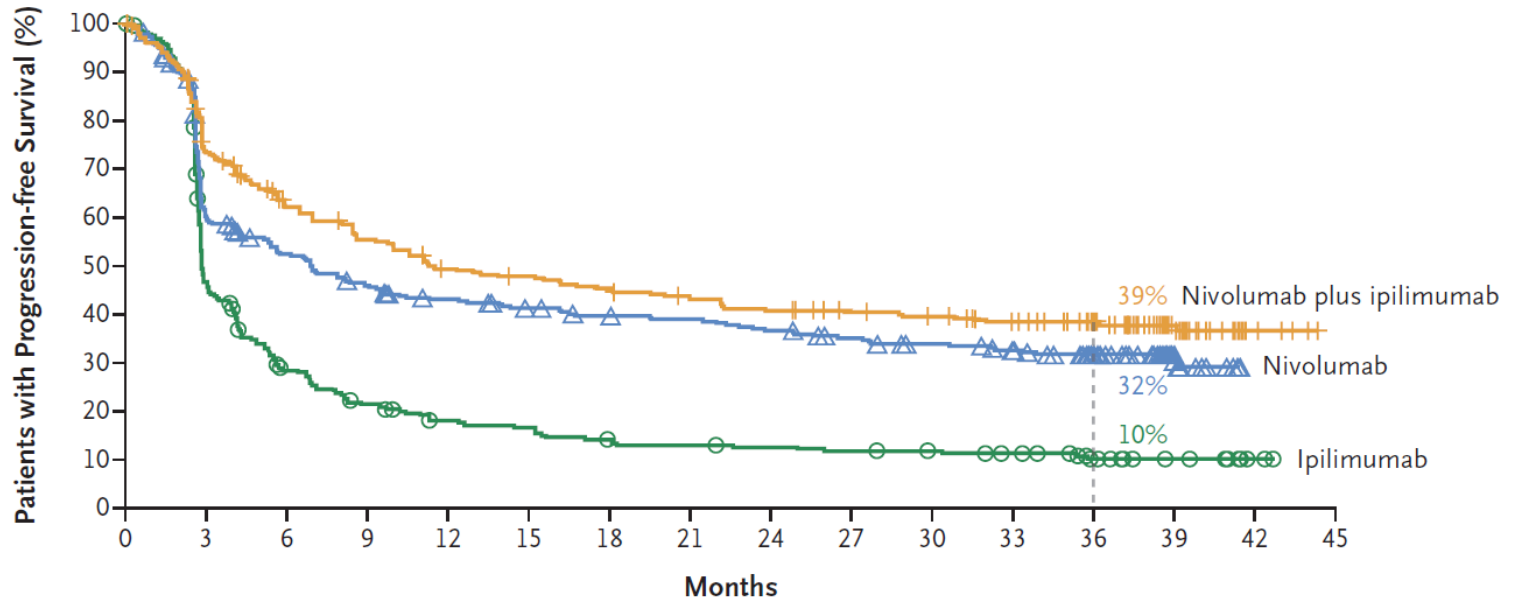


ORIGINAL ARTICLE

Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma

J.D. Wolchok, V. Chiarion-Sileni, R. Gonzalez, P. Rutkowski, J.-J. Grob, C.L. Cowey, C.D. Lao, J. Wagstaff, D. Schadendorf, P.F. Ferrucci, M. Smylie, R. Dummer, A. Hill, D. Hogg, J. Haanen, M.S. Carlino, O. Bechter, M. Maio, I. Marquez-Rodas, M. Guidoboni, G. McArthur, C. Lebbé, P.A. Ascierto, G.V. Long, J. Cebon, J. Sosman, M.A. Postow, M.K. Callahan, D. Walker, L. Rollin, R. Bhole, F.S. Hodi, and J. Larkin

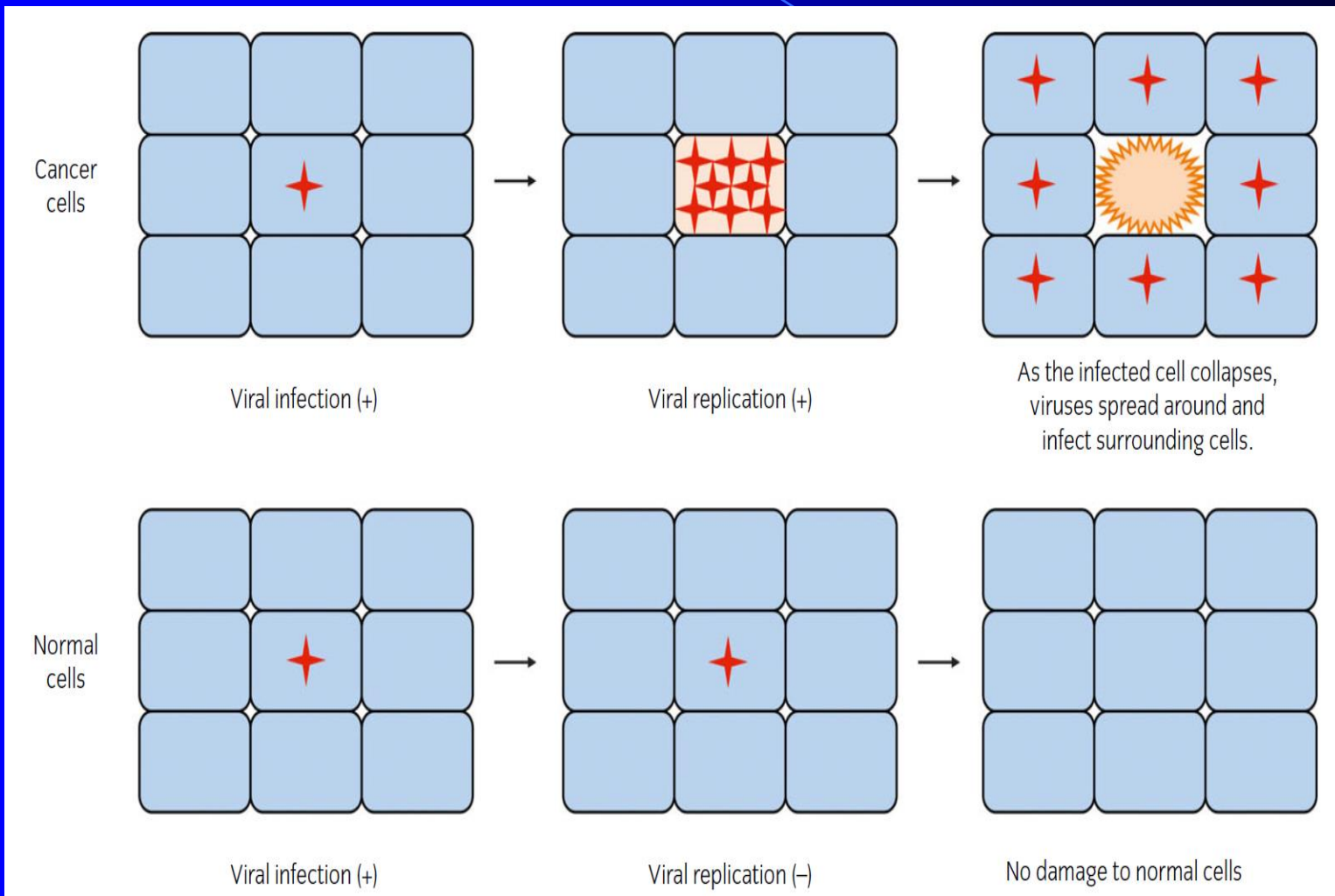
A Progression-free Survival



No. at Risk

Nivolumab plus ipilimumab	314	218	175	155	136	131	124	117	110	104	100	92	75	29	5	0
Nivolumab	316	177	151	131	119	111	105	102	96	87	81	75	61	24	0	0
Ipilimumab	315	136	78	58	46	42	34	32	30	28	26	23	15	8	2	0

Koncepcja leczenia z wykorzystaniem wirusów onkolitycznych



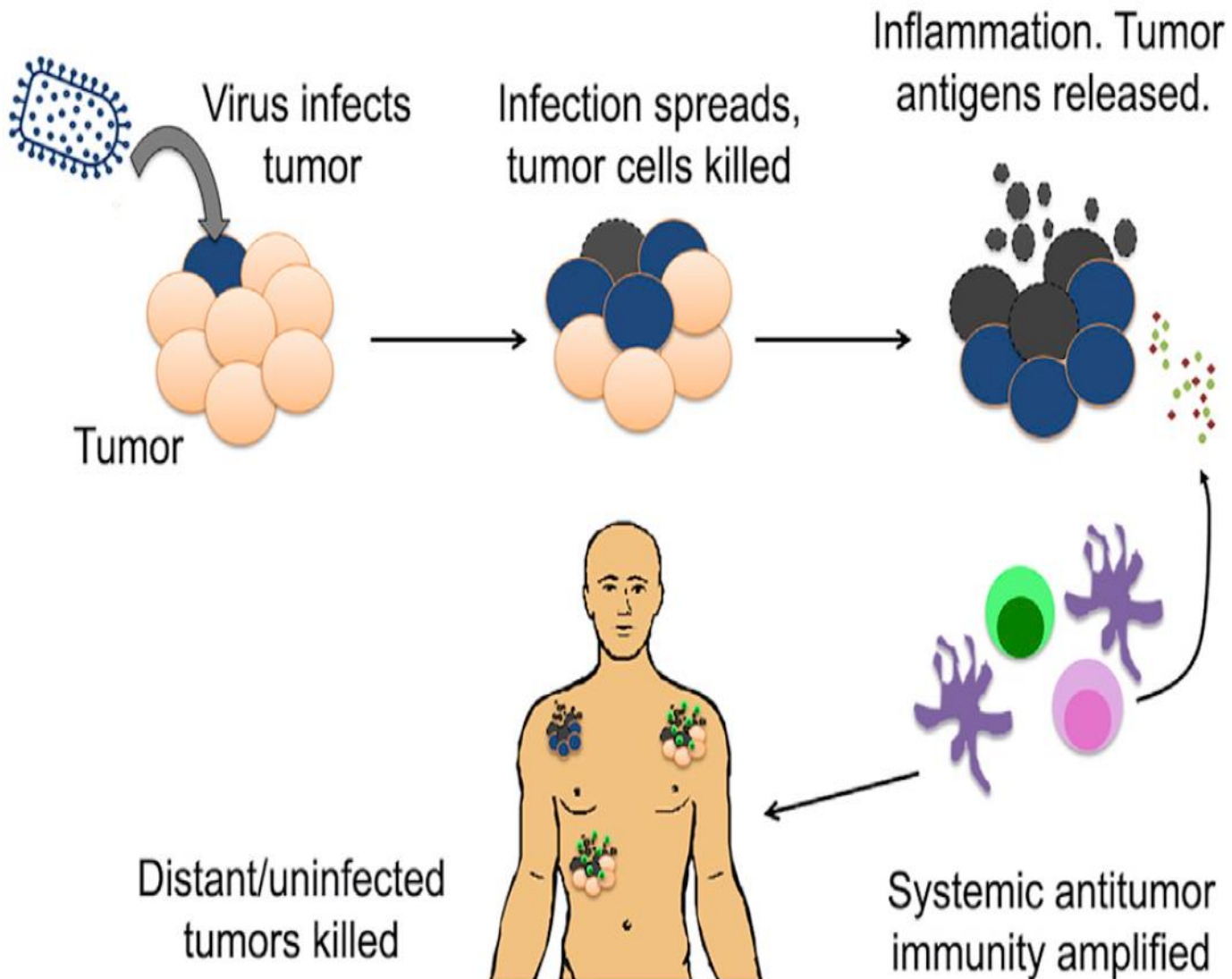


Figure 1. Oncolytic Virotherapy Is Not Just Immunotherapy

Talimogen laherparepvec

- W październiku 2015 FDA zaaprobowało T-VEC do leczenia nieoperacyjnych czerniaków
- Terapia wirusowa została następnie zaaprobowana w Europie i Australii (2016).

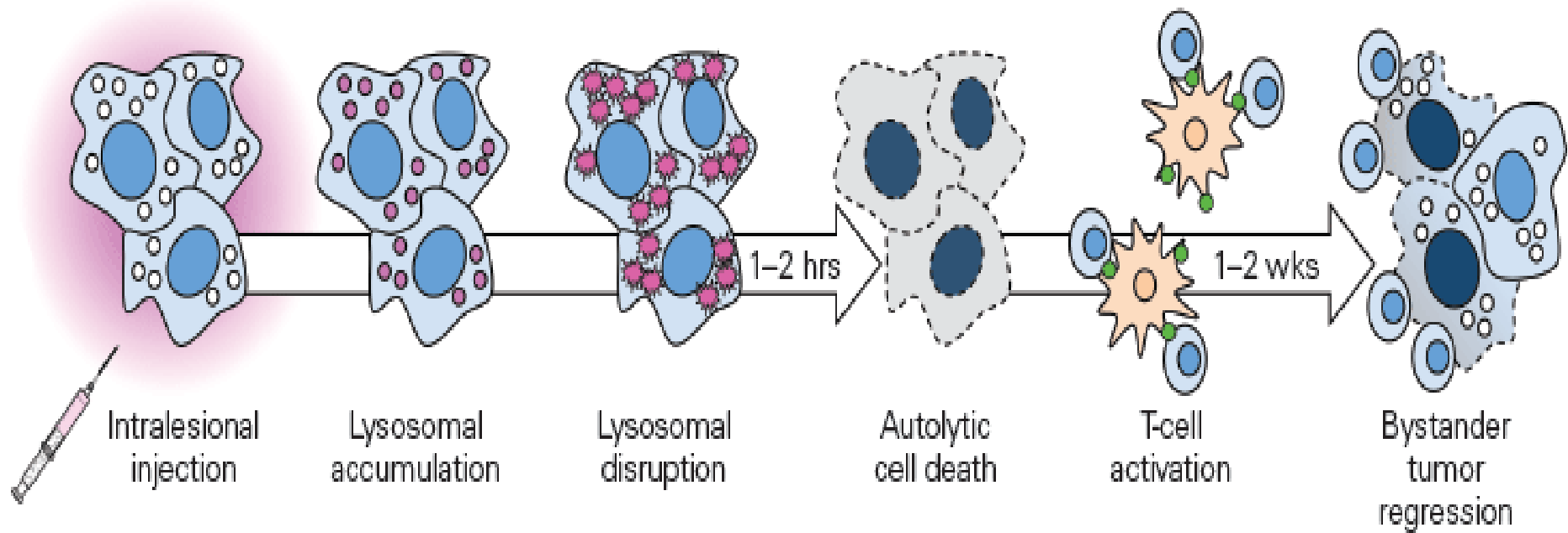
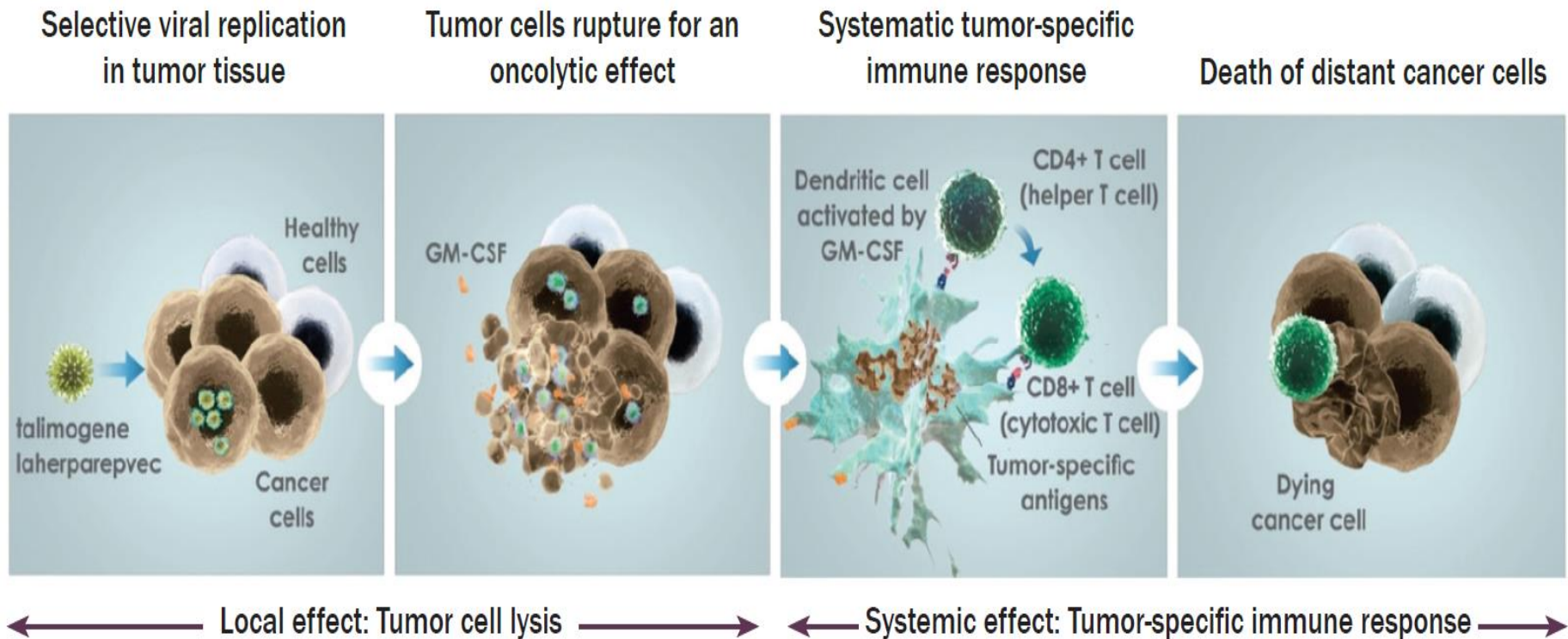


Figure. Mechanism of Action of Talimogene Laherparepvec (T-VEC)—This is a two-phase mechanism, consisting of primary ablation and a secondary tumor-specific immune response.

FIGURE 3. Talimogene Laherparepvec Proposed Mechanism of Action

GM-CSF—granulocyte macrophage–colony-stimulating factor

Note. Image courtesy of Amgen Inc. Used with permission

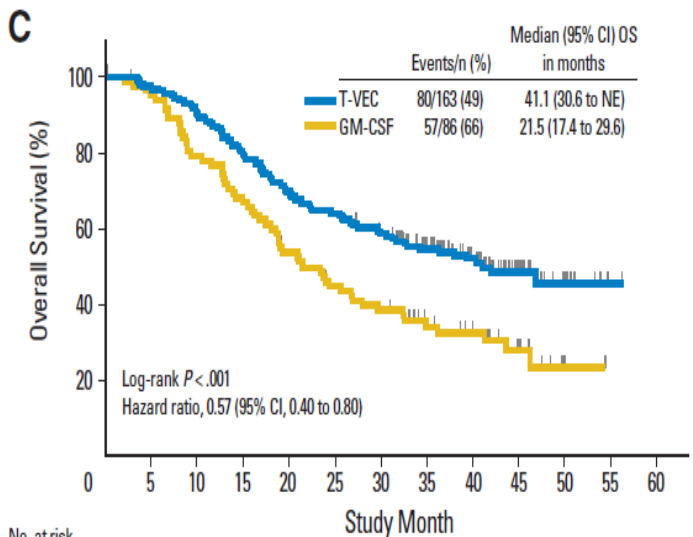




Baseline

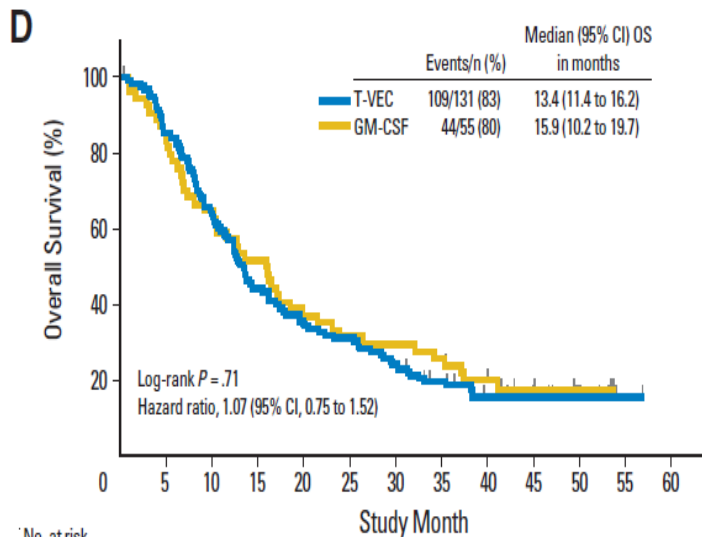


12 months



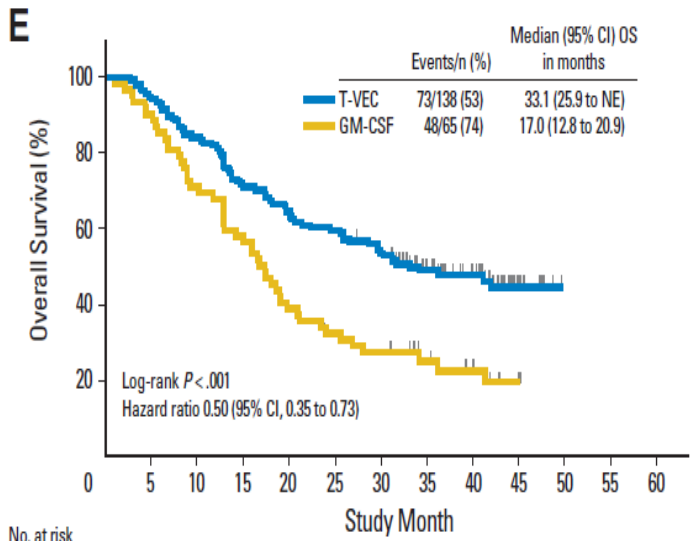
No. at risk

	0	5	10	15	20	25	30	35	40	45	50	55	60
GM-CSF	86	78	65	55	43	35	30	22	17	10	2		
T-VEC	163	157	146	129	113	104	93	73	51	23	10	1	



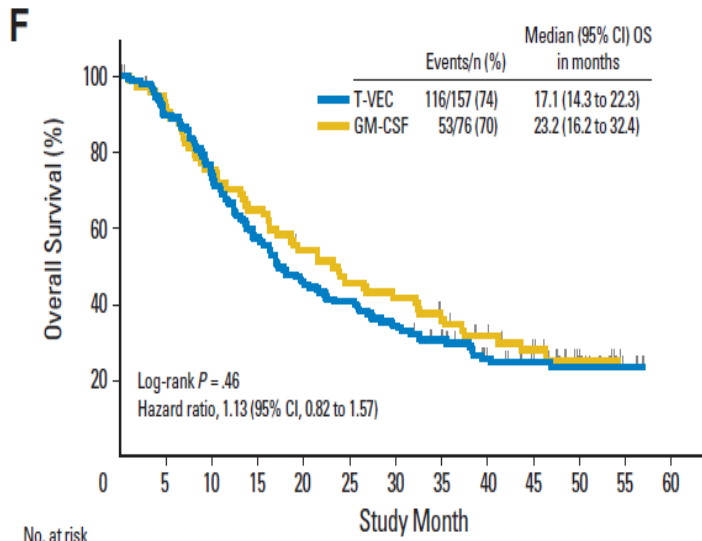
No. at risk

	0	5	10	15	20	25	30	35	40	45	50	55	60
GM-CSF	55	46	35	28	20	17	16	14	10	5	3		
T-VEC	131	112	84	58	46	41	32	22	15	13	6	1	



No. at risk

	0	5	10	15	20	25	30	35	40	45	50	55	60
GM-CSF	65	56	44	35	24	19	16	11	8	2			
T-VEC	138	130	116	98	89	82	72	50	37	12			



No. at risk

	0	5	10	15	20	25	30	35	40	45	50	55	60
GM-CSF	76	68	56	48	39	33	30	25	19	13	5		
T-VEC	157	139	114	89	70	63	53	45	29	24	16	2	

**IIIb, IIIc,
IVa vs.
IVb, IVc**

**First-line
vs.
second
line
therapy**

Thank you for your attention

