Moderne onkologisch/hämatologische Therapie und Palliativmedizin Ein Widerspruch ?

Palliativmedizin und Hospizarbeit

Bonn 26.10.2022

Y. Ko

JOHANNITER

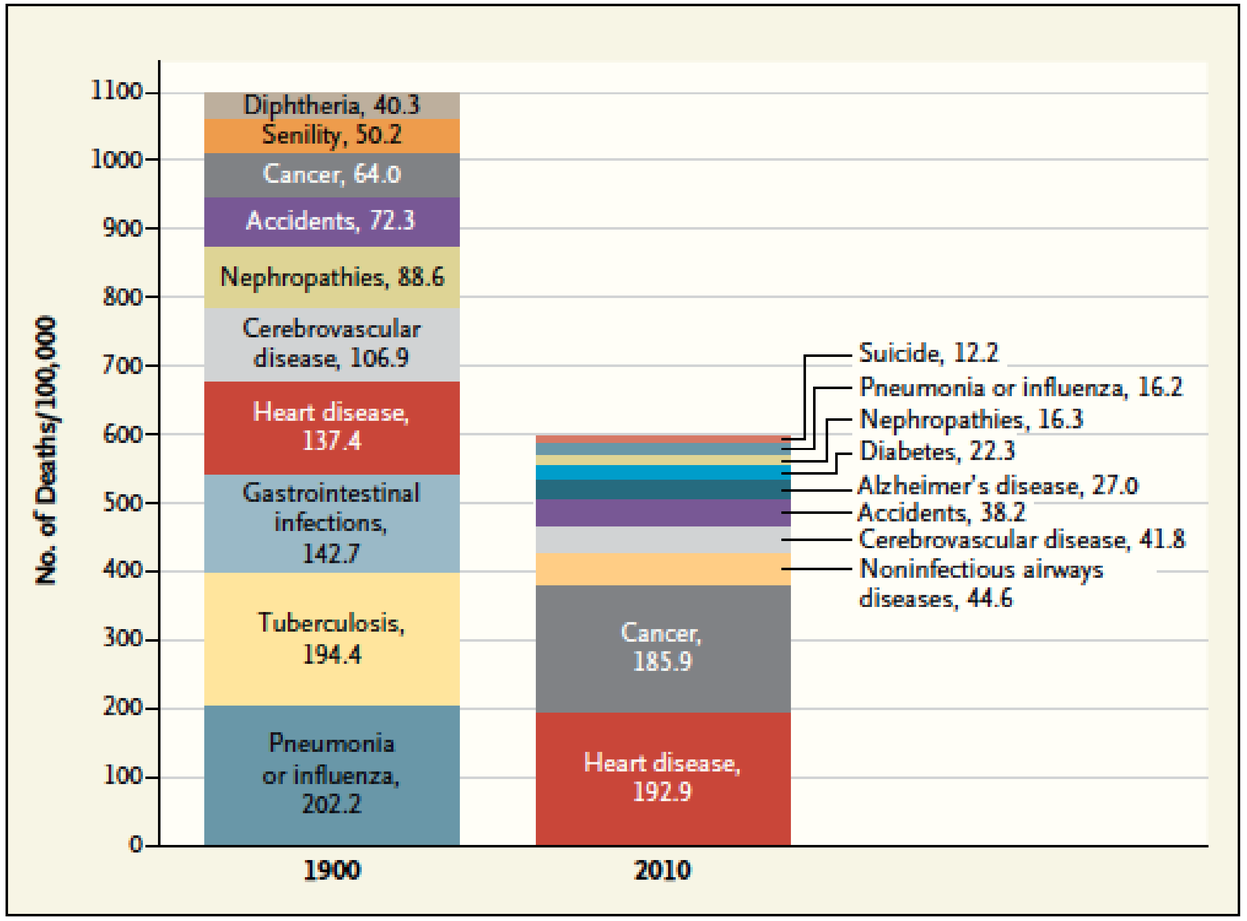
Aus Liebe zum Leben

Volksgesundheit - Todesursachen

The DEATHS preceding were caused by Diseases and Casualties as follows, viz.

Abscesses	1	Hernia, or Rupture	3
Aneurism	1	Jaundice	10
Apoplexy	13	Inflammation of the bowels	1
Burns or Scalds	6	——— of the stomach	1
Cancer	5	Killed by lightning	1
Casualties	15	Insanity	1
Childbed	14	Intemperance	2
Cholera Morbus	6	Locked jaw	2
Colic	2	Mortification	11
Consumption	221	Old Age	26
Convulsions	36	Palsy	12
Cramp in the stomach	2	Pleurisy	8
Croup	1	Quinsy	15
Debility	28	Rheumatism	1
Decay	20	Rupture of blood vessels	1
Diarrhœa	15	Small-Pox,(at Rainsford's Island)	2
Drinking cold water	2	Sore throat	1
Dropsy	21	Spasms	2
——— in the head	23	Stillborn	49
Drowned	13	Suicide	1
Dysentery	14	Sudden death	25
Dispepsia or Indigestion	15	Syphilis	12
Fever, bilious	7	Teething	15
——— pulmonic	46	Worms	11
——— inflammatory	24	Whooping Cough	14
——— putrid	6	White swelling	2
——— typhus	33	Diseases not mentioned	48
Flux infantile	57		
Gout	3	Total,	942
Hoemorrhage	4		

Causes of Death in 1811. Abstract of the Bill of Mortality for the Town of Boston.

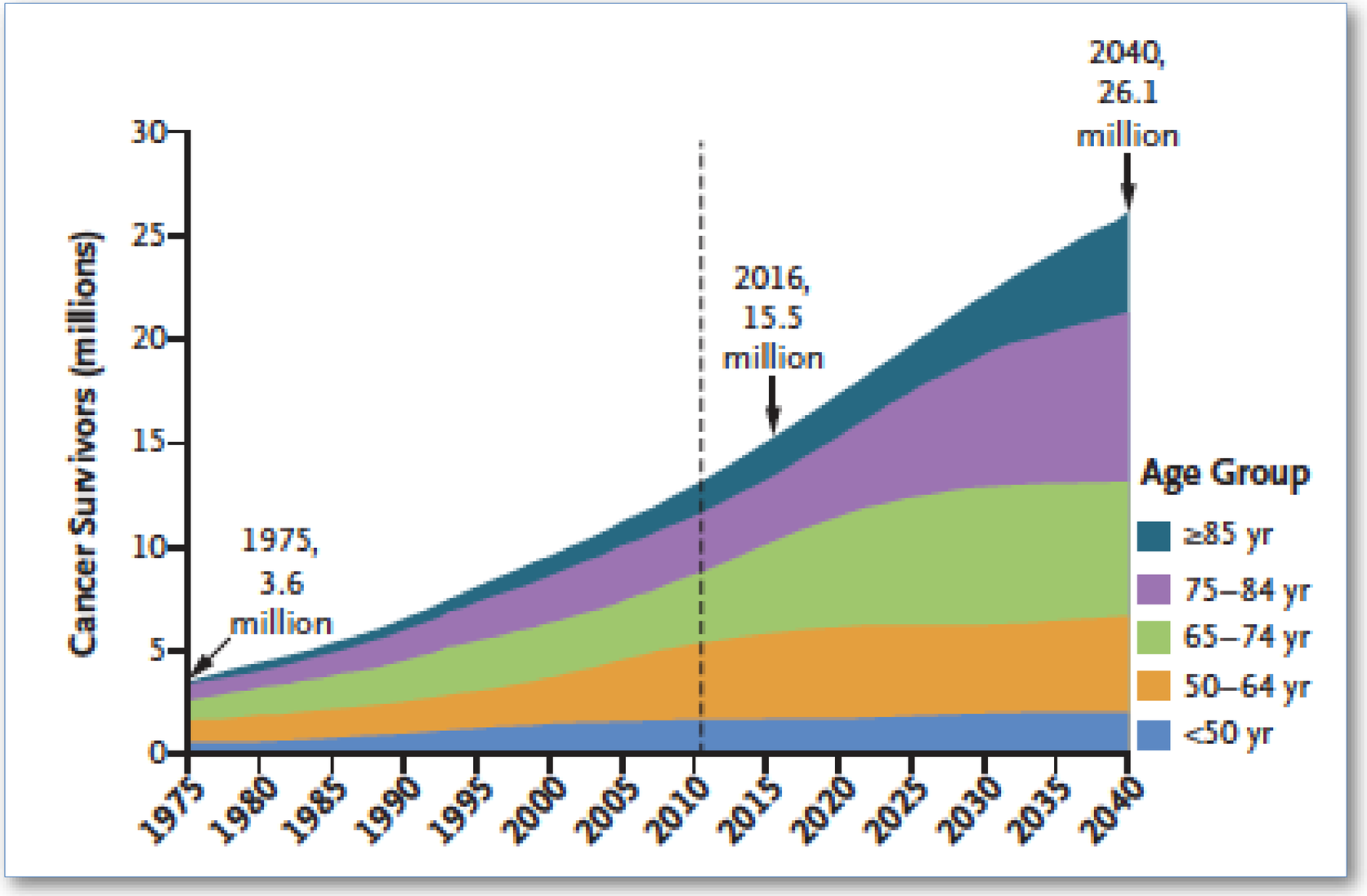


Top 10 Causes of Death: 1900 vs. 2010.

Data are from the Centers for Disease Control and Prevention.

Jones et al. NEJM 2012;25:2333-8

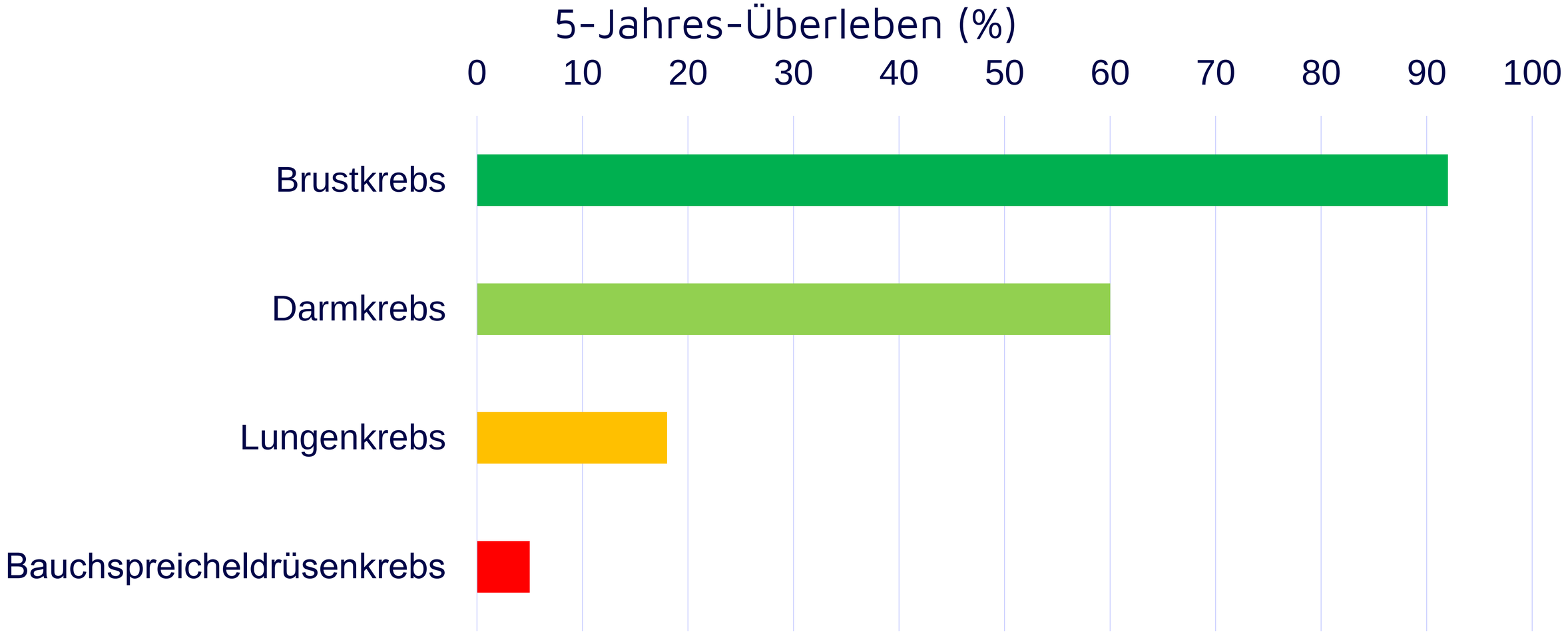
Cancer Survivors – Überlebende nach Krebs in den USA



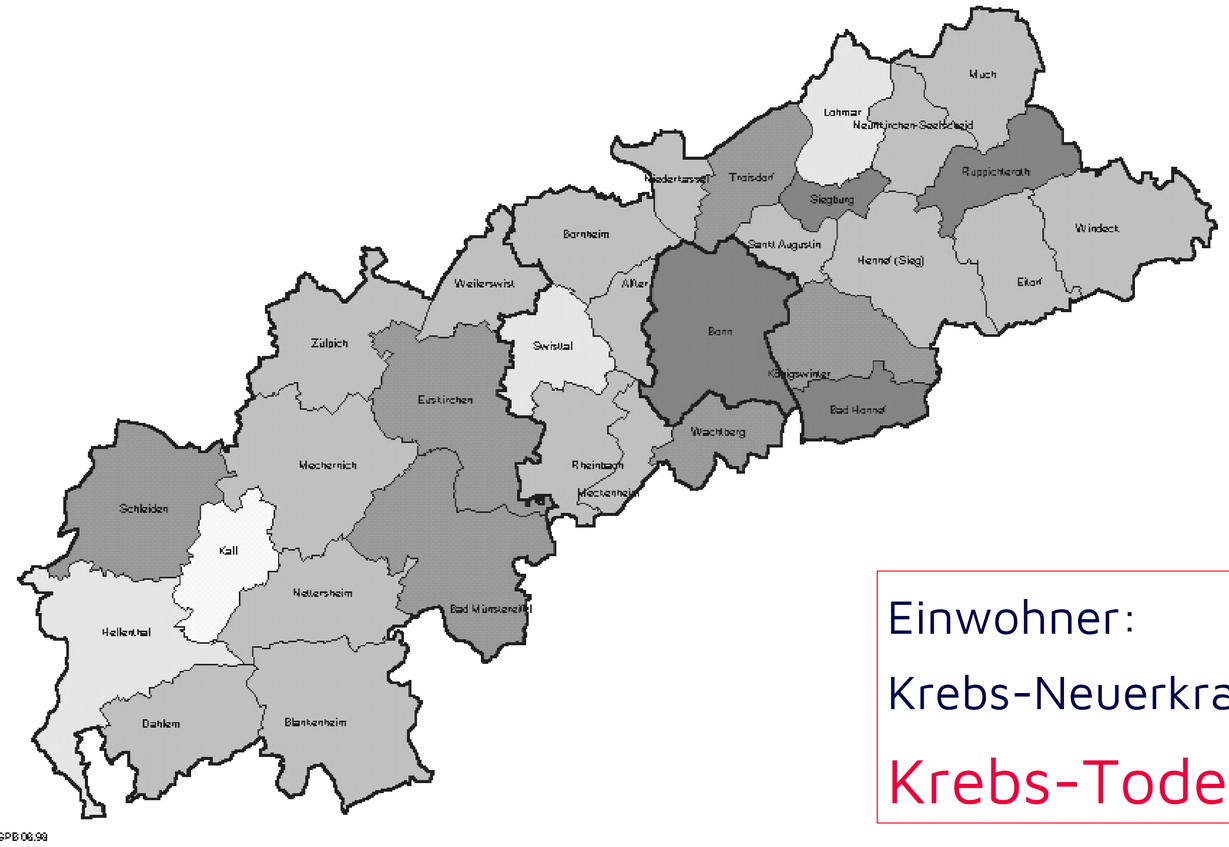
Shapiro NEJM 2018;379:2438-50

Überleben mit Krebs

Mehr Heilung



Versorgungsgebiet Bonn und Umland



aber

Einwohner:	1.122.224
Krebs-Neuerkrankungen:	~ 7000 pro Jahr
Krebs-Todesfälle:	~ 3000 pro Jahr

"Go around and see what is being done and then see how your own circumstances can produce another version; there is need for diversity in this field."

Dame Cicely Saunders, Founder
St. Christopher's Hospice

1918-2005

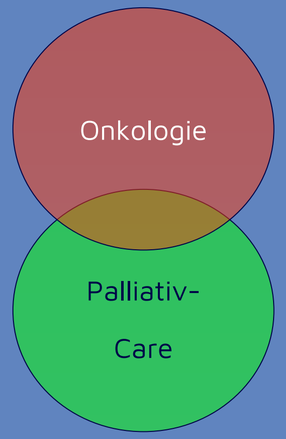
1967: St. Christopher`s-Hospiz

Symptomkontrolle

1983: 1. Deutsche Palliativstation in Köln

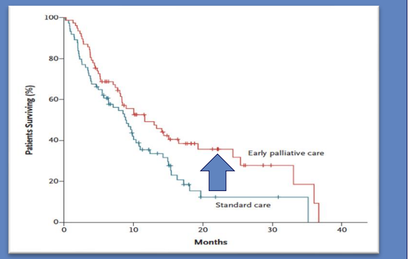
2005

Integration



2015

Lebens-
erwartung



Soll (noch) behandelt werden ?

Chemotherapie am Ende des Lebens

Chemotherapie-refraktäre Situation

Research

Original Investigation

Chemotherapy Use, Performance Status, and Quality of Life at the End of Life

Holly G. Prigerson, PhD; Yuhua Bao, PhD; Manish A. Shah, MD; M. Elizabeth Paulk, MD; Thomas W. LeBlanc, MD, MA; Bryan J. Schneider, MD; Melissa M. Garrido, PhD; M. Carrington Reid, MD, PhD; David A. Berlin, MD; Kerin B. Adelson, MD; Alfred I. Neugut, MD, PhD; Paul K. Maciejewski, PhD

Patienten:

- Fernmetastasen ("End-Stage-Cancer")
- Refraktäre Erkrankung (≥1 refraktäre CTX)
- Lebenserwartung < 6 Monate

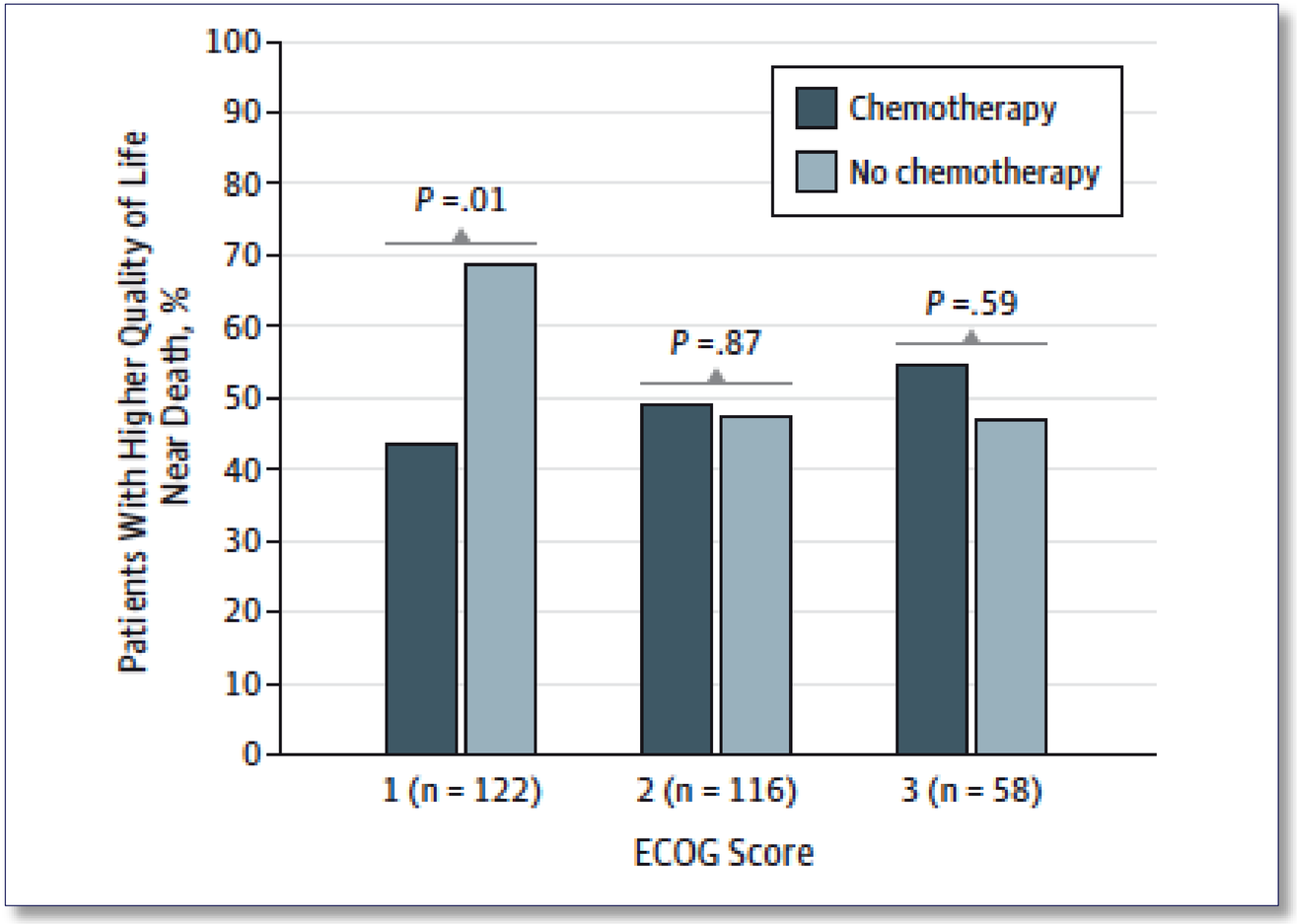
↓

ECOG 1: ambulant
ECOG 2: <50% bettlägerig
ECOG 3: >50% bettlägerig

Chemotherapie

↓

Lebensqualität in der letzten Lebens-Woche

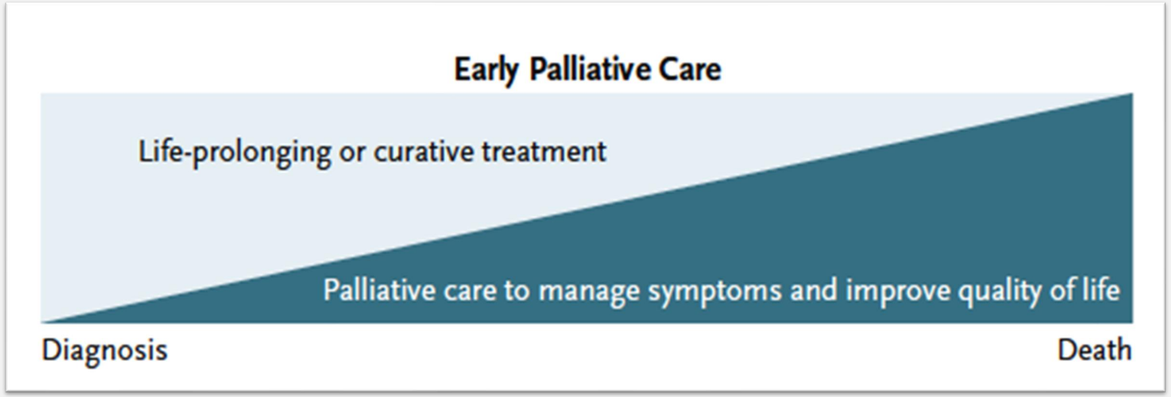


Prigerson et al. JAMA Oncol 2015;1:778-84

Palliativmedizin am Anfang der Erkrankung

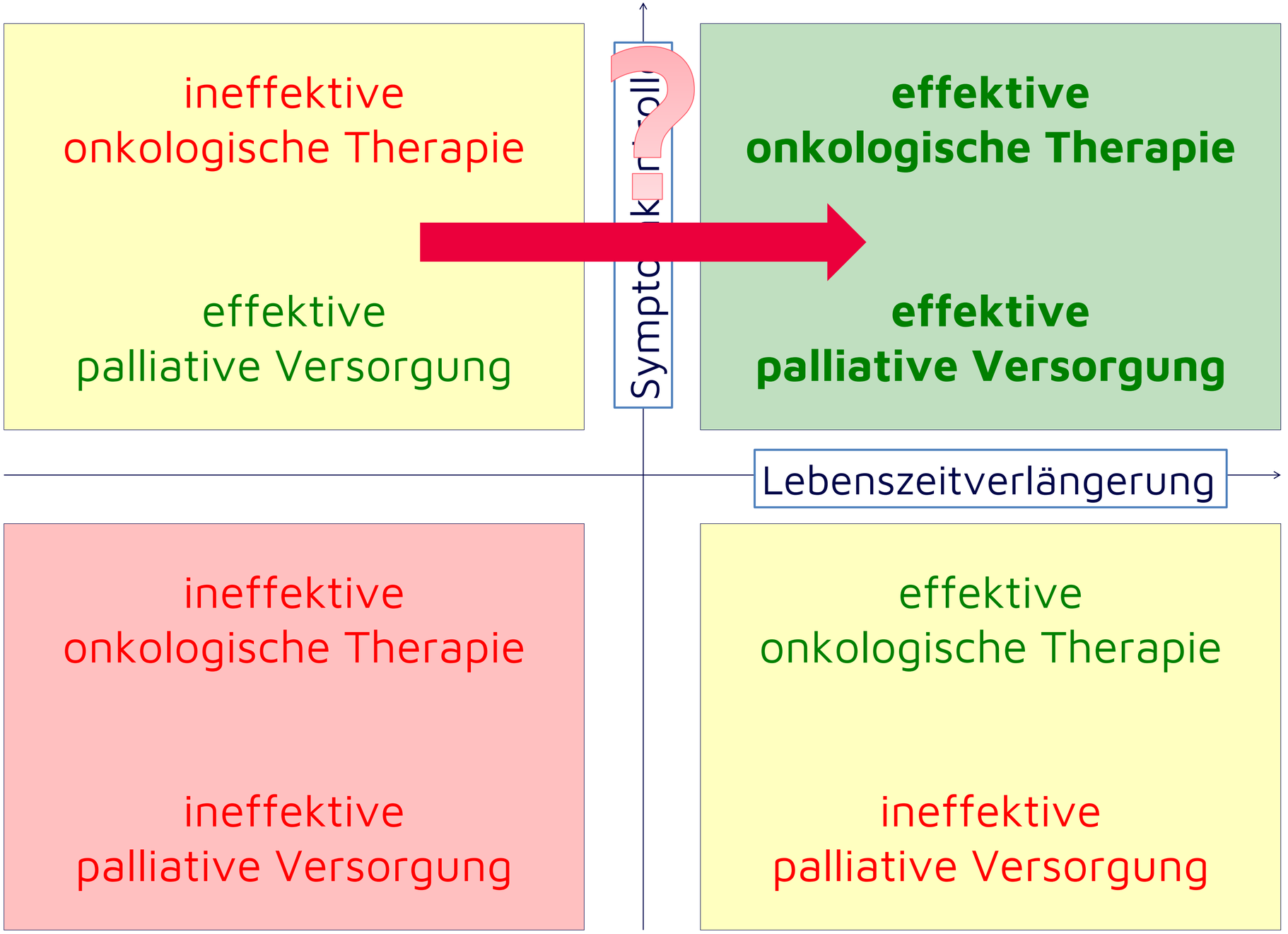
Situation mit hoher Symptomlast

Parikh et al. NEJM 2010;369:2347-51



Antizipation statt Reaktion

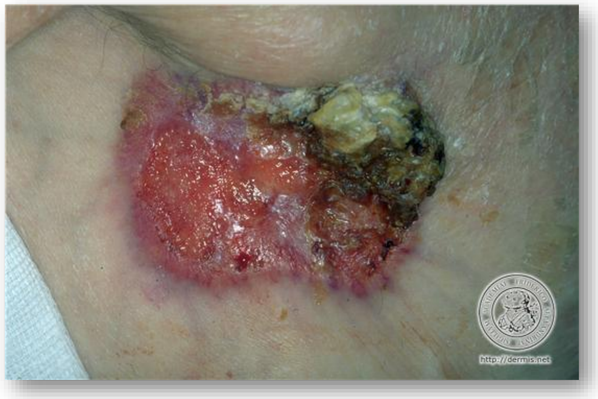
Gomez et al. JCO 2015;22:1438-46


ineffektive
onkologische Therapie
effektive
palliative Versorgung
Symptomkontrolle
?
effektive
onkologische Therapie
effektive
palliative Versorgung
Lebenszeitverlängerung
ineffektive
onkologische Therapie
ineffektive
palliative Versorgung
effektive
onkologische Therapie
ineffektive
palliative Versorgung

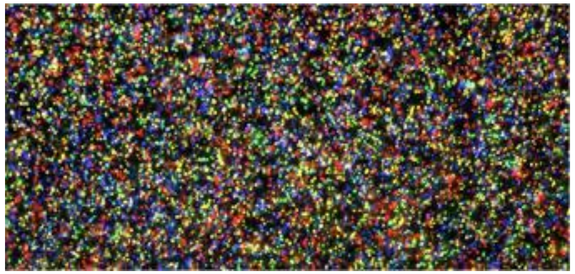
Onkologie im Wandel der Zeit

„… und an der Brust sahen wir häufig Tumoren, die der Gestalt eines Krebses sehr ähnlich waren. So wie die Beine des Tieres an beiden Seiten des Körpers liegen, so verlassen die Venen den Tumor, der seiner Form nach dem Krebskörper gleicht."

Galenos von Pergamon 2. Jh. n. Chr.



Next-Generation-Sequencing



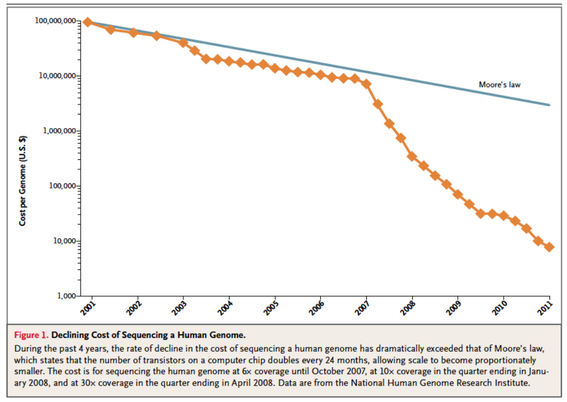
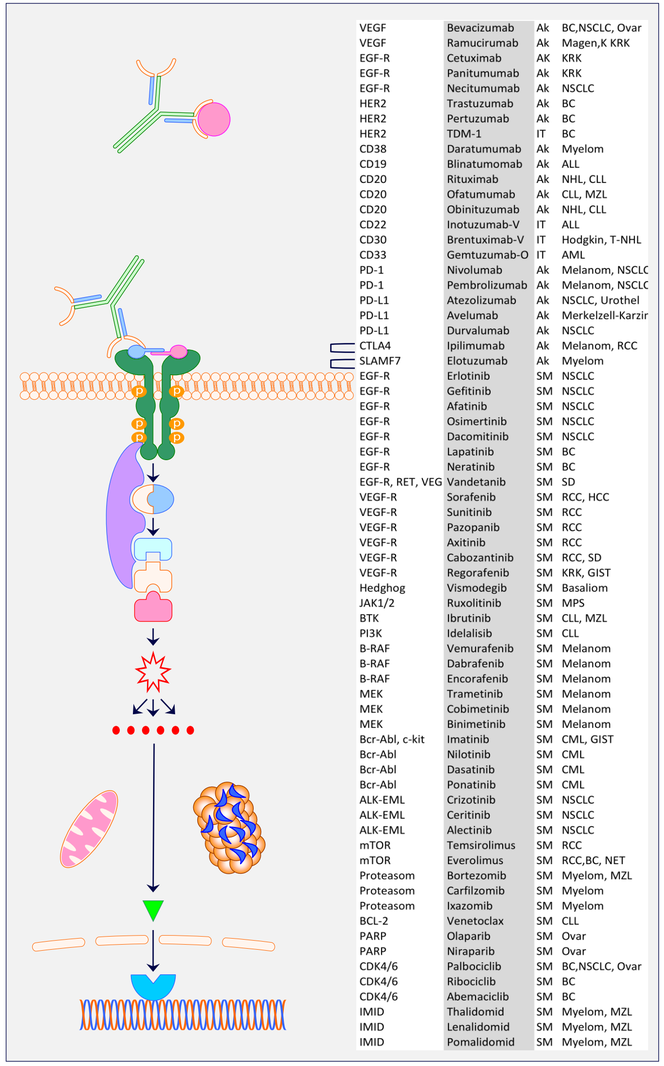
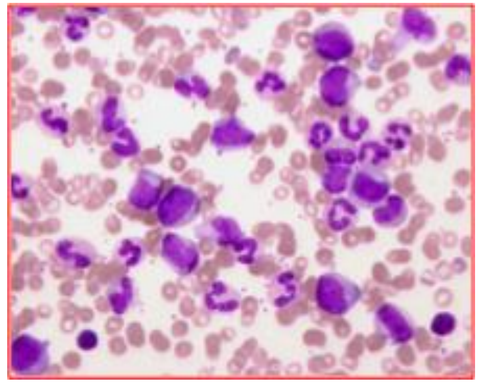


Figure 1. Declining Cost of Sequencing a Human Genome.
During the past 4 years, the rate of decline in the cost of sequencing a human genome has dramatically exceeded that of Moore's law, which states that the number of transistors on a computer chip doubles every 24 months, allowing scale to become proportionately smaller. The cost is for sequencing the human genome at 6× coverage until October 2007, at 10× coverage in the quarter ending in January 2008, and at 30× coverage in the quarter ending in April 2008. Data are from the National Human Genome Research Institute.

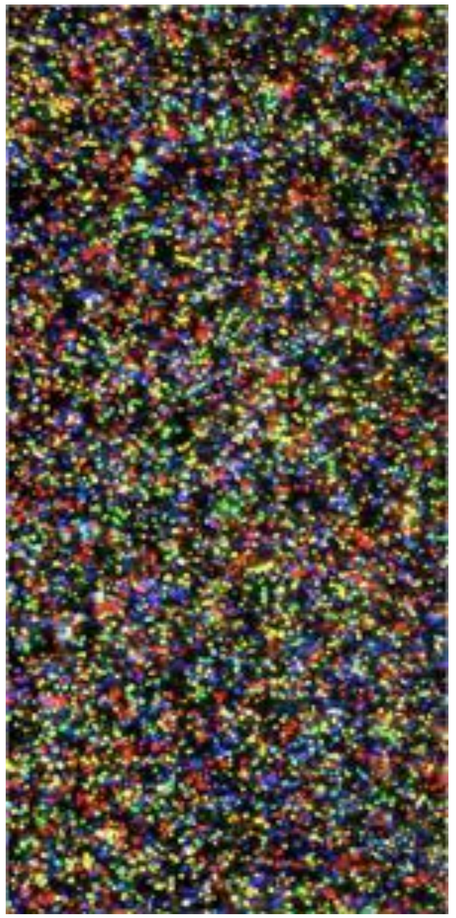


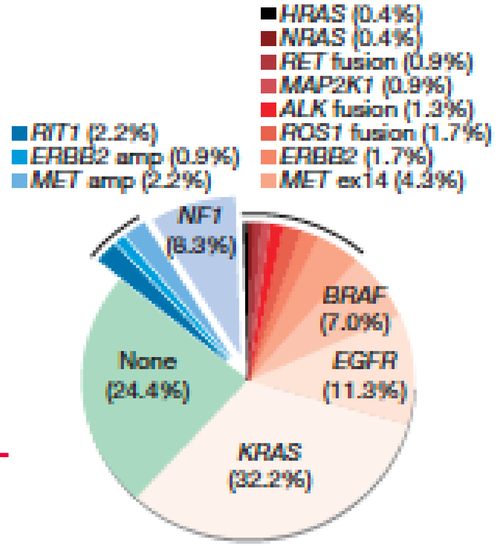
VEGF	Bevacizumab	Ak	BC,NSCLC, Ovar
VEGF	Ramucirumab	Ak	Magen,K KRK
EGF-R	Cetuximab	AK	KRK
EGF-R	Panitumumab	Ak	KRK
EGF-R	Necitumumab	Ak	NSCLC
HER2	Trastuzumab	Ak	BC
HER2	Pertuzumab	Ak	BC
HER2	TDM-1	IT	BC
CD38	Daratumumab	Ak	Myelom
CD19	Blinatumomab	Ak	ALL
CD20	Rituximab	Ak	NHL, CLL
CD20	Ofatumumab	Ak	CLL, MZL
CD20	Obinituzumab	Ak	NHL, CLL
CD22	Inotuzumab-V	IT	ALL
CD30	Brentuximab-V	IT	Hodgkin, T-NHL
CD33	Gemtuzumab-O	IT	AML
PD-1	Nivolumab	Ak	Melanom, NSCLC
PD-1	Pembrolizumab	Ak	Melanom, NSCLC
PD-L1	Atezolizumab	Ak	NSCLC, Urothel
PD-L1	Avelumab	Ak	Merkelzell-Karzir
PD-L1	Durvalumab	Ak	NSCLC
CTLA4	Ipilimumab	Ak	Melanom, RCC
SLAMF7	Elotuzumab	Ak	Myelom
EGF-R	Erlotinib	SM	NSCLC
EGF-R	Gefitinib	SM	NSCLC
EGF-R	Afatinib	SM	NSCLC
EGF-R	Osimertinib	SM	NSCLC
EGF-R	Dacomitinib	SM	NSCLC
EGF-R	Lapatinib	SM	BC
EGF-R	Neratinib	SM	BC
EGF-R, RET, VEG	Vandetanib	SM	SD
VEGF-R	Sorafenib	SM	RCC, HCC
VEGF-R	Sunitinib	SM	RCC
VEGF-R	Pazopanib	SM	RCC
VEGF-R	Axitinib	SM	RCC
VEGF-R	Cabozantinib	SM	RCC, SD
VEGF-R	Regorafenib	SM	KRK, GIST
Hedghog	Vismodegib	SM	Basaliom
JAK1/2	Ruxolitinib	SM	MPS
BTK	Ibrutinib	SM	CLL, MZL
PI3K	Idelalisib	SM	CLL
B-RAF	Vemurafenib	SM	Melanom
B-RAF	Dabrafenib	SM	Melanom
B-RAF	Encorafenib	SM	Melanom
MEK	Trametinib	SM	Melanom
MEK	Cobimetinib	SM	Melanom
MEK	Binimetinib	SM	Melanom
Bcr-Abl, c-kit	Imatinib	SM	CML, GIST
Bcr-Abl	Nilotinib	SM	CML
Bcr-Abl	Dasatinib	SM	CML
Bcr-Abl	Ponatinib	SM	CML
ALK-EML	Crizotinib	SM	NSCLC
ALK-EML	Ceritinib	SM	NSCLC
ALK-EML	Alectinib	SM	NSCLC
mTOR	Temsirolimus	SM	RCC
mTOR	Everolimus	SM	RCC,BC, NET
Proteasom	Bortezomib	SM	Myelom, MZL
Proteasom	Carfilzomib	SM	Myelom
Proteasom	Ixazomib	SM	Myelom
BCL-2	Venetoclax	SM	CLL
PARP	Olaparib	SM	Ovar
PARP	Niraparib	SM	Ovar
CDK4/6	Palbociclib	SM	BC,NSCLC, Ovar
CDK4/6	Ribociclib	SM	BC
CDK4/6	Abemaciclib	SM	BC
IMID	Thalidomid	SM	Myelom, MZL
IMID	Lenalidomid	SM	Myelom, MZL
IMID	Pomalidomid	SM	Myelom, MZL

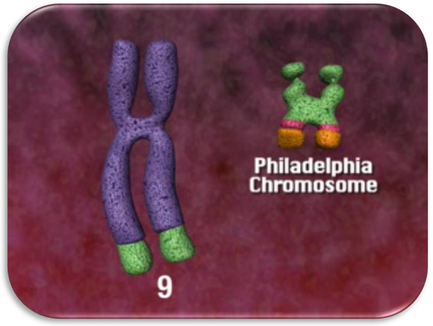
Vom Tumor zur Target-Mutation



NGS Illumina







24 Stunden

Monoklonale Antikörper

EGF-R | CD20 | CD19 | HER2 | IL6 | EGF-R | CD38 | VEGF

CD79a | TROP2 | Nectin-4

CD30 | HER2 | BMCA

Antikörper-Drug Konjugate (ADC)

Chemotherapie

CTLA4 | PD1 | PD-L1 | LAG-3

CART | BITE

Immuntherapie

HER2 | ALK | bcr-abl | EGF-R | PDGF-R | ROS1 | Apoptose | MET | JAK

VEGF-R | RAS | Hedghog | MEK | PI3CA | BTK | RAS | mTOR | Proteasom

Small Molecules

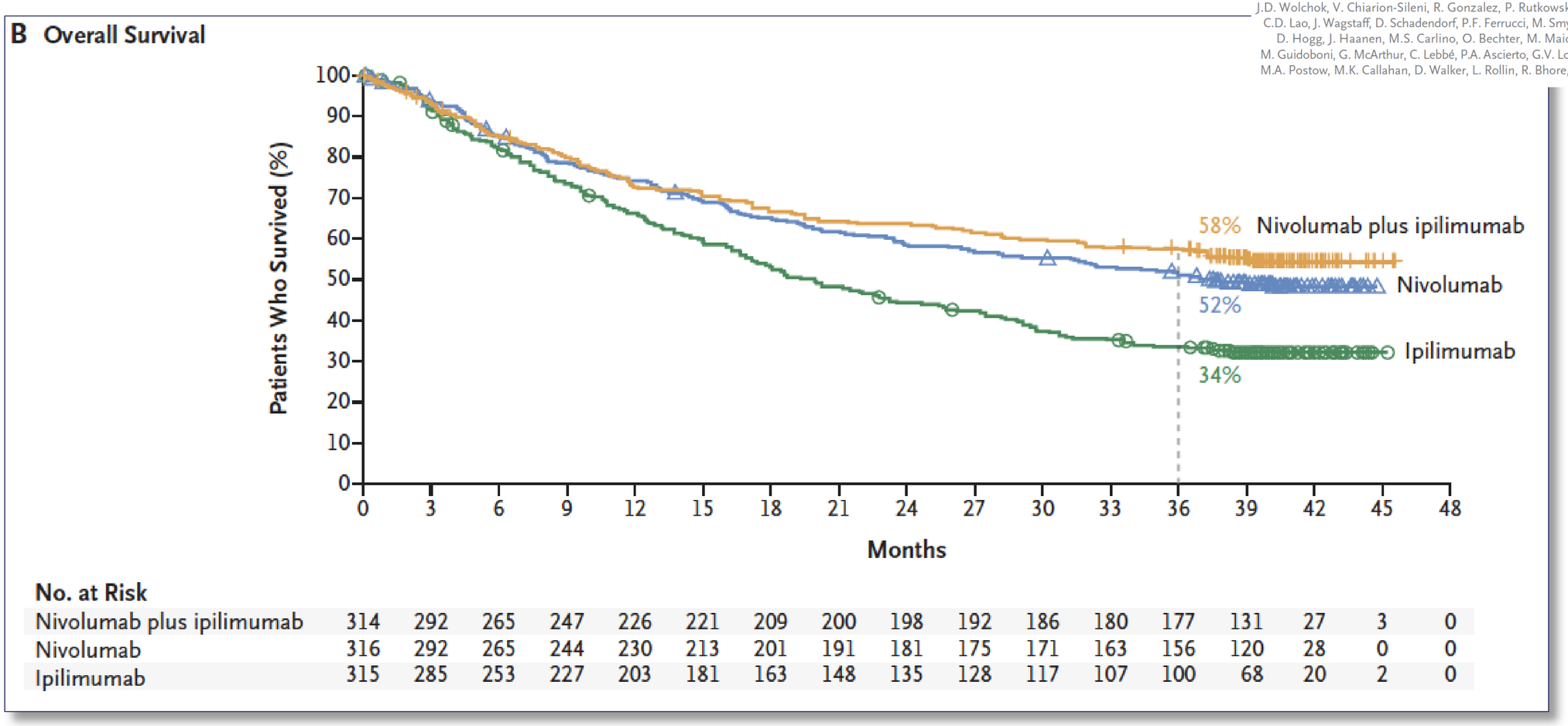
Malignes Melanom
Immuntherapie

The NEW ENGLAND JOURNAL of MEDICINE

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. Bhore, F.S. Hodi, and J. Larkin



No. at Risk

Nivolumab plus ipilimumab	314	292	265	247	226	221	209	200	198	192	186	180	177	131	27	3	0
Nivolumab	316	292	265	244	230	213	201	191	181	175	171	163	156	120	28	0	0
Ipilimumab	315	285	253	227	203	181	163	148	135	128	117	107	100	68	20	2	0

Wochok et al. NEJM 2017;377:1345-56

Brustkrebs – HR positiv

CDK4/6 Inhibitoren in der palliativen Situation

Ribociclib 600mg d1-21 q28 + Letrozol 2,5mg

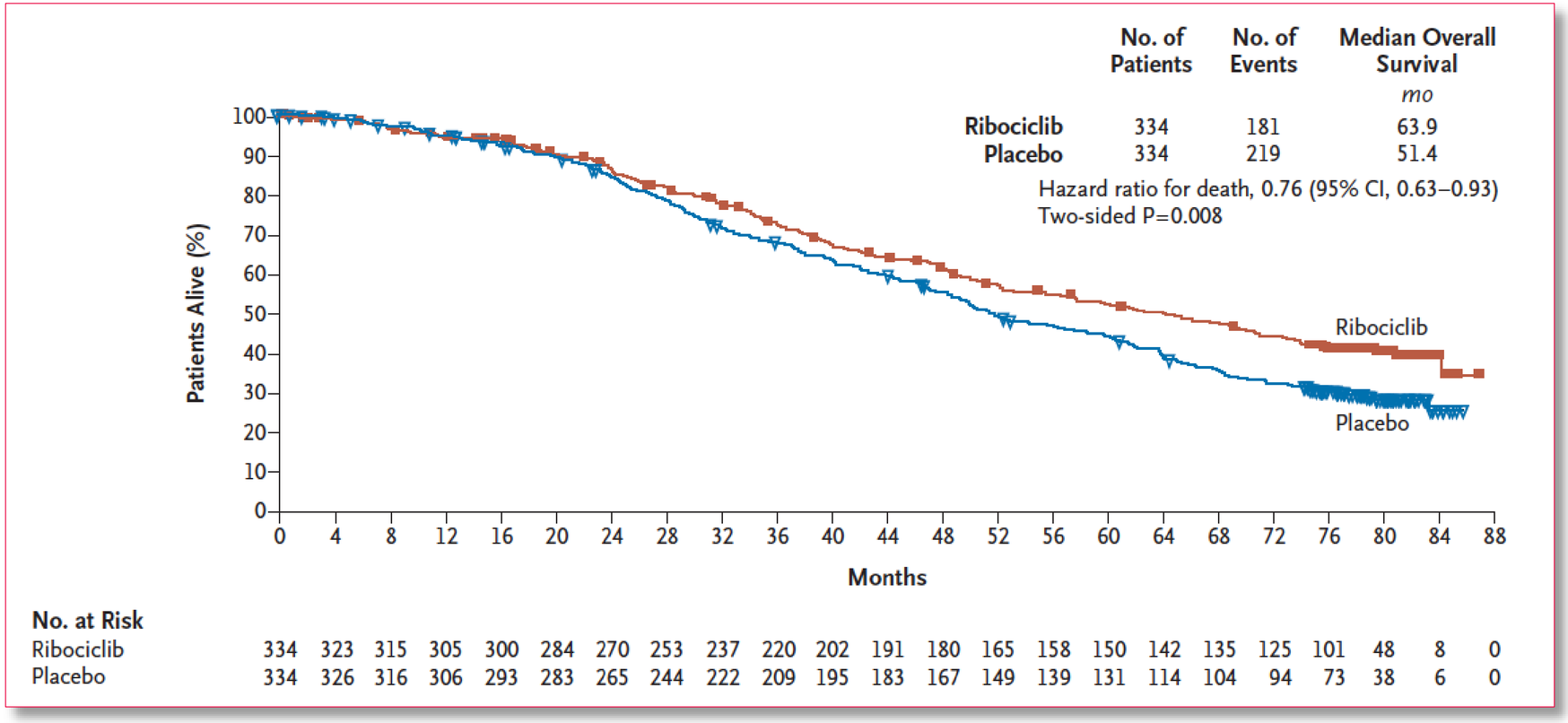
verbessert das Gesamtüberleben

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

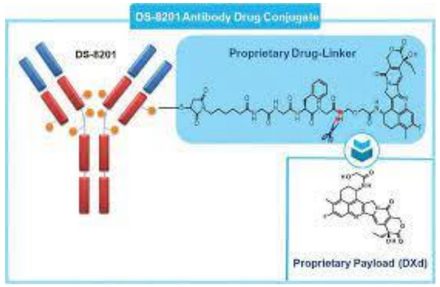
Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer

Gabriel N. Hortobagyi, M.D., Salomon M. Stemmer, M.D., Howard A. Burris, M.D., Yoon-Sim Yap, M.D., Gabe S. Sonke, M.D., Ph.D., Lowell Hart, M.D., Mario Campone, M.D., Ph.D., Katarina Petrakova, M.D., Ph.D., Eric P. Winer, M.D., Wolfgang Janni, M.D., Ph.D., Pierfranco Conte, M.D., Ph.D., David A. Cameron, M.D., Fabrice André, M.D., Ph.D., Carlos L. Arteaga, M.D., Juan P. Zarate, M.D., Arunava Chakravartty, Ph.D., Tetiana Taran, M.D., Fabienne Le Gac, Ph.D., Pharm.D., Paolo Serra, M.Sc., and Joyce O'Shaughnessy, M.D.



Brustkrebs - HER-positiv

Trastuzumab-Deruxtecan (TDx)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

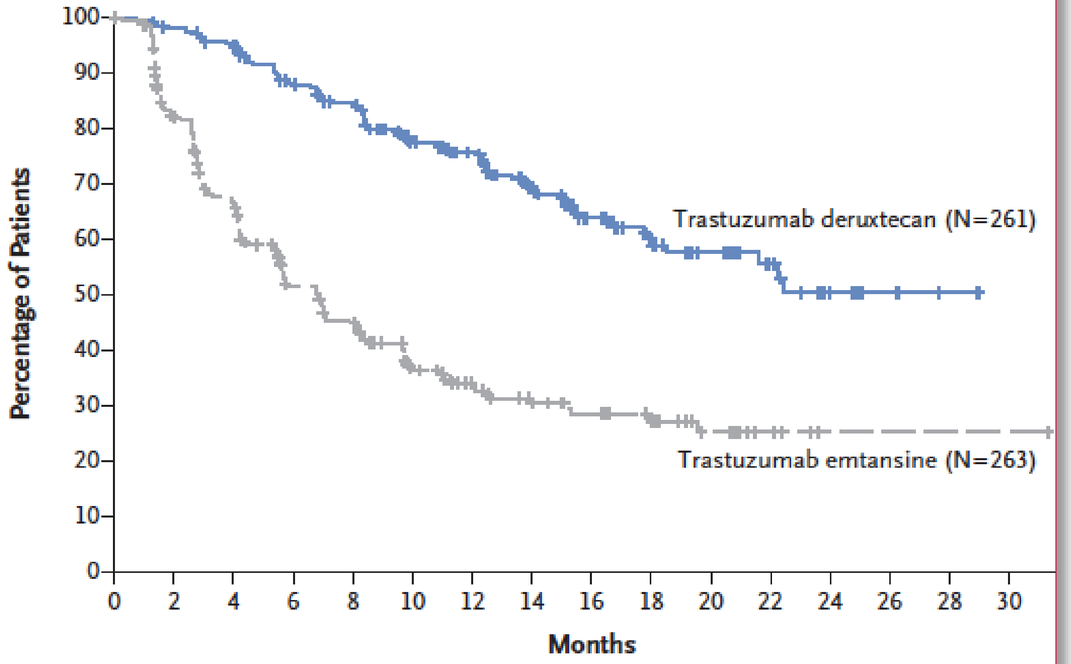
Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer

J. Cortés, S.-B. Kim, W.-P. Chung, S.-A. Im, Y.H. Park, R. Hegg, M.H. Kim, L.-M. Tseng, V. Petry, C.-F. Chung, H. Iwata, E. Hamilton, G. Curigliano, B. Xu, C.-S. Huang, J.H. Kim, J.W.Y. Chiu, J.L. Pedrini, C. Lee, Y. Liu, J. Cathcart, E. Bako, S. Verma, and S.A. Hurvitz, for the DESTINY-Breast03 Trial Investigators*

Trastuzumab-Emsantine (TDM1) vs. TDx

2. Linie nach mindestens Trastuzumab/Taxan

A Progression-free Survival

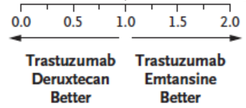


No. at Risk

Trastuzumab deruxtecan	261	250	240	214	200	168	150	112	79	53	36	25	10	5	2
Trastuzumab emtansine	263	200	155	108	93	65	51	37	29	21	12	6	1	1	1	1

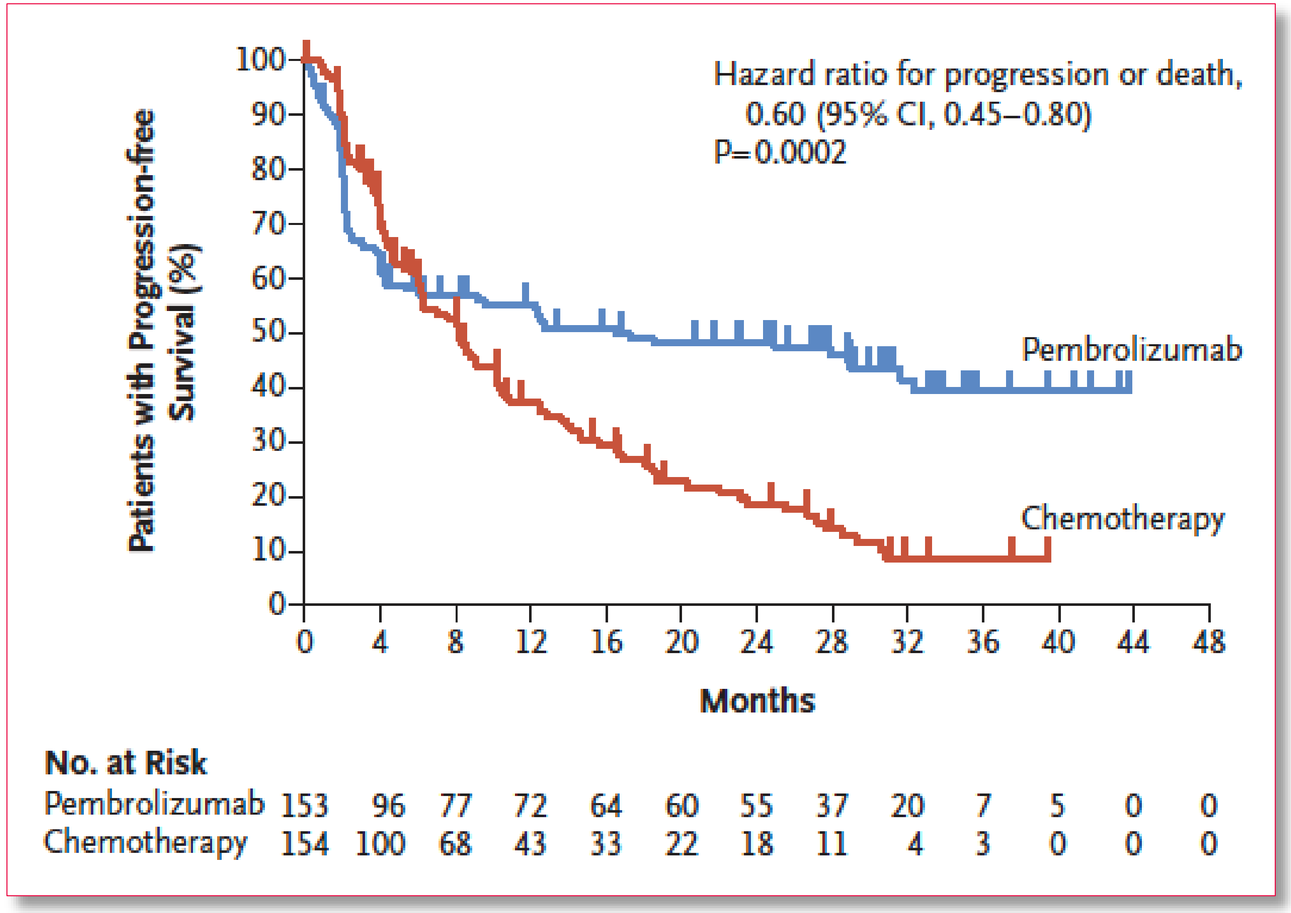
B Progression-free Survival in Prespecified Subgroups

Subgroup	No. of Patients	No. of Events/No. of Patients		Median Progression-free Survival (95% CI) *mo*		Hazard Ratio for Disease Progression or Death (95% CI)
		Trastuzumab deruxtecan	Trastuzumab emtansine	Trastuzumab deruxtecan	Trastuzumab emtansine	
All patients		87/261	158/263	NE (18.5–NE)	6.8 (5.6–8.2)	0.28 (0.22–0.37)
Hormone-receptor status						
Positive	272	46/133	84/139	22.4 (17.7–NE)	6.9 (4.2–9.8)	0.32 (0.22–0.46)
Negative	248	41/126	73/122	NE (18.0–NE)	6.8 (5.4–8.3)	0.30 (0.20–0.44)
Previous pertuzumab treatment						
Yes	320	57/162	98/158	NE (18.5–NE)	6.8 (5.4–8.3)	0.30 (0.22–0.43)
No	204	30/99	60/105	NE (16.5–NE)	7.0 (4.2–9.7)	0.30 (0.19–0.47)
Visceral disease						
Yes	384	72/195	123/189	22.2 (16.5–NE)	5.7 (4.2–7.0)	0.28 (0.21–0.38)
No	140	15/66	35/74	NE (NE–NE)	11.3 (6.8–NE)	0.32 (0.17–0.58)
Lines of previous therapy						
0 or 1	258	46/132	75/126	22.4 (17.9–NE)	8.0 (5.7–9.7)	0.33 (0.23–0.48)
≥2	266	41/129	83/137	NE (16.8–NE)	5.6 (4.2–7.1)	0.28 (0.19–0.41)
Stable brain metastases						
Yes	114	31/62	31/52	15.0 (12.6–22.2)	5.7 (2.9–7.1)	0.38 (0.23–0.64)
No	410	56/199	127/211	NE (22.4–NE)	7.0 (5.5–9.7)	0.27 (0.19–0.37)



Kolorektales Karziom - MSI-dMMR

1. Linie: FOLFOX6/FOLFIRI + Cetuximab/Bevacizumab vs. Pembrolizumab-Mono



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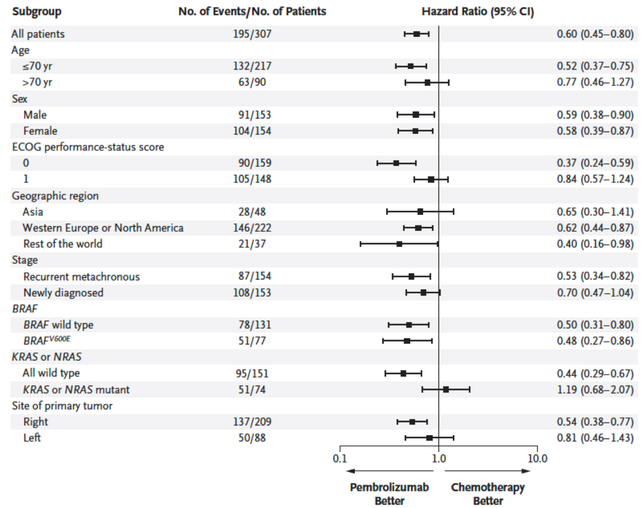
Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*

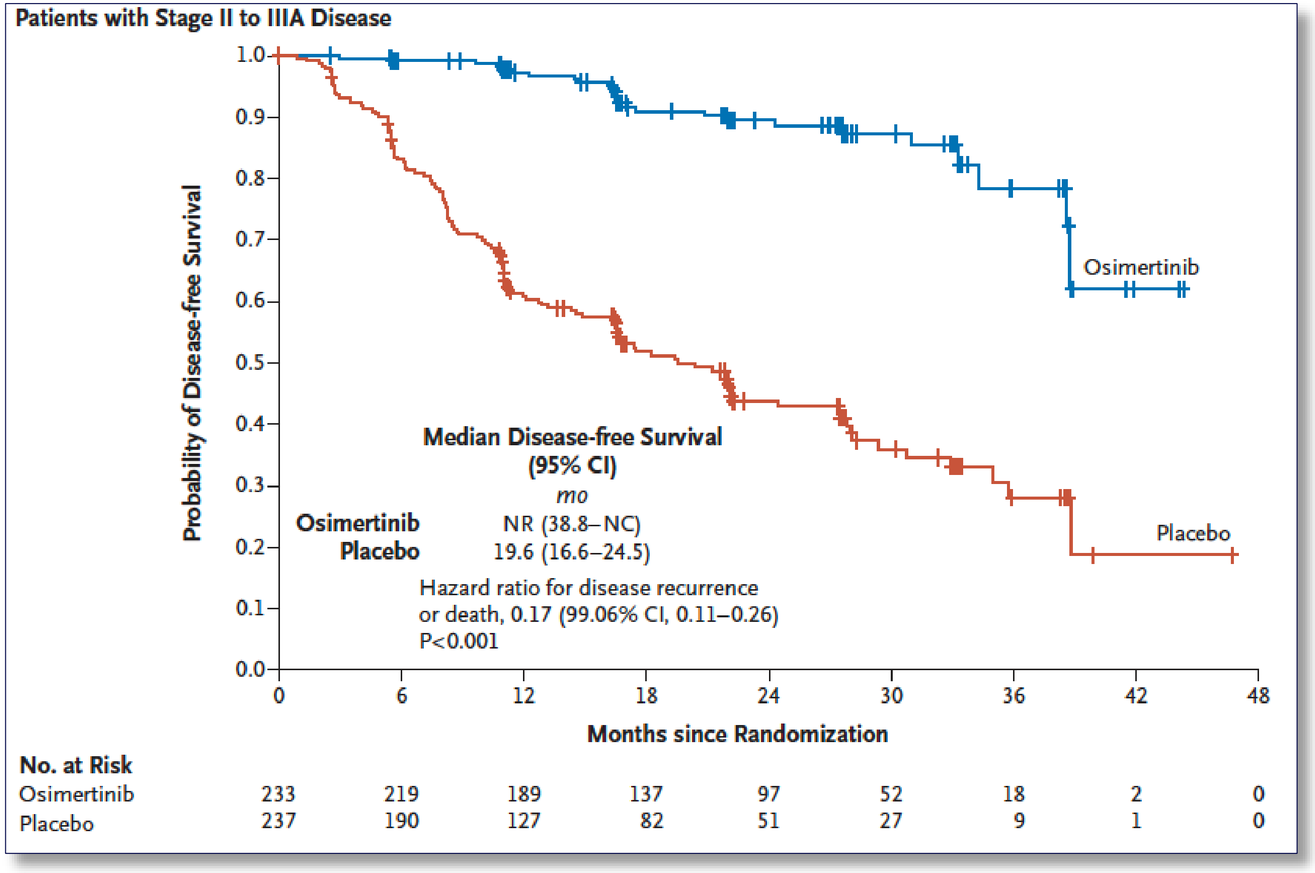


Andre et al. NEJM 2020;383:2207-18

Lungenkrebs adjuvante Therapie

Exon19-Deletion, Exon21 L858R

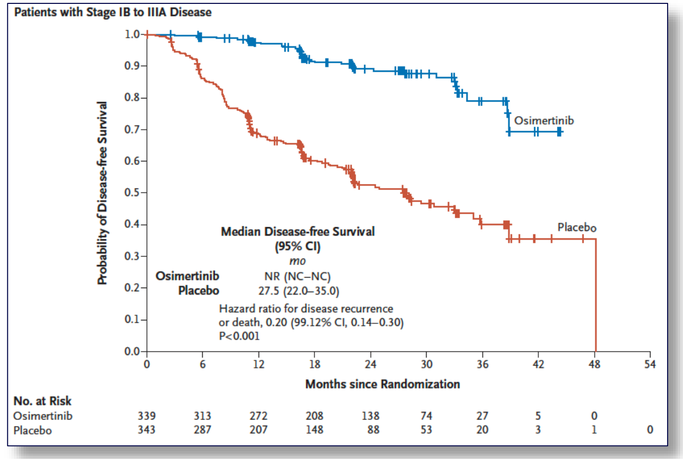
Nach Chemotherapie Osimertinib 80mg über 3 Jahre



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 OCTOBER 29, 2020 VOL. 383 NO. 18

Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA Investigators*

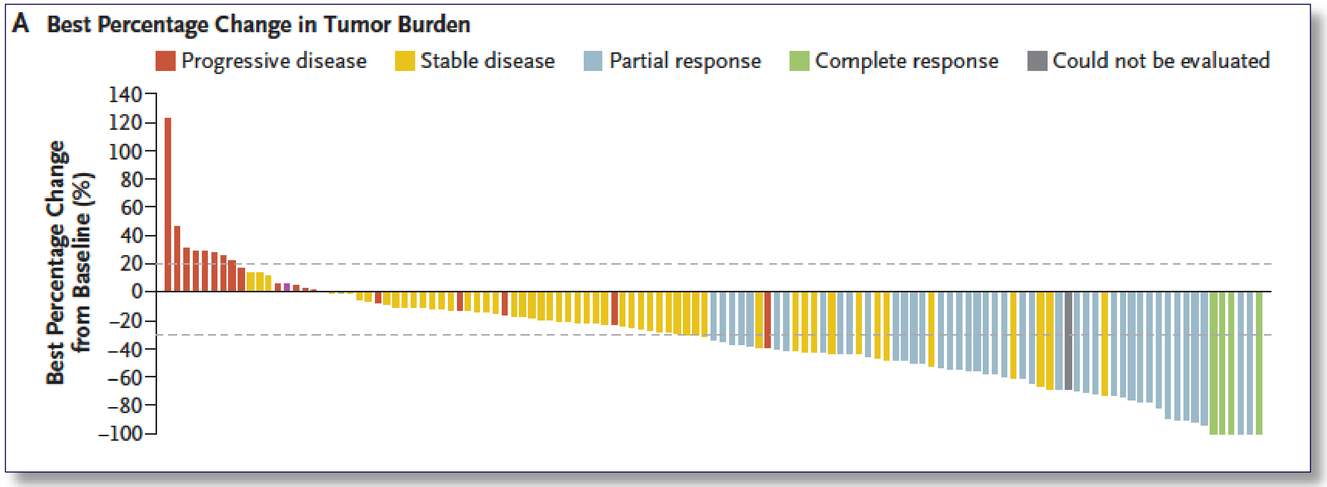


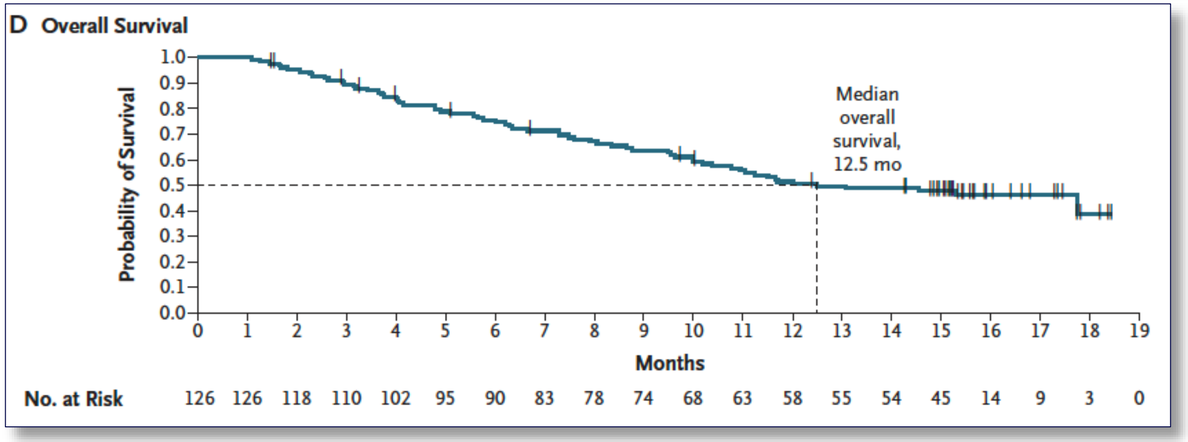
Wu et al. NEJM 2020;383:1711-23

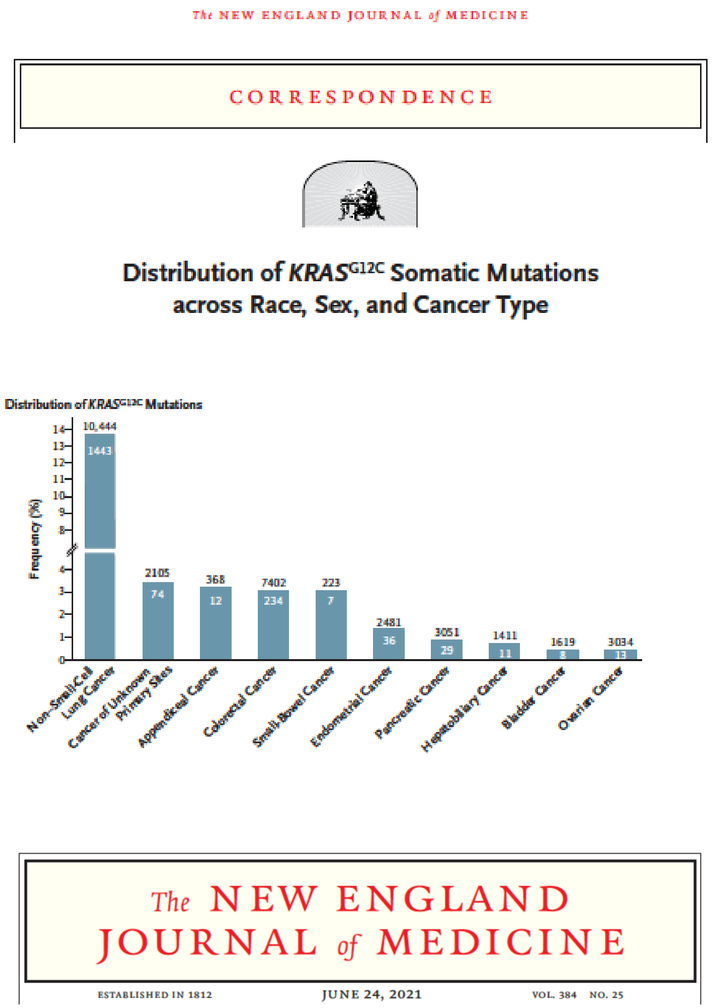
Lungenkrebs - KRAS p.G12C

Mindestens 1 Vortherpie

- Sotorasib 960 mg tgl. oral.







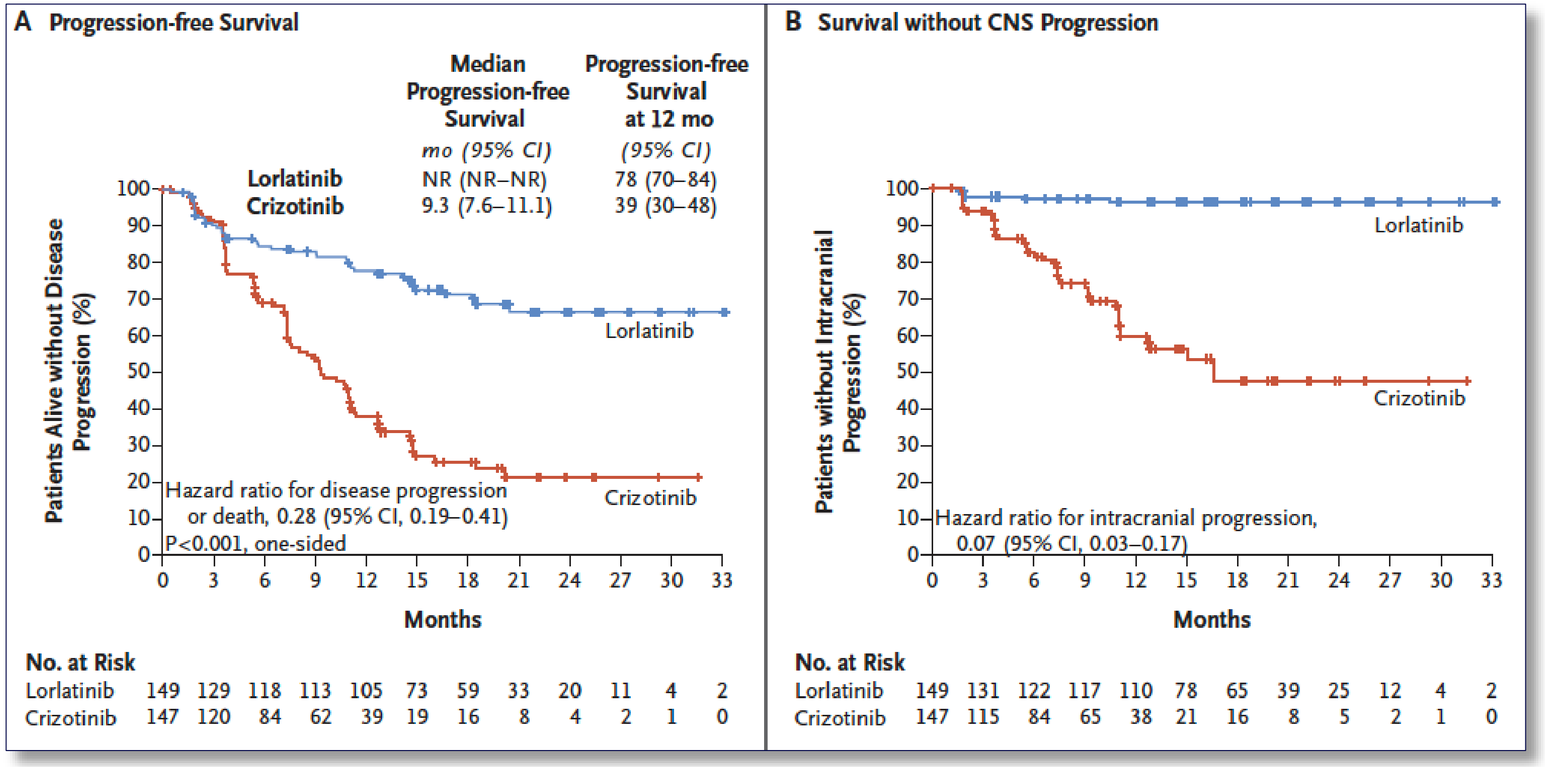
Sotorasib for Lung Cancers with *KRAS* p.G12C Mutation

F. Skoulidis, B.T. Li, G.K. Dy, T.J. Price, G.S. Falchook, J. Wolf, A. Italiano, M. Schuler, H. Borghaei, F. Barlesi, T. Kato, A. Curioni-Fontecedro, A. Sacher, A. Spira, S.S. Ramalingam, T. Takahashi, B. Besse, A. Anderson, A. Ang, Q. Tran, O. Mather, H. Henary, G. Ngarmchamnanrith, G. Friberg, V. Velcheti, and R. Govindan

Skoulidis et al. NEJM 2021:384:2371-81

Lungenkrebs - ALK

Lorlatinib

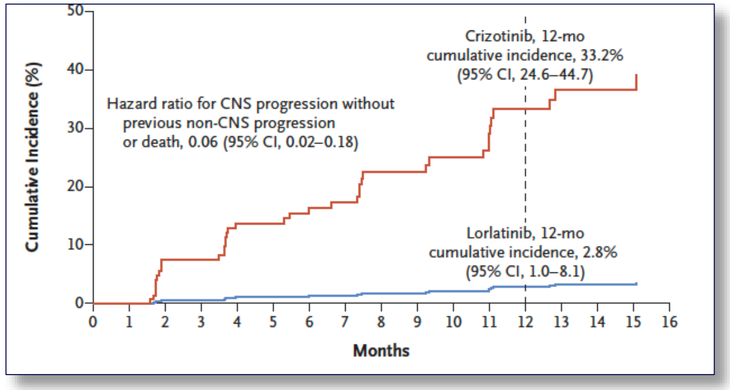


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

First-Line Lorlatinib or Crizotinib in Advanced *ALK*-Positive Lung Cancer

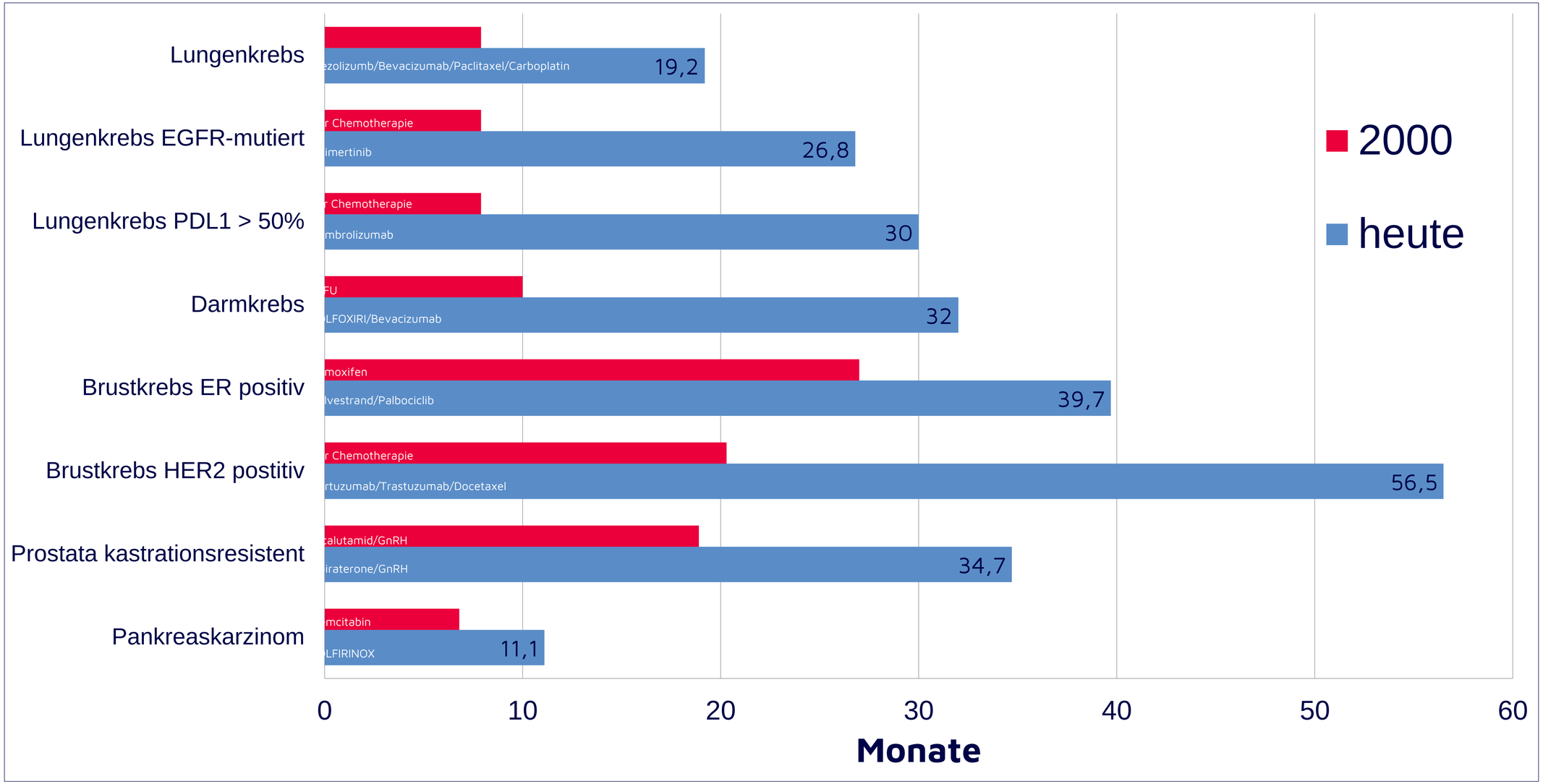
Alice T. Shaw, M.D., Ph.D., Todd M. Bauer, M.D., Filippo de Marinis, M.D., Ph.D., Enriqueta Felip, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Geoffrey Liu, M.D., Julien Mazieres, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Tony Mok, M.D., Anna Polli, B.Sc., Holger Thurm, M.D., Anna M. Calella, Ph.D., Gerson Peltz, M.D., M.P.H., and Benjamin J. Solomon, M.B., B.S., Ph.D., for the CROWN Trial Investigators*



Shaw et al. NEJM 2020:3843:2018-29

Überleben mit Krebs und Metastasen
Gestern und Heute

Länger Leben



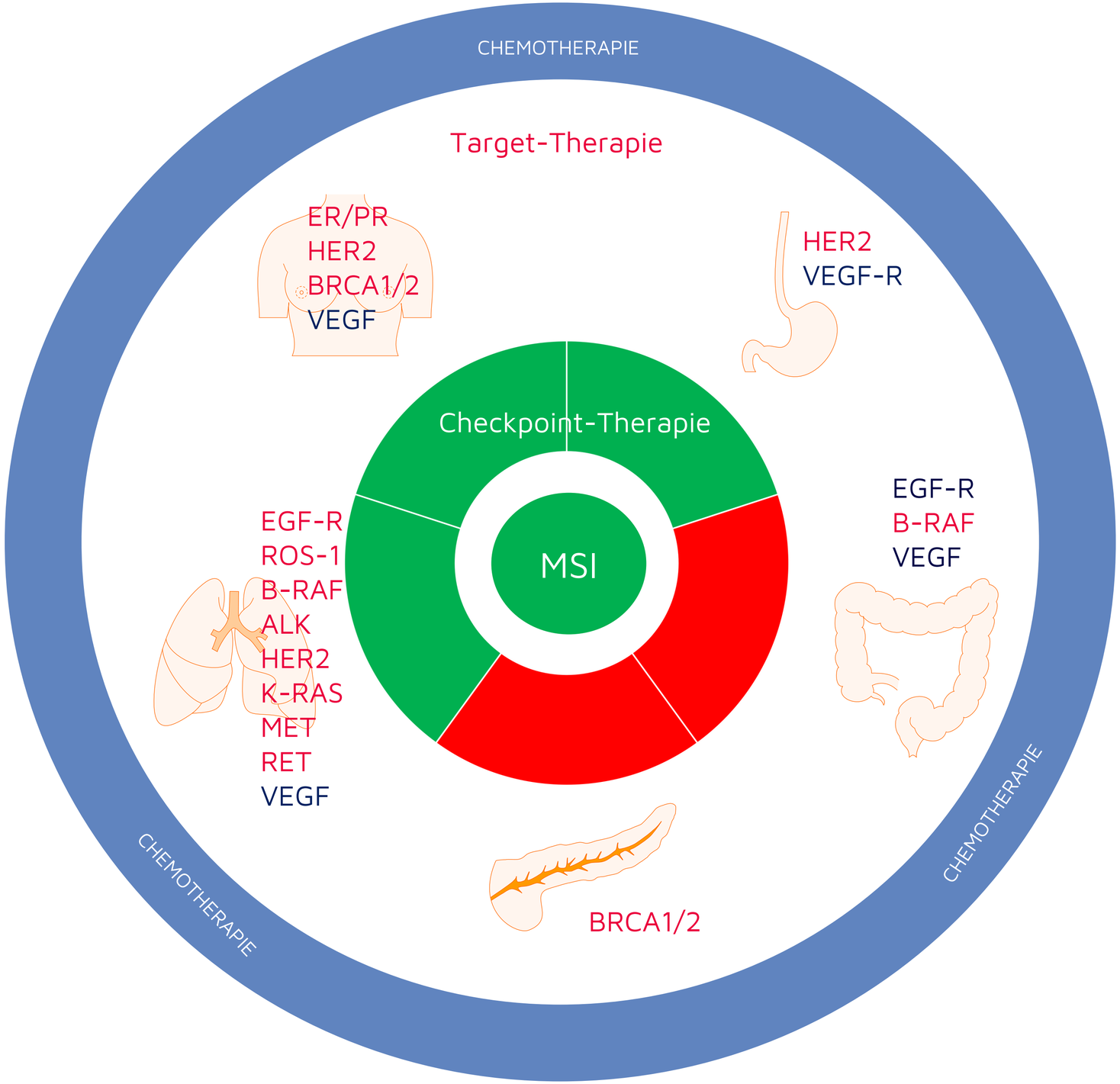
Mutationsspezifische Therapien

	adjuvant	1st	2nd	3rd
EGF-R (Ex19/21)	Osimertinib (delEx19, Ex21 L858R)	Erlotinib Gefitinib Afatinib Osimertinib	Osimertinib (T790M)	Afatinib (Mutation Ex18 p.G724S)
EGF-R T790M		Osimertinib	Osimertinib	
EGF-R Exon (18)20			Mobocertinib Poziotinib	
ALK		Crizotinib Ceritinib Alectinib Brigatinib	Ceritinib (nach Crizotinib) Lorlatinib Brigatinib (nach Crizotinib)	Lorlatinib
ROS-1		Crizotinib	Lorlatinib	
B-RAF V600E		Dabrafenib+Trametinib		
RAS p.G12C		Sotorasib		
MET Ex14		Tepotinib Capmatinib	Tepotinib Capmatinib	
HER2 (ERBB2)			Trastuzumab-Deruxtecan	
NTRK			Larotrectinib	
RET			Selpercatinib Pralsetinib	

Immuntherapie 2022

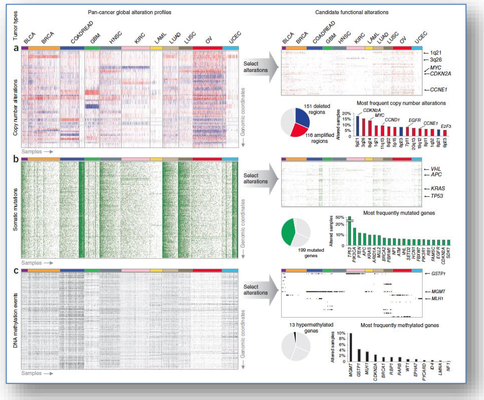
Immuntherapie 20222		**Melanom**	**Merkelzell-Karzinom**	**Plattenepithel-karzinom der Haut**	**Basalzellkarzinom**	**Lungenkrebs** NSCLC Adeno	**Lungenkrebs** NSCLC Platte	**Lungekrebs** SCLC	**Pleurameotheliom**	**Brustkrebs** TNBC	**Ösopahgus-karzinom/AEG**	**Magenkarzinom**	**Darmkrebs** MSI-high	**HCC**	**Nierenkrebs**	**Urothel-karzinom**	**Kopf-Hals-Krebs**	**Endometrium-karzinom**	**M. Hodgkin**
Ipilimumab Yervoy®	CTLA-4	+				+	+		+				+ 2nd		+				
Nivolumab Opdivo®	PD-1	+				+	+		+		+	(+)	+ 2nd		+	+	+		+
Pembrolizumab Keytruda®	PD-1	+				+	+				+		+ 1st		+	+	+		+
Avelumab Bavenico®	PD-L1		+												+				
Durvalumab Imfinzi®	PD-L1					+	+												
Atezolizumab Tecentric®	PD-L1					+		+		+				+		+			
Cemiplimab Libtayo®	PD-L1			+	+	+	+												
Dostarlimab Jemperli®	PD-1																	+	

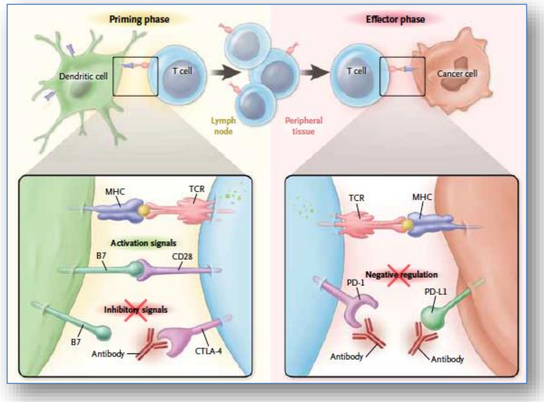
Systemtherapie 2022



Target-spezifisch
Mutations-spezifisch

Systemtherapie/ die 3 Säulen der Therapie heute



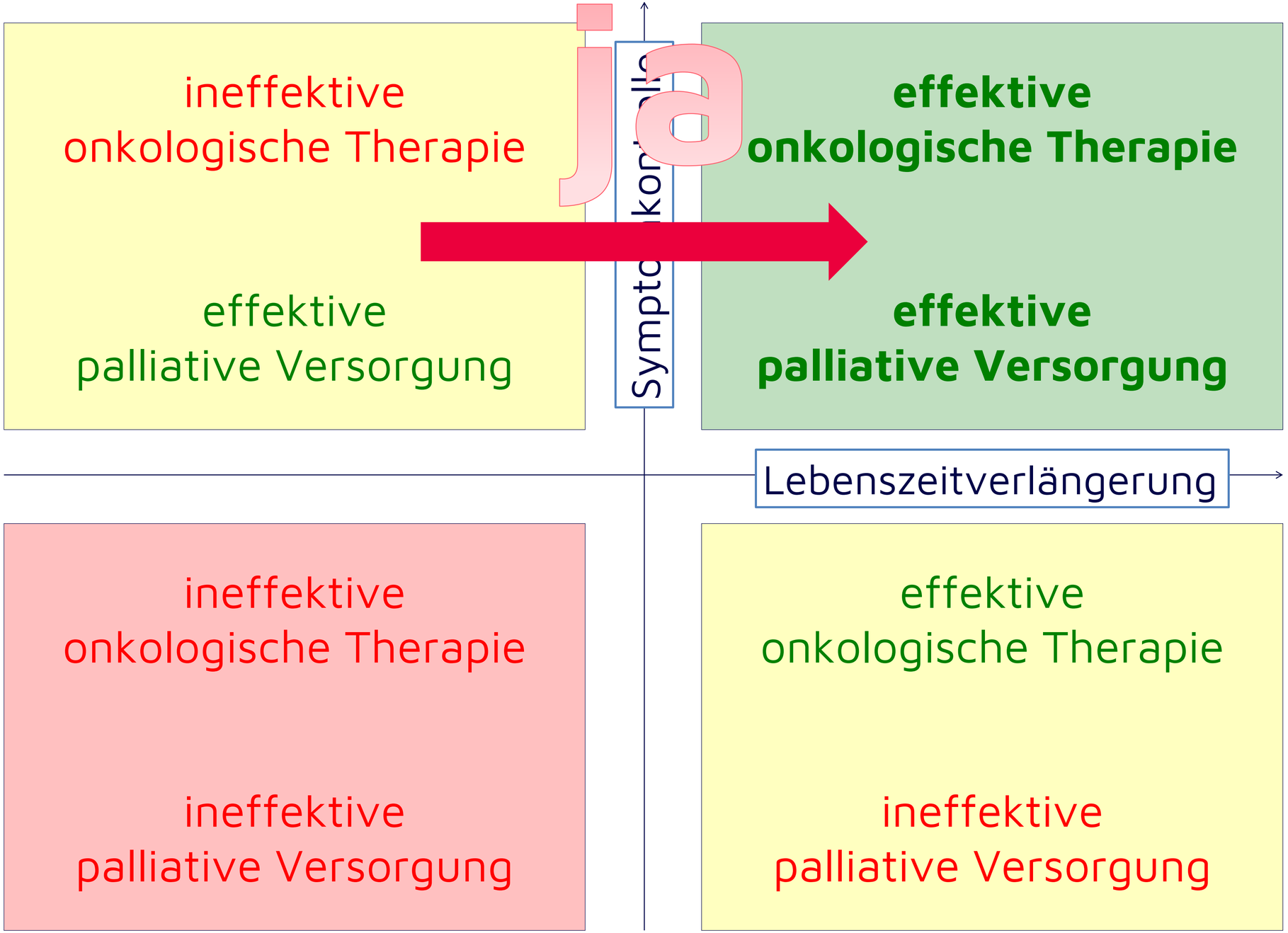


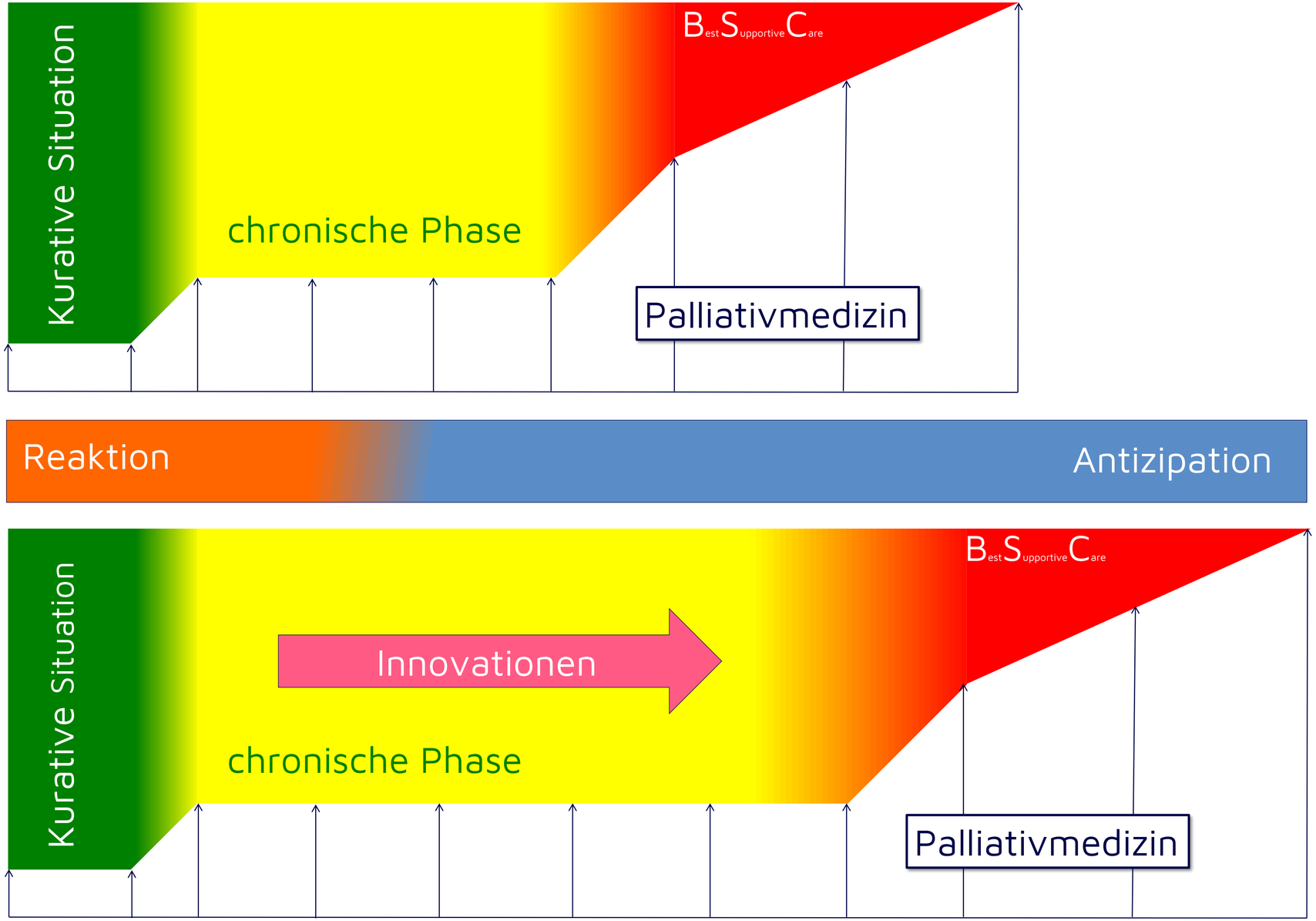
Immun-Therapie

Molekulare Target-Therapie

Konventionelle Therapie

2005 2010 2015


ineffektive
onkologische Therapie
effektive
palliative Versorgung
Ja
Symptomkontrolle
effektive
onkologische Therapie
effektive
palliative Versorgung
Lebenszeitverlängerung
ineffektive
onkologische Therapie
ineffektive
palliative Versorgung
effektive
onkologische Therapie
ineffektive
palliative Versorgung


Kurative Situation
chronische Phase
Best Supportive Care
Palliativmedizin
Reaktion
Antizipation
Kurative Situation
Innovationen
chronische Phase
Best Supportive Care
Palliativmedizin

"Go around and see what is being done and then see how your own circumstances can produce another version; there is need for diversity in this field."

Dame Cicely Saunders, Founder
St. Christopher's Hospice

1918-2005

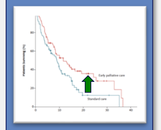
1967: St. Christopher`s-Hospiz

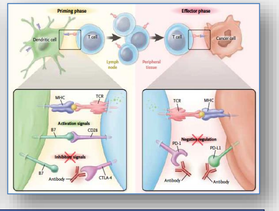
Symptomkontrolle

1983: 1. Deutsche Palliativstation in Köln

2005
Integration

2015
Lebens-
erwartung





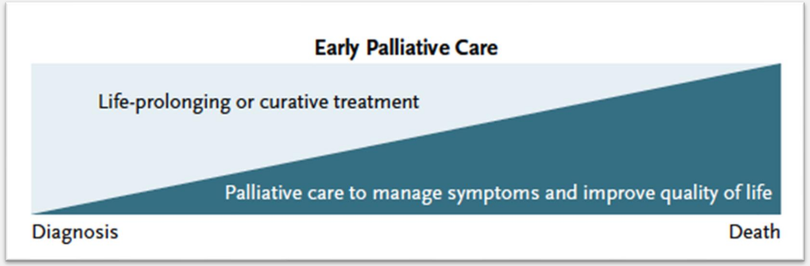
Immun-Therapie

Molekulare Target-Therapie

Konventionelle Therapie

2005 2010 2015

Parikh et al. NEJM 2010;369:2347-51

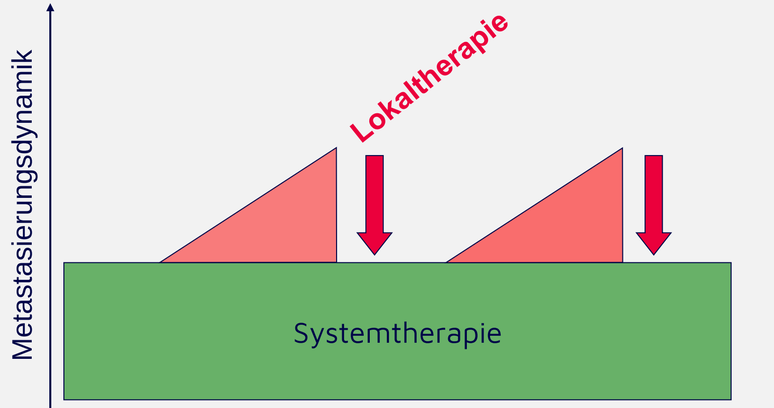


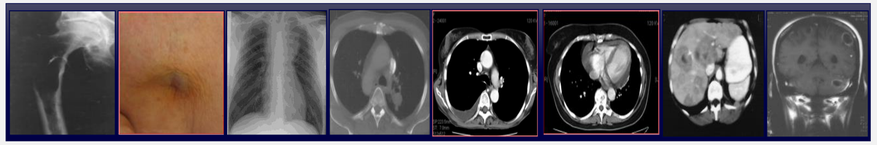
Reaktion Antizipation

Antizipation statt Reaktion

Reaktion Antizipation

Gomez et al. JCO 2015;22:1438-46





Vielen Dank

Aus Liebe zum Leben