

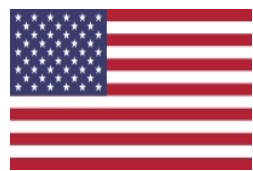
ESMO 2015
Patiententag
Melanom/Hauttumore

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Therapie des metastasierten Melanoms: 1970–2015



Proleukin
(high-dose IL-2)
Jan 1998

DTIC-Dome
(dacarbazine)
May 1975

Yervoy
(ipilimumab)
Mar 2011

Zelboraf
(vemurafenib)
Aug 2011

Tafinlar/Mekinist
monotherapies
(dabrafenib/trametinib)
May 2013

Tafinlar + Mekinist
(dabrafenib + trametinib)
dual therapy
Jan 2014

Keytruda
(pembrolizumab)
Sep 2014

Opdivo
(nivolumab)
Dec 2014

<1990 2000 2010 2011 2012 2013 2014 2015

DTIC-Dome
(dacarbazine)
1970s



Yervoy
(ipilimumab)
Jul 2011

Zelboraf
(vemurafenib)
Feb 2012

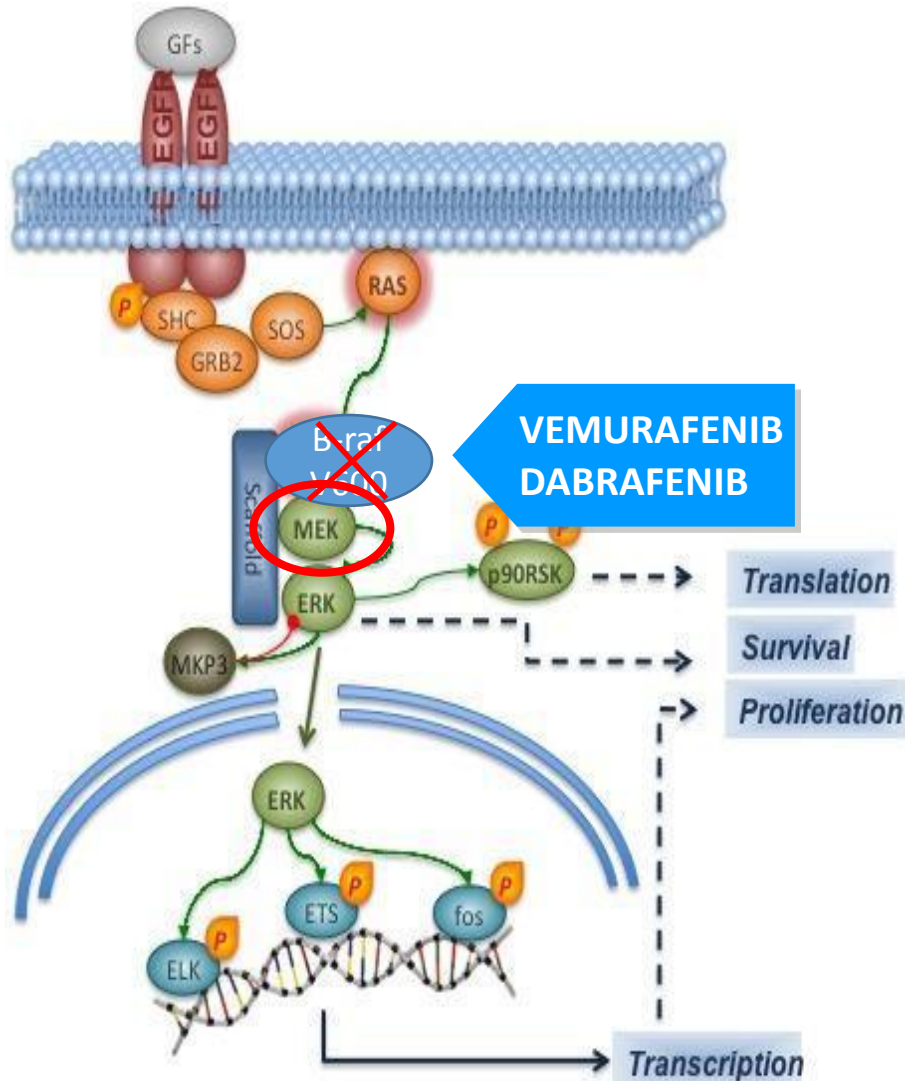
Tafinlar
(dabrafenib)
Sept 2013

Opdivo
(nivolumab)
June 2015

Keytruda
(pembrolizumab)
July 2015

Tafinlar + Mekinist
dual therapy
(dabrafenib + trametinib)
Aug 2015

B-raf Mutation



Ungefähr 40% der Patienten mit Melanom weisen im Tumor eine genetische Veränderung in B-raf auf

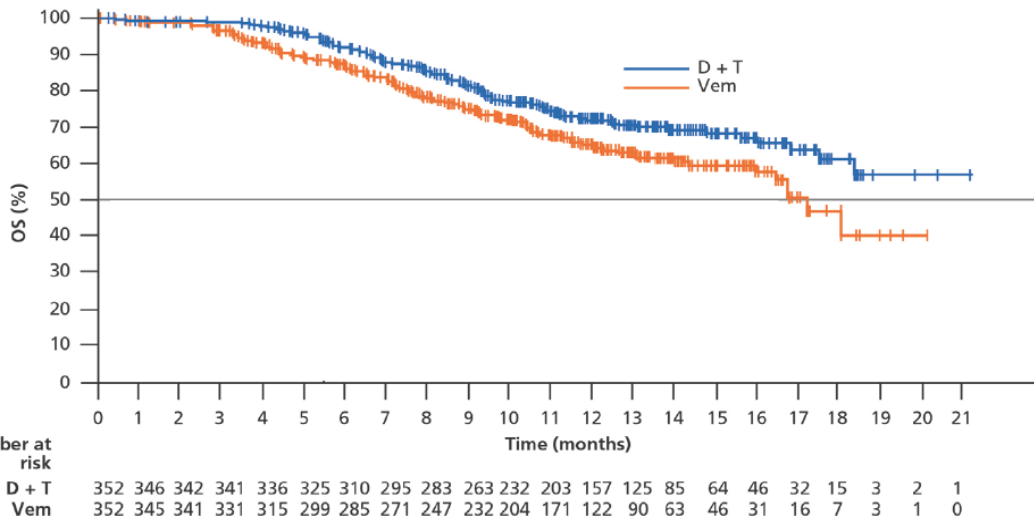
Diese führt zu verstärktem Tumorwachstum

Molekular gezielte Medikamente können speziell das veränderte B-raf Molekül blockieren

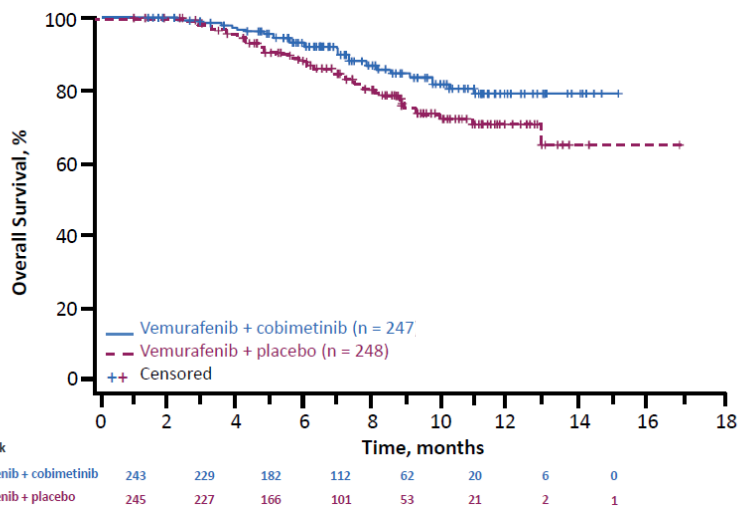
Die Therapie mit B-raf Inhibitoren wirkt bei mehr als 50% der Patienten

Die Wirkung halt im Mittel aber nur ca. 7 Monate an

Combi-V/Co-Brim - OS



	D+T (n = 352)	Vem (n = 352)
Died, n (%)	100 (28)	122 (35)
Median, months (95% CI)	NR (18.3-NR)	17.2 (16.4-NR)
Adjusted HR (95% CI)	0.69 (0.53-0.89)	
2-sided P-value	0.005 (<0.0214)	



	Vemurafenib + Placebo	Vemurafenib + Cobimetinib
OS events, n	51	34
Median OS	NE	NE
9-month OS (95% CI), %	72.5 (65.2-79.8)	81.1 (74.7-87.5)
HR (95% CI) P value two-sided	0.65 (0.42-1.00) P = 0.046*	

COMBI-v: B-raf + MEK Kombinationstherapie

COMBI-v¹

Eligibility criteria included:

- ≥18 years
- Stage IIIC/IV melanoma
- BRAF V600E/K positive
- ECOG PS status 0 or 1
- No prior systemic therapy
- No prior treatment with a BRAF inhibitor or MEK inhibitor
- Treated/stable brain metastases

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BRAF
V600E/K

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Dabrafenib + trametinib
n=352

150mg BID +
2mg QD

Vemurafenib
n=352

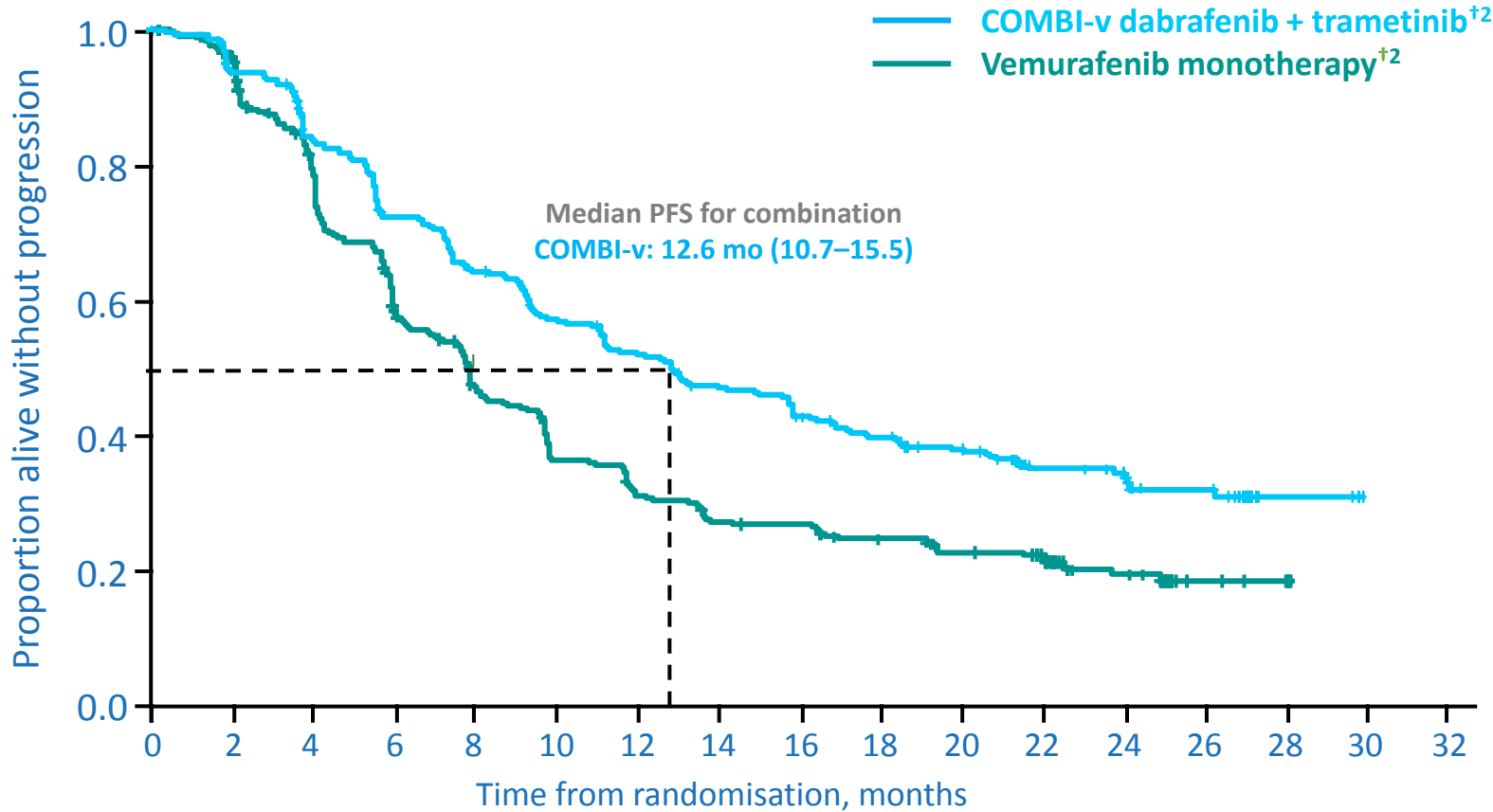
960mg BID

Interim OS
analysis

Final OS
analysis

COMBI-v: B-raf + MEK Kombination

Zeit bis zum Fortschreiten

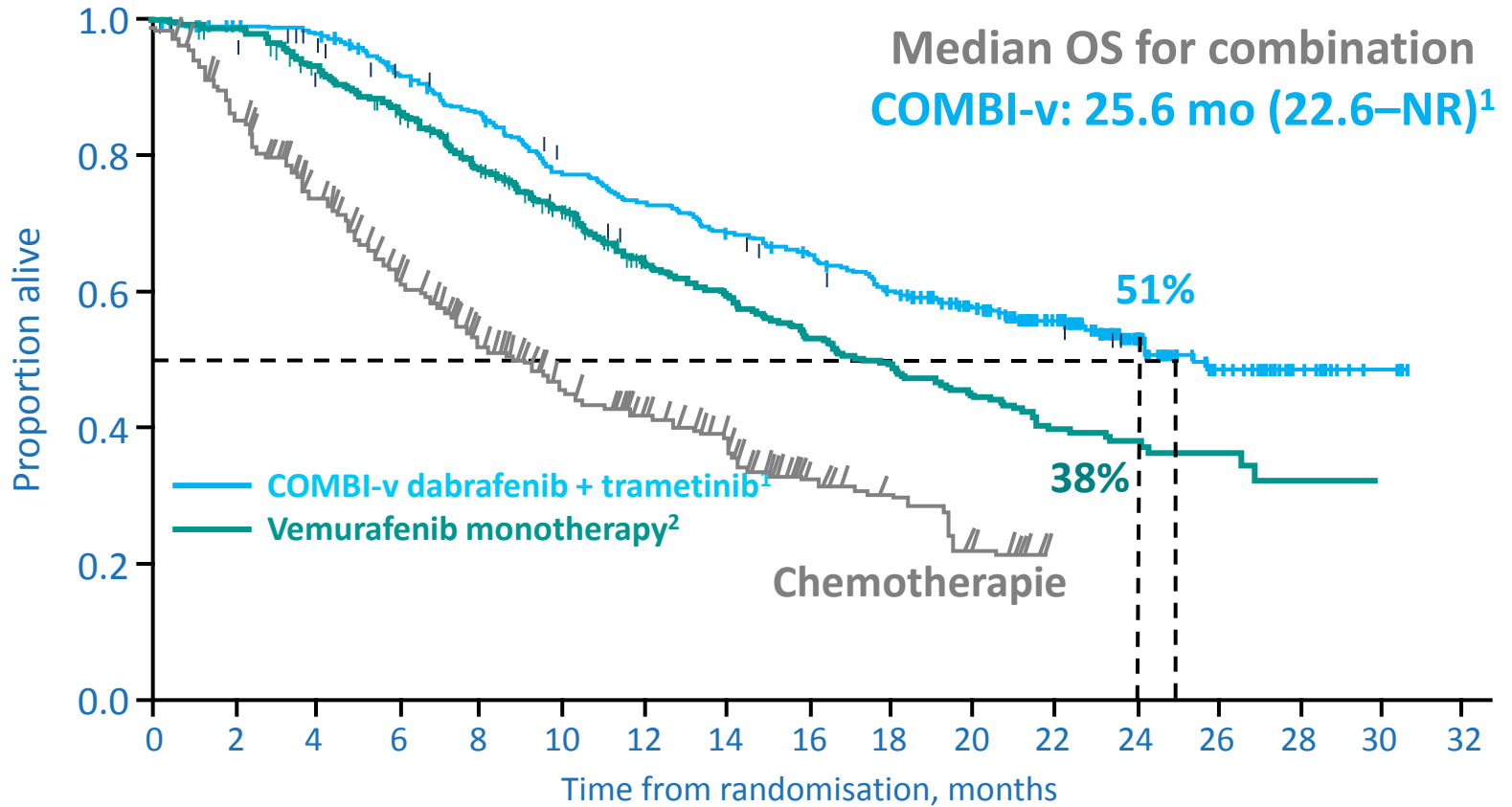


Number at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32
COMBI-v D + T ²	352	310	270	229	202	175	158	140	125	115	98	56	30	26	4	0	0
Vemurafenib ²	352	281	216	162	127	100	81	69	61	59	49	23	8	4	0	0	0

*Data cut-off: January 2015; †Data cut-off: March 2015.

1. Long GV, et al. *Lancet* 2015;386:444–51;
2. Robert C, et al. Oral presentation at ECC 2015, Abstract 3301.

COMBI-v: B-raf + MEK Kombination Überlebenszeit



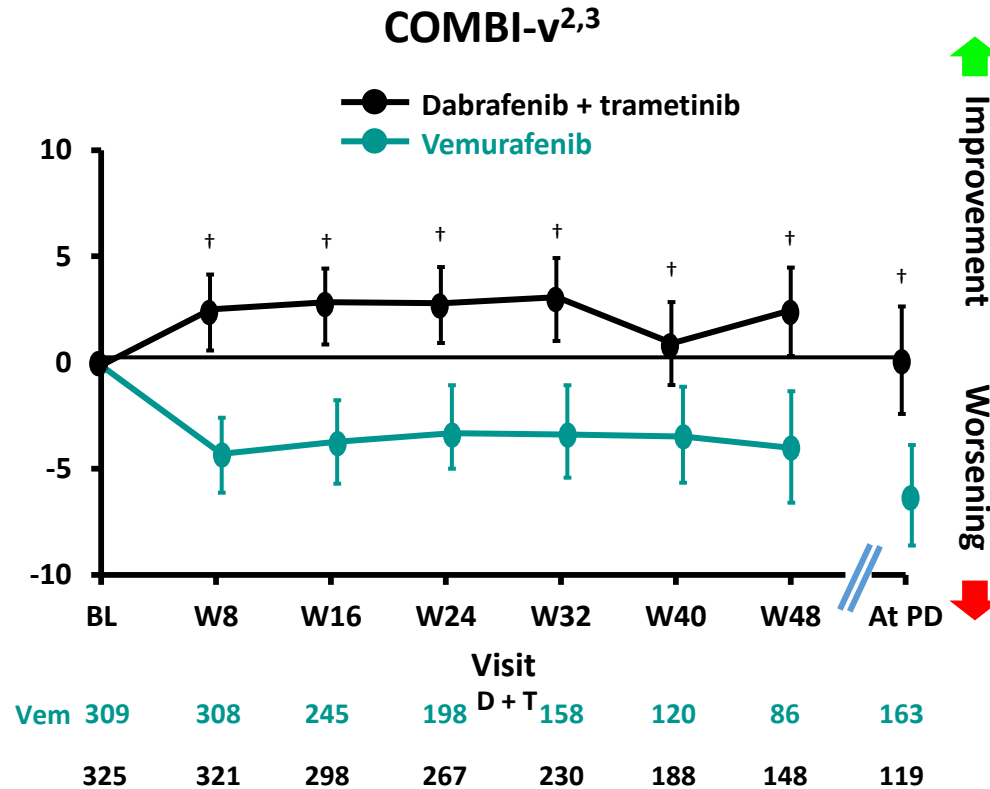
COMBI-v D + T ¹	352	342	336	311	286	260	245	230	217	198	173	128	68	38	16	5	0
Vemurafenib ²	352	341	315	286	252	231	201	187	166	152	129	88	46	28	7	0	0

*Adjusted stopping boundaries: two-sided $p < 0.0214$ for the efficacy analysis and $p > 0.2210$ for the futility analysis.

1. Robert C, et al. Oral presentation at ECC 2015, Abstract 3301;

2. Long GV, et al. *Lancet* 2015;386:444–51.

COMBI-v: B-raf + MEK Kombinationstherapie

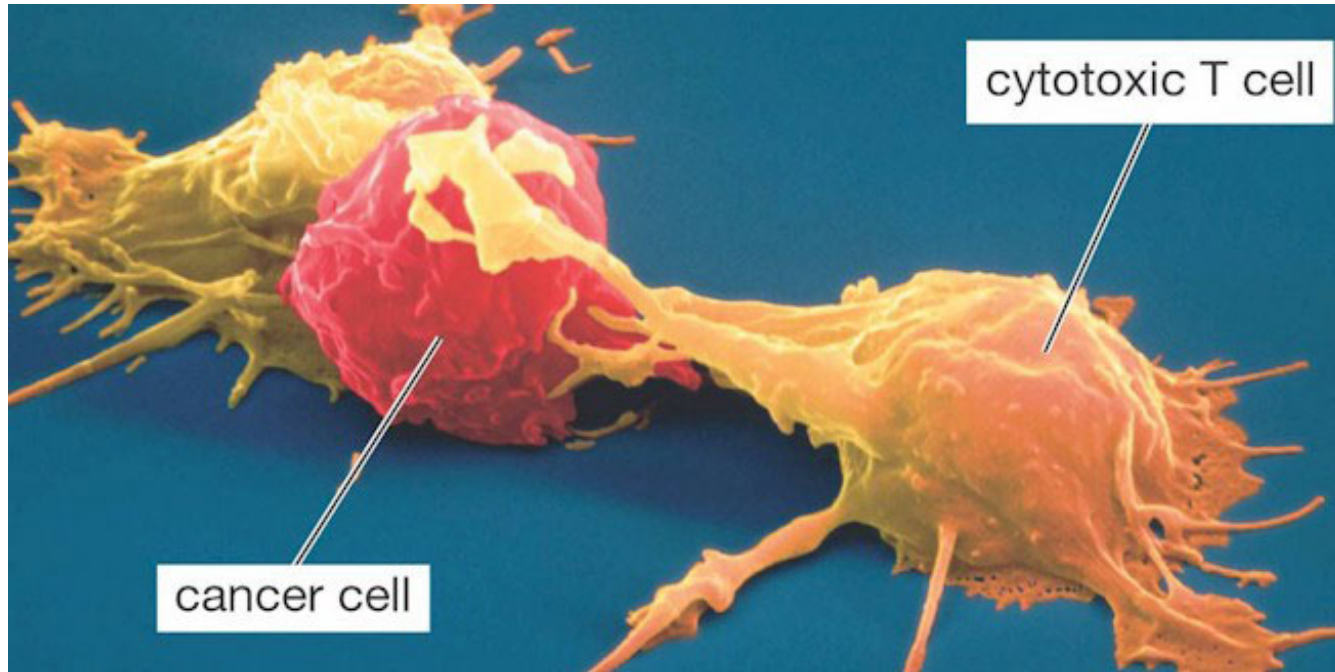


*Denotes statistically significant; Week 8, p=0.049; Week 16, p=0.035; Week 24, p=0.045; †Clinically meaningful and statistically significant difference between the arms. BL=baseline; D=dabrafenib; T=trametinib; HRQOL=health-related quality of life; SE=standard error; W=week. ITT population.

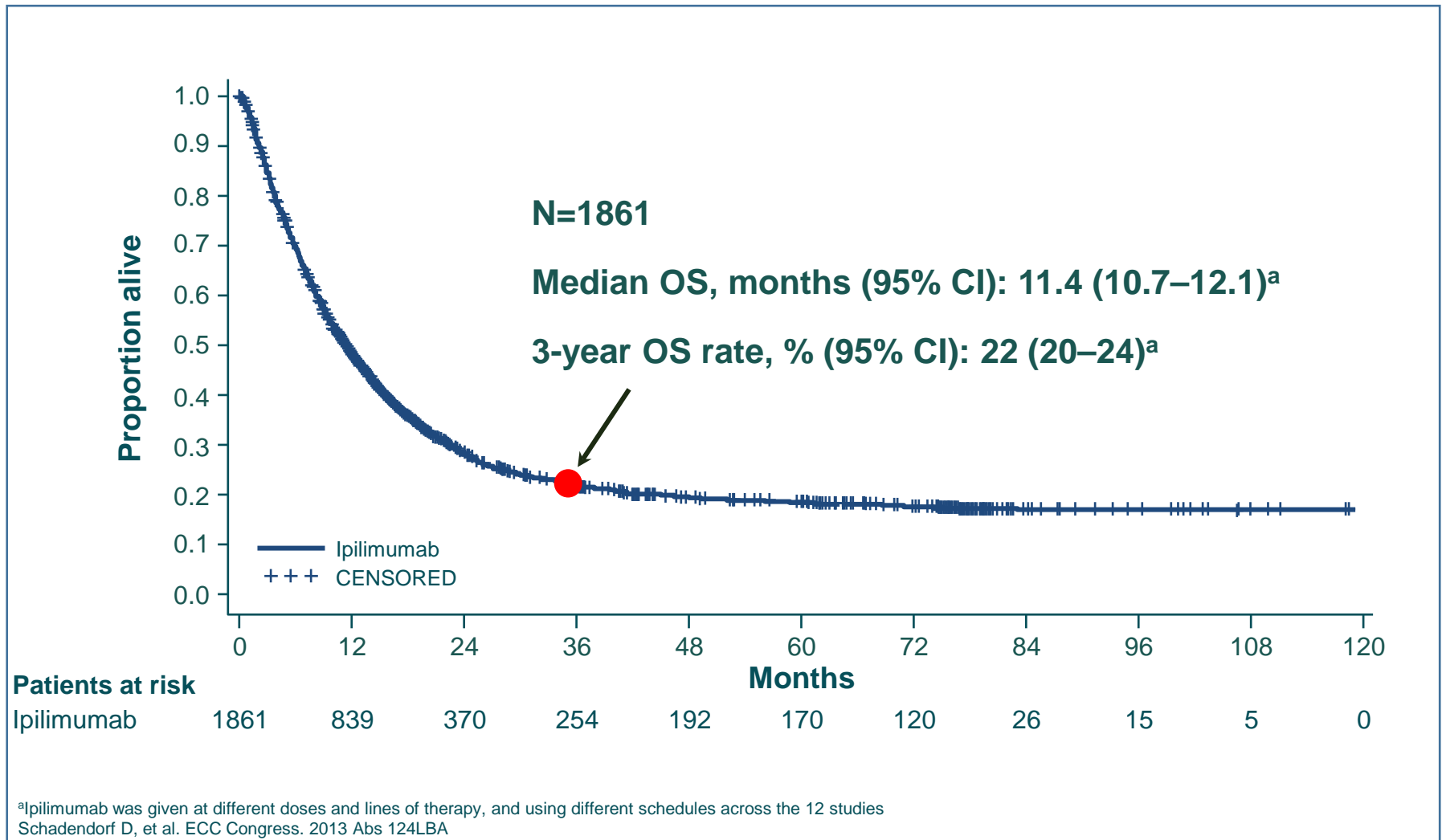
1. Schadendorf D, et al. *Eur J Cancer* 2015;51:833-840;

2. Grob JJ, et al. Poster presented at ECC 2015, Abstract 3345;
3. Grob JJ, et al. *Lancet Oncol* 2015. In press.

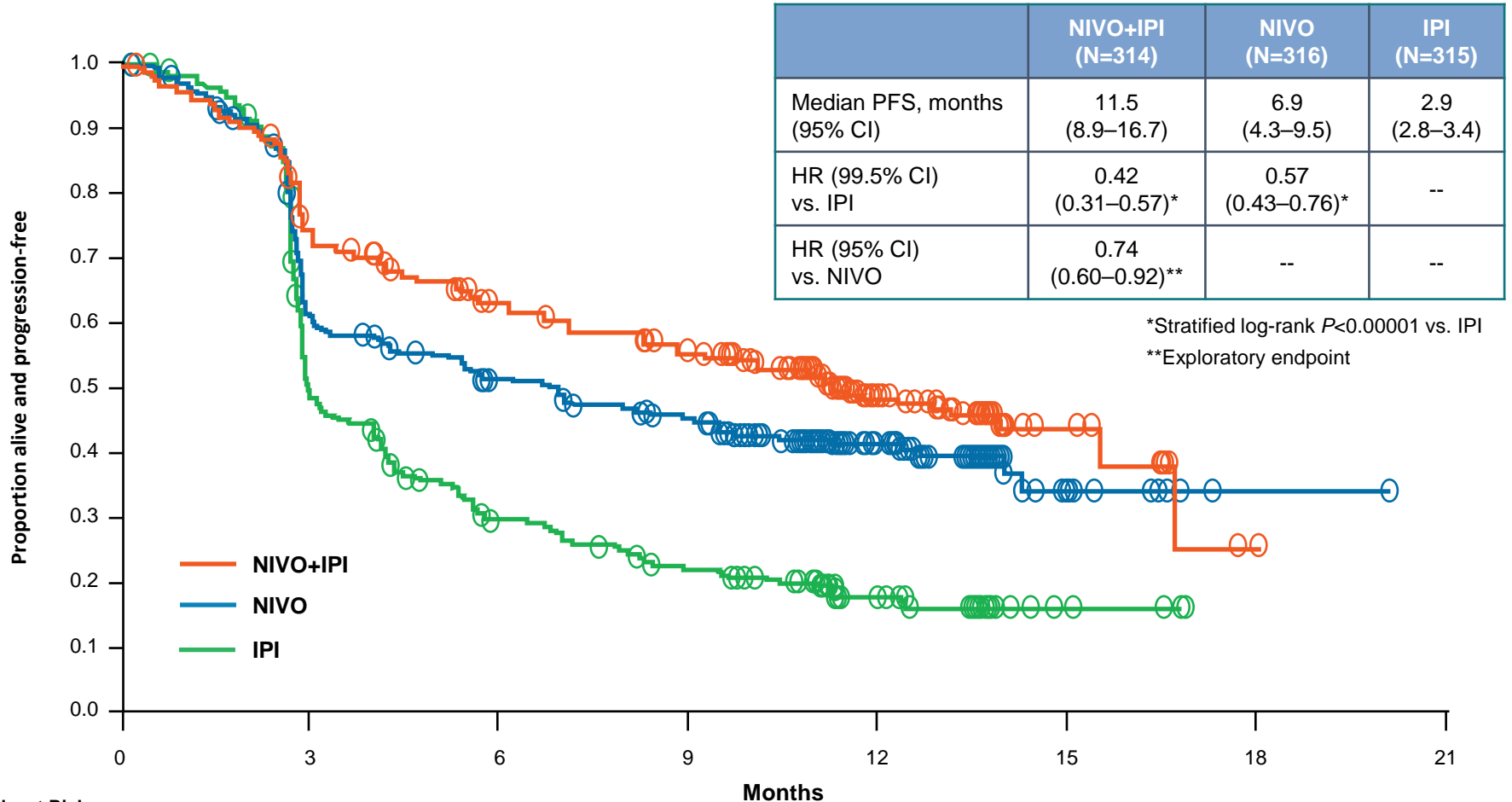
Immuntherapie des Melanoms



Unter Ipilimumab kann ein Teil der Patienten ein lang anhaltendes Überleben erreichen



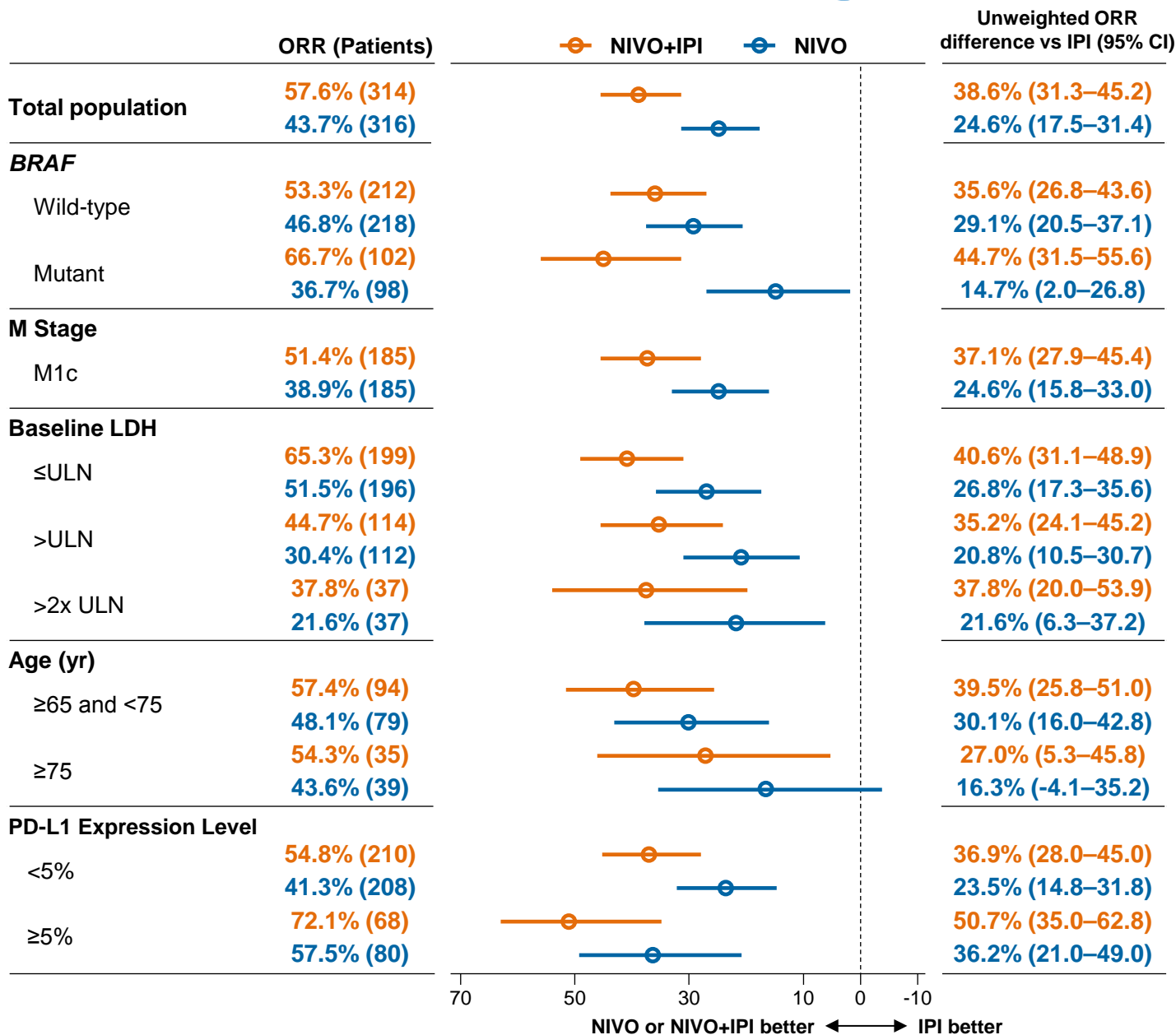
Zeit bis zum Fortschreiten der Erkrankung



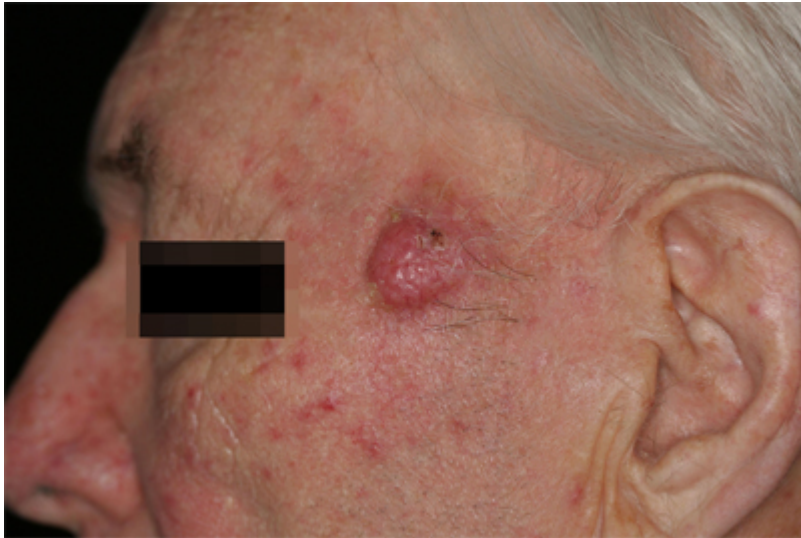
No. at Risk

	0	3	6	9	12	15	18	21
NIVO+IPI	314	219	173	151	65	11	1	0
NIVO	316	177	147	124	50	9	1	0
IPI	315	137	77	54	24	4	0	0

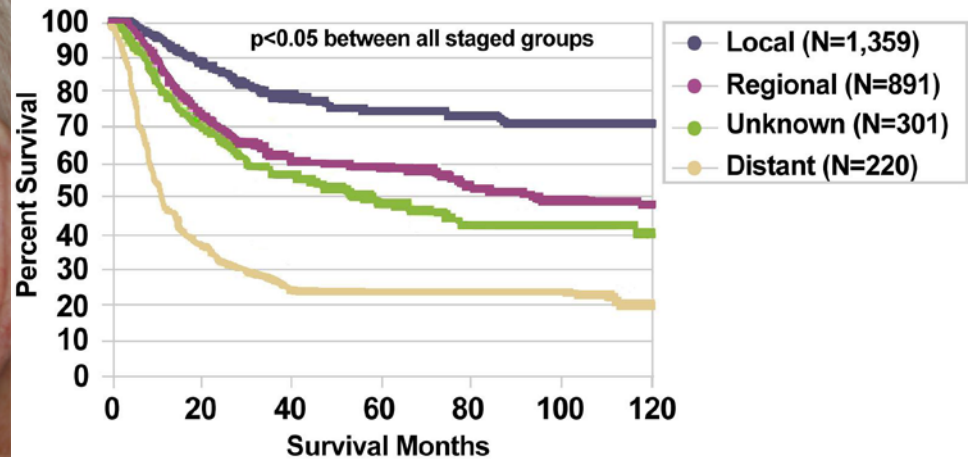
ORR in Patient Subgroups



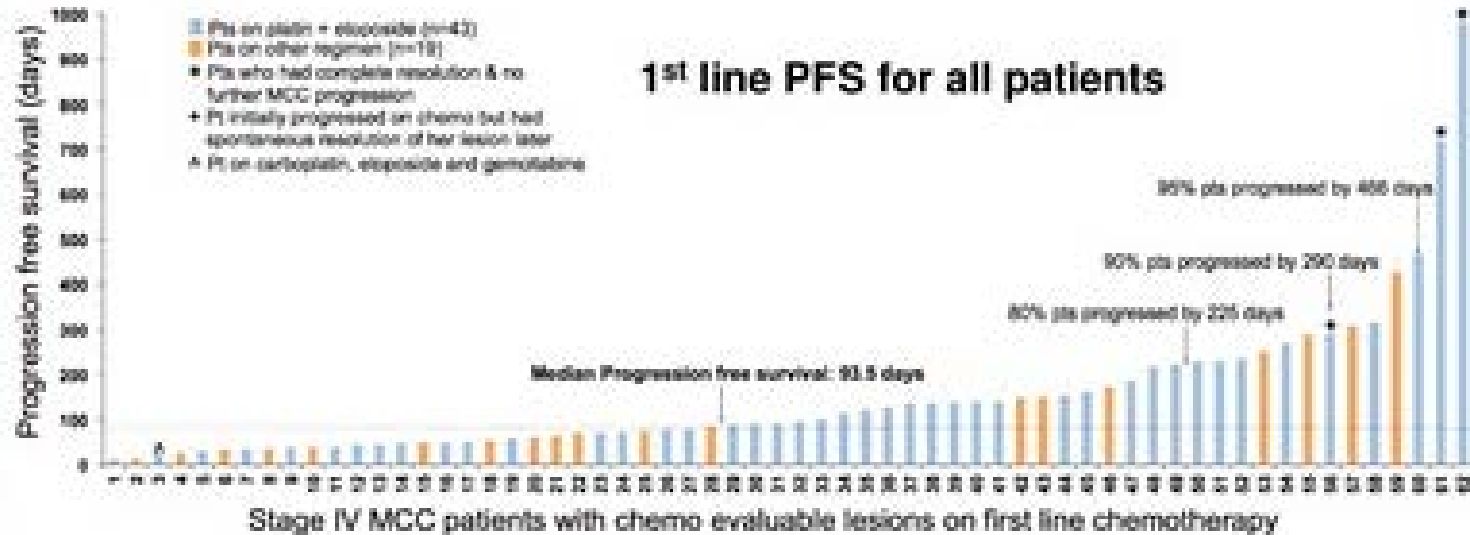
Merkelzellkarzinom



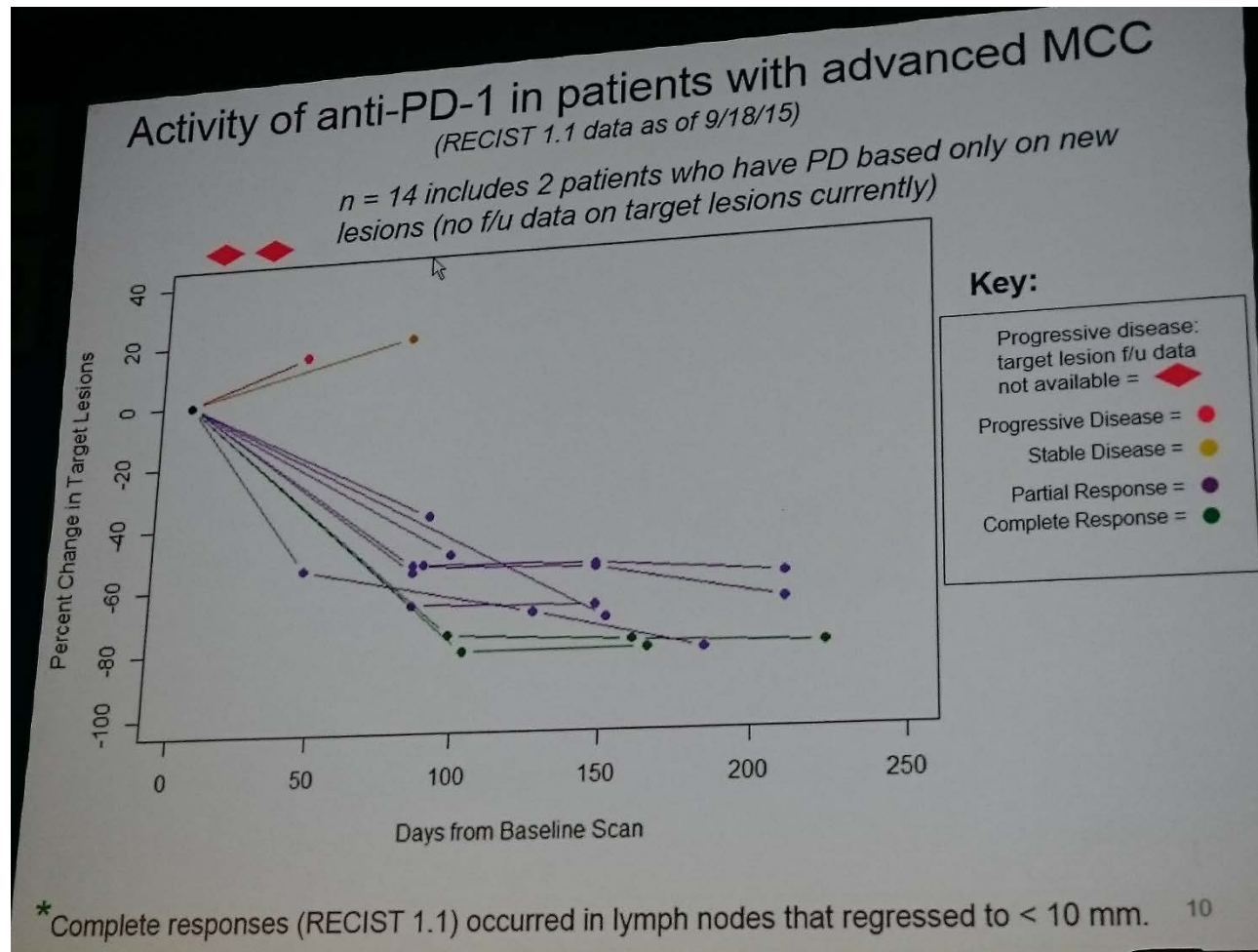
Relative ten year survival rates for Merkel cell carcinoma by stage (SEER 1973-2006)



Merkelzellkarzinom – vorübergehendes Ansprechen auf Chemotherapie



PD-1 Antikörper bei Merkelzellkarzinom



Danke für Ihre Aufmerksamkeit



Ausficht des allgemeinen Krankenhauses

Vue de l'Hopital General a Vienne

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