ESMO 2024 - Wichtig zu wissen

Prof. Dr. med. Bernhard Wörmann

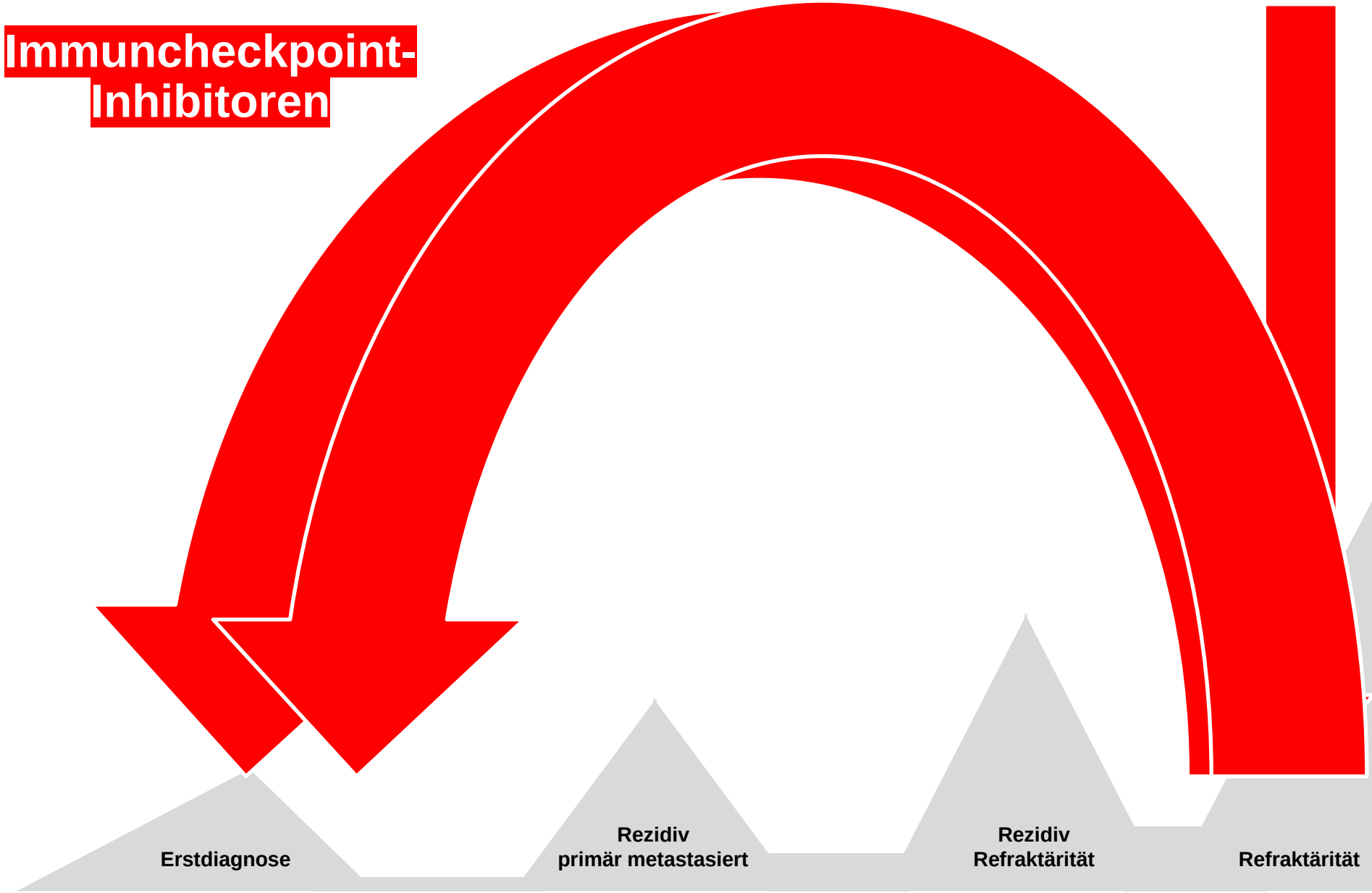
Barcelona, 14. – 17. September 2024

20. September 2024

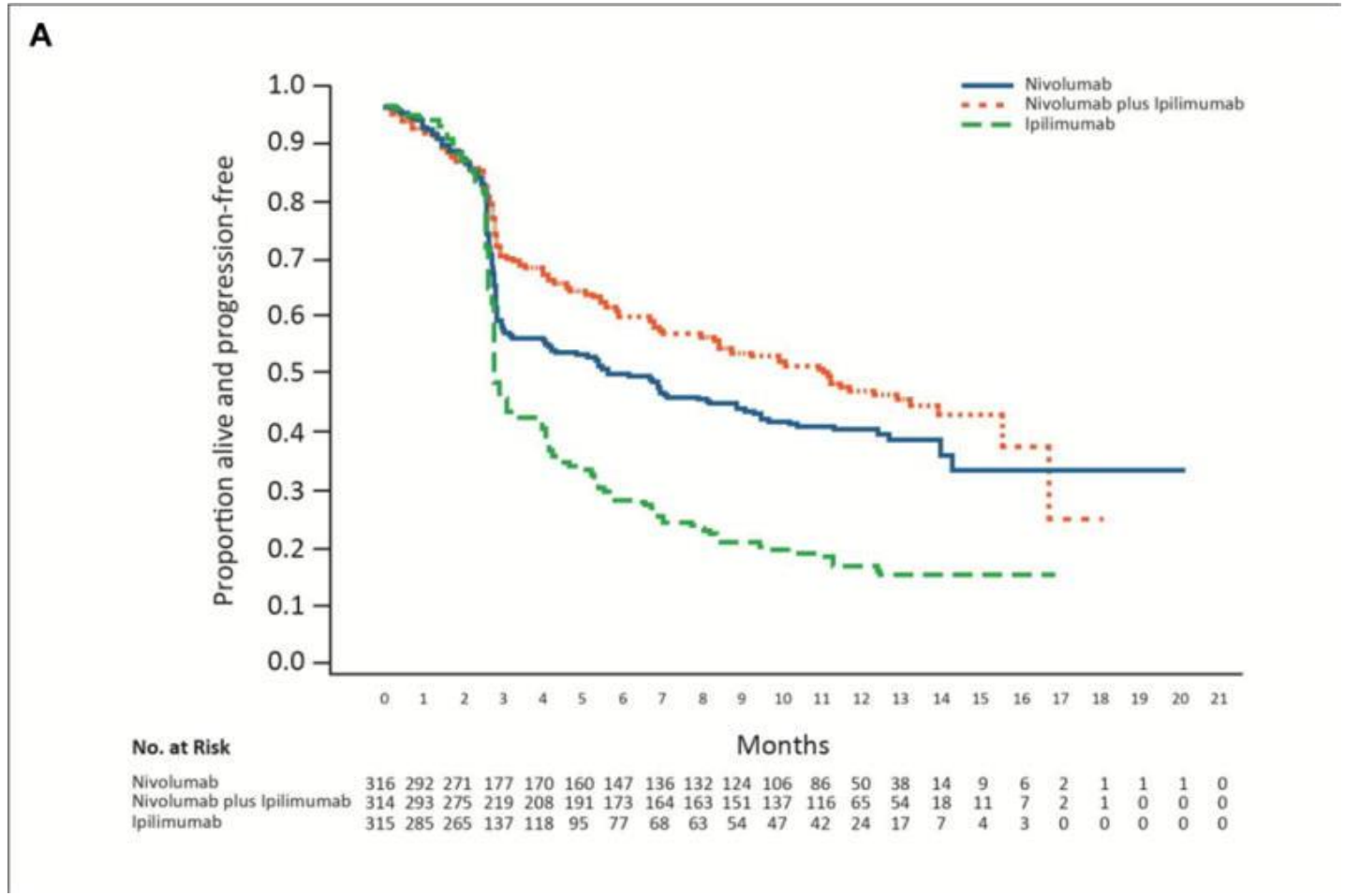
ESMO 2024

Wichtig zu wissen

• Analkarzinom	
• Lungenkarzinom	
• Magenkarzinom	N Engl J Med
• Mammakarzinom	N Engl J Med
• Melanom	N Engl J Med
• Prostatakarzinom	
• Neuroendokrine Tumoren	N Engl J Med
• Tumorkachexie	N Engl J Med
• Urothelkarzinom	N Engl J Med
• Zervixkarzinom	Lancet

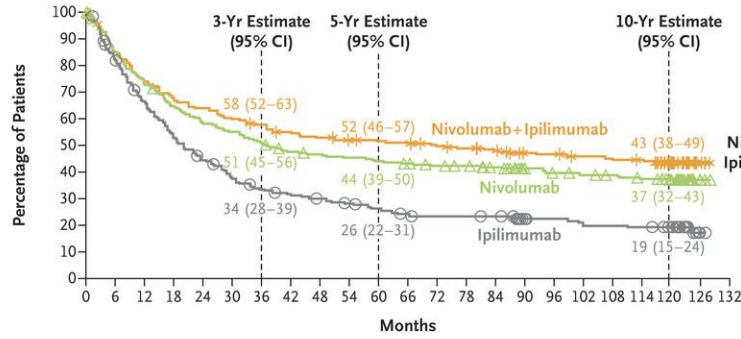

Immuncheckpoint-Inhibitoren
Erstdiagnose
Rezidiv primär metastasiert
Rezidiv Refraktärität
Refraktärität

Melanom, metastasiert



Larkin et al., NEJM 2015

A Overall Survival



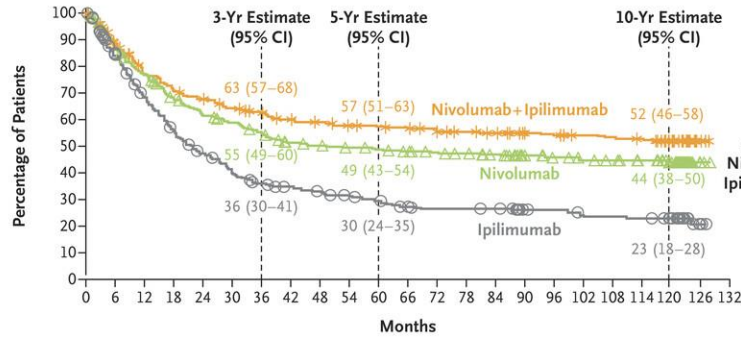
	No. of Patients with Event	Median Overall Survival (95% CI)
		mo
Nivo+Ipi (N=314)	173	71.9 (38.2–114.4)
Nivolumab (N=316)	192	36.9 (28.2–58.7)
Ipilimumab (N=315)	243	19.9 (16.8–24.6)

Hazard ratio for death, nivo+ipi vs. ipilimumab, 0.53 (95% CI, 0.44–0.65)
Hazard ratio for death, nivolumab vs. ipilimumab, 0.63 (95% CI, 0.52–0.76)
Hazard ratio for death, nivo+ipi vs. nivolumab, 0.85 (95% CI, 0.69–1.05)

No. at Risk

Nivo+ipi	314	265	227	210	199	187	179	169	163	158	156	153	147	144	139	126	124	120	117	115	92	10	0
Nivolumab	316	265	231	201	181	171	158	145	141	137	134	130	126	123	118	107	102	98	96	92	77	4	0
Ipilimumab	315	253	203	163	135	113	100	94	87	81	75	68	64	64	63	50	49	44	43	42	35	3	0

B Melanoma-Specific Survival



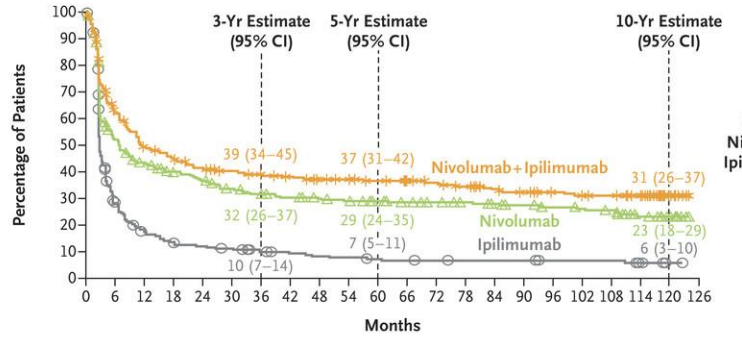
	No. of Patients with Event	Median Melanoma-Specific Survival (95% CI)
		mo
Nivo+Ipi (N=314)	139	NR (71.8–NR)
Nivolumab (N=316)	163	49.4 (35.1–119.4)
Ipilimumab (N=315)	221	21.9 (18.1–27.4)

Hazard ratio for death from melanoma, nivo+ipi vs. ipilimumab, 0.48 (95% CI, 0.39–0.59)
Hazard ratio for death from melanoma, nivolumab vs. ipilimumab, 0.59 (95% CI, 0.49–0.73)
Hazard ratio for death from melanoma, nivo+ipi vs. nivolumab, 0.81 (95% CI, 0.64–1.01)

No. at Risk

Nivo+ipi	314	265	227	210	199	187	179	169	163	158	156	153	147	144	139	126	124	120	117	115	92	10	0
Nivolumab	316	265	231	201	181	171	158	145	141	137	134	130	126	123	118	107	102	98	96	92	77	4	0
Ipilimumab	315	253	203	163	135	113	100	94	87	81	75	68	64	64	63	50	49	44	43	42	35	3	0

C Progression-free Survival



	No. of Patients with Event	Median Progression-free Survival (95% CI)
		mo
Nivo+Ipi (N=314)	192	11.5 (8.9–20.0)
Nivolumab (N=316)	212	6.9 (5.1–10.2)
Ipilimumab (N=315)	262	2.9 (2.8–3.1)

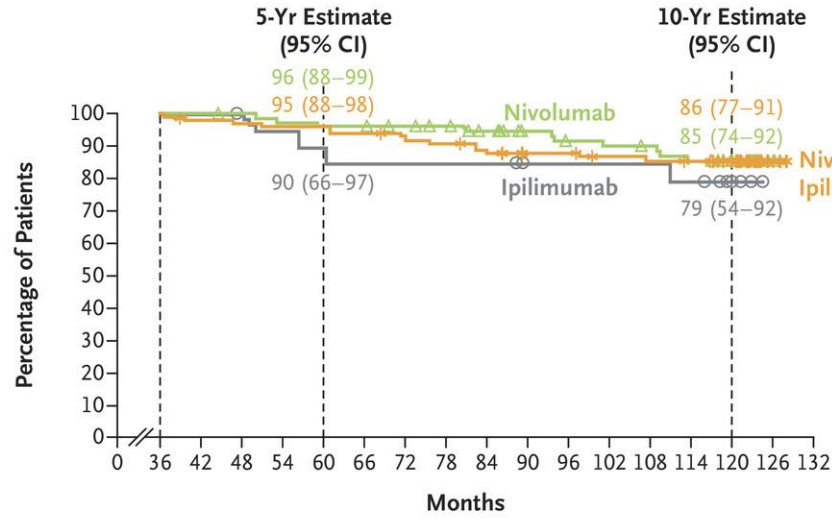
Hazard ratio for disease progression or death, nivo+ipi vs. ipilimumab, 0.42 (95% CI, 0.35–0.51)
Hazard ratio for disease progression or death, nivolumab vs. ipilimumab, 0.54 (95% CI, 0.45–0.65)
Hazard ratio for disease progression or death, nivo+ipi vs. nivolumab, 0.79 (95% CI, 0.65–0.96)

No. at Risk

Nivo+ipi	314	175	138	126	112	104	100	94	88	85	80	78	72	68	62	58	53	51	49	42	15	0	
Nivolumab	316	151	120	106	97	84	78	73	69	66	62	58	55	52	49	45	42	40	38	24	12	0	
Ipilimumab	315	78	46	34	31	28	21	18	16	15	13	12	11	10	10	10	8	8	8	4	1	0	

Wolchok et al., NEJM 2024

A Overall Survival among Patients Alive and Progression-free at 3 Yr

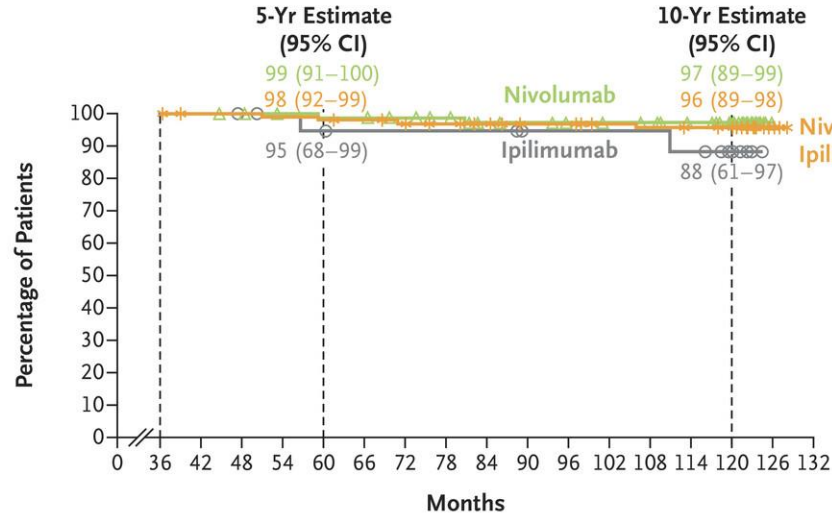


	No. of Patients with Event	Median Overall Survival (95% CI)
		mo
Nivo+Ipi (N=100)	14	NR
Nivolumab (N=78)	10	NR
Ipilimumab (N=21)	4	NR

No. at Risk

Nivo+ipi	314	100	97	96	95	94	93	91	89	85	80	80	77	76	75	61	6	0
Nivolumab	316	78	78	77	75	74	74	72	70	65	61	58	57	56	53	47	1	0
Ipilimumab.	315	21	21	20	19	18	17	17	17	17	15	15	15	15	14	10	0	0

B Melanoma-Specific Survival among Patients Alive and Progression-free at 3 Yr



	No. of Patients with Event	Median Melanoma-Specific Survival (95% CI)
		mo
Nivo+Ipi (N=100)	4	NR
Nivolumab (N=78)	2	NR
Ipilimumab (N=21)	2	NR

No. at Risk

Nivo+ipi	314	100	97	96	95	94	93	91	89	85	80	80	77	76	75	61	6	0
Nivolumab	316	78	78	77	75	74	74	72	70	65	61	58	57	56	53	47	1	0
Ipilimumab	315	21	21	20	19	18	17	17	17	17	15	15	15	15	14	10	0	0

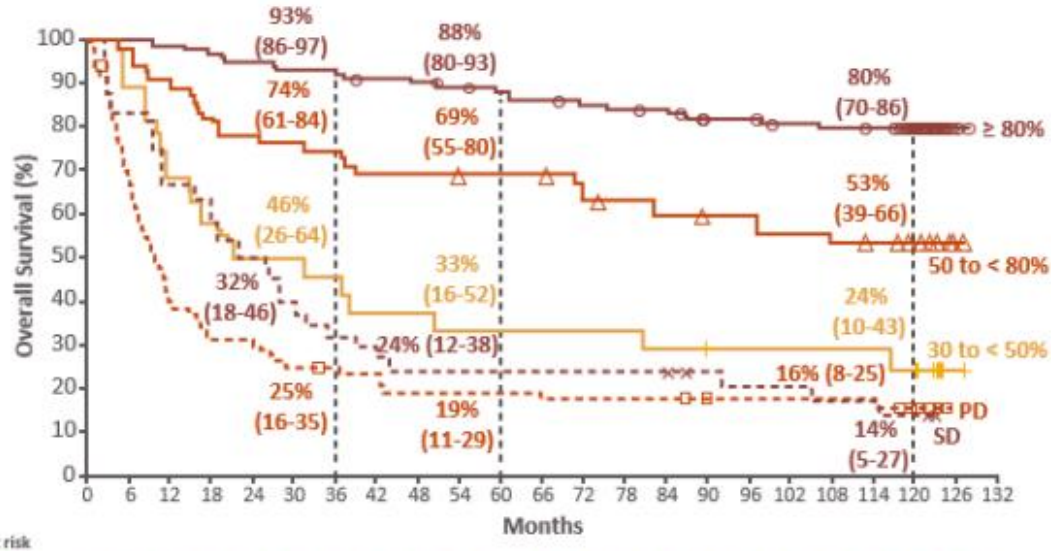
Wolchok et al., NEJM 2024

Melanom, metastasiert

B. Overall Survival by Best Depth of Response

NIVO + IPI

	≥ 80% (n = 102)	50 to < 80% (n = 55)	30 to < 50% (n = 24)	SD (n = 38)	PD (n = 74)
Events	20	25	18	32	61
Median, mo (95% CI)	NR	NR (72.1-NR)	27.0 (10.9-80.8)	23.7 (14.8-31.8)	10.0 (7.1-12.5)
HR vs SD/PD (95% CI)	0.16 (0.10-0.27)	0.23 (0.15-0.37)	0.54 (0.32-0.90)	—	—



No. at risk

≥ 80%	102	102	101	99	97	95	95	92	91	89	87	85	83	82	80	75	73	70	69	68	55	7	0
50 to < 80%	55	53	49	45	43	42	41	38	38	37	37	37	34	32	30	29	28	27	26	25	20	2	0
30 to < 50%	24	20	16	14	12	12	11	9	9	8	8	8	8	8	7	6	6	6	6	6	5	1	0
SD	38	34	26	24	19	15	12	11	9	9	9	9	9	9	9	7	6	6	5	5	4	0	0
PD	74	50	30	23	23	18	17	16	13	13	13	12	12	12	12	10	10	10	10	10	7	0	0

Wolchok et al., NEJM 2024

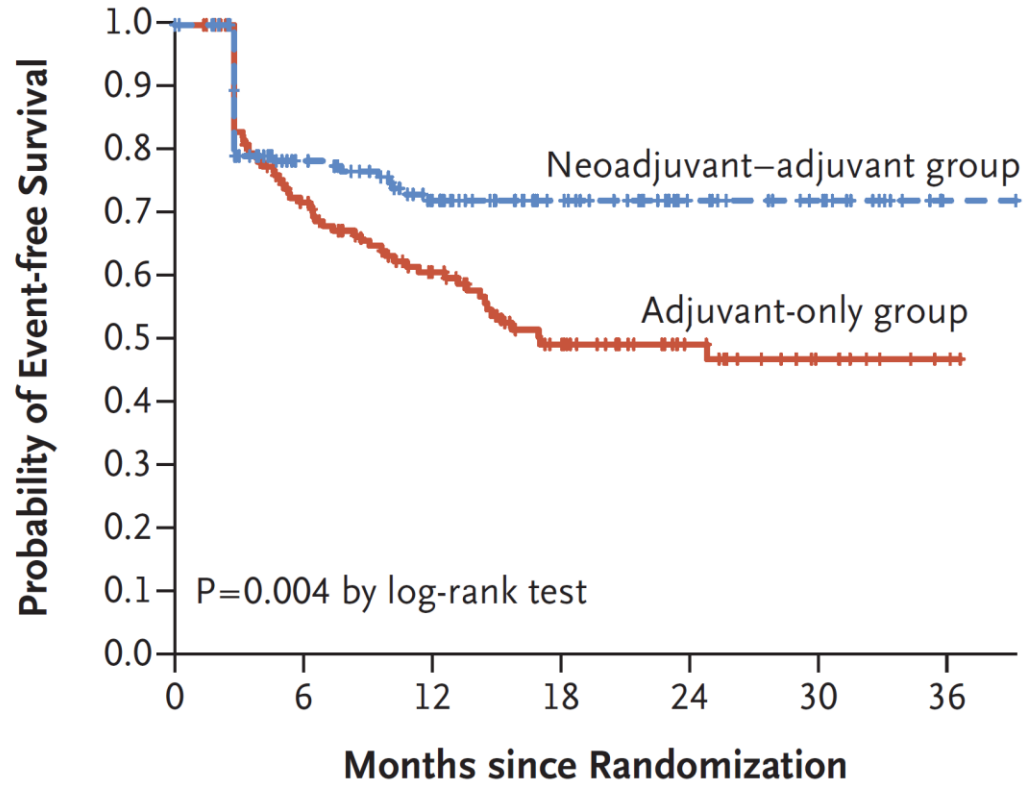
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

S.P. Patel, M. Othus, Y. Chen, G.P. Wright, Jr., K.J. Yost, J.R. Hyngstrom, S. Hu-Lieskovan, C.D. Lao, L.A. Fecher, T.-G. Truong, J.L. Eisenstein, S. Chandra, J.A. Sosman, K.L. Kendra, R.C. Wu, C.E. Devoe, G.B. Deutsch, A. Hegde, M. Khalil, A. Mangla, A.M. Reese, M.I. Ross, A.S. Poklepovic, G.Q. Phan, A.A. Onitilo, D.G. Yasar, B.C. Powers, G.C. Doolittle, G.K. In, N. Kokot, G.T. Gibney, M.B. Atkins, M. Shaheen, J.A. Warneke, A. Ikeguchi, J.E. Najera, B. Chmielowski, J.G. Crompton, J.D. Floyd, E. Hsueh, K.A. Margolin, W.A. Chow, K.F. Grossmann, E. Dietrich, V.G. Prieto, M.C. Lowe, E.I. Buchbinder, J.M. Kirkwood, L. Korde, J. Moon, E. Sharon, V.K. Sondak, and A. Ribas

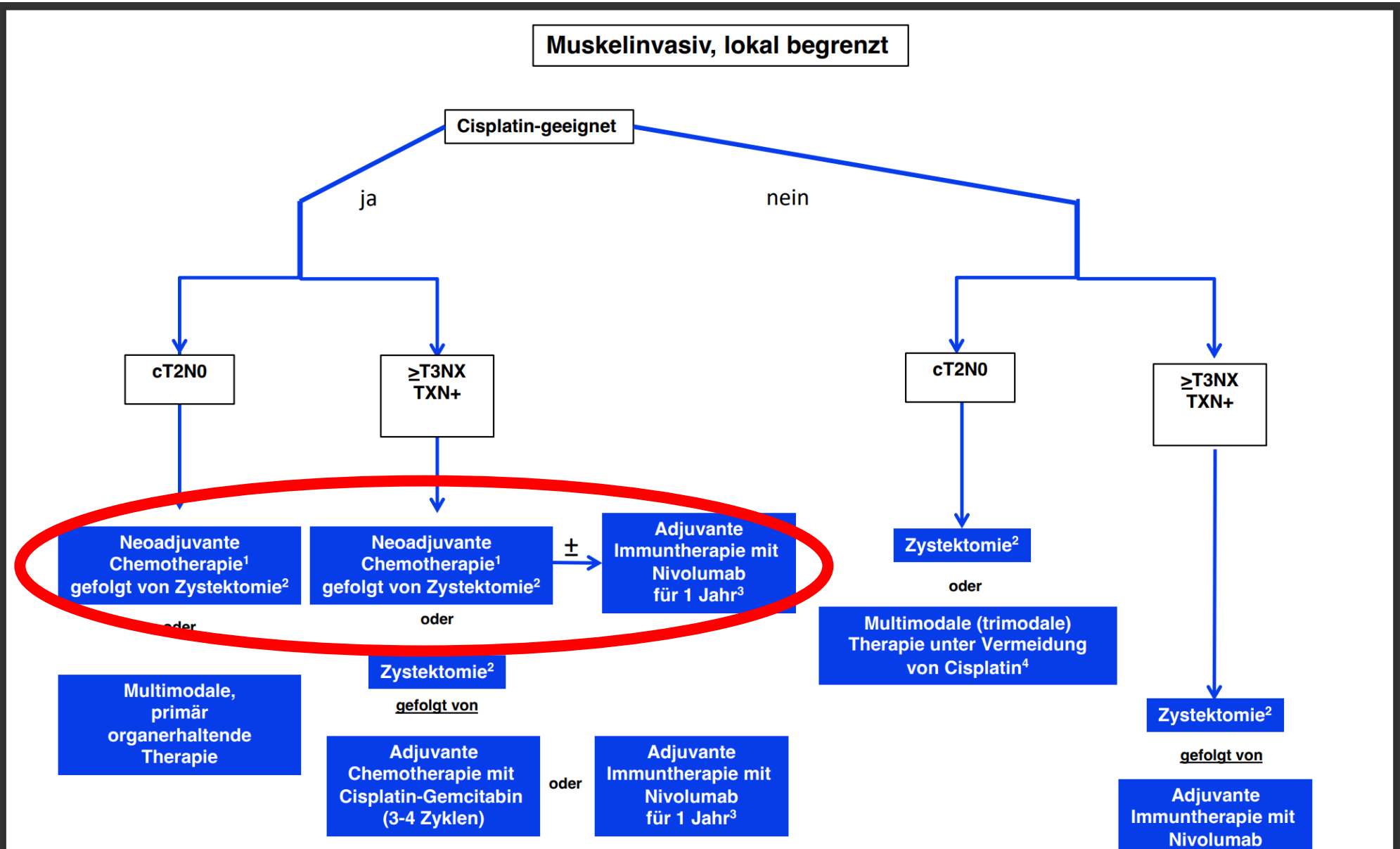
Stadium IIIB-IVC, resektabel



No. at Risk

Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

Urothelkarzinom, muskelinvasiv



BARCELONA 2024 ESMO congress

A Randomised Phase 3 Trial of Neoadjuvant Durvalumab Plus Chemotherapy Followed by Radical Cystectomy and Adjuvant Durvalumab in Muscle-invasive Bladder Cancer (NIAGARA)

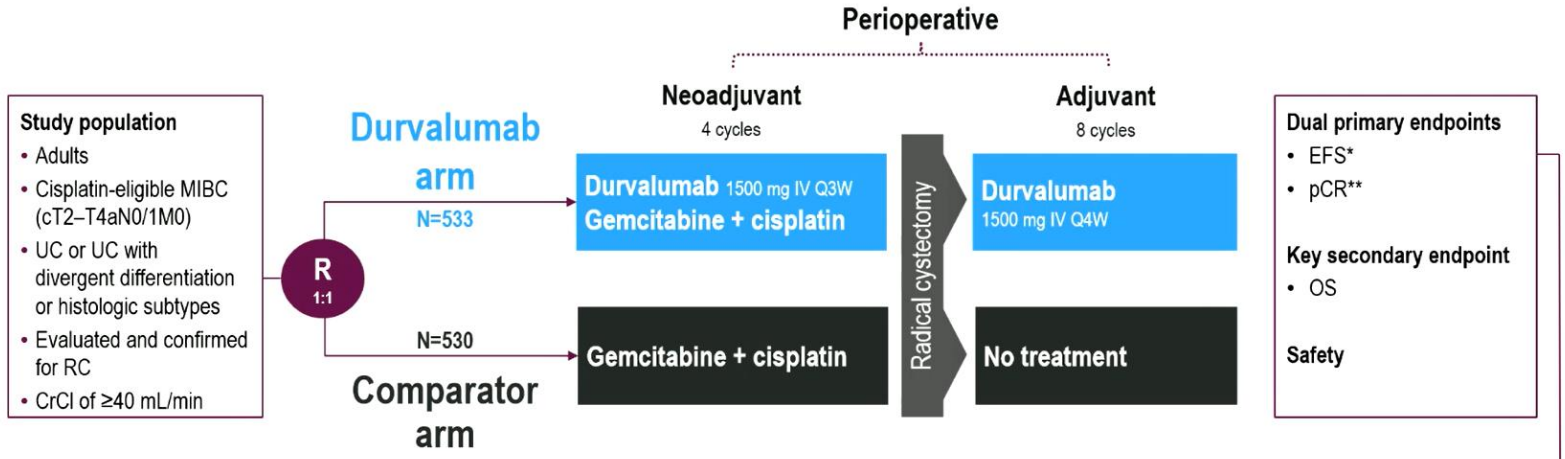
Thomas Powles,[1] Michiel S. van der Heijden,[2] Matthew D. Galsky,[3] Hikmat Al-Ahmadie,[4] Joshua J. Meeks,[5] Hiroyuki Nishiyama,[6] Toan Quang Vu,[7] Lorenzo Antonuzzo,[8] Paweł Wiechno,[9] Vagif Atduev,[10] Ariel G. Kann,[11] Tae-Hwan Kim,[12] Cristina Suarez,[13] Chao-Hsiang Chang,[14] Florian Roghmann,[15] Mustafa Özgüroğlu,[16] Jon Armstrong,[17] Svetlana Ho,[18] Stephan Hois,[18] James W. F. Catto[19]

[1]Barts Cancer Institute ECMC/BRC, Queen Mary University of London, Barts Health NHS Trust, London, UK; [2]Department of Medical Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]Memorial Sloan Kettering Cancer Center, Department of Pathology, New York, NY, USA; [5]Departments of Urology, Biochemistry and Molecular Genetics, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [6]Department of Urology, University of Tsukuba, Tsukuba, Japan; [7]Department of Internal Medicine 3, Vietnam National Cancer Hospital, Hanoi, Vietnam; [8]Sodc Ematologia - Azienda Ospedaliera - Universitaria Careggi, Florence, Italy; [9]Department of Uro-oncology, Maria Sklodowska-Cune National Research Institute of Oncology, Warsaw, Poland; [10]Volga District Medical Center, Federal Medical-Biological Agency, Nizhny Novgorod, Russia; [11]Clinical Oncology, Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; [12]Department of Urology, Kyungpook National University Chilgok Hospital, Daegu, Korea; [13]Vall d'Hebron Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain; [14]Department of Urology and School of Medicine, China Medical University and Hospital, Taichung, Taiwan; [15]Department of Urology, University Hospital of Ruhr-University Bochum, Marien Hospital, Herne, Germany; [16]Cerrahpaşa School of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye; [17]AstraZeneca, Cambridge, UK; [18]AstraZeneca, Gaithersburg, MD, USA; [19]University of Sheffield, Sheffield, UK

LBA5

Presenter: Thomas Powles, MBBS, MRCP, MD, London, UK

NIAGARA: Study Design



Stratification factors

Clinical tumour stage (T2N0 vs >T2N0)

Renal function (CrCl ≥60 mL/min vs ≥40–<60 mL/min)

PD-L1 status (high vs low/negative expression)

Gemcitabine/cisplatin dosing

CrCl ≥60 mL/min: Cisplatin 70 mg/m^2 + gemcitabine 1000 mg/m^2 Day 1, then gemcitabine 1000 mg/m^2 Day 8, Q3W for 4 cycles

CrCl ≥40–<60 mL/min: Split-dose cisplatin 35 mg/m^2 + gemcitabine 1000 mg/m^2 Days 1 and 8, Q3W for 4 cycles

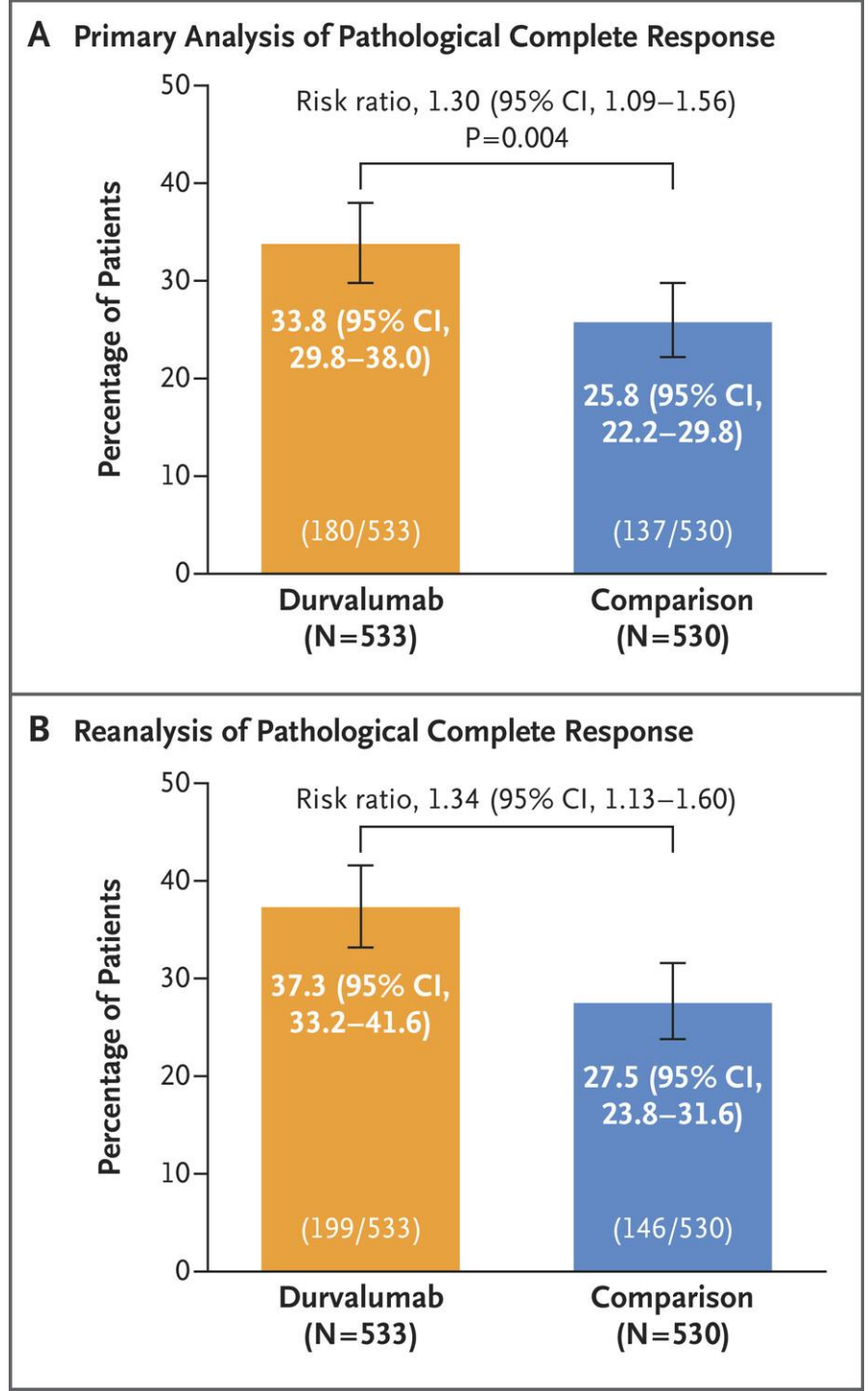
EFS was defined as:

- Progressive disease that precluded RC
- Recurrence after RC
- Date of expected surgery in patients who did not undergo RC
- Death from any cause

Other endpoints (not reported here): DFS, DSS, MFS, HRQoL, 5-year OS

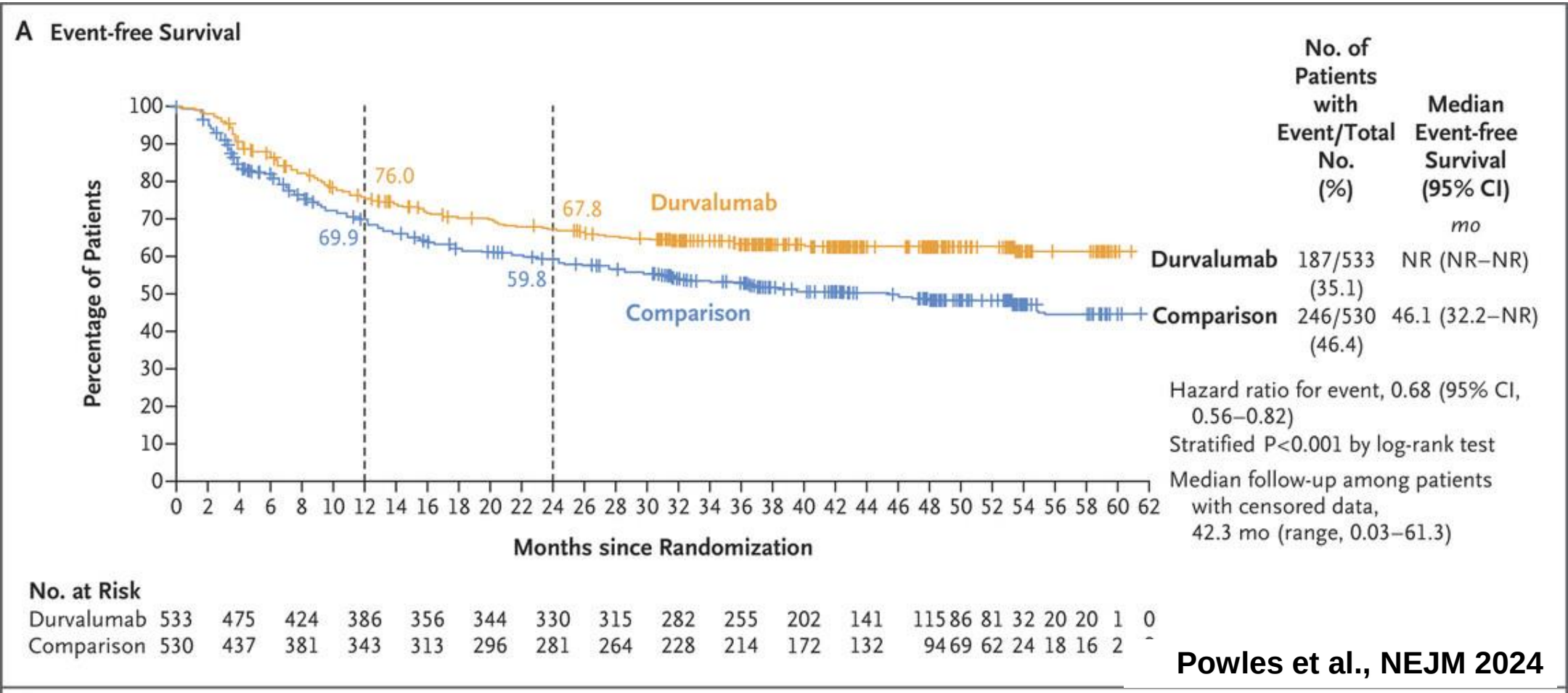
*Evaluated by blinded independent central review or central pathology review (if a biopsy was required for a suspected new lesion). **Evaluated by blinded central pathology review.

ClinicalTrials.gov, NCT03732677; EudraCT number, 2018-001811-59. CrCl, creatinine clearance; DFS, disease-free survival; DSS, disease-specific survival; EFS, event-free survival; HRQoL, health-related quality of life; IV, intravenous; MFS, metastasis-free survival; MIBC, muscle-invasive bladder cancer; OS, overall survival; pCR, pathologic complete response; PD-L1, programmed cell death ligand-1; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomised; RC, radical cystectomy; UC, urothelial carcinoma.



Powles et al., NEJM 2024

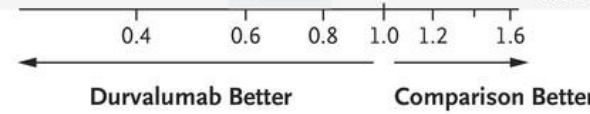
Urothelkarzinom, neoadjuvant



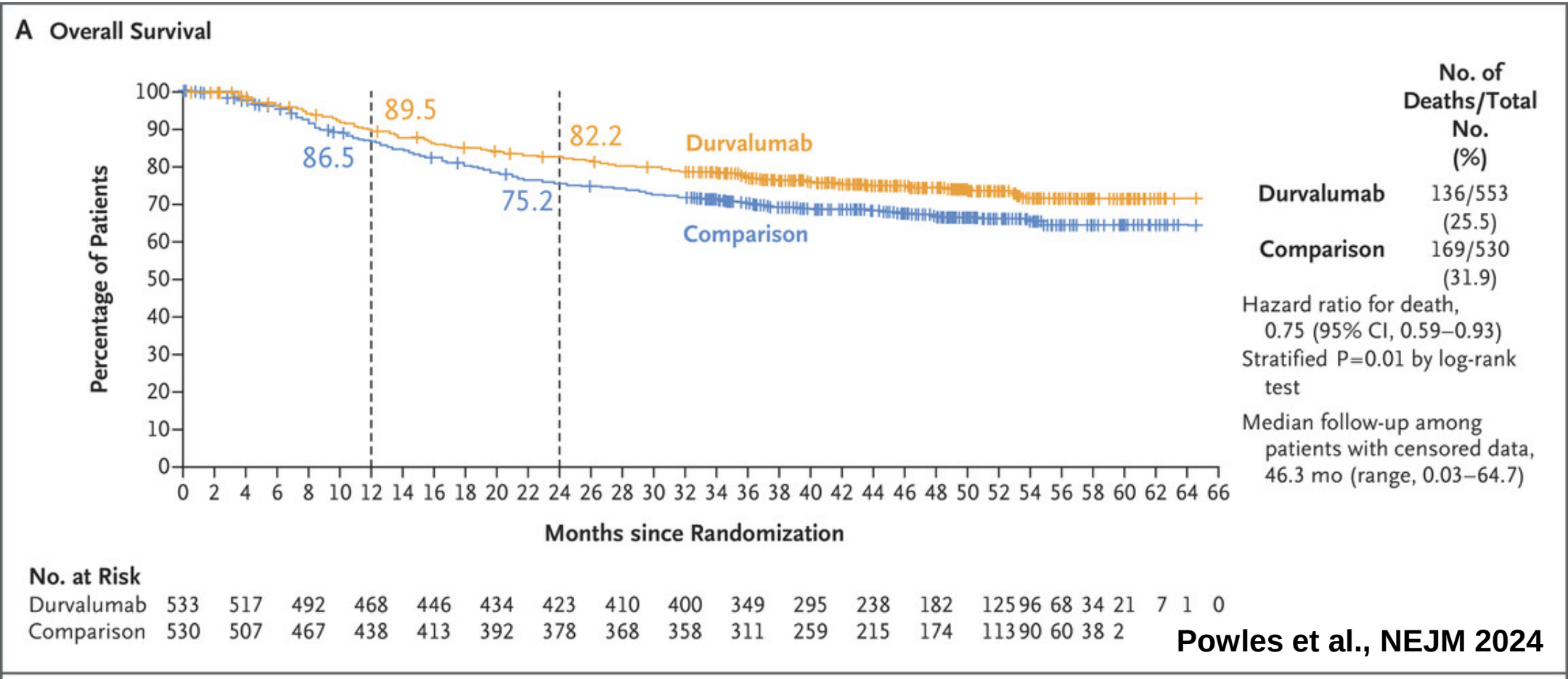
Powles et al., NEJM 2024

B Subgroup Analysis for Event-free Survival

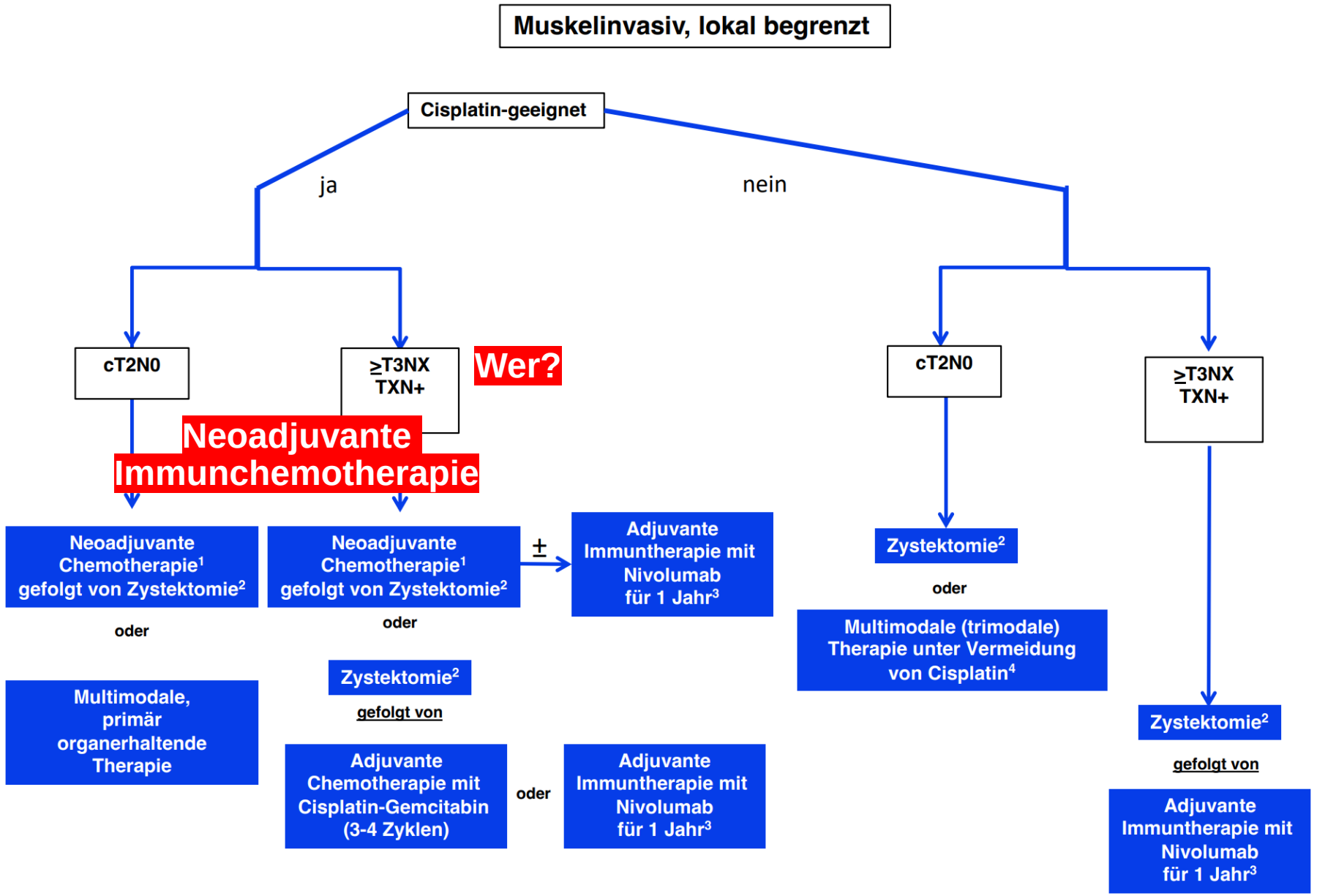
Subgroup	No. of Patients	Durvalumab	Comparison	Hazard Ratio for Event (95% CI)
		no. of patients with event/total no.		
All patients	1063	187/533	246/530	0.68 (0.56–0.82)
Age at randomization				
<65 yr	499	86/258	105/241	0.71 (0.53–0.94)
≥65 yr	564	101/275	141/289	0.67 (0.52–0.86)
Sex				
Male	870	157/437	199/433	0.71 (0.58–0.88)
Female	193	30/96	47/97	0.56 (0.35–0.88)
Race				
White	712	130/354	169/358	0.71 (0.56–0.89)
Non-White	315	54/165	67/150	0.65 (0.45–0.92)
Geographic region				
Asia	294	50/151	63/143	0.68 (0.46–0.98)
Europe	552	102/265	134/287	0.76 (0.58–0.98)
North America and Australia	128	17/66	27/62	0.50 (0.27–0.92)
South America	89	18/51	22/38	0.55 (0.29–1.03)
Histologic type at baseline				
Urothelial carcinoma	898	163/457	197/441	0.72 (0.58–0.89)
Urothelial carcinoma with divergent differentiation or histologic subtypes	165	24/76	49/89	0.52 (0.32–0.84)
Previous BCG therapy				
Yes	57	11/31	12/26	0.66 (0.29–1.51)
No	1006	176/502	234/504	0.68 (0.56–0.83)
Regional lymph-node stage at baseline				
N0	1005	176/505	232/500	0.68 (0.56–0.82)
N1	58	11/28	14/30	0.75 (0.33–1.64)
Tumor stage at baseline				
T2N0	428	78/215	88/213	0.81 (0.60–1.10)
Higher than T2N0	635	109/318	158/317	0.61 (0.48–0.78)
Creatinine clearance at baseline				
≥60 ml/min/1.73 m^2	862	141/432	189/430	0.68 (0.54–0.84)
40 to <60 ml/min/1.73 m^2	201	46/101	57/100	0.69 (0.46–1.01)
PD-L1 expression level at baseline				
High	777	129/389	168/388	0.70 (0.56–0.88)
Low or none	286	58/144	78/142	0.62 (0.44–0.87)

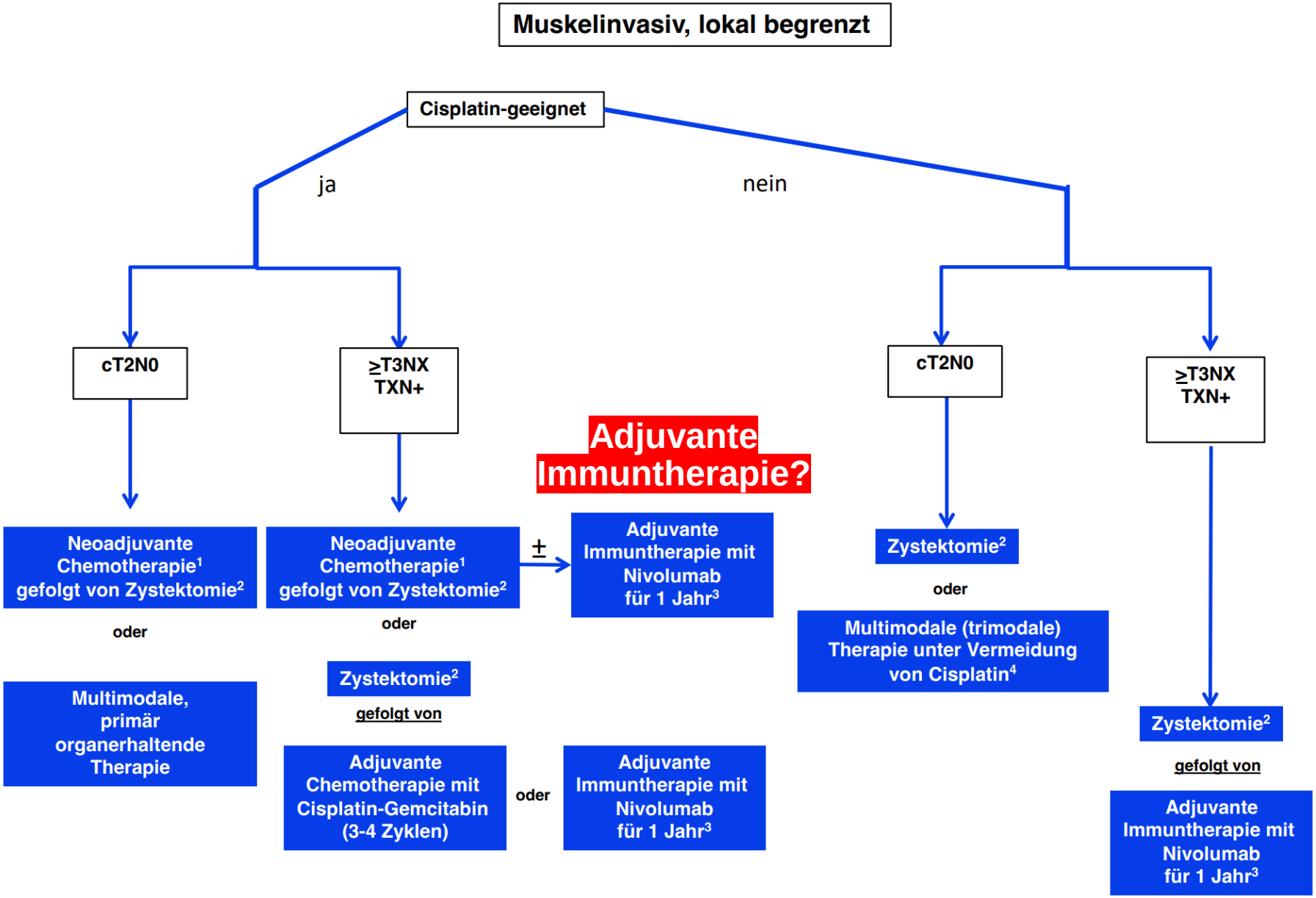


Urothelkarzinom, neoadjuvant



Powles et al., NEJM 2024


Muskelinvasiv, lokal begrenzt
Cisplatin-geeignet
ja
nein
cT2N0
≥T3NX TXN+
Wer?
Neoadjuvante Immunchemotherapie
cT2N0
≥T3NX TXN+
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
oder
Multimodale, primär organerhaltende Therapie
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
±
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]
oder
Zystektomie[2]
gefolgt von
Adjuvante Chemotherapie mit Cisplatin-Gemcitabin (3-4 Zyklen)
oder
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]
Zystektomie[2]
oder
Multimodale (trimodale) Therapie unter Vermeidung von Cisplatin[4]
Zystektomie[2]
gefolgt von
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]


Muskelinvasiv, lokal begrenzt
Cisplatin-geeignet
ja
nein
cT2N0
≥T3NX TXN+
cT2N0
≥T3NX TXN+
Adjuvante Immuntherapie?
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
oder
Multimodale, primär organerhaltende Therapie
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
±
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Zystektomie[2]
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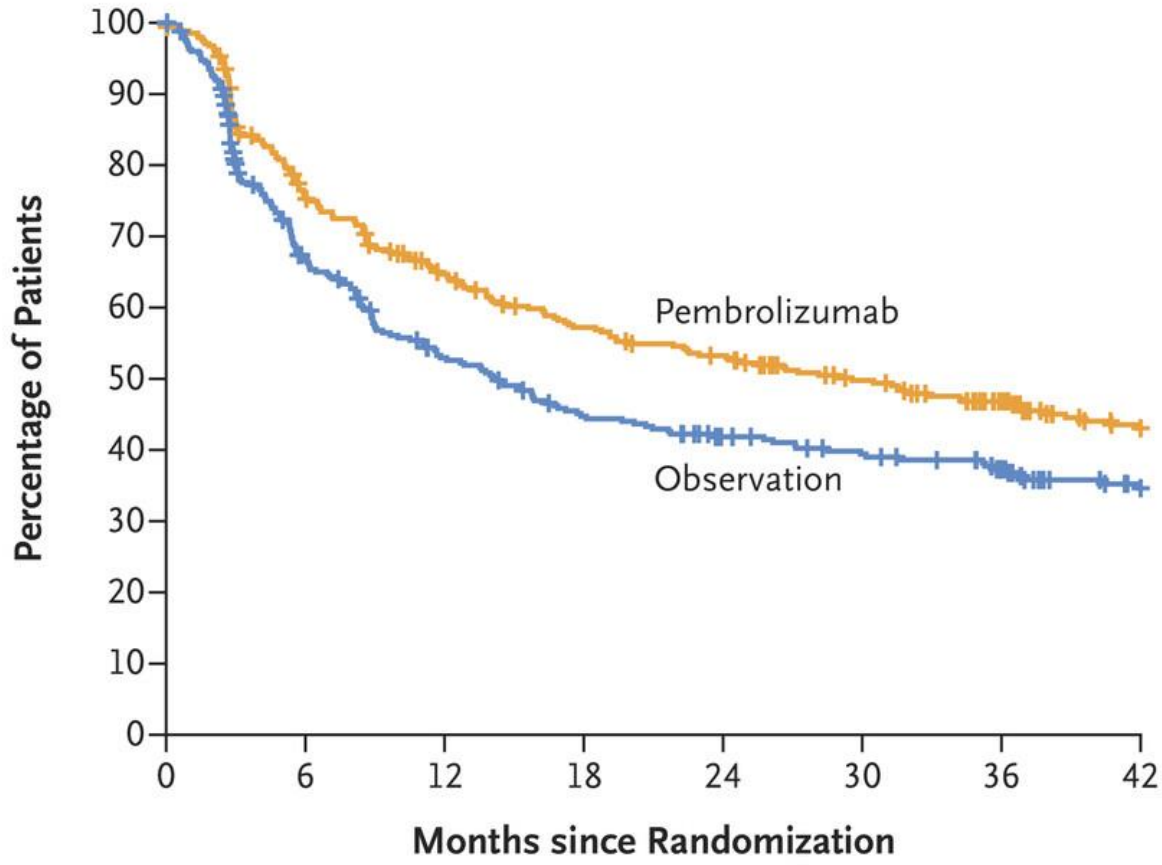
Zystektomie[2]
gefolgt von
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]

Urothelkarzinom, adjuvant



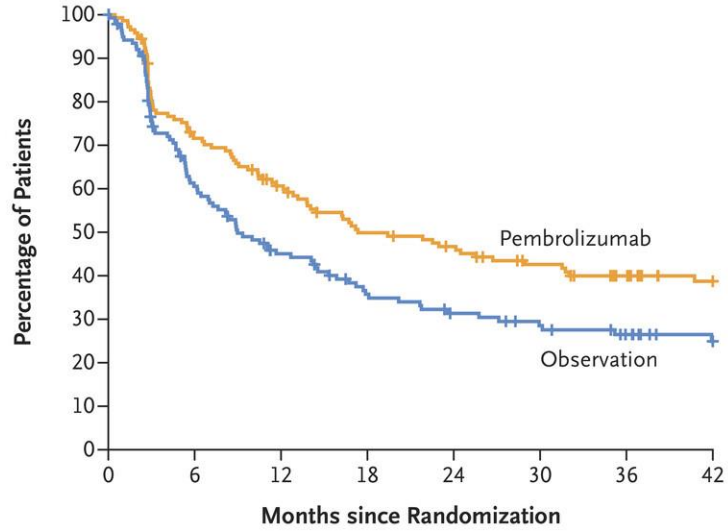
No. at Risk								
Pembrolizumab	354	247	202	174	159	137	114	85
Observation	348	198	150	124	107	96	81	58

	No. of Events/ Total No. of Patients	Median Disease-free Survival (95% CI)
		mo
Pembrolizumab	185/354	29.6 (20.0–40.7)
Observation	194/348	14.2 (11.0–20.2)

Hazard ratio for disease progression or death, 0.73 (95% CI, 0.59–0.90)
Stratified P=0.003 by log-rank test

Apolo et al., NEJM 2024

A Disease-free Survival, PD-L1 Negative

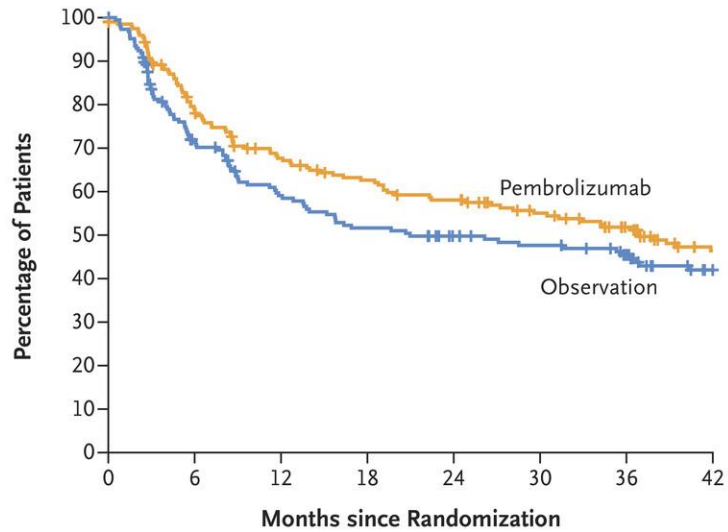


No. at Risk								
Pembrolizumab	151	99	80	64	58	49	40	31
Observation	147	79	55	41	34	29	23	16

	No. of Events/ Total No. of Patients	Median Disease-free Survival (95% CI)
		mo
Pembrolizumab	89/151	17.3 (13.2–32.0)
Observation	97/147	9.0 (6.9–15.3)

Hazard ratio for disease progression or death, 0.71 (95% CI, 0.53–0.95)

B Disease-free Survival, PD-L1 Positive



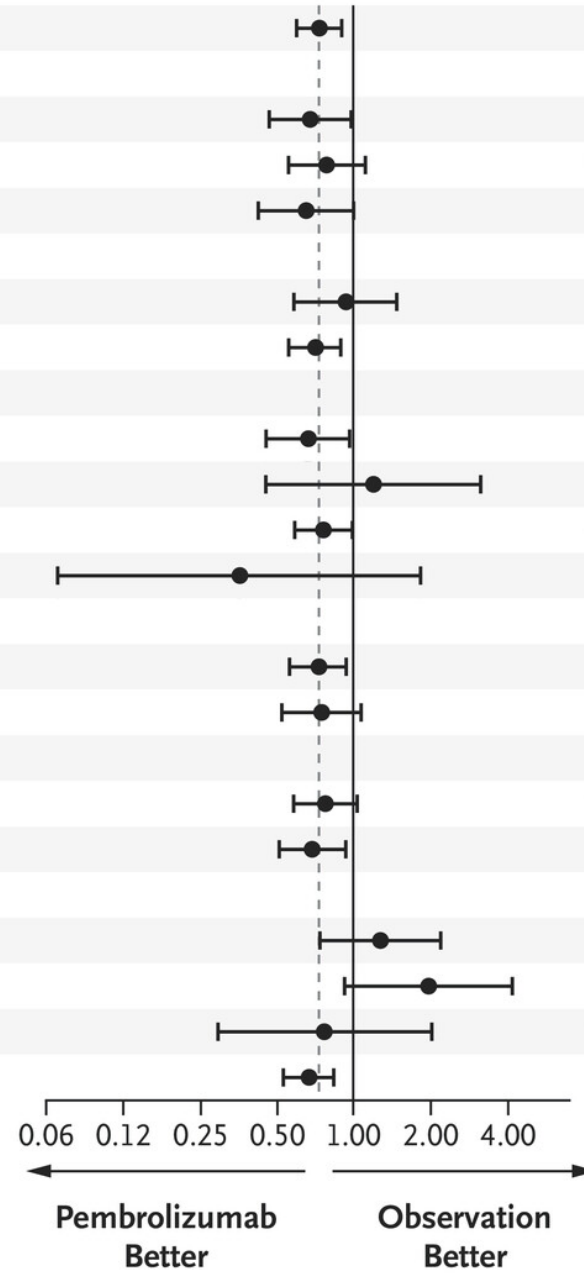
No. at Risk								
Pembrolizumab	203	148	122	110	101	88	74	54
Observation	201	119	95	83	73	67	58	42

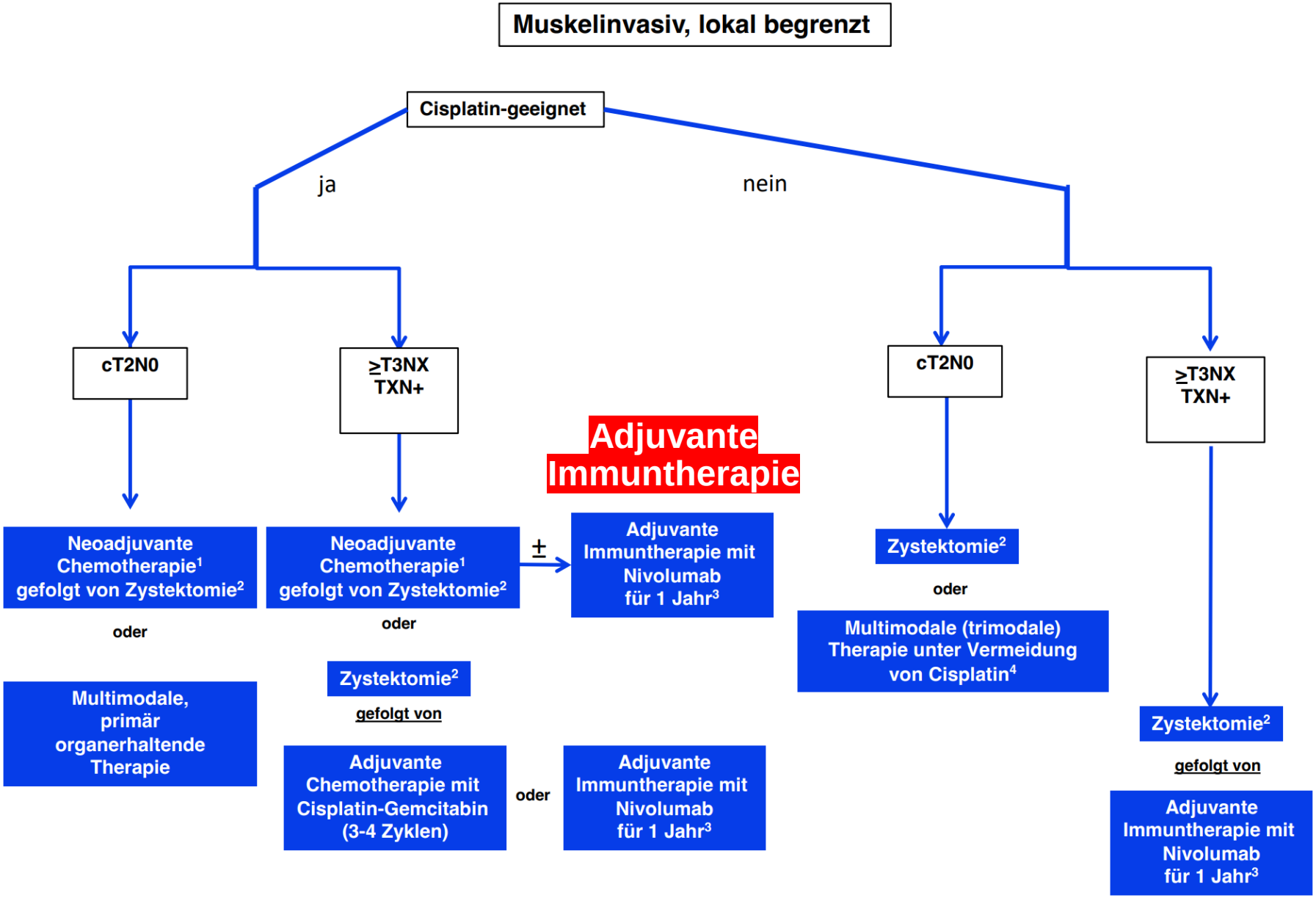
	No. of Events/ Total No. of Patients	Median Disease-free Survival (95% CI)
		mo
Pembrolizumab	96/203	36.9 (27.2–NE)
Observation	97/201	21.0 (13.6–53.3)

Hazard ratio for disease progression or death, 0.81 (95% CI, 0.61–1.08)

Apolo et al., NEJM 2024

Subgroup	Pembrolizumab	Observation	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/total no.		
All patients	185/354	194/348	0.73 (0.59–0.90)
Age			
<65 yr	60/120	63/125	0.67 (0.47–0.97)
65–75 yr	82/145	70/135	0.78 (0.55–1.10)
>75 yr	43/89	61/88	0.65 (0.42–1.00)
Sex			
Female	39/83	44/95	0.92 (0.58–1.47)
Male	146/271	150/253	0.70 (0.56–0.89)
Pathological stage			
pT2/3N0 or NX	49/146	62/150	0.66 (0.45–0.96)
pT4N0 or NX	11/19	10/20	1.19 (0.45–3.14)
Any pT or any N+	117/180	115/170	0.76 (0.58–0.98)
Positive surgical margins	8/9	7/8	0.36 (0.07–1.82)
Previous neoadjuvant therapy			
Yes	120/229	125/218	0.72 (0.56–0.93)
No	65/125	69/130	0.75 (0.53–1.06)
PD-L1 status			
Positive	96/203	97/201	0.77 (0.58–1.03)
Negative	89/151	97/147	0.69 (0.51–0.92)
Primary tumor site			
Upper tract	36/81	27/73	1.27 (0.74–2.18)
Renal pelvis	26/53	11/40	1.96 (0.92–4.17)
Ureter	10/28	16/33	0.77 (0.29–2.02)
Lower tract	149/273	167/275	0.66 (0.53–0.83)




Muskelinvasiv, lokal begrenzt
Cisplatin-geeignet
ja
nein
cT2N0
≥T3NX TXN+
cT2N0
≥T3NX TXN+
Adjuvante Immuntherapie
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
oder
Multimodale, primär organerhaltende Therapie
Neoadjuvante Chemotherapie[1] gefolgt von Zystektomie[2]
±
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]
oder
Zystektomie[2]
gefolgt von
Adjuvante Chemotherapie mit Cisplatin-Gemcitabin (3-4 Zyklen)
oder
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]
Zystektomie[2]
oder
Multimodale (trimodale) Therapie unter Vermeidung von Cisplatin[4]
Zystektomie[2]
gefolgt von
Adjuvante Immuntherapie mit Nivolumab für 1 Jahr[3]


CELEBRATING
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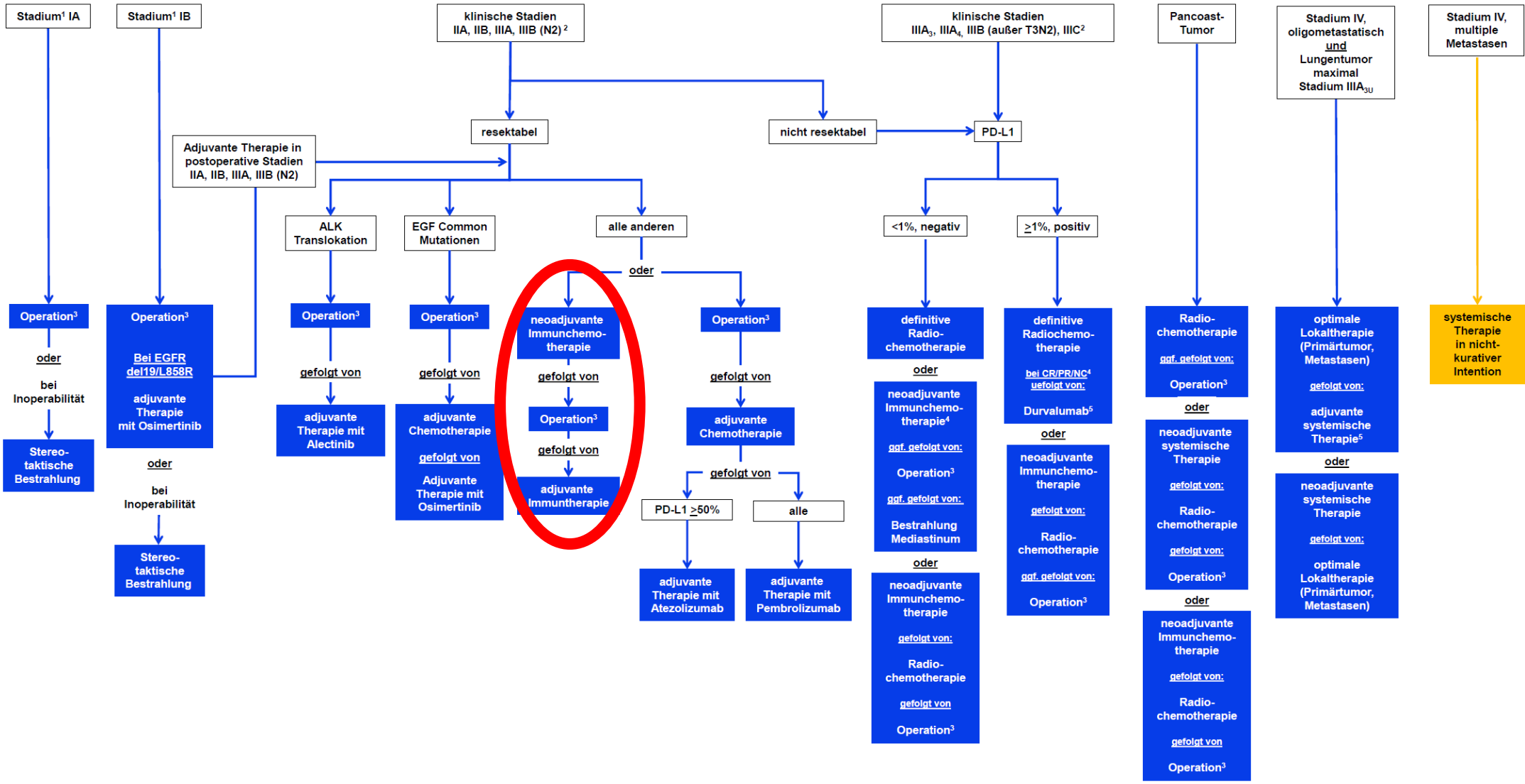
2024 World Conference on Lung Cancer
SEPTEMBER 7-10, 2024 | SAN DIEGO, CA USA

Lungenkarzinom, NSCLC



2024 World Conference on Lung Cancer
SEPTEMBER 7-10, 2024 | SAN DIEGO, CA USA

Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

Patrick M. Forde,[1] Solange Peters,[2] Jessica Donington,[3] Stephanie Meadows-Shropshire,[4] Phuong Tran,[4] Stefano Lucherini,[5] Cinthya Coronado Erdmann,[6] Hong Sun,[6] Tina Cascone[7]

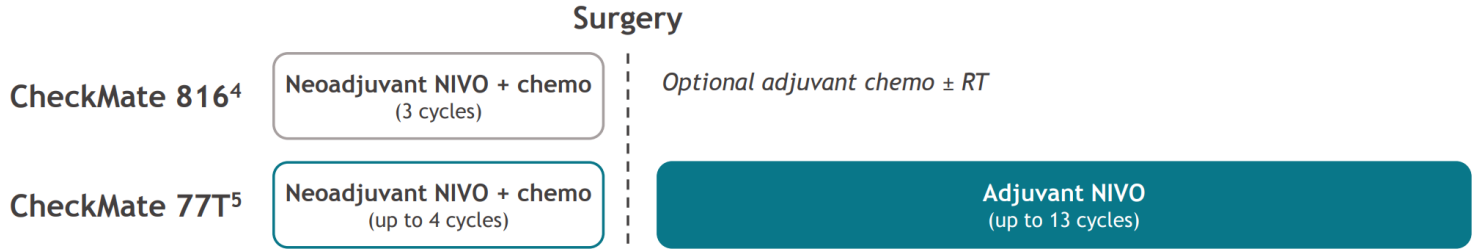
[1]The Bloomberg-Kimmel Institute for Cancer Immunotherapy, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medicine, Baltimore, MD, USA; [2]Lausanne University Hospital, Lausanne, Switzerland; [3]The University of Chicago, Chicago, IL, USA; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]Bristol Myers Squibb, Uxbridge, UK; [6]Bristol Myers Squibb, Boudry, Switzerland; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Presentation number 3589

Lungenkarzinom, NSCLC

Introduction

- NIVO + chemo is an approved and guideline-recommended neoadjuvant-only immunotherapy-containing regimen for eligible patients with resectable NSCLC[1-3]
  - EFS benefit was demonstrated vs neoadjuvant chemo (HR = 0.63[a])[4]
- Perioperative NIVO built on neoadjuvant NIVO + chemo and demonstrated significant EFS benefit vs placebo (HR = 0.58[b])[5]
- pCR rates with neoadjuvant NIVO + chemo were 24%–25%[4,5]

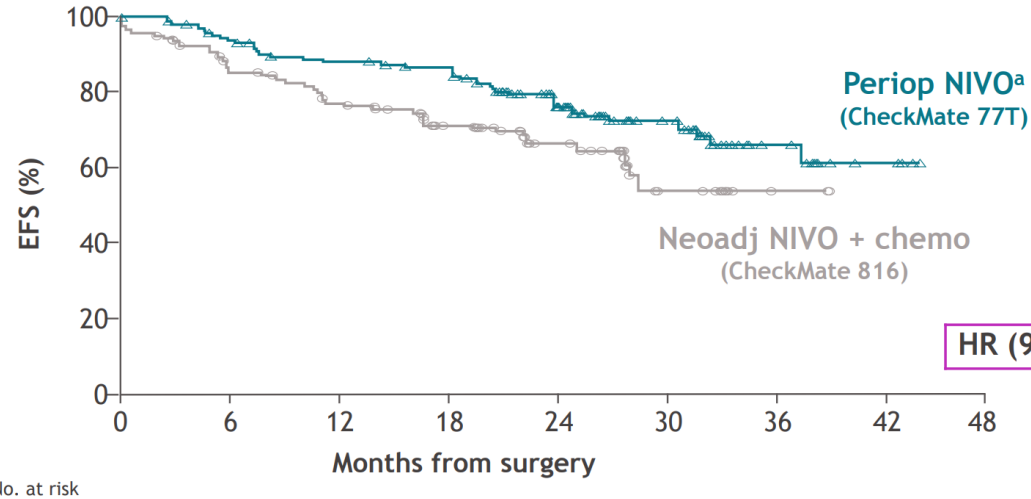


[a]97.38% CI, 0.43-0.91. [b]97.36% CI, 0.42-0.81.

1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; February 2023. 2. OPDIVO® (nivolumab) [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb Pharma EEIG; July 2023. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer. V7.2024. 4. Forde PM, et al. *N Engl J Med* 2022;386:1973–1985. 5. Cascone T, et al. *N Engl J Med* 2024;390:1756–1769.

Lungenkarzinom, NSCLC

Landmark EFS (BICR) from definitive surgery



No. at risk

Periop NIVO	139.4	128.0	118.1	112.9	79.7	42.5	13.0	3.1	0
Neoadj N+C	147.5	121.0	106.2	84.2	39.1	12.1	2.2	0	0

	Weighted (ATE)[b]	
	Periop NIVO[a] (n = 139.4[c])	Neoadj NIVO + chemo (n = 147.5[c])
HR (95% CI)	0.61 (0.39-0.97)	

- HR (95% CI): ATT[d] weighted analysis, 0.56 (0.35-0.90); unweighted analysis, 0.59 (0.38-0.92)

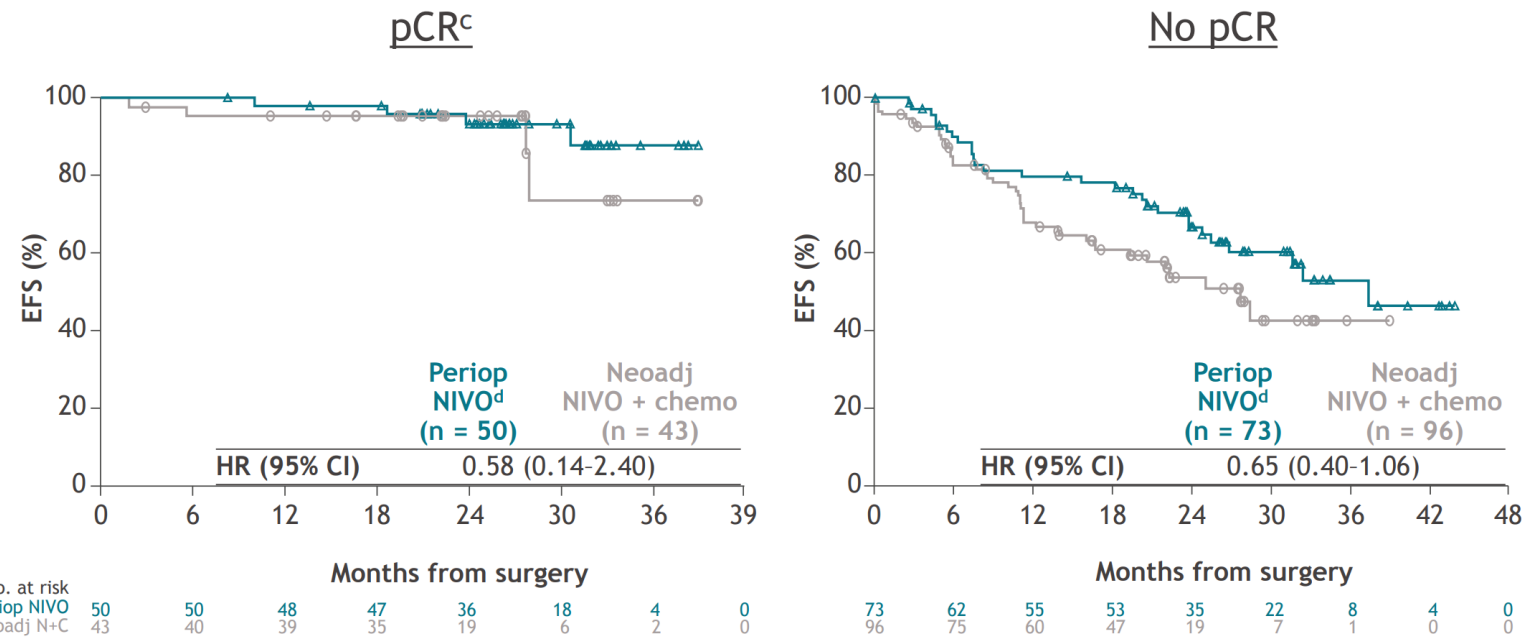
Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [b]ATE: varying weights were applied to all patients in both neoadjuvant NIVO + chemo arm (CheckMate 816) and perioperative NIVO (CheckMate 77T) to make them comparable to one another. [c]N values fractional due to weighting. [d]ATT: varying weights were applied to patients in the neoadjuvant NIVO + chemo arm (CheckMate 816) to make them comparable to those in the perioperative NIVO arm (CheckMate 77T).

In the unweighted analysis population, 89 patients (64%) completed adjuvant therapy, and median number of doses (range) was 13.0 (1-13). Unweighted landmark EFS from surgery among all patients who had surgery (regardless of whether they received adjuvant NIVO in CheckMate 77T) for periop NIVO vs neoadj NIVO + chemo: HR = 0.82 (95% CI, 0.55-1.21).

Lungenkarzinom, NSCLC

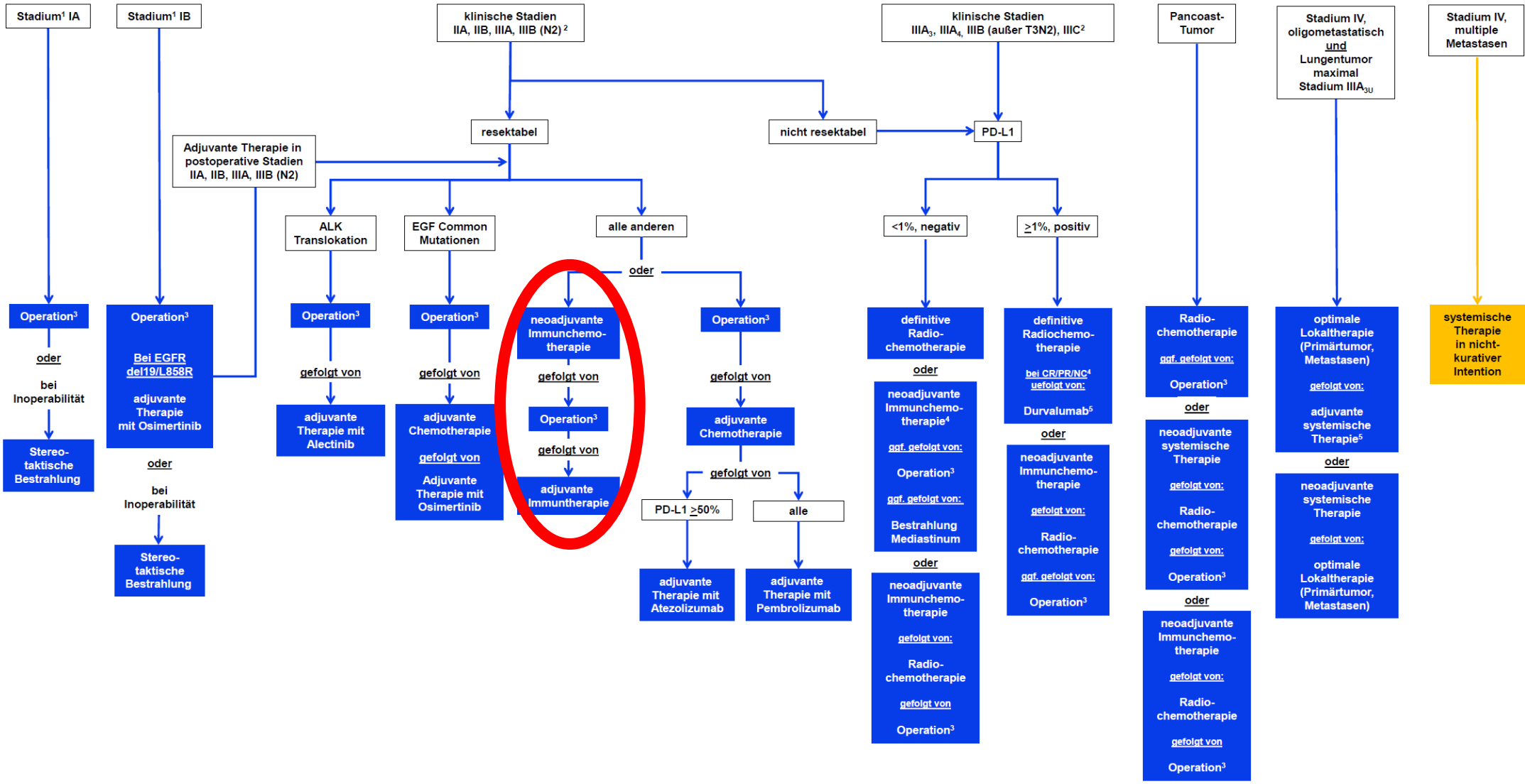
Perioperative vs neoadjuvant NIVO: Patient-level analysis

Landmark EFS[a] (analysis population) by pCR status[a,b]

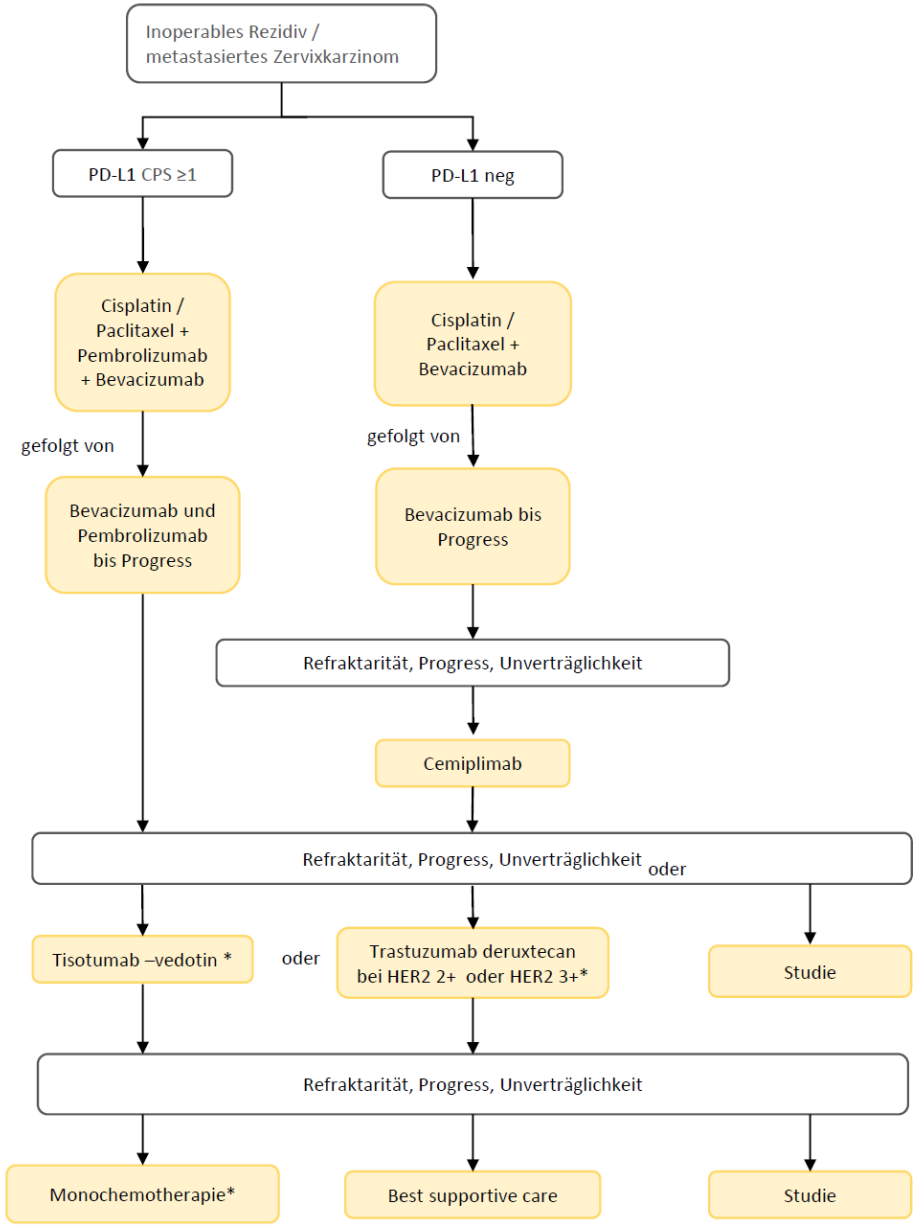


Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable pCR status were excluded. [b]Unweighted analyses.
[c]pCR rates in this analysis population: perioperative NIVO, 40.7%; neoadjuvant NIVO + chemo, 30.5%. [d]Includes only patients who received ≥ 1 dose of adjuvant NIVO.

Lungenkarzinom, NSCLC



Zervixkarzinom



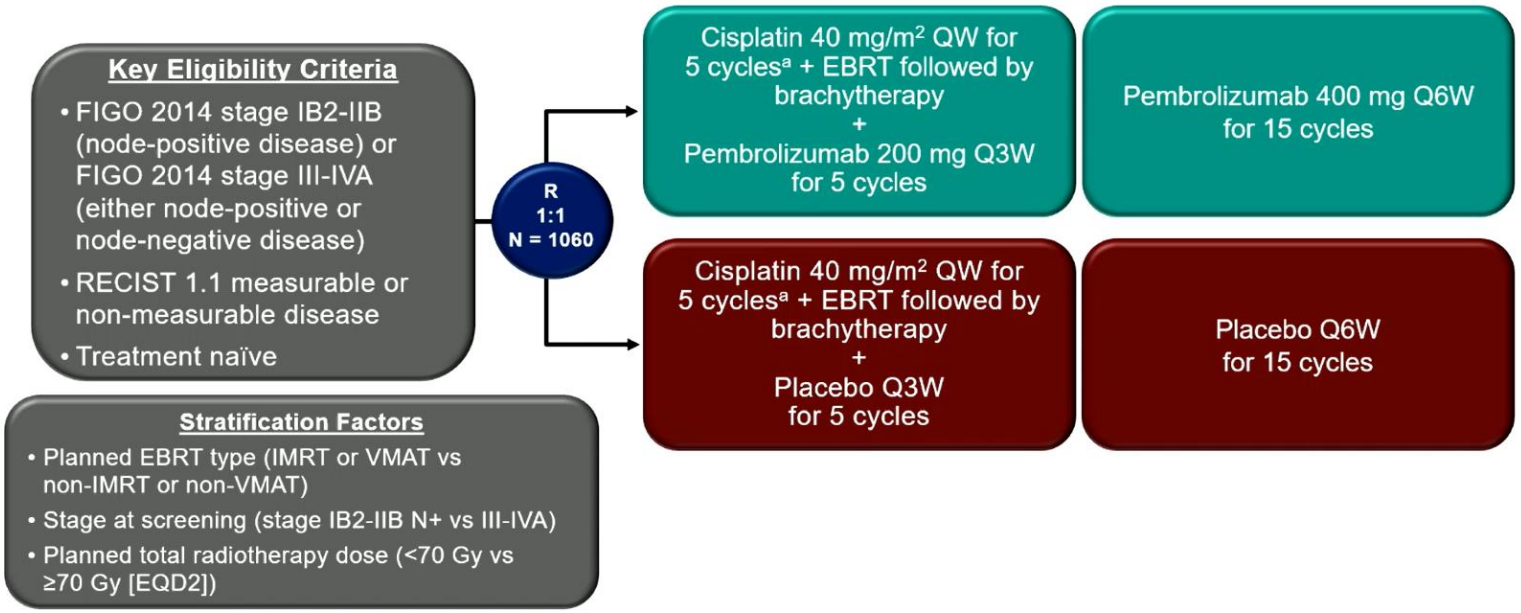
* Zulassungsstatus beachten, aktuell off-lable

Zervixkarzinom, lokal fortgeschritten

16:30 - 18:15 Presidential Symposium I: Practice-changing trials

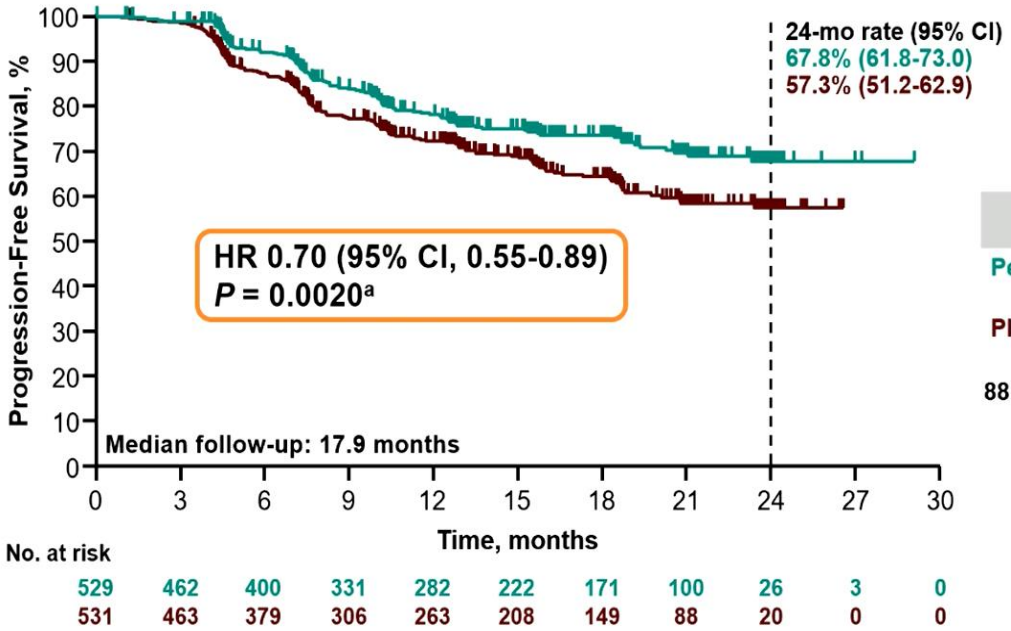
CHAIRS: ANDRES CERVANTES, KARIN JORDAN

ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study



[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Progression-Free Survival at IA1

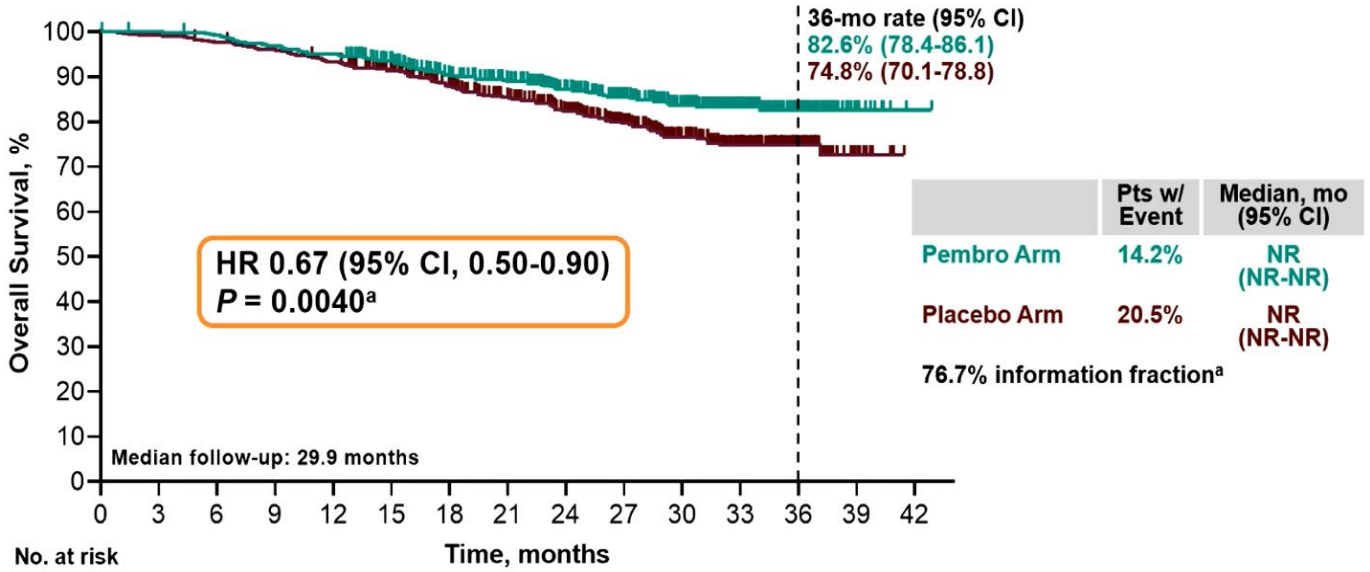


	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	21.7%	NR (NR-NR)
Placebo Arm	29.0%	NR (NR-NR)

88.5% information fraction[a]

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. [a]With 269 events (88.5% information fraction), the observed $P = 0.0020$ (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) at this planned first interim analysis. The success criterion of the PFS hypothesis was met, and thus no formal testing of PFS will be performed at a later analysis. Data cutoff date: January 9, 2023.

Primary Endpoint: Overall Survival at IA2



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	14.2%	NR (NR-NR)
Placebo Arm	20.5%	NR (NR-NR)

76.7% information fraction[a]

[a]With 184 of the 240 deaths expected at the final analysis (76.7% information fraction), the observed *P* = 0.0040 (1-sided) crossed the prespecified nominal boundary of 0·01026 (1-sided) at this planned second interim analysis. At this time, 66 patients had received immunotherapy as post-progression treatment, including 15/138 patients (10.9%) in the pembro arm and 51/193 patients (26.4%) in the placebo arm; of those, 10 (7.2%) and 41 (21.2%), respectively, had received pembro. Data cutoff date: January 8, 2024.

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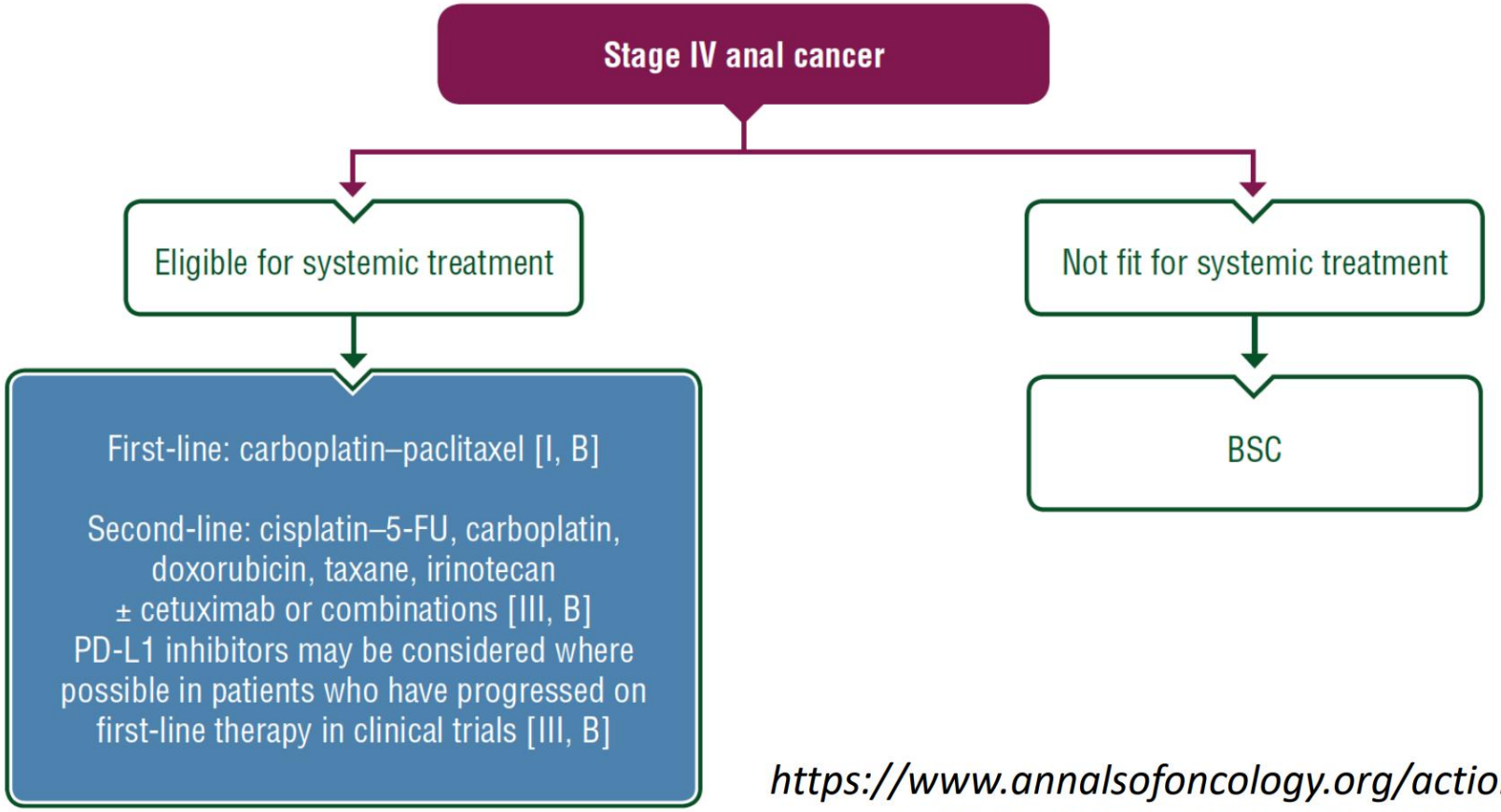
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up☆

S. Rao[1], M. G. Guren[2], K. Khan[3,4], G. Brown[5], A. G. Renehan[6], S. E. Steigen[7], E. Deutsch[8], E. Martinelli[9] & D. Arnold[10], on behalf of the ESMO Guidelines Committee*



https://www.annalsofoncology.org/action/showPdf?pii=S0923-7534%2821%2902064-0

Analkarzinom, lokal fortgeschritten/metastasiert

BARCELONA 2024 ESMO congress

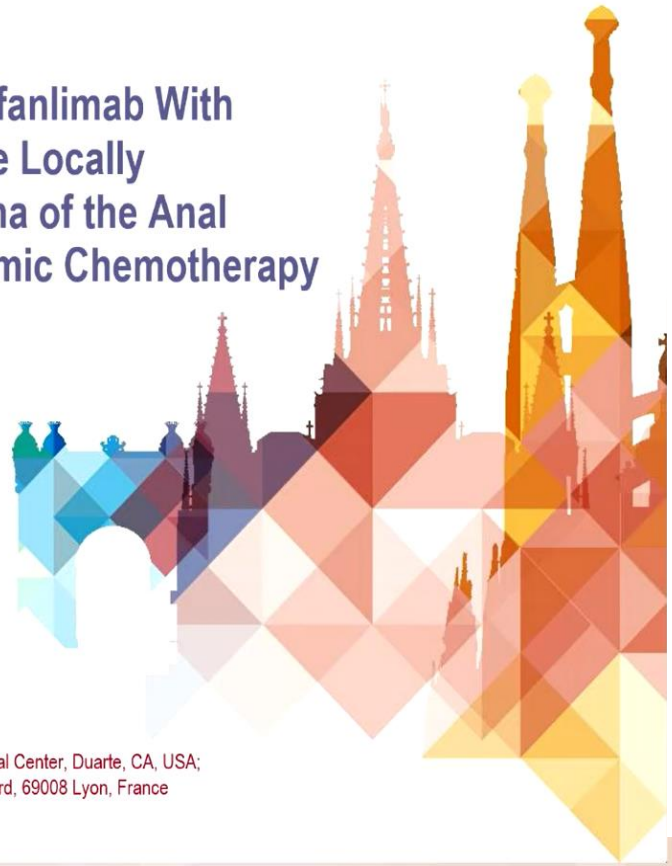
POD1UM-303/InterAACT 2: Phase 3 Study of Retifanlimab With Carboplatin-Paclitaxel in Patients With Inoperable Locally Recurrent or Metastatic Squamous Cell Carcinoma of the Anal Canal (SCAC) Not Previously Treated With Systemic Chemotherapy

Sheela Rao,[1,*] Emmanuelle Samalin-Scalzi,[2] Ludovic Evesque,[3] Meher Ben Abdelghani,[4] Federica Morano,[5] Amitesh Roy,[6] Laetitia Dahan,[7] Stefano Tamberi,[8] Amandeep (Singh) Dhadda,[9] Mark Saunders,[10] Nathalie Casanova,[11] Rosine Guimbaud,[12] Astrid Lievre,[13] Joan Maurel,[14] Marwan Fakih,[15] Peixin Zhang,[16] Jill Harrison,[16] Mark Jones,[16] Jean-Philippe Spano,[17,†] Pauline Rochefort[18,†]

*Corresponding author; †Co-senior authors

[1]Royal Marsden Hospital NHS Foundation Trust, Sutton, Surrey, UK; [2]Institut Régional du Cancer de Montpellier, 34090 Montpellier, France; [3]Centre Antoine Lacassagne, 06100 Nice, France; [4]Centre Paul Strauss, 67100 Strasbourg, France; [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [6]Flinders Medical Centre, Flinders University, Bedford Park, Adelaide, South Australia, Australia; [7]Hôpital de la Timone, Marseille, France; [8]Presidio Ospedaliero Ravenna–Ospedale Santa Maria delle Croci, Ravenna, Italy; [9]Castle Hill Hospital, Cottingham, UK; [10]The Christie Hospital, Manchester, UK; [11]Leeds Cancer Centre, Leeds, UK; [12]CHU de Toulouse, Toulouse, France; [13]CHU Rennes - Hopital Pontchaillou, 35000 Rennes, France; [14]Hospital Clinic de Barcelona, CIBEREHD, Barcelona, Spain; [15]City of Hope National Medical Center, Duarte, CA, USA; [16]Incyte Corporation, Wilmington, DE, USA; [17]Groupe Hospitalier Pitie-Salpetriere, Paris, France; [18]Centre Léon Bérard, 69008 Lyon, France

Abstract #5348



Analkarzinom, lokal fortgeschritten/metastasiert

Background

- Advanced SCAC is a neglected orphan disease; incidence is increasing ~3% per year mainly due to endemic HPV, the causative agent for most anogenital cancers[1-4]
  - HIV is an important amplifier of SCAC; people with HIV are 25- to 35-fold more likely to develop SCAC[5,6]
- Relapse after primary therapy (chemo-radiotherapy) is common; standard of care treatment has not changed since the early 1980s[7]
  - Prognosis is poor for patients who relapse or with de novo metastatic disease, and quality of life is greatly diminished[8]
- The InterAACT phase 2 study established carboplatin–paclitaxel as 1L treatment. Responses were meaningful and durable, but overall PFS (8 months) and OS (20 months) remained short[9]
- HPV-driven malignancy is an attractive target for immunotherapy approaches
  - Improved survival in head and neck squamous cell carcinoma[10] and cervical cancer[11] serve as proof of concept for SCAC
- Retifanlimab, a humanised anti–PD-1 monoclonal antibody, showed anti-tumour activity in platinum-refractory SCAC in the phase 2 POD1UM-202 study[12]
- The phase 3 POD1UM-303/InterAACT 2 study was designed to evaluate retifanlimab in combination with standard of care chemotherapy in patients with locally advanced or metastatic SCAC not previously treated with systemic therapy

1. Gondal TA, et al. *Curr Oncol*. 2023;30:3232-3250. **2.** Islami F, et al. *Int J Epidemiol*. 2017;46:924-938. **3.** Giuliano AR, et al. *Int J Cancer*. 2015;136:2752-2760. **4.** Morris V, Eng C. *J Gastrointest Oncol*. 2016;7:721-726. **5.** Wang C-CJ, et al. *Surg Oncol Clin N Am*. 2017;26:17-31. **6.** NCCN Clinical Practice Guidelines in Oncology: Cancer in People with HIV. Version 1.2021. 2021. **7.** Pessia B, et al. *Ann Med Surg (Lond)*. 2020;55:36-46. **8.** Rao S, et al. *Ann Oncol*. 2021;32:1087-1100. **9.** Rao S, et al. *J Clin Oncol*. 2020;38:2510-2518. **10.** Ferris RL, et al. *N Engl J Med*. 2016;375:1856-1867. **11.** Colombo N, et al. *N Engl J Med*. 2021;385:1856-1867. **12.** Rao S, et al. *ESMO Open*. 2022;7:100529.
1L, first-line; HIV, human immunodeficiency virus; HPV, human papillomavirus; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; SCAC, squamous cancer of the anal canal.

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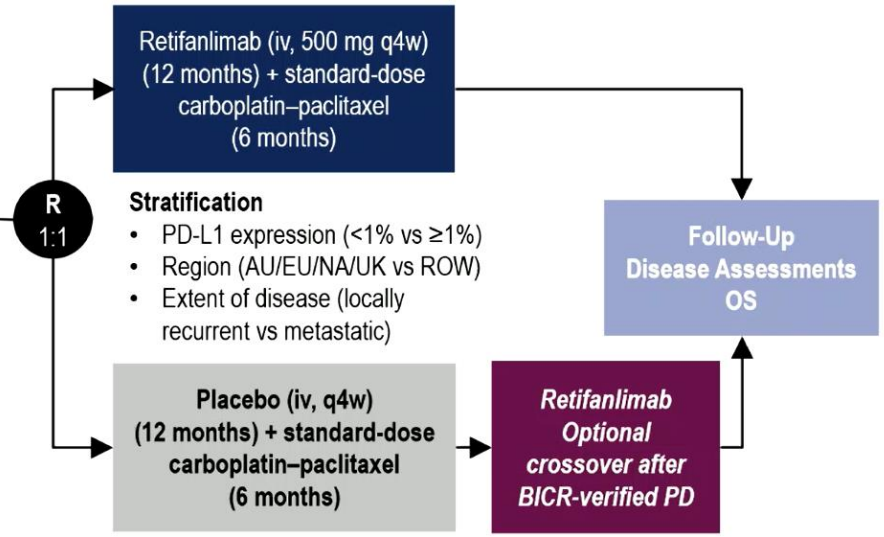
POD1UM-303/InterAACT 2 Study Design

Patients with locally recurrent or metastatic SCAC

- No prior chemotherapy except as radiosensitising treatment or (neo) adjuvant therapy ≥6 months prior to study entry
- Patients with HIV and well-controlled infection were eligible
- **Planned enrolment: N=300**

Study Endpoints	
Primary	PFS by BICR (HR=0.67 at >80% power, alpha=0.025 [1-sided])
Secondary	OS (key secondary, alpha=0.025 [1-sided] if PFS is statistically significant), ORR, DOR, safety, PK
Exploratory	PFS2, PROs, HIV control, immunogenicity



Standard-dose carboplatin–paclitaxel: carboplatin AUC5 iv: day 1. Paclitaxel 80 mg/m² iv: days 1, 8 and 15. Each cycle = 28 days. 6 months/24 weeks (6 cycles).
AU, Australia; AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; EU, European Union; HIV, human immunodeficiency virus; HR, hazard ratio; iv, intravenous; NA, North America; ORR, overall response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; q4w, every 4 weeks; R, randomisation; ROW, rest of the world; SCAC, squamous cancer of the anal canal; UK, United Kingdom.

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Patient Demographics and Characteristics (ITT Population)

Characteristic	Placebo + Carboplatin–Paclitaxel (n=154)	Retifanlimab + Carboplatin–Paclitaxel (n=154)
Median age, years	61	62
Female, %	77	68
White, %	89	86
Prior RT, %	73	68
Metastatic disease, %*	**83**	**82**
Liver, %	36	36
ECOG PS 0, %	56	53
HIV+, %	3	4
PD-L1 expression status ≥1, %*,†	**91**	**90**

*Stratification factor. †PD-L1 expression <1 also includes non-evaluable patients.
ECOG PS, Eastern Cooperative Oncology Group performance status; HIV+, human immunodeficiency virus positive; ITT, intention-to-treat; PD-L1, programmed cell death ligand 1; RT, radiotherapy.

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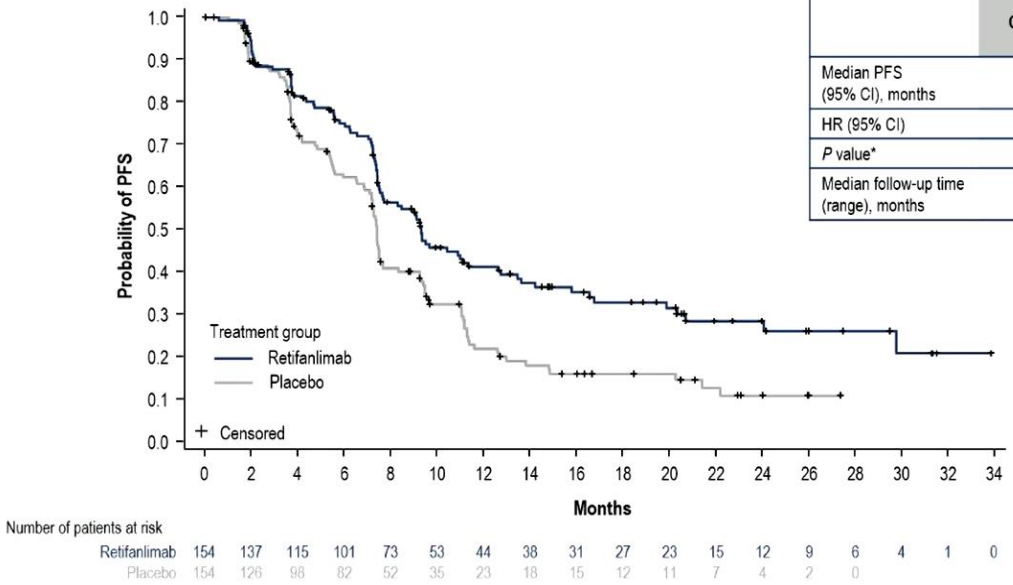
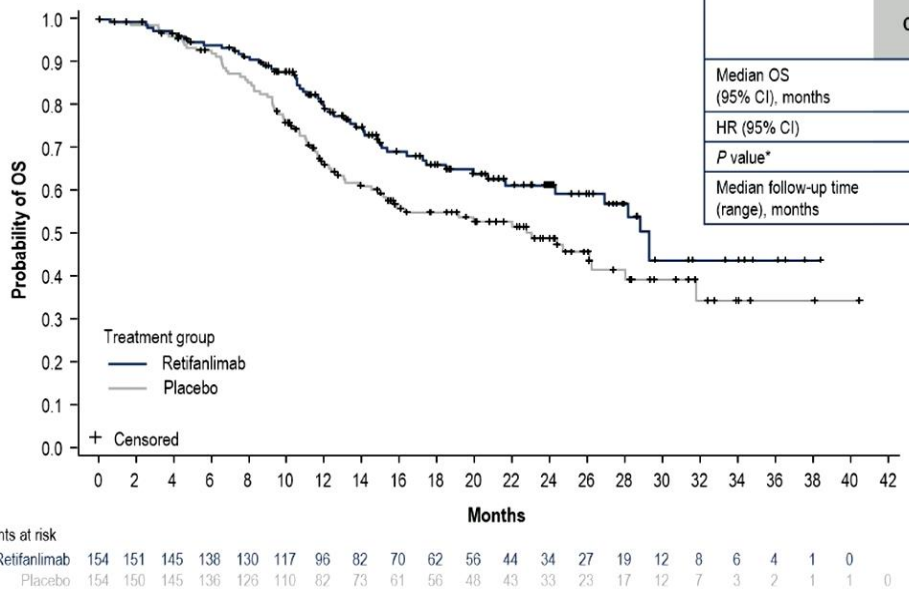
PFS by BICR (Primary Endpoint)



	Placebo + Carboplatin–Paclitaxel (n=154)	Retifanlimab + Carboplatin–Paclitaxel (n=154)
Median PFS (95% CI), months	7.4 (7.1, 7.7)	9.3 (7.5, 11.3)
HR (95% CI)		**0.63 (0.47, 0.84)**
P value*		**0.0006**
Median follow-up time (range), months	7.1 (0.0, 27.4)	7.6 (0.0, 33.9)

*Stratified log-rank test with a 1-sided significance level of 2.5%. Stratification factors: region of the world, extent of disease and PD-L1 expression status.
BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PD-L1, programmed cell death ligand 1; PFS, progression-free survival.

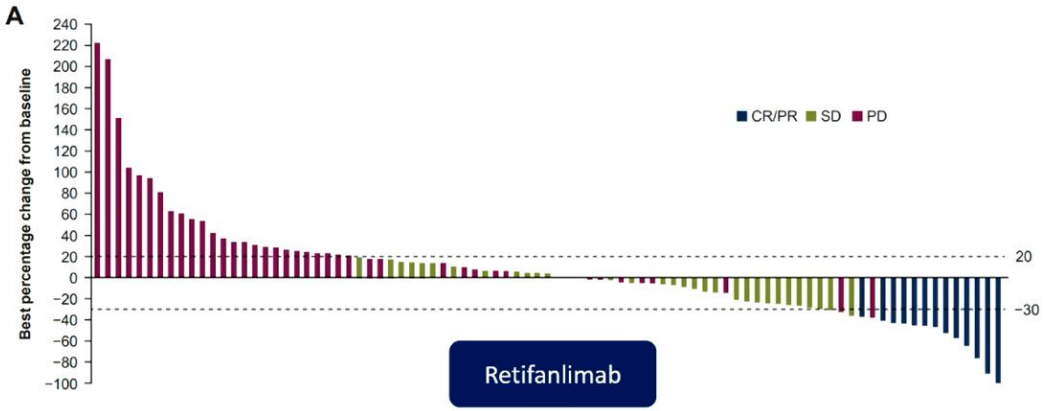
OS (Interim Analysis)

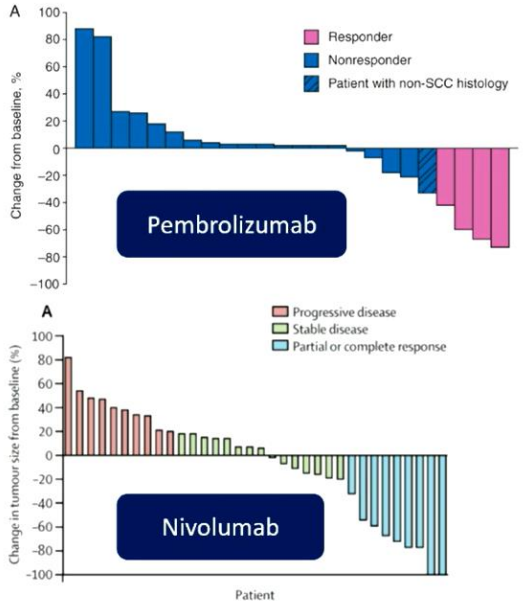


	Placebo + Carboplatin–Paclitaxel (n=154)	Retifanlimab + Carboplatin–Paclitaxel (n=154)
Median OS (95% CI), months	23.0 (15.1, 27.9)	29.2 (24.2, NE)
HR (95% CI)		**0.70 (0.49, 1.01)**
P value*		**0.0273**
Median follow-up time (range), months	12.9 (0.0, 40.4)	14.8 (0.6, 38.3)

*Stratified log-rank test with a 1-sided significance level of 1.2% at this interim look. Stratification factors: region of the world, extent of disease and PD-L1 expression status.
CI, confidence interval; HR, hazard ratio; NE, not estimable; PD-L1, programmed cell death ligand 1; OS, overall survival.

Experience with anti-PD-1 in pretreated SCAC





Ott PA et al Ann Oncol 2017, Rao S et al ESMO open 2022, Van Morris K et al Lancet Oncol 2017

Dominik Modest

Invited Discussant LBA2

Summary

- POD1UM-303/InterAACT 2 is a positive phase-3 trial in a rare cancer entity demonstrating superior efficacy in an acceptable primary endpoint (PFS)
    - The trial provides consistent efficacy data in secondary endpoints (ORR, OS)
    - The gain of benefit in this first-line trial is greater than expected based on monotherapy with checkpoint-inhibitors in pretreated patients
    - Crossover rates of retifanlimab did not impact on OS (due to only 45% exposition but likely also due to lack of efficacy)
    - With a PFS of 7.4 months and an OS of 23 months in the control arm, more information on the use of further-line therapy might help to understand the role of sequential therapy in SCAC

- Safety and tolerability are as expected, retifanlimab adds some immune-related events, but the regimen is manageable

- The external consistency of the trial is limited by lacking availability of randomized trials in this disease or their result (SCARCE C17-02/ Prodige 60)

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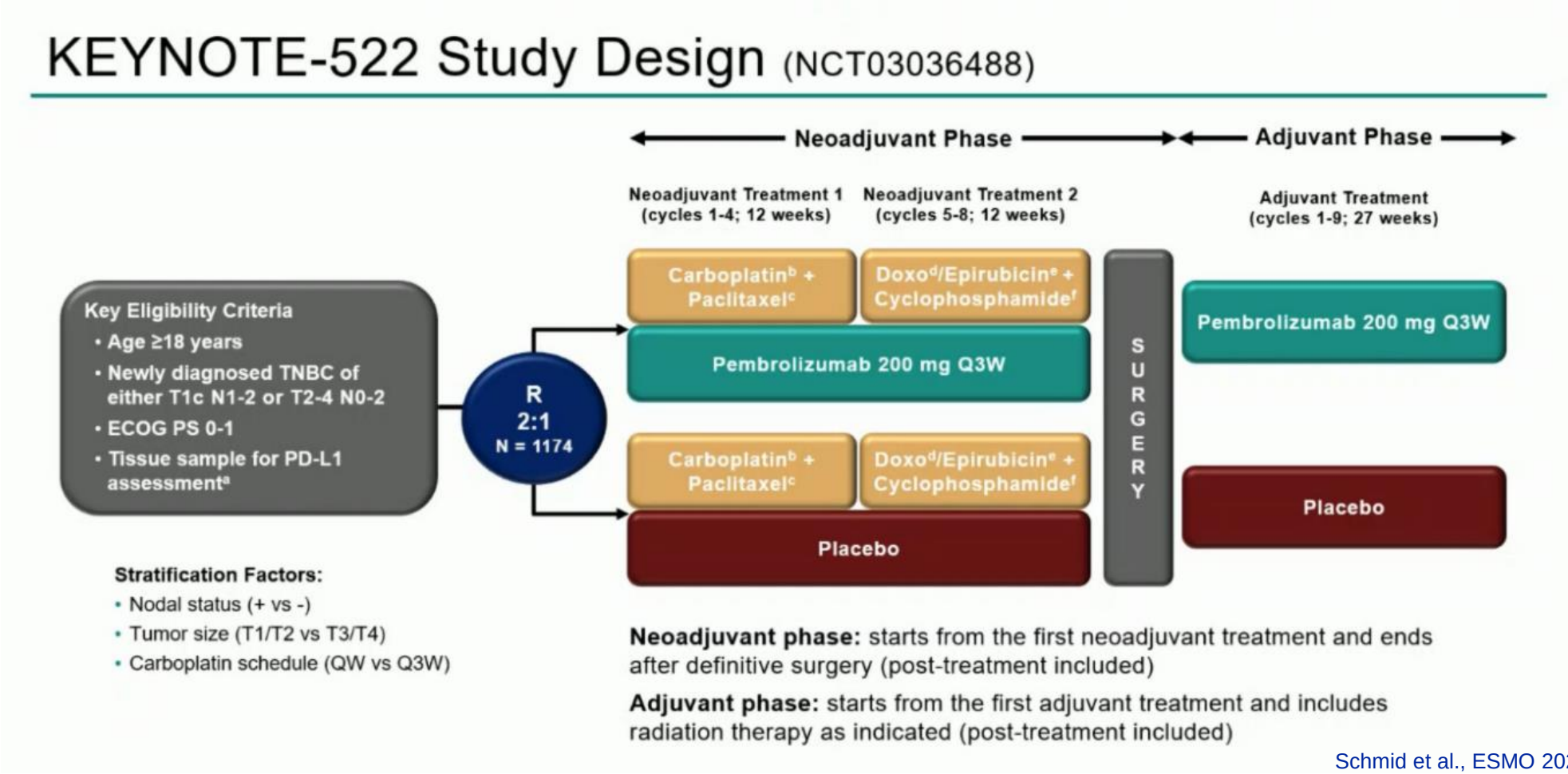
Neoadjuvant Pembrolizumab or Placebo + Chemotherapy Followed by Adjuvant Pembrolizumab or Placebo for High-Risk Early-Stage Triple-Negative Breast Cancer: Overall Survival Results from the Phase 3 KEYNOTE-522 Study

Peter Schmid,[1] Javier Cortes,[2] Rebecca Dent,[3] Heather McArthur,[4] Lajos Pusztai,[5] Sherko Kümmel,[6] Carsten Denkert,[7] Yeon Hee Park,[8] Rina Hui,[9] Nadia Harbeck,[10] Masato Takahashi,[11] Seock-Ah Im,[12] Michael Untch,[13] Peter A. Fasching,[14] Fatima Cardoso,[15] Jing Zhao,[16] Xuan Zhou,[16] Konstantinos Tryfonidis,[16] Gursel Aktan,[16] Joyce O'Shaughnessy[17]

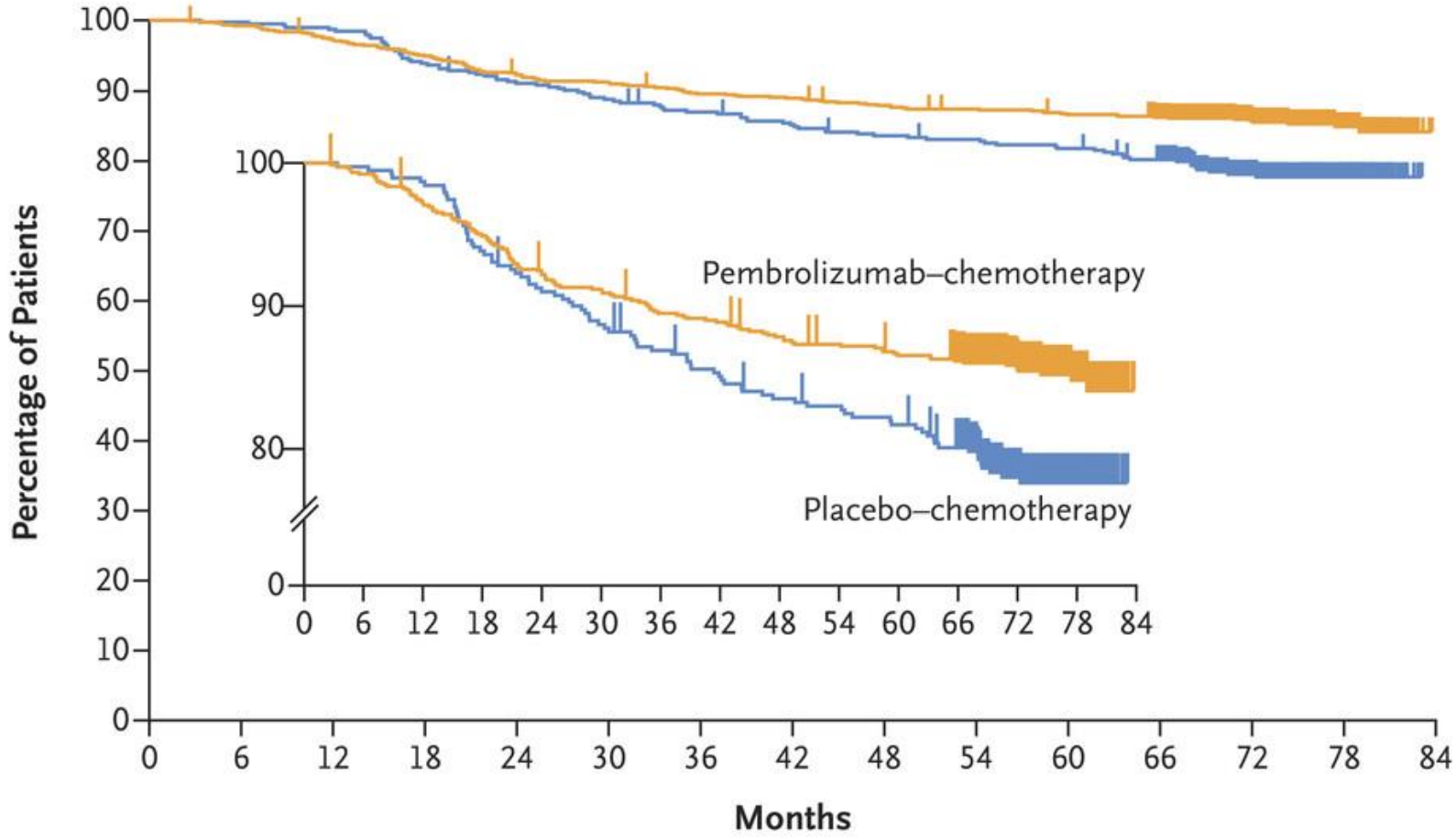
[1]Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University London, London, UK; [2]International Breast Cancer Center (IBCC), Pangaea Oncology, Quironsalud Group, Barcelona, Spain; Medical Scientia Innovation Research (MedSIR), Barcelona, Spain; Faculty of Biomedical and Health Sciences, Department of Medicine, Universidad Europea de Madrid, Madrid, Spain; [3]National Cancer Centre Singapore, Duke – National University of Singapore Medical School, Singapore; [4]University of Texas Southwestern Medical Center, Dallas, TX, USA; [5]Yale School of Medicine, Yale Cancer Center, New Haven, CT, USA; [6]Breast Unit, Kliniken Essen-Mitte, Essen, Germany and Charité – Universitätsmedizin Berlin, Department of Gynecology with Breast Center, Berlin, Germany; [7]Institute of Pathology, Philipps-University Marburg and University Hospital Marburg, Marburg, Germany; [8]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [9]Westmead Breast Cancer Institute, Westmead Hospital and the University of Sydney, Sydney, NSW, Australia and Centre of Cancer Medicine, School of Clinical Medicine, University of Hong Kong, Hong Kong; [10]Breast Center, Dept. OB&GYN, LMU University Hospital, Munich, Germany; [11]Hokkaido University Hospital, Sapporo, Japan; [12]Seoul National University Hospital, Cancer Research Institute, Seoul National University, Seoul, Republic of Korea; [13]Breast Cancer Center, Helios Klinikum Berlin-Buch, Berlin, Germany; [14]University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany; [15]Breast Unit, Champalimaud Clinical Center/ Champalimaud Foundation, Lisbon, Portugal; [16]Oncology, Merck & Co., Inc., Rahway, NJ, USA; [17]Baylor University Medical Center, Texas Oncology, Sarah Cannon Research Institute, Dallas, TX, USA

Mammakarzinom, neoadjuvant / adjuvant



Schmid et al., ESMO 2024

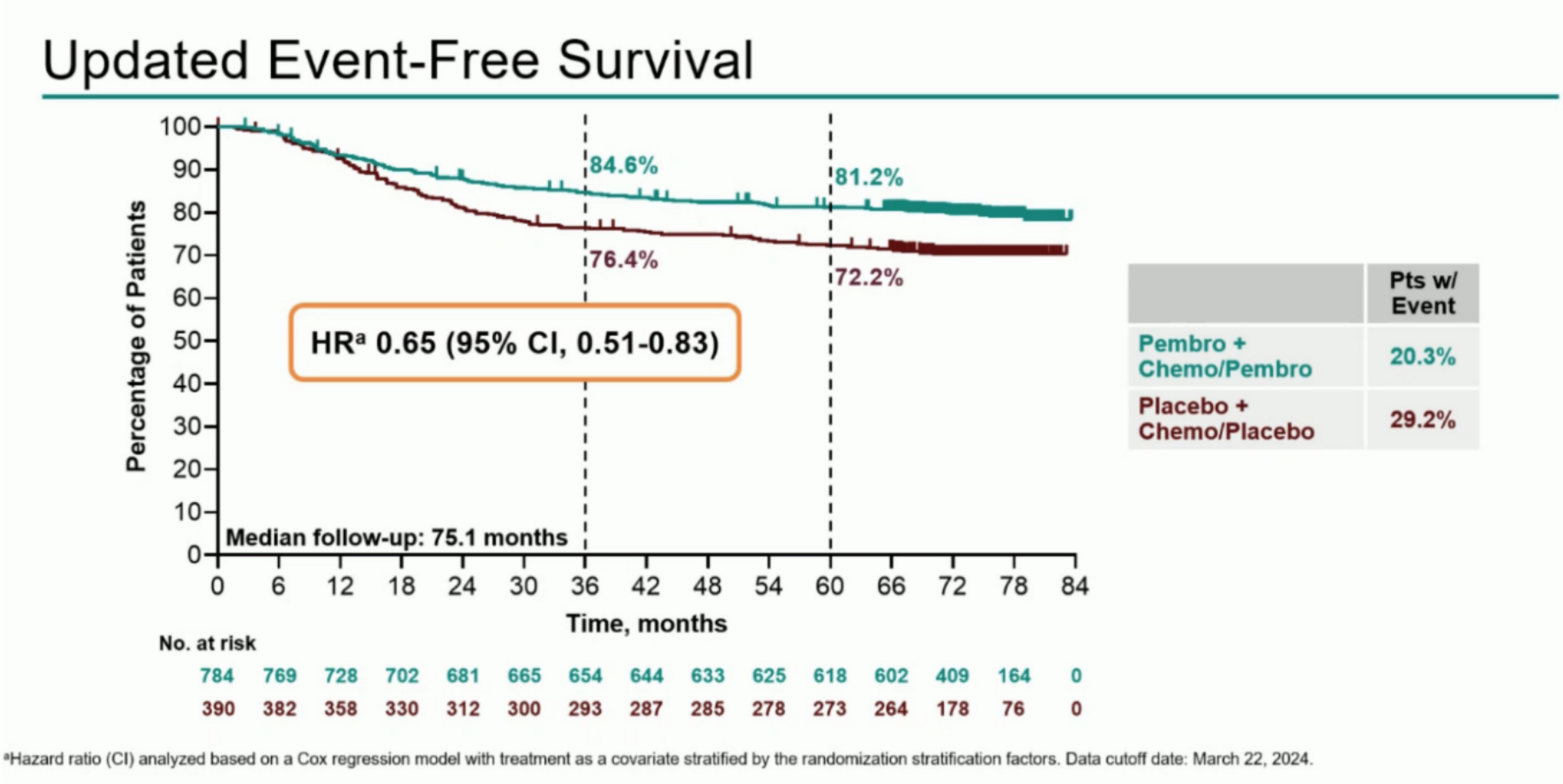
A **Overall Survival According to Treatment Group in the Intention-to-Treat Population**



No. at Risk

Pembrolizumab–chemotherapy	784	777	760	742	720	712	698	693	683	677	670	656	448	176	0
Placebo–chemotherapy	390	389	385	366	354	345	336	328	321	318	313	300	199	82	0

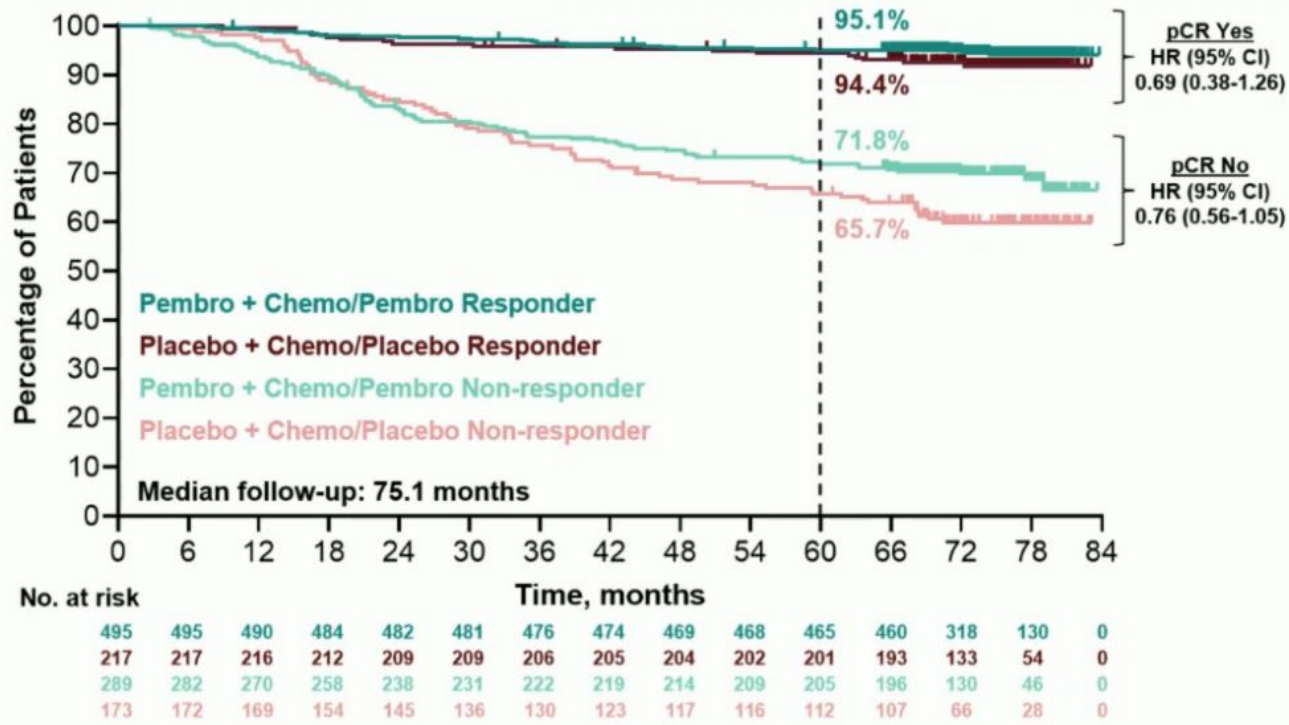
Mammakarzinom, neoadjuvant / adjuvant



Schmid et al., ESMO 2024

Mammakarzinom, neoadjuvant / adjuvant

Overall Survival by Pathologic Complete Response (yp T0/Tis ypN0)

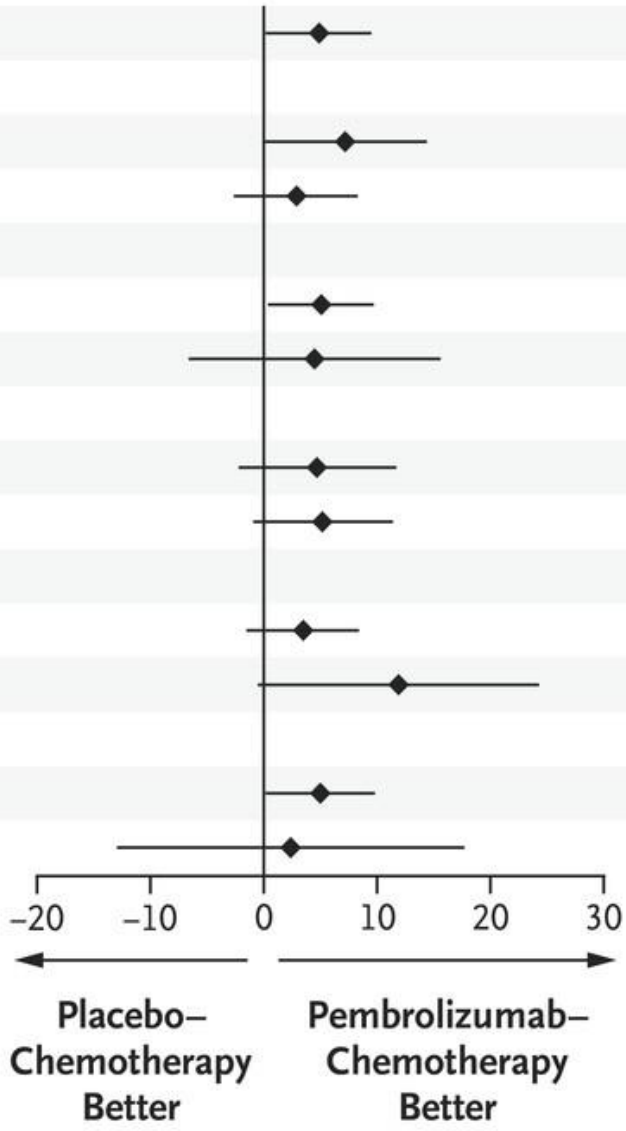


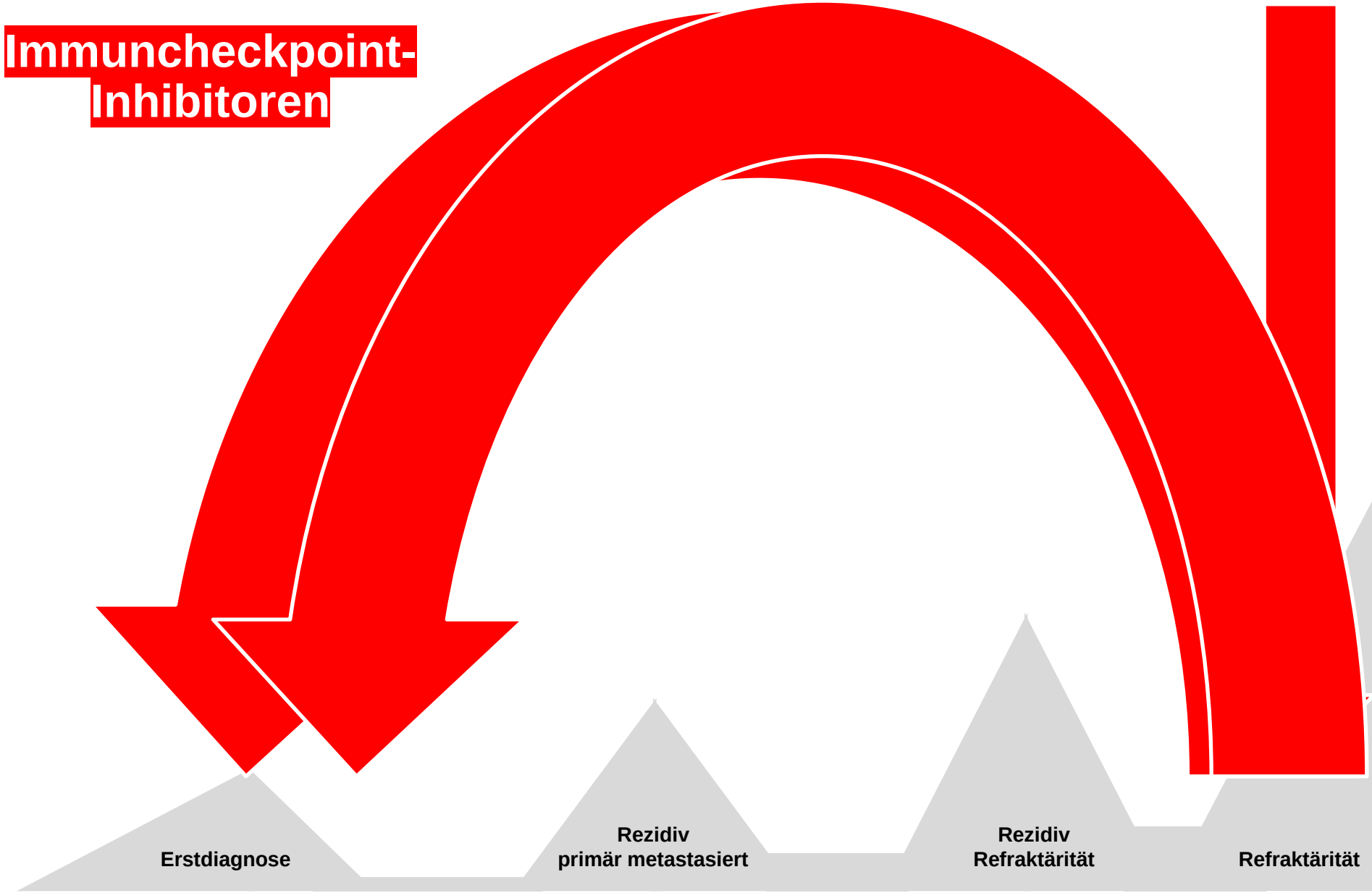
This is a non-randomized subgroup analysis based on the post-treatment outcome of pCR and HRs should therefore be interpreted with caution. Data cutoff date: March 22, 2024.

Schmid et al., ESMO 2024

B Subgroup Analyses of Overall Survival

Subgroup	Pembrolizumab–Chemotherapy	Placebo–Chemotherapy	Difference in 5-Year Overall Survival (95% CI)
	no. of patients who died/total no. (%)		*percentage points*
Overall	115/784 (14.7)	85/390 (21.8)	4.9 (0.3 to 9.4)
Nodal status			
Positive	78/408 (19.1)	56/196 (28.6)	7.2 (0.0 to 14.3)
Negative	37/376 (9.8)	29/194 (14.9)	2.9 (–2.5 to 8.2)
Tumor size			
T1 to T2	54/580 (9.3)	51/290 (17.6)	5.1 (0.5 to 9.6)
T3 to T4	61/204 (29.9)	34/100 (34.0)	4.5 (–6.5 to 15.5)
Carboplatin schedule			
Every 3 wk	46/334 (13.8)	36/167 (21.6)	4.7 (–2.1 to 11.6)
Weekly	68/444 (15.3)	49/220 (22.3)	5.2 (–0.8 to 11.3)
PD-L1 status			
CPS ≥1	92/656 (14.0)	62/317 (19.6)	3.5 (–1.4 to 8.3)
CPS <1	23/128 (18.0)	23/69 (33.3)	11.9 (–0.4 to 24.2)
Age			
<65 yr	93/700 (13.3)	72/342 (21.1)	5.0 (0.3 to 9.7)
≥65 yr	22/84 (26.2)	13/48 (27.1)	2.4 (–12.8 to 17.6)




Immuncheckpoint-Inhibitoren
Erstdiagnose
Rezidiv primär metastasiert
Rezidiv Refraktärität
Refraktärität

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Locoregional hypo vs normofractionated radiation therapy in breast early cancer

5 years results of the **HypoG-01** phase 3 UNICANCER trial

Sofia Rivera MD, PhD
On behalf of the HypoG-01 trialists

Villejuif, France, 15/09/2024

hypog-01@unicancer.fr

Mammakarzinom, Bestrahlung

HypoG-01: Study design

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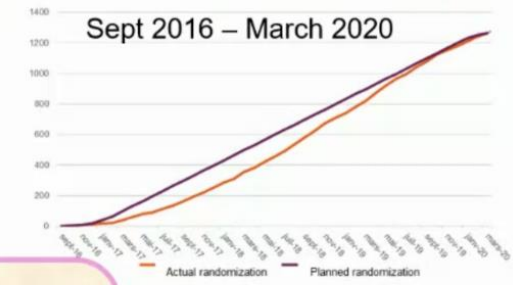
Non inferiority, phase III, 29 centers

N= 1265 randomized patients

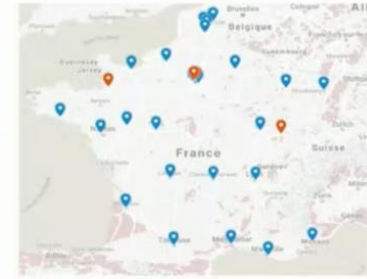


Woman≥18 years, operated for T1-3, N0-3, M0 breast cancer with an indication for **regional nodes RT**

R

Hypofractionated RT: 40 Gy/ 15 fr/ 3 weeks +/- boost (investigator's choice)

Normofractionated RT: 50 Gy/ 25 fr/ 5 weeks +/- boost (investigator's choice)



Primary endpoint: 3-year cumulative incidence of **Arm lymphedema**

Stratification:
- Mastectomy vs lumpectomy
- Radiotherapy technique
- Center of treatment
- Nodes cleared : 0, 1-3, ≥4
- BMI ≤25 vs >25

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HypoG-01: Methods

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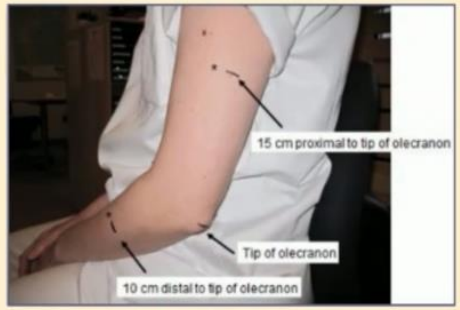
Primary endpoint

- **Arm lymphedema** defined as ≥10% increase in arm circumference 15 cm proximal and/or 10 cm distal of the olecranon relative to baseline, compared to the contralateral circumference



Secondary endpoints

- **Overall Survival (OS)**
- **Loco Regional-Free survival (LRFS)**
- **Distant disease-Free survival (DDFS)**
- **Breast cancer specific survival (BCSS)**
- **Shoulder range of motion** impairment defined as a reduction ≥25° in active abduction or flexion

Statistics

- one-sided logrank test at 5% significance in **per-protocol population (PP)**
- **pre-specified non-inferiority margin**
- 80% power → 131 events; 1012 patients needed
- Assuming up to 20% excluded from per-protocol population **1265 patients** were needed

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HypoG-01: Primary endpoint

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Non inferiority of hypofractionated RT

In per protocol analysis :

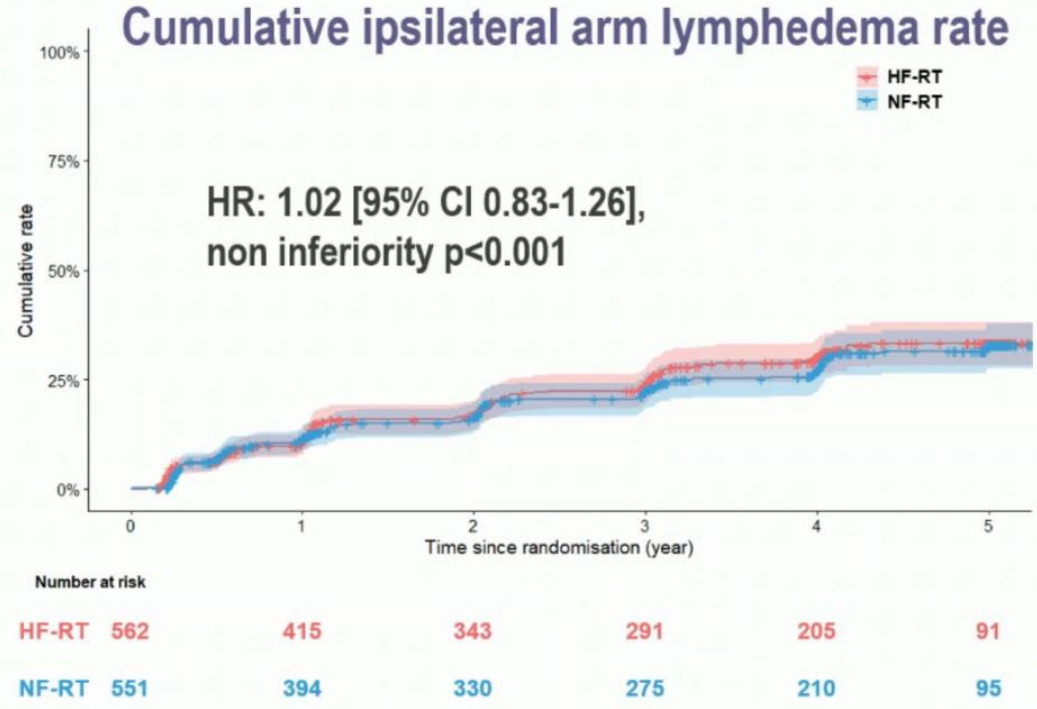
Median follow up: **4.8 years**

Arm lymphedema occurred in 275/ 1113 pts with baseline and end of RT measurements

Non inferiority in cumulative ipsilateral arm lymphedema rate p<0.001

Cumulative 5-year rate (PP):

- **33.3%** (95% CI: 28.7 - 38.4) in HF
- **32.8%** (95% CI: 27.9 - 38.1) in NF



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HypoG-01: Secondary endpoint

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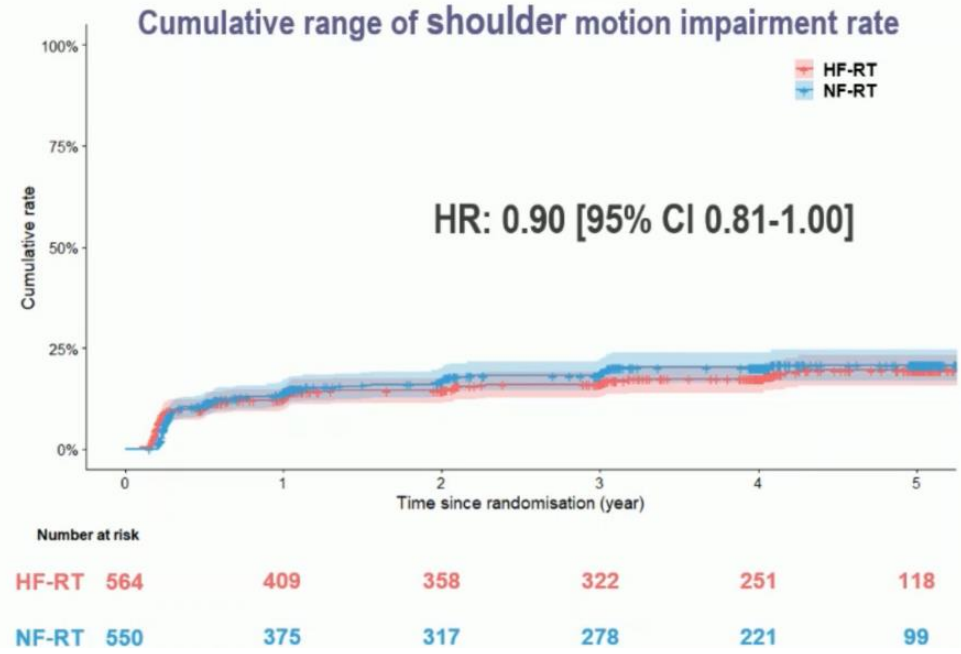
No sign of a detrimental effect on **shoulder motion** (ROM) of hypofractionated RT

In per protocol analysis:

Cumulative **5-year ROM impairment** rate:
19.6% (95% CI 16.1-23.7) in HF
vs 20.7% (95% CI 17.2-24.8) in NF

No obvious difference in cumulative ROM impairment rate was observed between arms



Rivera et al., ESMO 2024

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HypoG-01: Secondary endpoint

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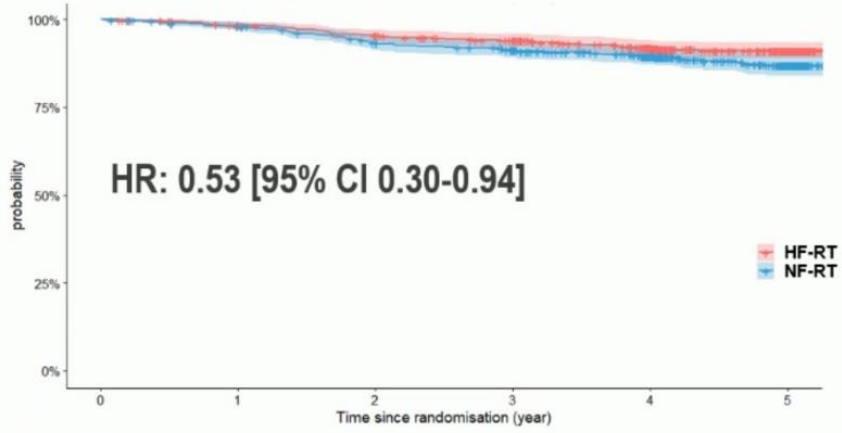
No sign of detrimental effect of hypofractionated RT on survival

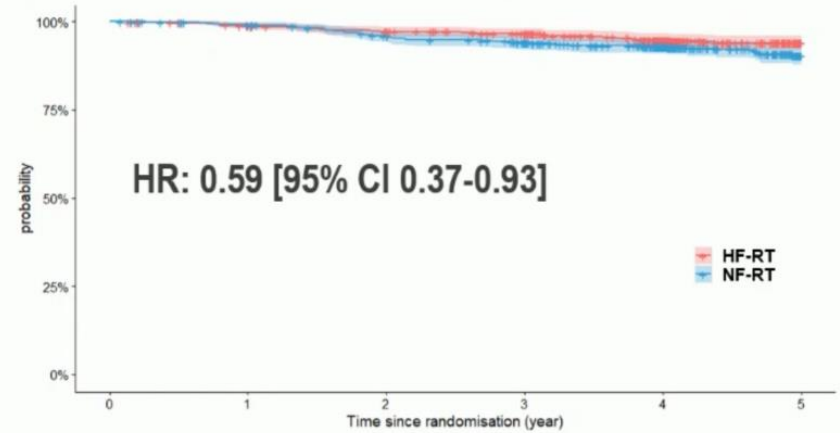
Breast Cancer-Specific Survival



Number at risk

HF-RT	614	590	567	541	438	201
NF-RT	607	586	550	526	433	172

Overall Survival



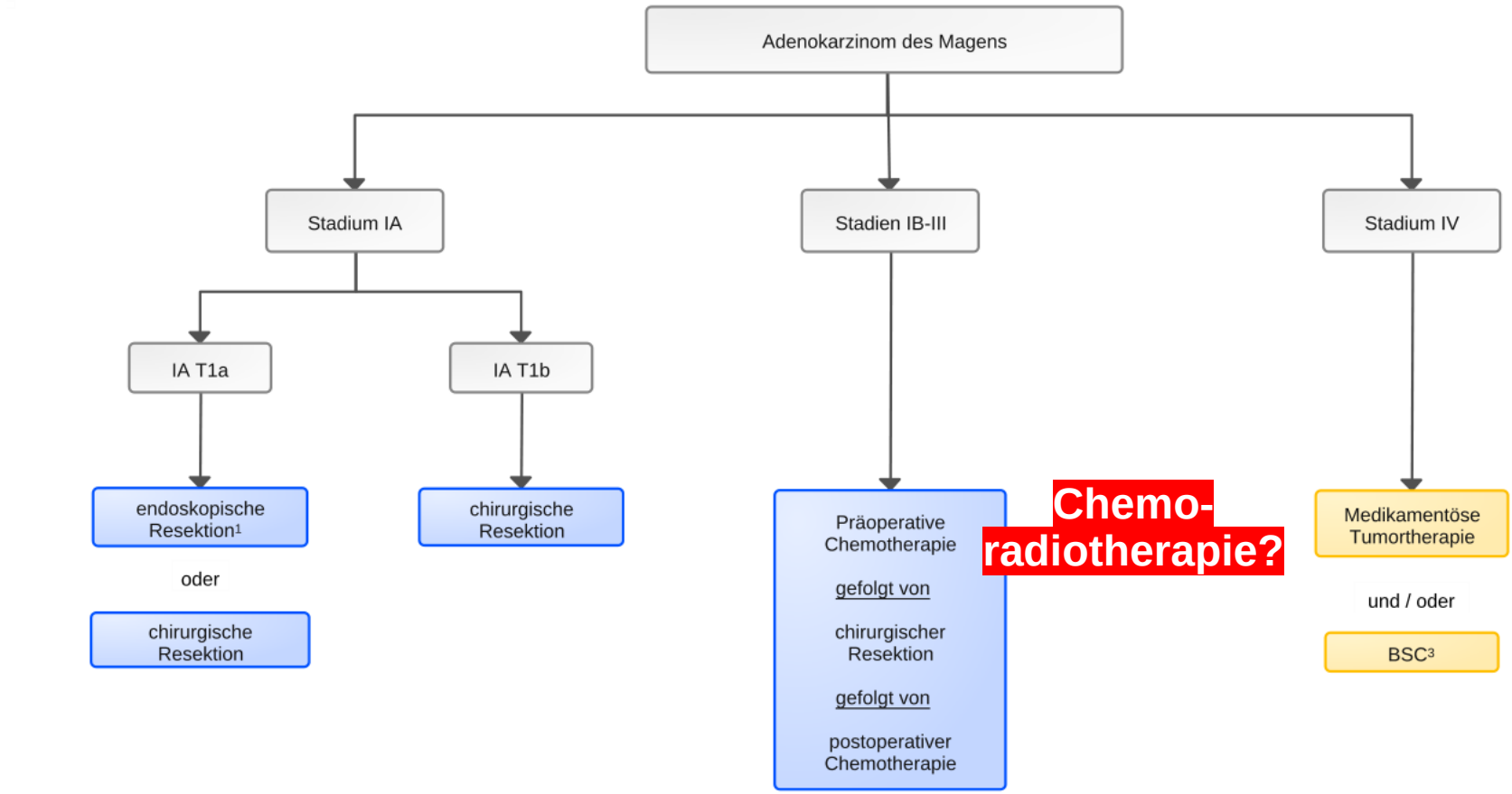
Number at risk

HF-RT	614	593	577	555	444	200
NF-RT	607	591	564	537	437	170

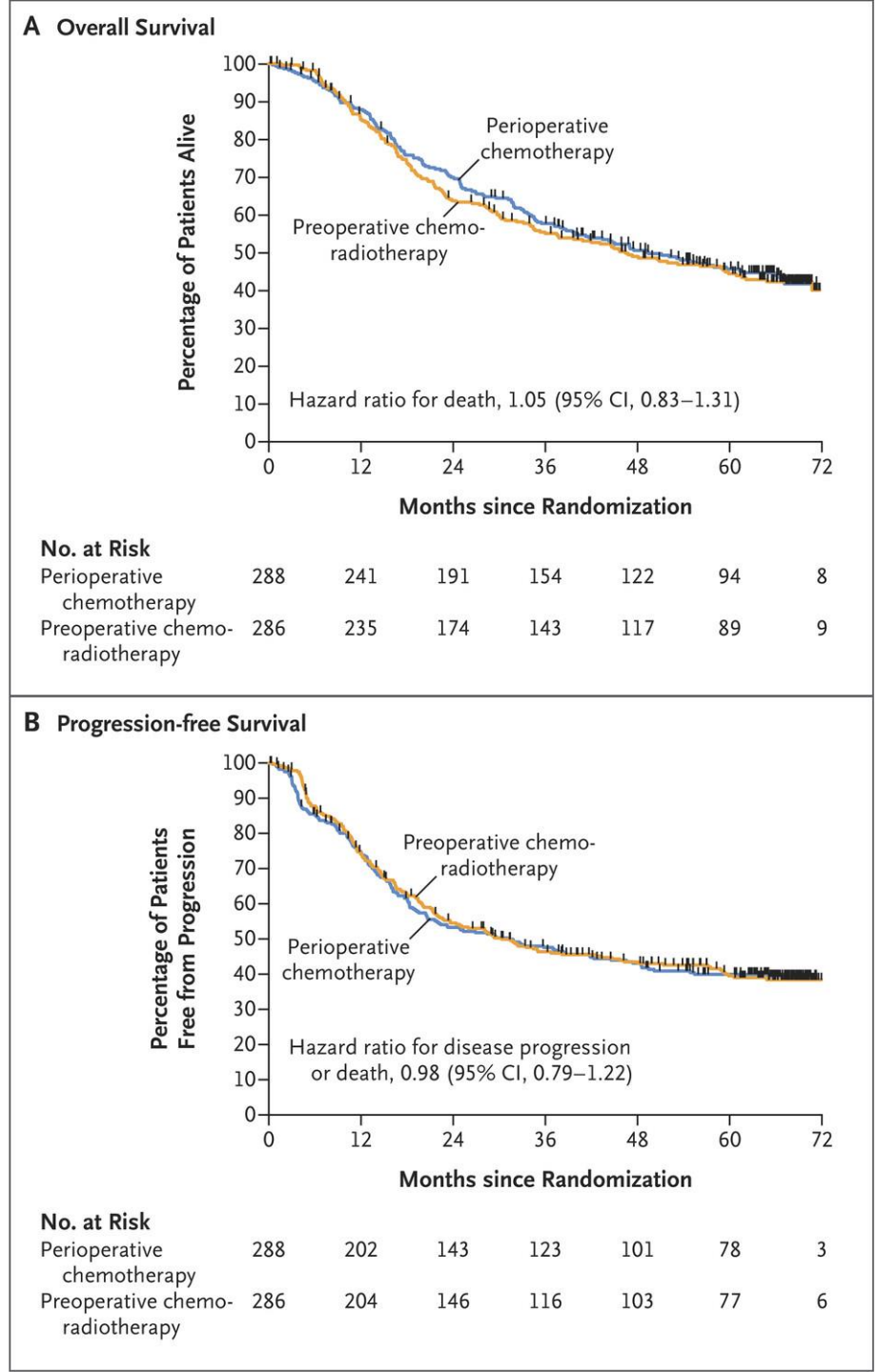
Rivera et al., ESMO 2024

Magenkarzinom, neoadjuvant / adjuvant

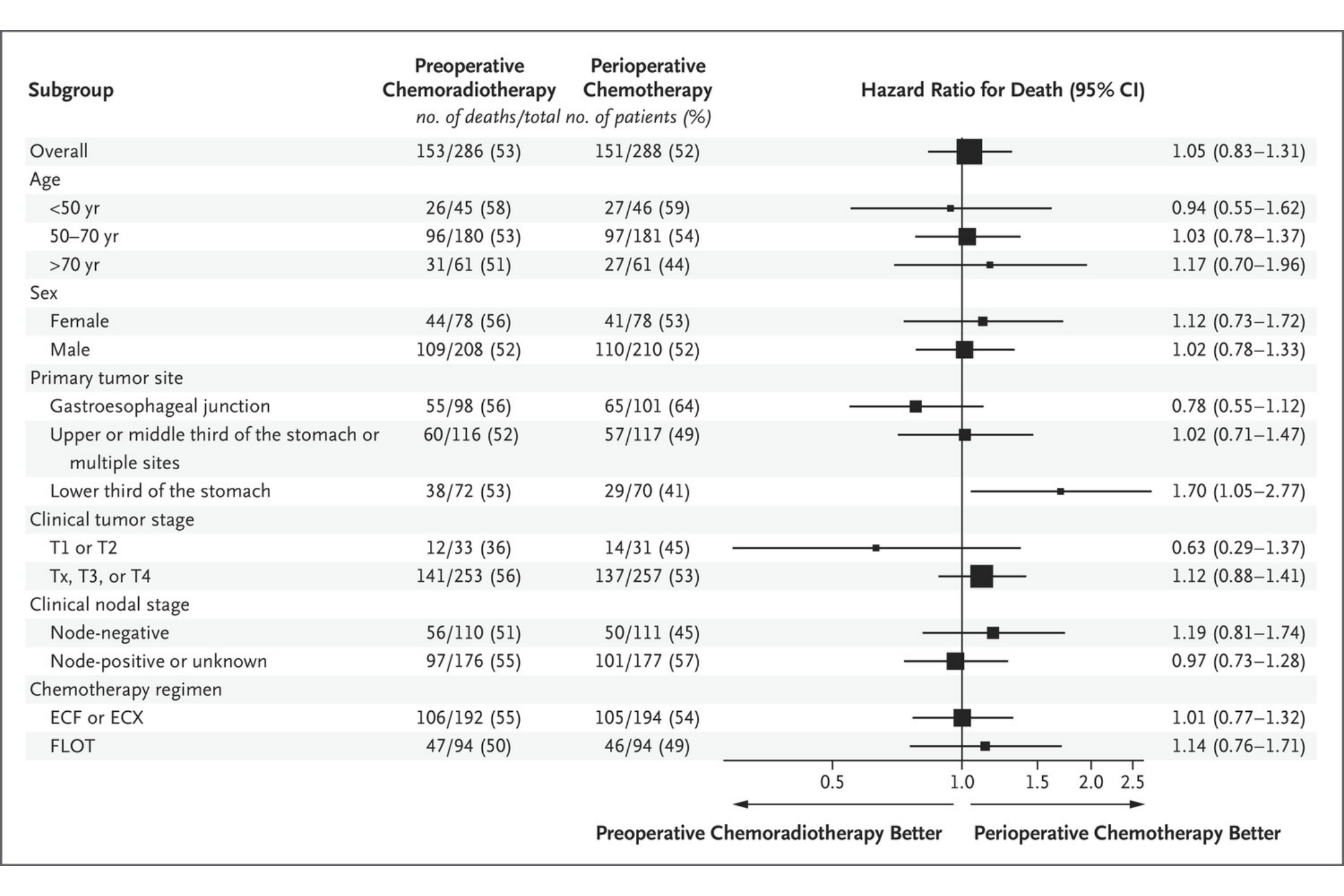
Algorithmus für die Primärtherapie



Legende:
kurativ intendierte Therapie; nicht-kurativ intendierte Therapie;
[1] *siehe Tabelle 4*
[2] *Best Supportive Care*

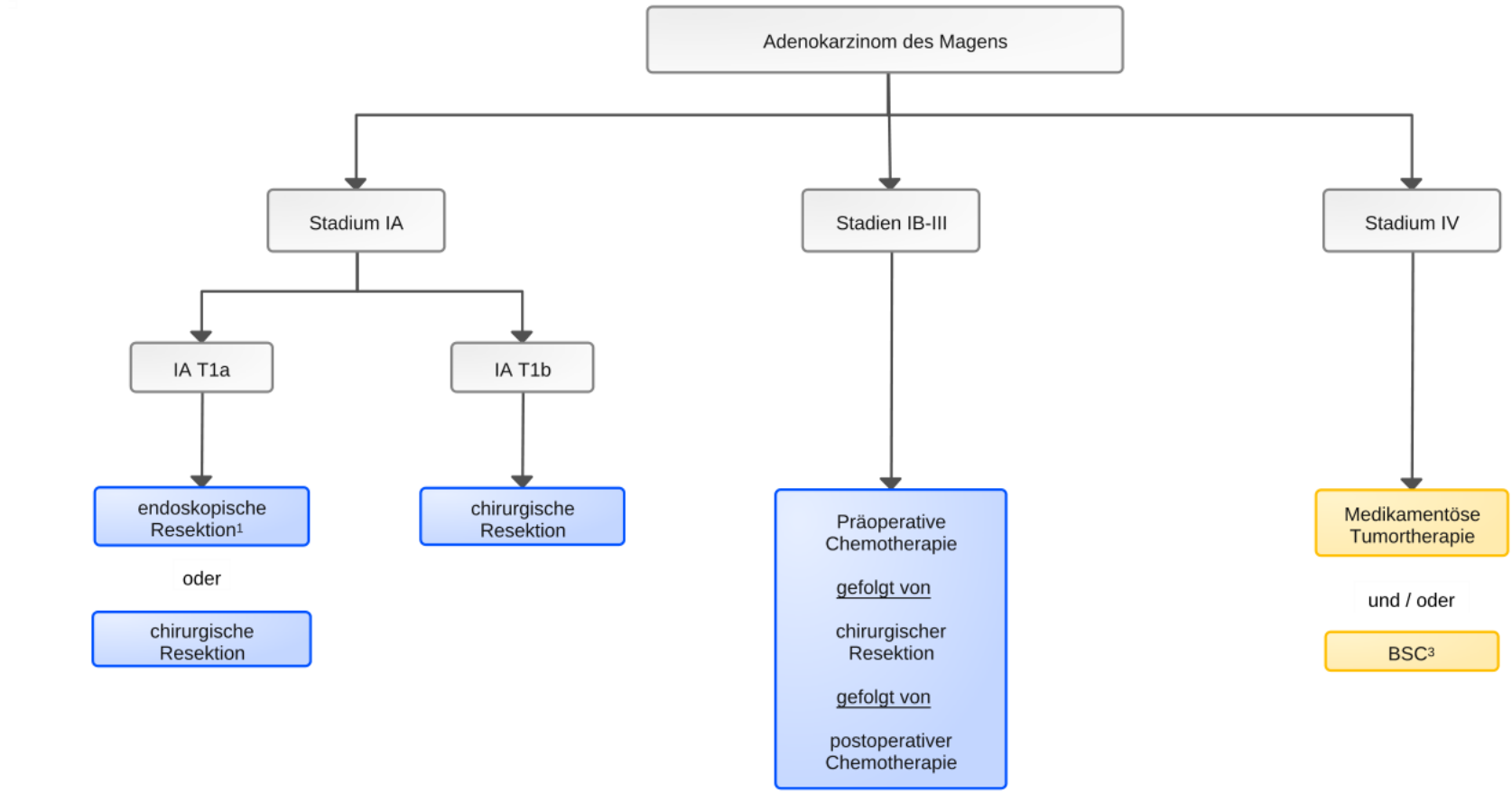


Leong et al., NEJM 2024


Subgroup
Preoperative Chemoradiotherapy
Perioperative Chemotherapy
no. of deaths/total no. of patients (%)
Hazard Ratio for Death (95% CI)
Overall 153/286 (53) 151/288 (52) 1.05 (0.83–1.31)
Age
<50 yr 26/45 (58) 27/46 (59) 0.94 (0.55–1.62)
50–70 yr 96/180 (53) 97/181 (54) 1.03 (0.78–1.37)
>70 yr 31/61 (51) 27/61 (44) 1.17 (0.70–1.96)
Sex
Female 44/78 (56) 41/78 (53) 1.12 (0.73–1.72)
Male 109/208 (52) 110/210 (52) 1.02 (0.78–1.33)
Primary tumor site
Gastroesophageal junction 55/98 (56) 65/101 (64) 0.78 (0.55–1.12)
Upper or middle third of the stomach or multiple sites 60/116 (52) 57/117 (49) 1.02 (0.71–1.47)
Lower third of the stomach 38/72 (53) 29/70 (41) 1.70 (1.05–2.77)
Clinical tumor stage
T1 or T2 12/33 (36) 14/31 (45) 0.63 (0.29–1.37)
Tx, T3, or T4 141/253 (56) 137/257 (53) 1.12 (0.88–1.41)
Clinical nodal stage
Node-negative 56/110 (51) 50/111 (45) 1.19 (0.81–1.74)
Node-positive or unknown 97/176 (55) 101/177 (57) 0.97 (0.73–1.28)
Chemotherapy regimen
ECF or ECX 106/192 (55) 105/194 (54) 1.01 (0.77–1.32)
FLOT 47/94 (50) 46/94 (49) 1.14 (0.76–1.71)
0.5
1.0
1.5
2.0
2.5
Preoperative Chemoradiotherapy Better
Perioperative Chemotherapy Better

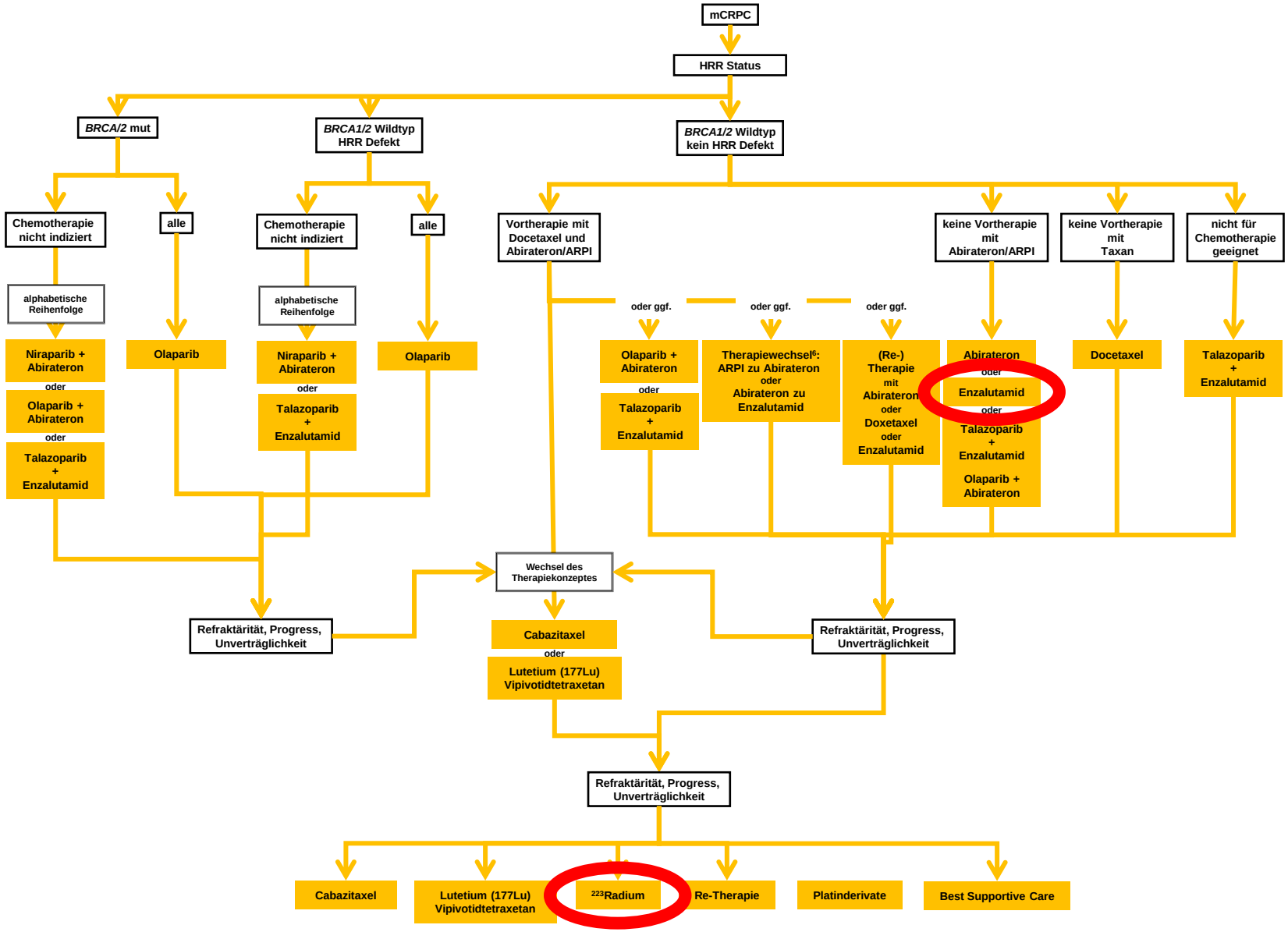
Adenokarzinom des Magens

Algorithmus für die Primärtherapie



Legende:
kurativ intendierte Therapie; nicht-kurativ intendierte Therapie;
[1] *siehe Tabelle 4*
[2] *Best Supportive Care*

Prostatakarzinom, mCRPC



Prostatakarzinom, mCRPC

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A randomized multicenter open-label phase III trial comparing enzalutamide vs a combination of Radium-223 and enzalutamide in asymptomatic or mildly symptomatic patients with bone metastatic mCRPC

Results of EORTC-GUCG 1333/PEACE-3, an EORTC/CTI/CUOG/LACOG/UNICANCER-GETUG cooperative study

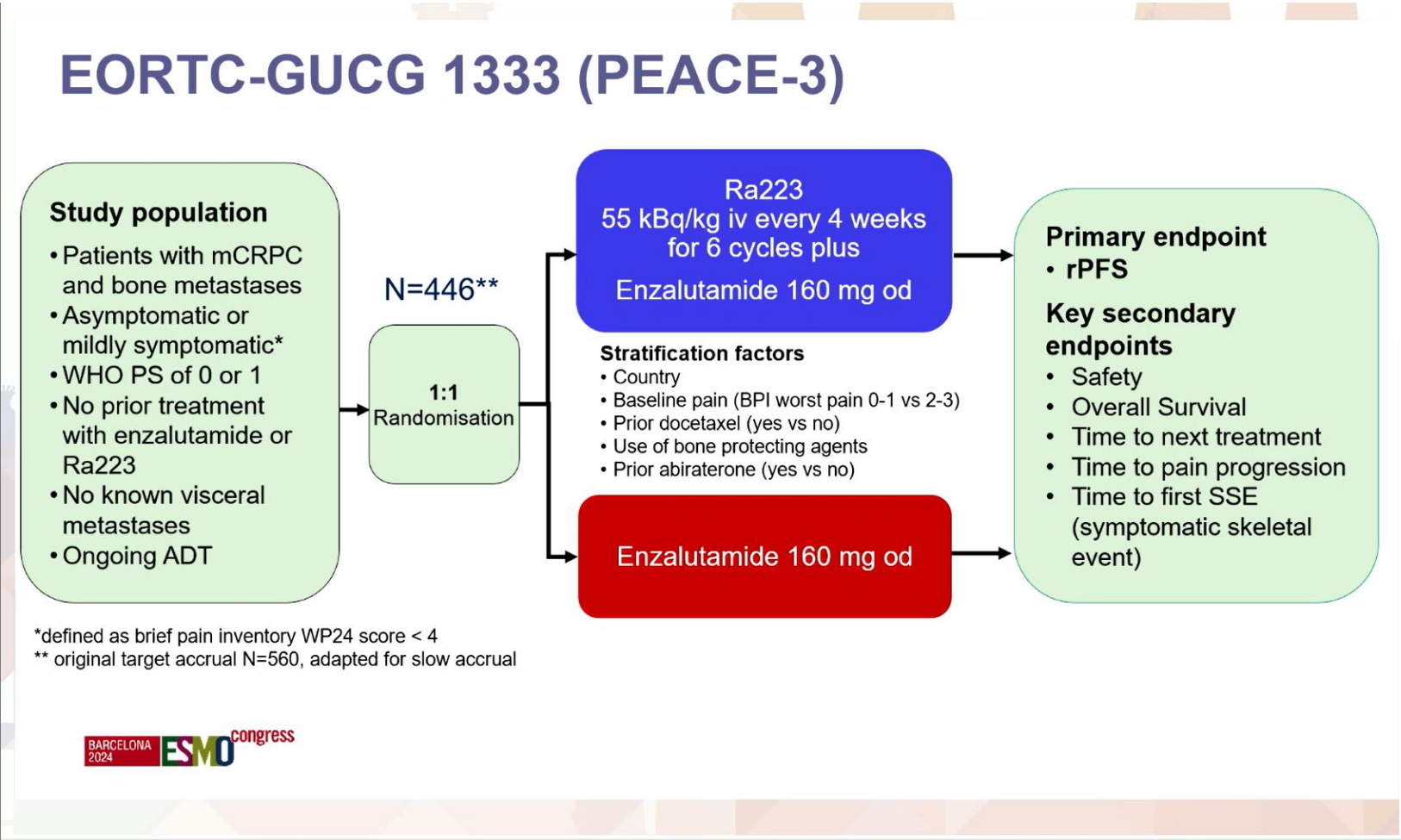
S. Gillessen
Oncology Institute of Southern Switzerland, EOC,
Bellinzona, Switzerland

On behalf of A. Choudhury, F. Saad , E. Gallardo Diaz, A. Soares, Y. Loriot, R. McDermott, A. Rodriguez-Vida, P. Isaacsson Velho, F. Nole, F. Cruz, T. Roumeguere, G. Daugaard, R. Yamamura, E. Bompas, P. Maroto, F. Gomez Veiga, I. Skoneczna, K. Martins da Trindade, F. Mavignier Carcano, F. Lecouvet, C.Coens, C. Poncet, B. Fournier, B. Tombal

PEACE Prostate Cancer Consortium Europe

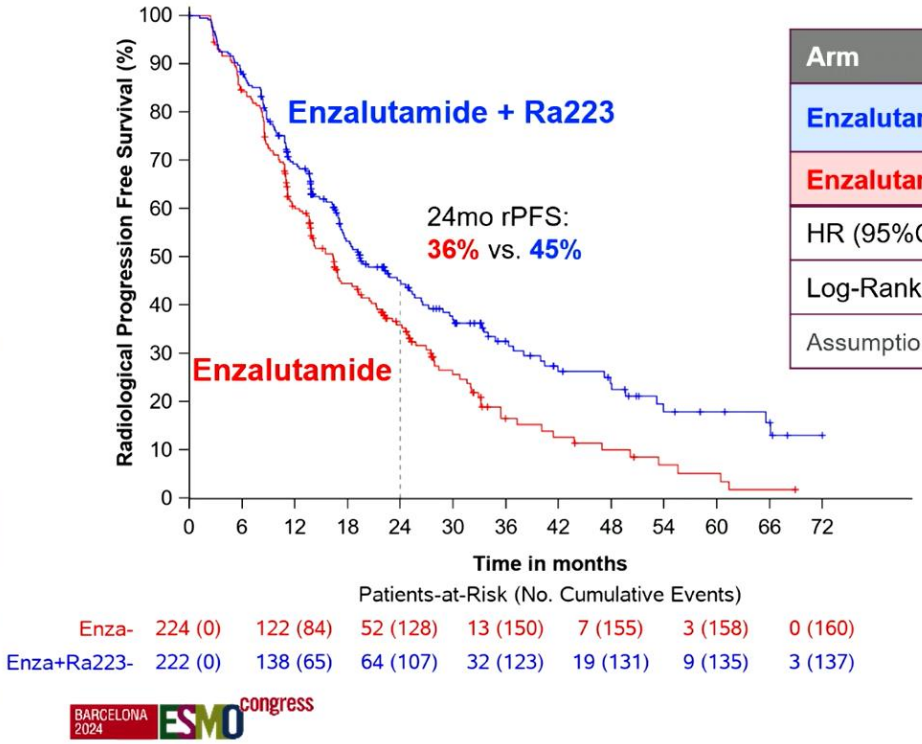
EORTC European Organisation for Research and Treatment of Cancer

Prostatakarzinom, mCRPC



Prostatakarzinom, mCRPC

Primary endpoint: rPFS



Arm	n/N	Median (95%CI)
Enzalutamide + Ra223	139/222	**19.4** (17.1-25.3) mo
Enzalutamide	160/224	**16.4** (13.8-19.2) mo
HR (95%CI)	**0.69** (0.54-0.87)	
Log-Rank p-value	**0.0009**	
Assumption of proportional hazard achieved		

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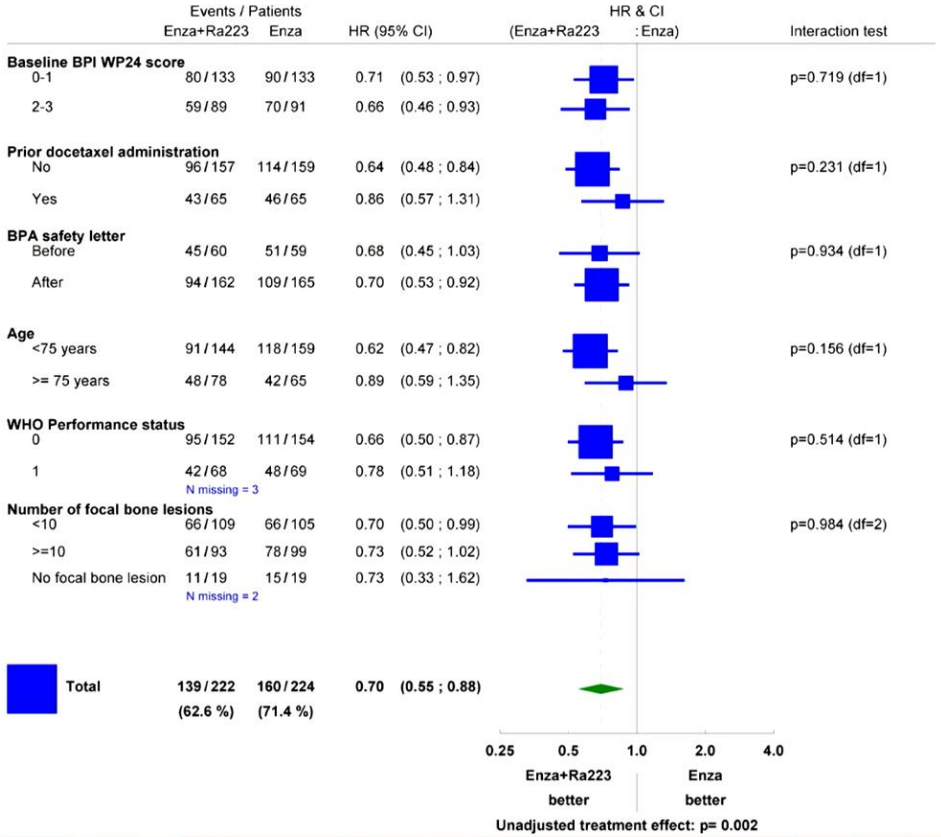
Prostatakarzinom, mCRPC

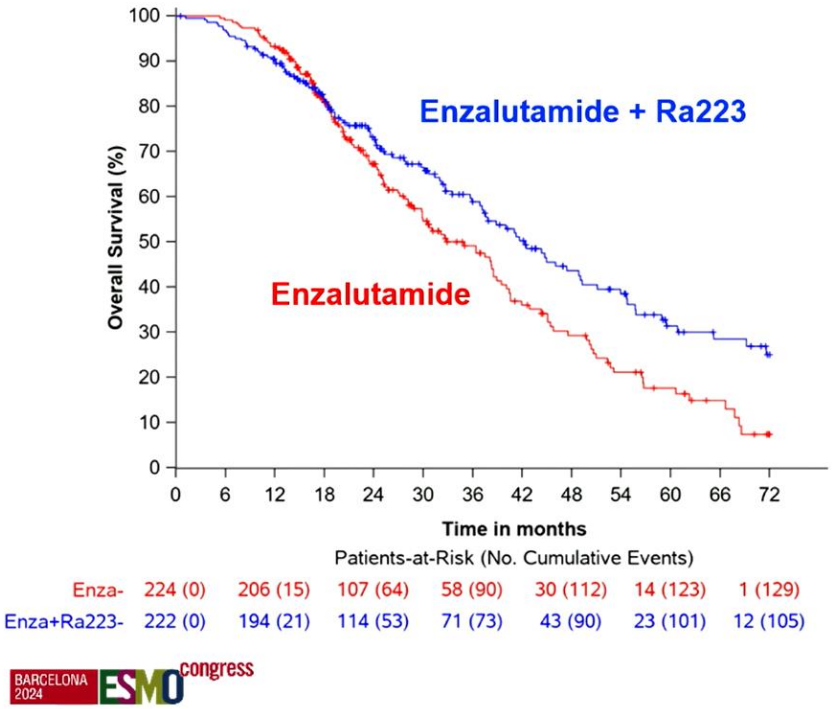
Forest plot for rPFS

As these analyses are exploratory, no adjustment for multiplicity was considered. Unadjusted (ie non-stratified) estimates and 2-sided p-values are presented



Prostatakarzinom, mCRPC

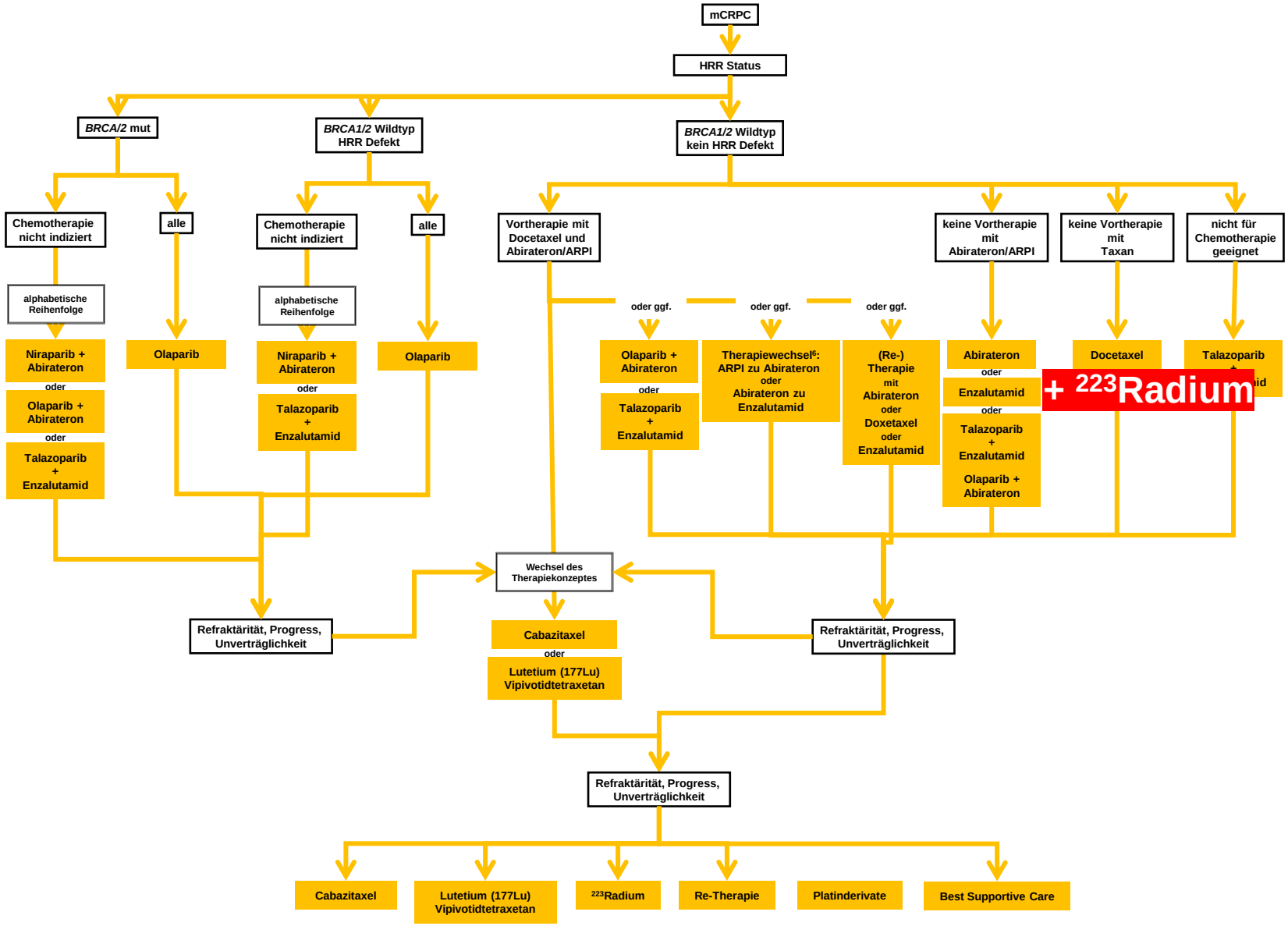
Overall Survival at interim analysis (80% of OS events)



Arm	n/N	Median (95%CI)
Enzalutamide + Ra223	110/222	**42.3** (36.8-49.1) mo
Enzalutamide	129/224	**35.0** (28.8-38.9) mo
HR (95%CI)	**0.69** (0.52-0.90)	
Log-Rank p-value	**0.0031**	<0.0034

- Pre-set level of significance for interim analysis was ≤ 0.0034
- Due to non-proportional hazards plus lack of unequivocal significance for RMST (restricted mean survival time) sensitivity analysis, study will continue to final OS analysis

Prostatakarzinom, mCRPC



Neuroendokrine Tumoren (NET), fortgeschritten

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 3 Trial of Cabozantinib to Treat Advanced Neuroendocrine Tumors

Jennifer A. Chan, M.D., M.P.H., Susan Geyer, Ph.D., Tyler Zemla, M.S., Michael V. Knopp, M.D., Ph.D., Spencer Behr, M.D., Sydney Pulsipher, M.P.H., Fang-Shu Ou, Ph.D., Amylou C. Dueck, Ph.D., Jared Acoba, M.D., Ardaman Shergill, M.D., Edward M. Wolin, M.D., Thorvardur R. Halfdanarson, M.D., Bhavana Konda, M.D., M.P.H., Nikolaos A. Trikalinos, M.D., Bernard Tawfik, M.D., Nitya Raj, M.D., Shagufta Shaheen, M.D., Namrata Vijayvergia, M.D., Arvind Dasari, M.D., Jonathan R. Strosberg, M.D., Elise C. Kohn, M.D., Matthew H. Kulke, M.D., Eileen M. O'Reilly, M.D., and Jeffrey A. Meyerhardt, M.D., M.P.H.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Extrapancreatic NET Cohort		Pancreatic NET Cohort	
	Cabozantinib (N=134)	Placebo (N=69)	Cabozantinib (N=64)	Placebo (N=31)
Median age (range) — yr	66 (28–86)	66 (30–82)	60 (29–79)	64 (39–79)
Female sex — no. (%)	74 (55)	31 (45)	27 (42)	13 (42)
ECOG performance-status score — no. (%)†				
0	49 (37)	32 (46)	35 (55)	15 (48)
1	84 (63)	36 (52)	28 (44)	16 (52)
Primary tumor site — no. (%)‡				
Gastrointestinal	70 (52)	46 (67)	2 (3)	1 (3)
Lung	27 (20)	12 (17)	NA	NA
Thymus	6 (4)	4 (6)	NA	NA
Pancreas	4 (3)	3 (4)	62 (97)	30 (97)
Other	5 (4)	2 (3)	NA	NA
Unknown	22 (16)	2 (3)	NA	NA
Tumor grade — no. (%)				
Grade 1	37 (28)	15 (22)	14 (22)	7 (22)
Grade 2	86 (64)	48 (70)	39 (61)	19 (61)
Grade 3	8 (6)	5 (7)	8 (12)	3 (10)
Unknown	3 (2)	1 (1)	3 (5)	2 (6)
Hormone syndrome present: functional tumor — no. (%)	41 (31)	25 (36)	11 (17)	5 (16)
Concurrent somatostatin analogue — no. (%)	92 (69)	48 (70)	35 (55)	17 (55)
Median no. (range) of previous systemic therapies not including somatostatin analogue A	2 (1–6)	2 (1–6)	3 (1–9)	2 (1–7)
Previous systemic therapy — no. (%)				
Somatostatin analogue	125 (93)	64 (93)	63 (98)	30 (97)
Lu-177 dotatate	80 (60)	41 (59)	38 (59)	18 (58)
Everolimus	96 (72)	44 (64)	51 (80)	25 (81)
Temozolomide with or without capecitabine	43 (32)	20 (29)	43 (67)	16 (52)
Cisplatin or carboplatin plus etoposide	11 (8)	8 (12)	NA	NA
Sunitinib	NA	NA	18 (28)	7 (22)

* Percentages may not total 100 because of rounding. NA denotes not applicable, and NET neuroendocrine tumors.
† Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 5, with higher scores indicating greater disability.
‡ The intention-to-treat population in the extrapancreatic neuroendocrine tumors cohort included seven patients with pancreatic neuroendocrine tumors (four in the cabozantinib group and three in the placebo group) who were misallocated to the extrapancreatic neuroendocrine tumors cohort by the registering site. The intention-to-treat population in the pancreatic neuroendocrine tumors cohort included three patients with extrapancreatic neuroendocrine tumors (two in the cabozantinib group and one in the placebo group) who were misallocated to the pancreatic neuroendocrine tumors cohort by the registering site.

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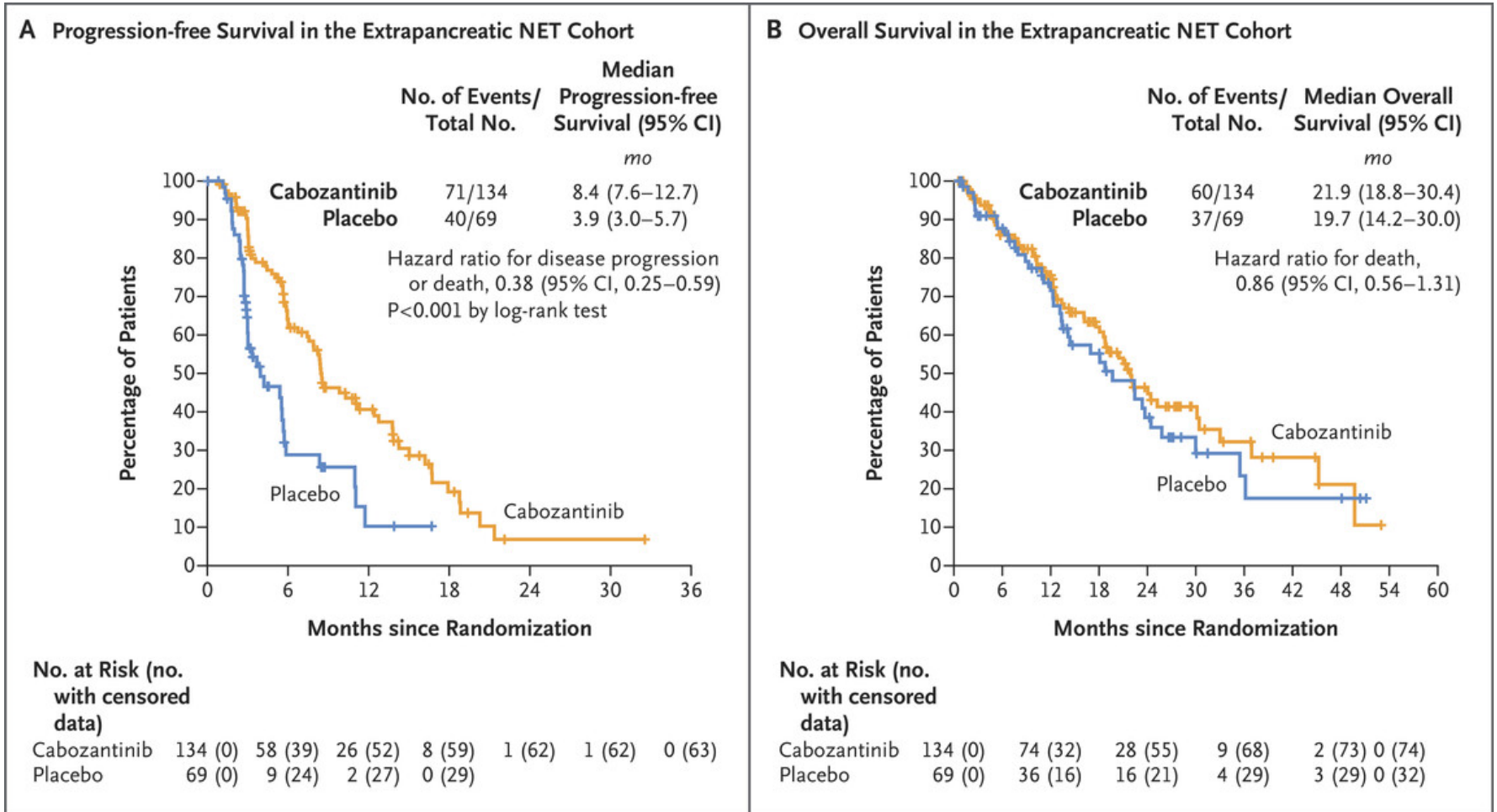
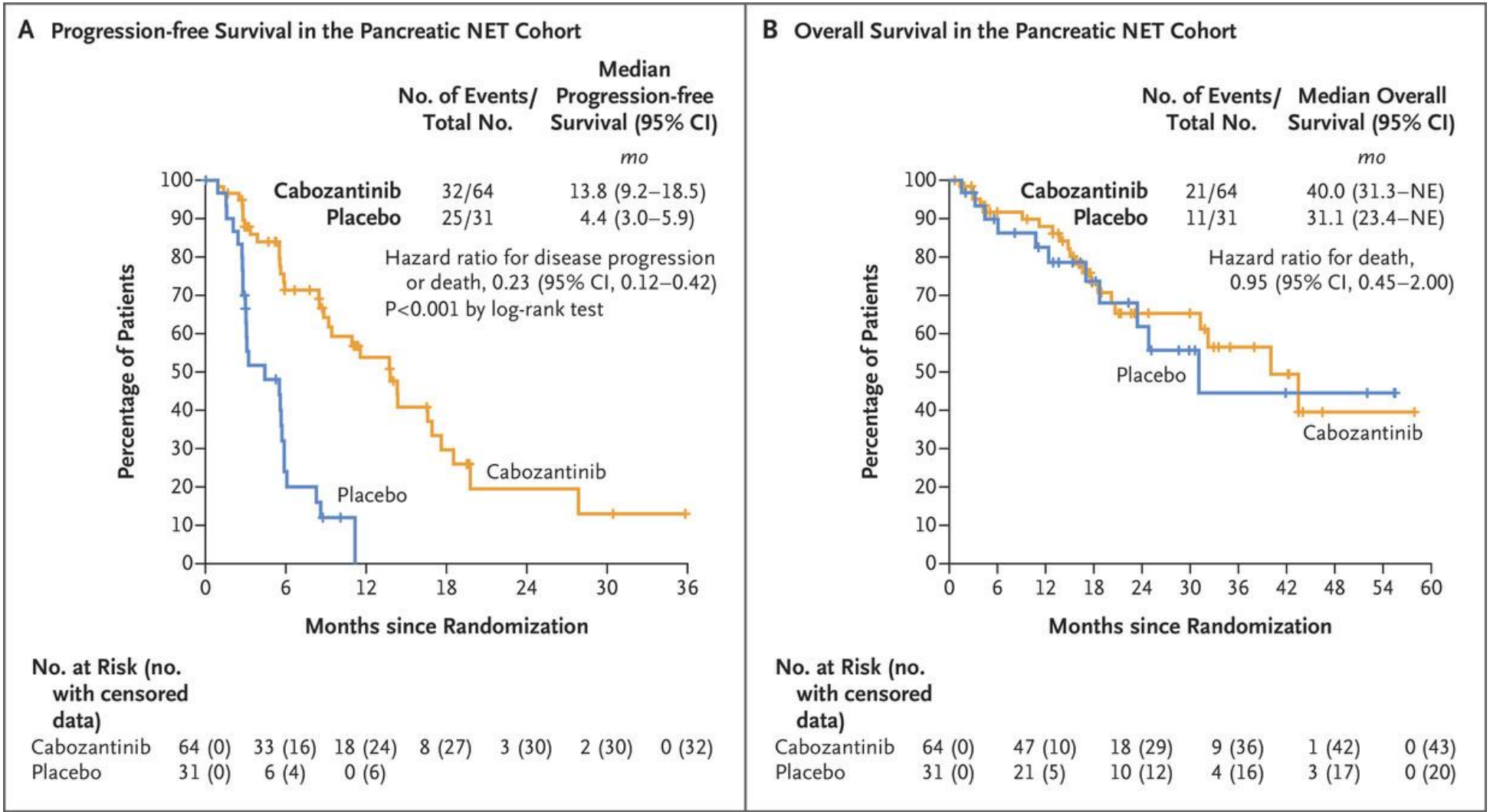
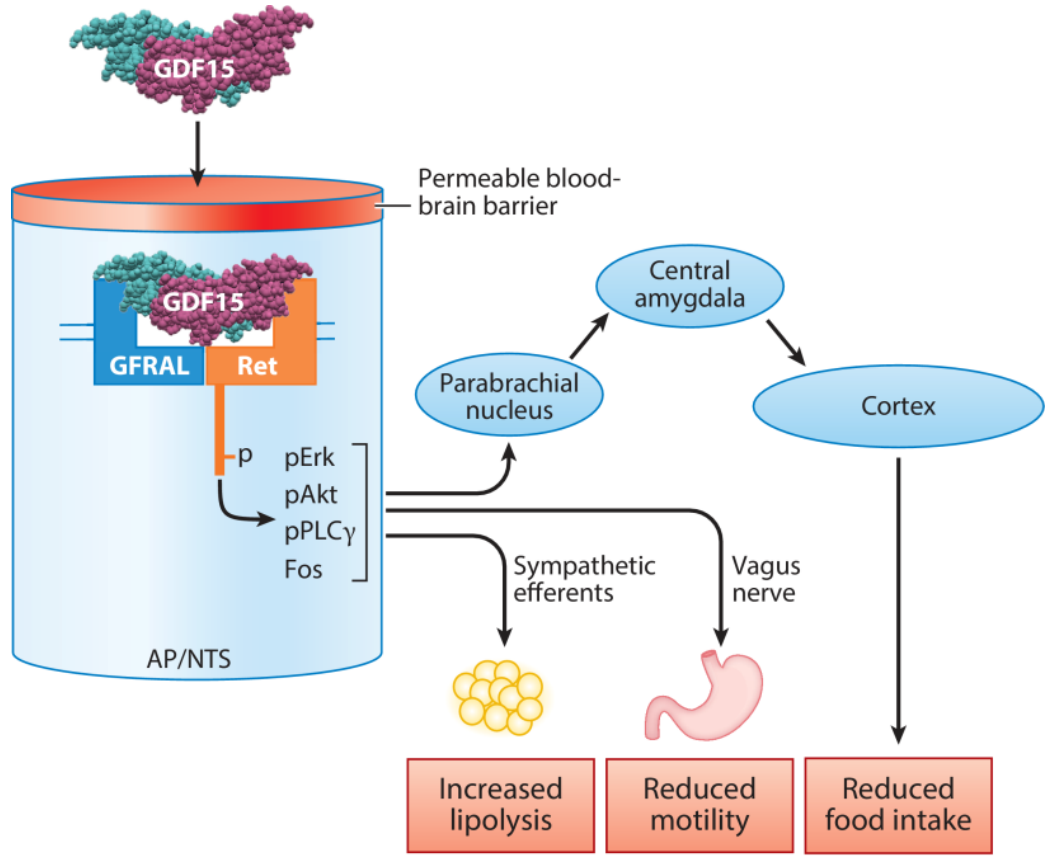
NET, fortgeschritten extrapankreatisch



NET, fortgeschritten pankreatisch

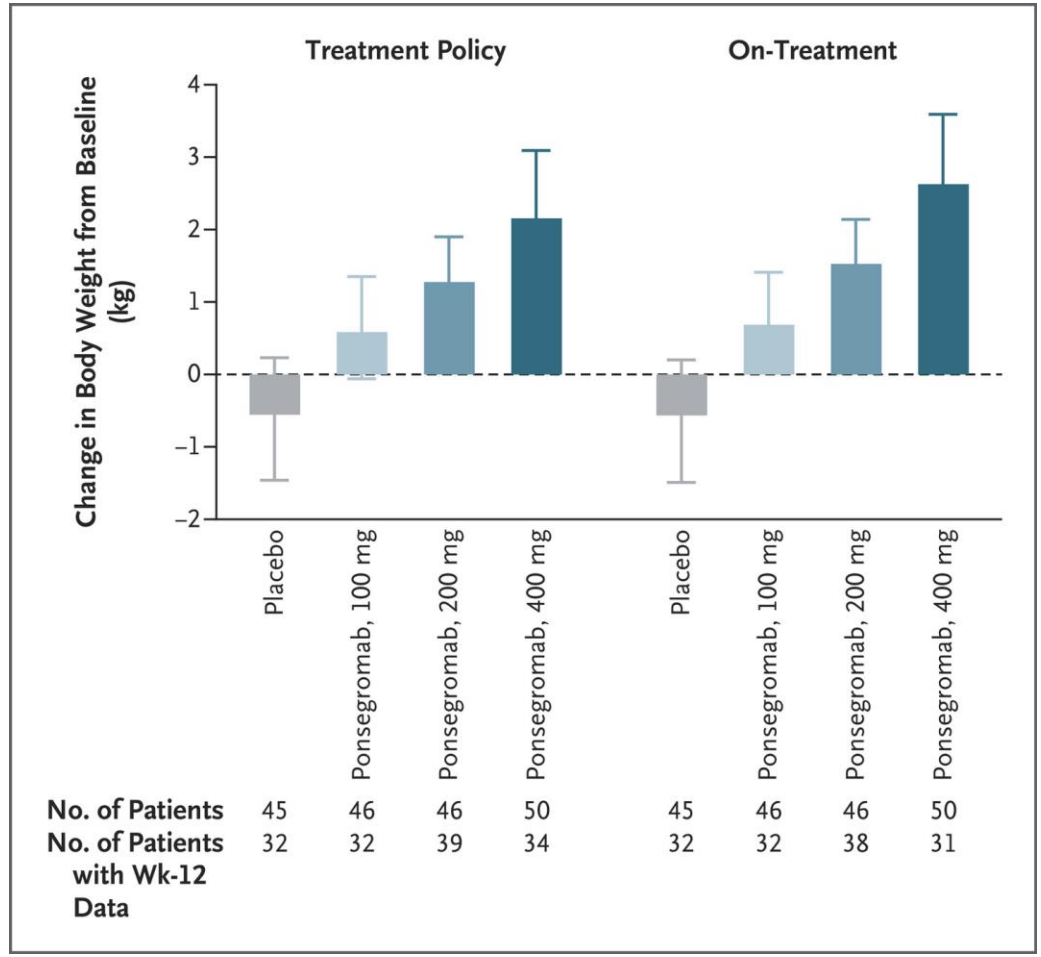


Tumorkachexie



Breit SN, et al. 2021
Annu. Rev. Physiol. 83:127–51

Tumorkachexie - Ponsegromab



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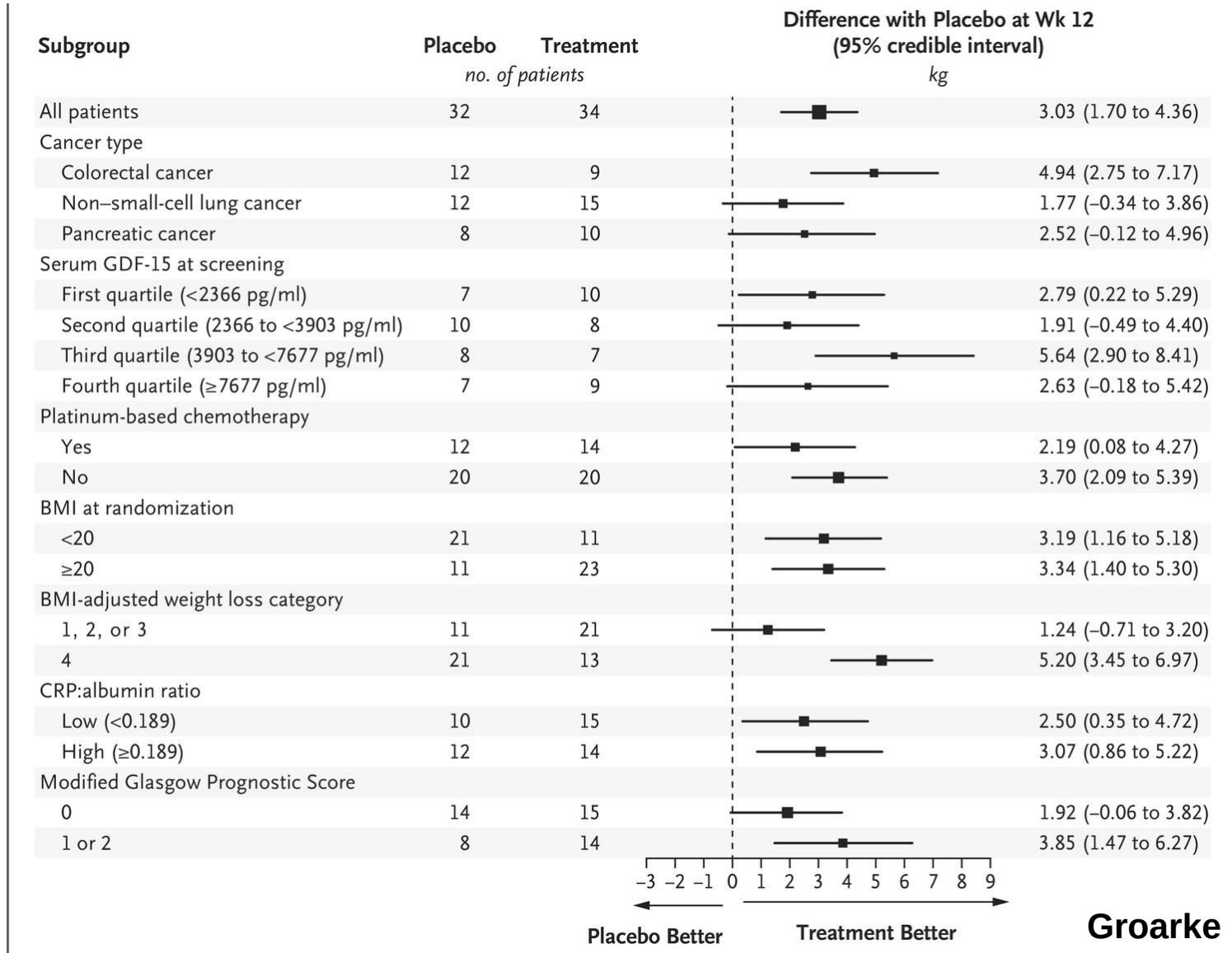
Tumorkachexie - Ponsegromab



Subgroup	Placebo	Treatment	Difference with Placebo at Wk 12 (95% credible interval)
	no. of patients		*kg*
All patients	32	34	3.03 (1.70 to 4.36)
Cancer type			
Colorectal cancer	12	9	4.94 (2.75 to 7.17)
Non–small-cell lung cancer	12	15	1.77 (–0.34 to 3.86)
Pancreatic cancer	8	10	2.52 (–0.12 to 4.96)
Serum GDF-15 at screening			
First quartile (<2366 pg/ml)	7	10	2.79 (0.22 to 5.29)
Second quartile (2366 to <3903 pg/ml)	10	8	1.91 (–0.49 to 4.40)
Third quartile (3903 to <7677 pg/ml)	8	7	5.64 (2.90 to 8.41)
Fourth quartile (≥7677 pg/ml)	7	9	2.63 (–0.18 to 5.42)
Platinum-based chemotherapy			
Yes	12	14	2.19 (0.08 to 4.27)
No	20	20	3.70 (2.09 to 5.39)
BMI at randomization			
<20	21	11	3.19 (1.16 to 5.18)
≥20	11	23	3.34 (1.40 to 5.30)
BMI-adjusted weight loss category			
1, 2, or 3	11	21	1.24 (–0.71 to 3.20)
4	21	13	5.20 (3.45 to 6.97)
CRP:albumin ratio			
Low (<0.189)	10	15	2.50 (0.35 to 4.72)
High (≥0.189)	12	14	3.07 (0.86 to 5.22)
Modified Glasgow Prognostic Score			
0	14	15	1.92 (–0.06 to 3.82)
1 or 2	8	14	3.85 (1.47 to 6.27)

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Table 3. Adverse Events.*

Event	Placebo (N=45)	Ponsegromab, 100 mg (N=46)	Ponsegromab, 200 mg (N=46)	Ponsegromab, 400 mg (N=50)	Ponsegromab, Total (N=142)	All Patients (N=187)
Any cause						
Any adverse event — no. (%)	36 (80)	32 (70)	31 (67)	37 (74)	100 (70)	136 (73)
Total no. of adverse events	138	122	118	184	424	562
Grades 1–2	102	83	86	131	300	402
Grade 3	27	32	22	42	96	123
Grade 4	4	1	4	2	7	11
Death	5†	6‡	6‡	9‡	21	26
Serious adverse event						
Patients with event — no. (%)	11 (24)	15 (33)	10 (22)	20 (40)	45 (32)	56 (30)
No. of serious events	18	20	16	35	71	89
Patients with adverse event leading to discontinuation of ponsegromab or placebo — no. (%)	6 (13)	4 (9)	5 (11)	7 (14)	16 (11)	22 (12)
Adverse events reported in ≥7% of patients — no. (%)						
Diarrhea	8 (18)	3 (7)	4 (9)	5 (10)	12 (8)	20 (11)
Neoplasm progression	4 (9)	3 (7)	5 (11)	5 (10)	13 (9)	17 (9)
Anemia	5 (11)	4 (9)	4 (9)	4 (8)	12 (8)	17 (9)
Hypokalemia	4 (9)	6 (13)	0	6 (12)	12 (8)	16 (9)
Nausea	7 (16)	1 (2)	1 (2)	4 (8)	6 (4)	13 (7)
Vomiting	6 (13)	2 (4)	3 (7)	2 (4)	7 (5)	13 (7)
Pyrexia	3 (7)	0	5 (11)	5 (10)	10 (7)	13 (7)
Event related to ponsegromab or placebo§						
Any adverse event — no. (%)	4 (9)	2 (4)	5 (11)	4 (8)	11 (8)	15 (8)
Total no. of adverse events¶	7	4	8	5	17	24
Grades 1–2	7	3	6	5	14	21
Grade 3	0	1	2	0	3	3
Serious adverse event						
Patients with event — no. (%)	0	1 (2)	1 (2)	0	2 (1)	2 (1)
No. of serious events	0	1	1	0	2	2
Patients with adverse event leading to discontinuation of ponsegromab or placebo — no. (%)	0	0	1 (2)	0	1 (1)	1 (1)
Adverse event occurring in ≥2 patients — no. (%)						
Malaise	0	1 (2)	1 (2)	0	2 (1)	2 (1)
Hypokalemia	1 (2)	0	0	1 (2)	1 (1)	2 (1)
Increase in aspartate aminotransferase	1 (2)	0	1 (2)	0	1 (1)	2 (1)

* All listed adverse events were reported after the first dose of ponsegromab or placebo and include all events that occurred either during the 12-week double-blind treatment period or during the subsequent follow-up until the first dose of open-label ponsegromab as part of the optional Part B extension period.
† One patient who was assigned to the placebo group completed the Part A period and entered Part B but did not receive any trial drug in Part B because of an adverse event. Thus, this death is not summarized in the Part A disposition (Fig. S5) but is listed in this table with Part A safety data.
‡ Among the patients who received ponsegromab, the deaths of 2 patients in the 100-mg group, 1 patient in the 200-mg group, and 3 patients in the 400-mg group that occurred during follow-up are not summarized in Figure S5.
§ The determination that an adverse event was related to ponsegromab or placebo was made by the investigator.
¶ No patient in any group had a grade 4 or fatal event that was determined to be related to ponsegromab or placebo.

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Wichtig zu wissen

• Analkarzinom, fortgeschritten/metastasiert		Immunchemotherapie
• Lungenkarzinom, NSCLC		perioperativ > adjuvant
• Magenkarzinom, lokal begrenzt		keine neoadjuvante Chemoradiotherapie
• Mammakarzinom,	TNBC neoadjuvant	Immunchemotherapie
	adjuvant	hypo = normofraktionierte Radiatio
• Melanom, metastasiert		Nivo / Ipi nach 10 Jahren
• Prostatakarzinom, mCRPC		Enzalutamid + Radium223
• NET, rezidiviert/refraktär		Cabozantinib
• Tumorkachexie		Ponsepromab
• Urothelkarzinom,	neoadjuvant	Durvalumab
	adjuvant	Pembrolizumab
• Zervixkarzinom lokal fortgeschritten		Immunradiochemotherapie

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