Updates in der Therapie lokal fortgeschrittener / metastasierter HNSCC

Sacha Rothschild

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EUROPEAN CANCER CENTRES | Zertifiziertes Onkologisches Zentrum

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Jahrestagung der Deutschen, Österreichischen und Schweizerischen Gesellschaften für Hämatologie und Medizinische Onkologie

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Patent, Urheberrecht, Verkaufslizenz
keine

Honorare
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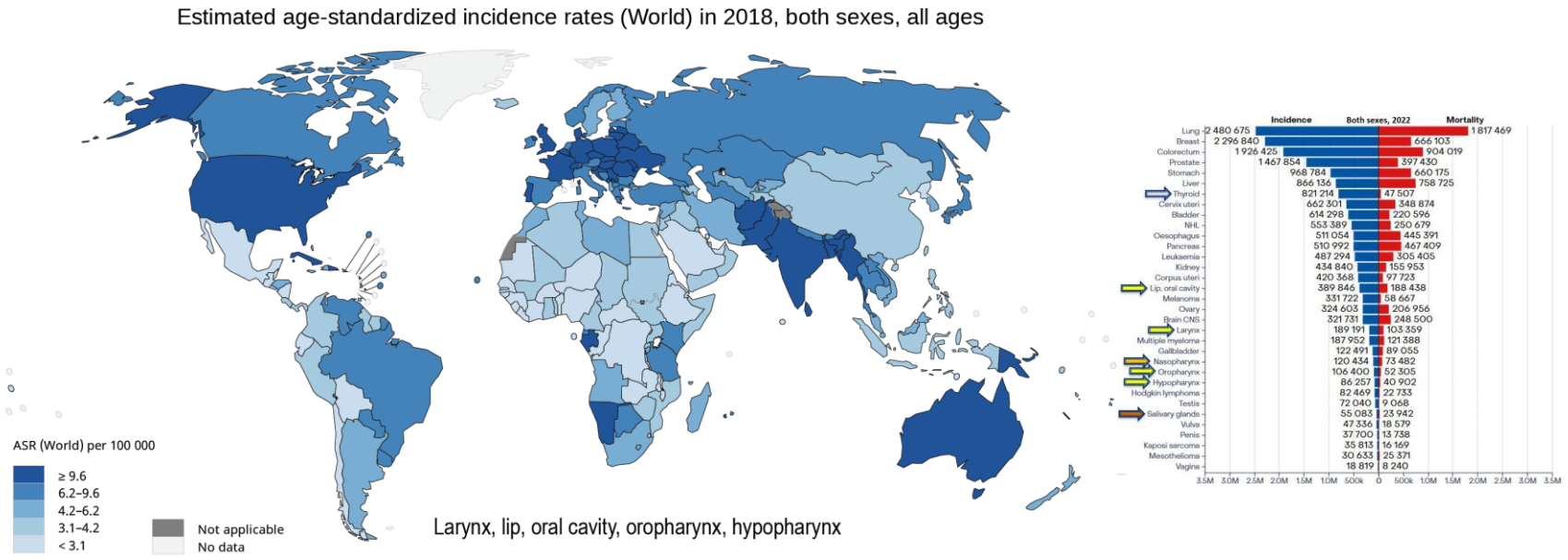
Finanzierung wissenschaftlicher Untersuchungen
AbbVie, Astra-Zeneca, BMS, Boehringer-Ingelheim, Merck, Roche

Andere finanzielle Beziehungen
keine

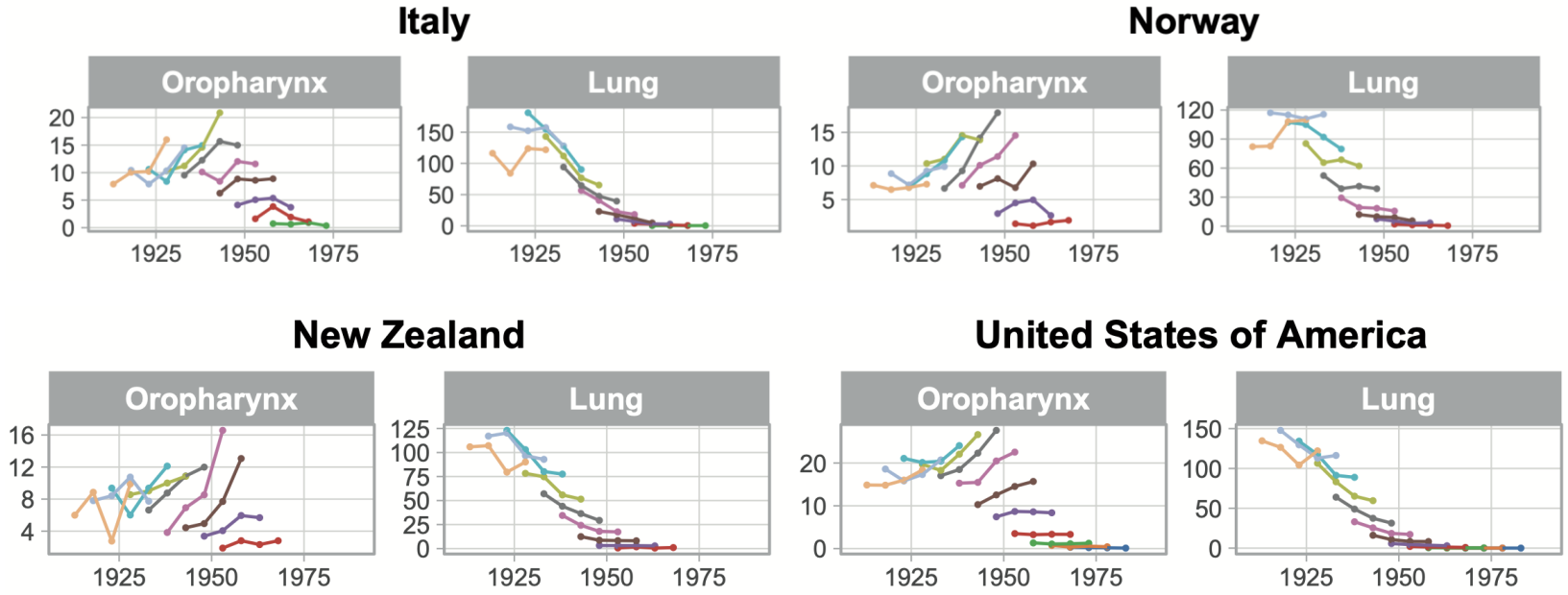
Immaterielle Interessenkonflikte
Vize-Präsident Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK); Gewähltes Mitglied der Eidgenössischen Arzneimittelkommission des Bundesamtes für Gesundheit

Kopf-Hals-Tumore - Epidemiologie



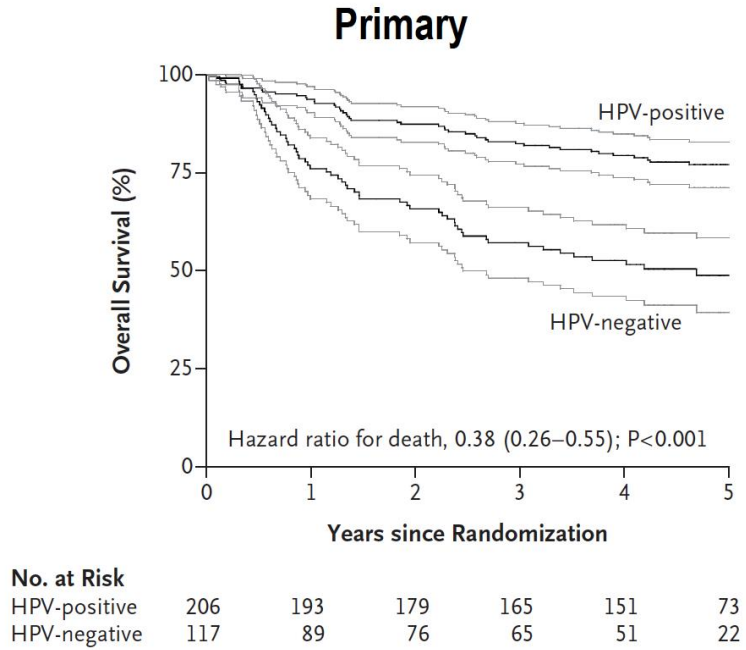
Sung H et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021.

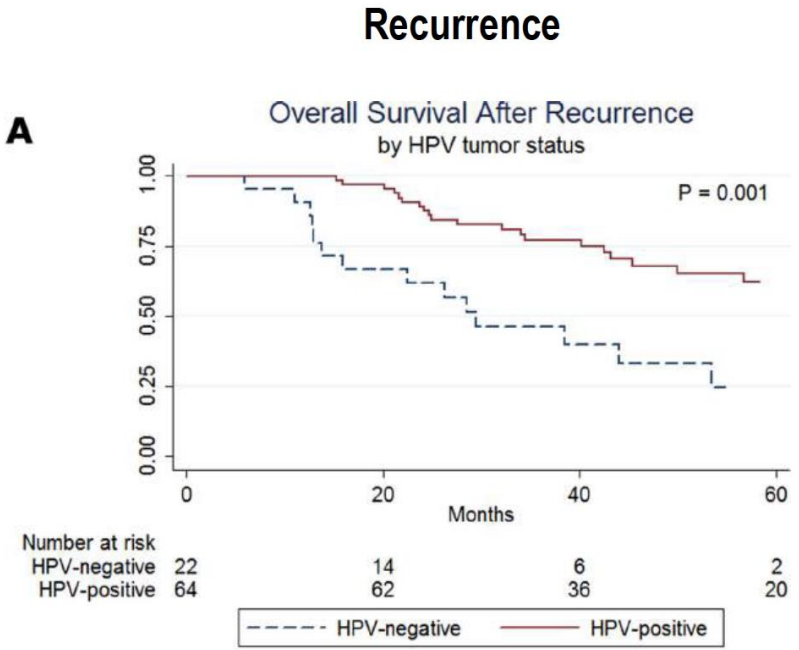
Oropharynx-Karzinome – Zunahme der Inzidenz



Zumsteg ZS, et al. J Natl Cancer Inst 2023;115:1544-1554.

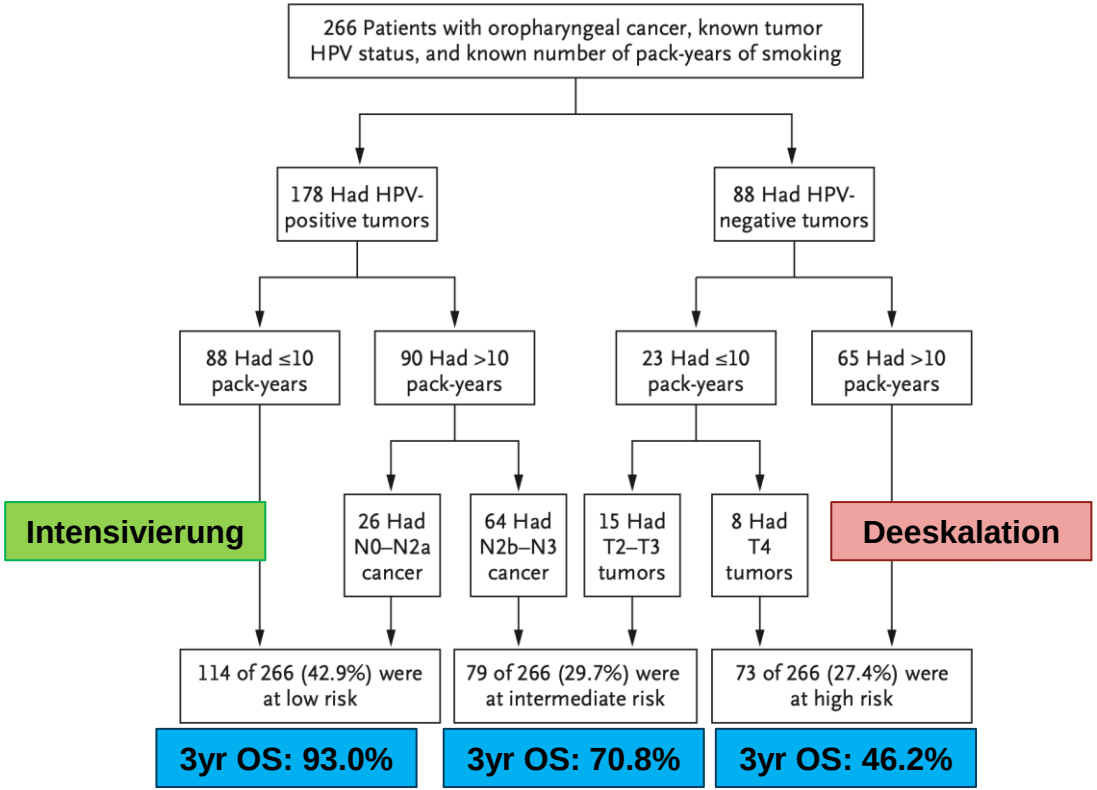
HPV-assoziierte Kopf-Hals-Tumoren – Prognose





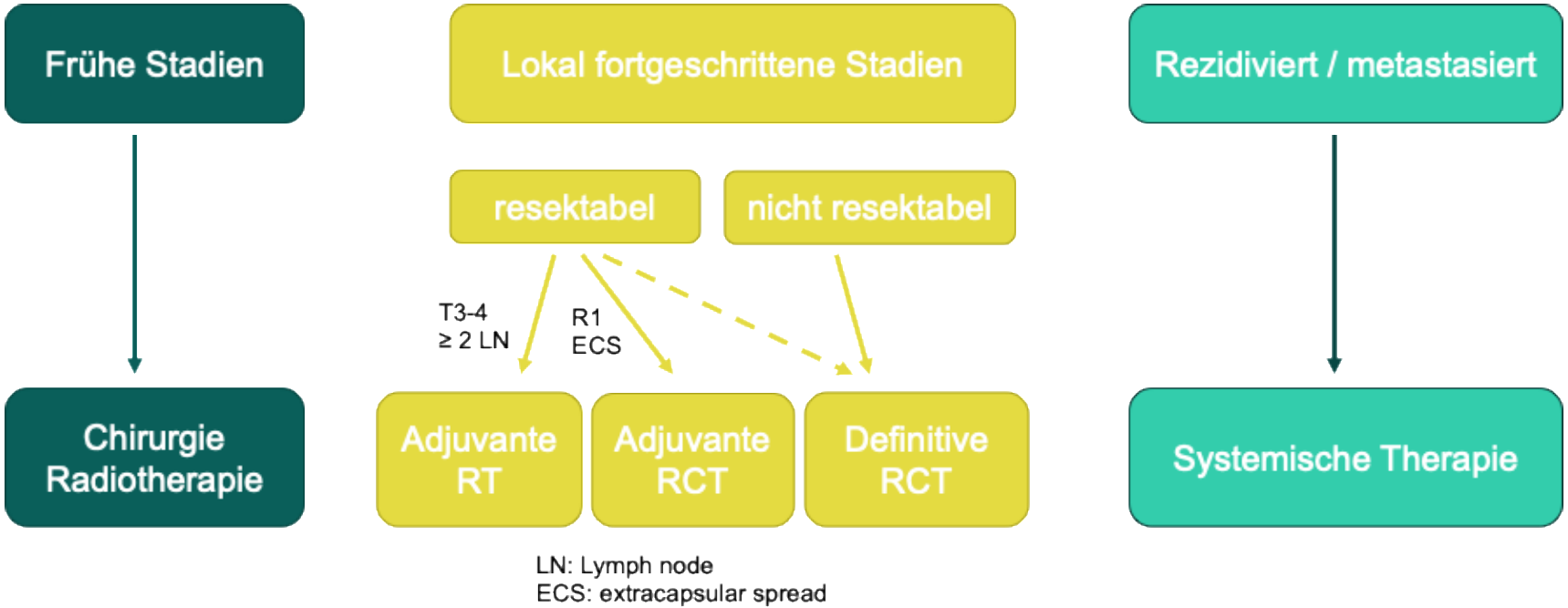
Ang K, et al. NEJM 2010;363:24-35; Josphe et al. Head & Neck 2016;28:E1501-9

Risikostratifizierung

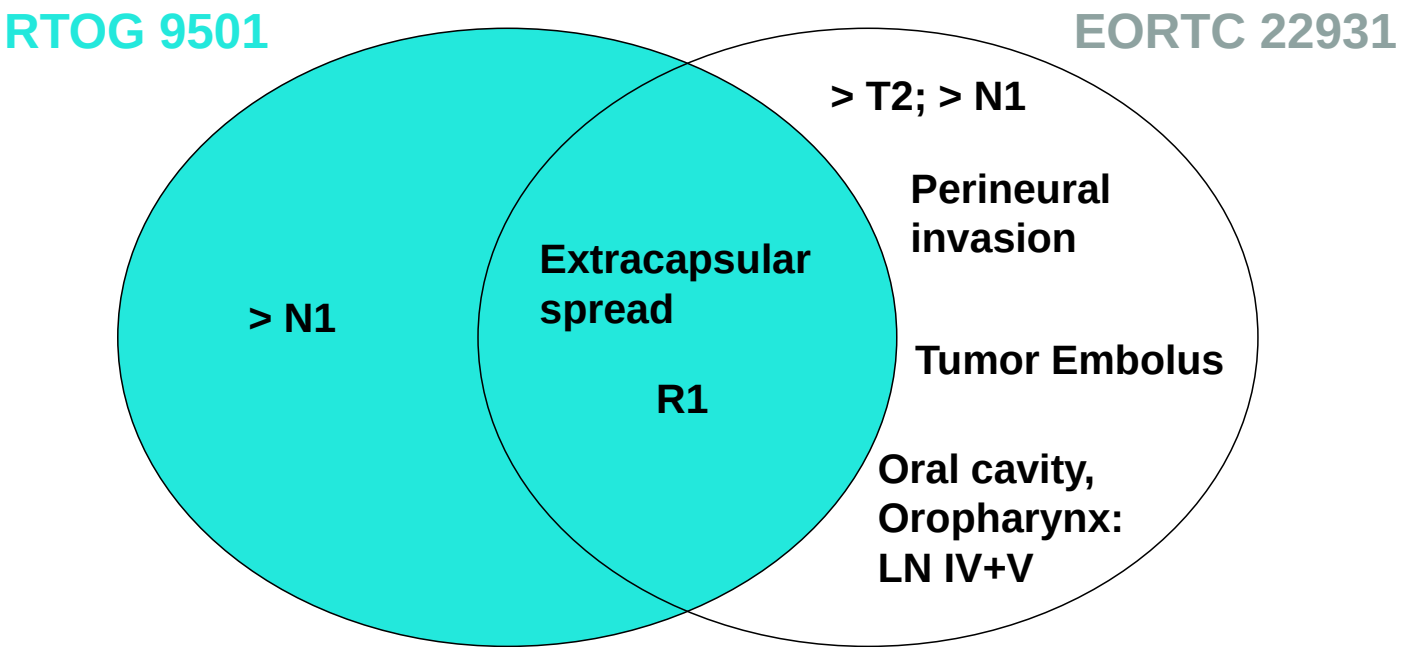


Ang K, et al. NEJM 2010;363:24-35

Behandlungskonzepte



Postoperative Radio-Chemotherapie



Cooper JS et al. NEJM 2004;350:1937-44; Bernier J et al. NEJM 2004;350:1945-52; Bernier J et al. Head Neck 2005;27:843-50

JCOG 1008 – Trial Design

Randomized non-inferiority trial

Resected HNSCC (n=261)
- Oral cavity, larynx, oro-/hypopharynx
- Stage III/IV
- R1 or ENE
- ECOG PS 0-1

R
1:1

RT + 3-weekly Cisplatin
100 mg/m^2 q3w
33x2 = 66 Gy

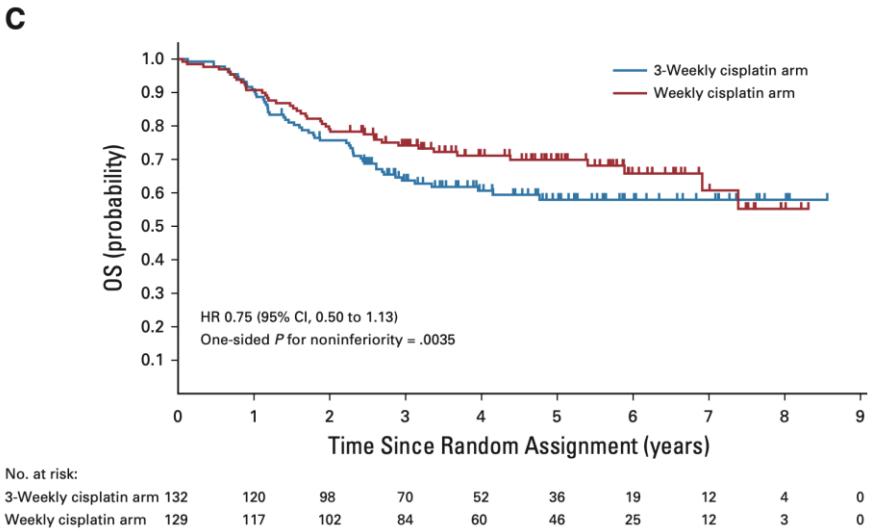
RT + weekly Cisplatin
40 mg/m^2 q1w
33x2 = 66 Gy

Primary endpoint: OS

Secondary endpoints: RFS, local RFS, nutrition-support-free survival, non-hospitalized treatment period, AEs

Kiyota N, et al. J Clin Oncol 2022;40(18):1980-1990

JCOG 1008 – Weekly Cisplatin



Parameter	3-Weekly Cisplatin (n = 132)	Weekly Cisplatin (n = 129)
Total RT dose (Gy), median (IQR)	66 (66-66)	66 (66-66)
Duration of RT (days), median (IQR)	49 (47-51)	49 (46-50)
Interval from surgery to RT initiation (days), median (IQR)	49 (42-56)	50 (43-56)
Cycles of cisplatin, median (IQR)	3 (3-3)	6 (5-7)
Cumulative dose of cisplatin (mg/m^2), median (IQR)	280 (250-299)	239 (199-277)
Proportion of actual to planned delivery of cisplatin (%), mean (SD)	88.9 (15.1)	84.1 (17.6)
Proportion of treatment completion (%), median (95% CI)	93.2 (87.5 to 96.8)	86.8 (79.7 to 92.1)

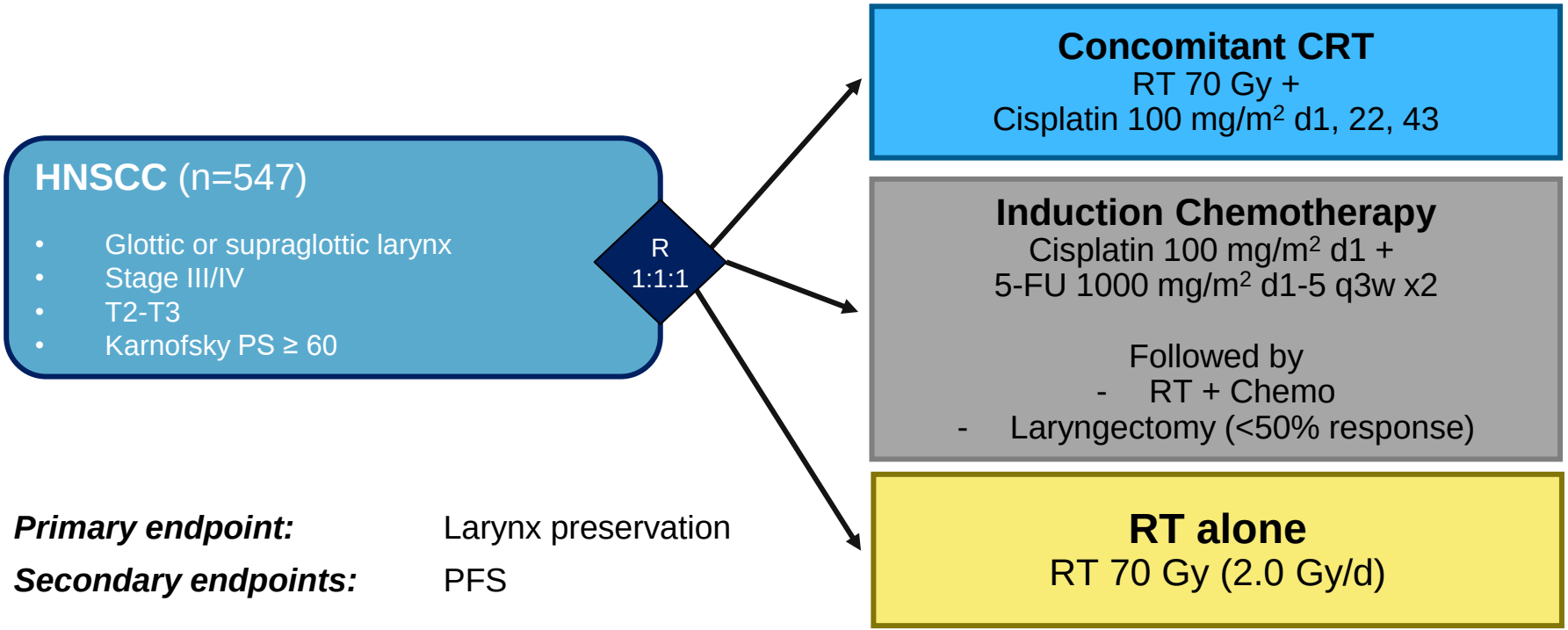
Kiyota N, et al. J Clin Oncol 2022;40(18):1980-1990

JCOG 1008 – Postoperative Radio-Chemotherapie

Non-hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade3-4(%)	Any grade	Grade3-4
Mucositis	118 (91.5%)	30 (23.3%)	113 (92.6%)	34 (27.9%)
Dysphagia	75 (58.1%)	24 (18.6%)	59 (48.4%)	14 (11.5%)
Dermatitis	118 (91.4%)	19 (14.7%)	112 (91.8%)	14 (11.5%)
Nausea	87 (67.4%)	17 (13.2%)	57 (46.7%)	6 (4.9%)
Infection	25 (19.4%)	15 (11.6%)	18 (14.8%)	8 (6.6%)
Hyponatremia	119 (92.2%)	13 (10.1%)	100 (82.0%)	13 (10.7%)
Renal impairment	51 (39.5%)	0 (0%)	36 (29.5%)	0 (0.0%)
Hearing impairment	22 (17.1%)	5 (3.9%)	9 (7.4%)	2 (1.6%)
Peripheral neuropathy	7 (5.4%)	0 (0.0%)	2 (1.6%)	0 (0.0%)

Kiyota N, et al. J Clin Oncol 2022;40(18):1980-1990

Kombinierte Radio-Chemotherapie (RTOG 91-11)



Primary endpoint: Larynx preservation

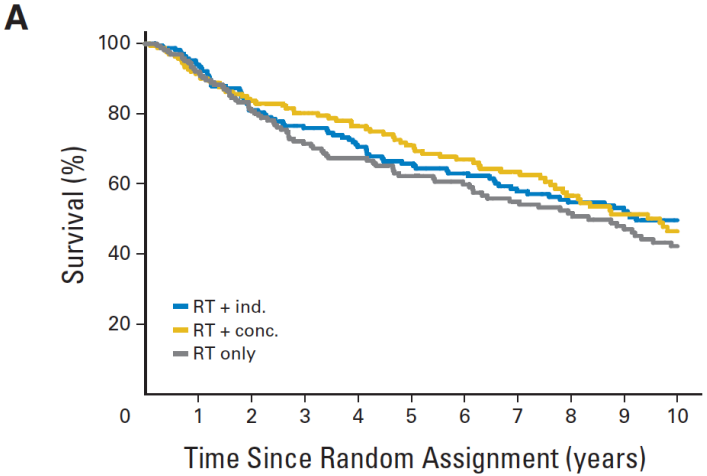
Secondary endpoints: PFS

Stratification: site of primary tumor, N stage, T stage

Forastiere AA, et al. NEJM 2003;349:2091-8

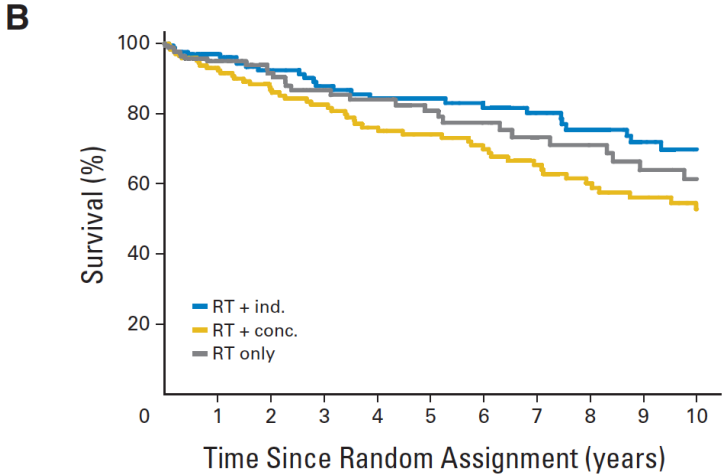
Kombinierte Radio-Chemotherapie (RTOG 91-11)

Survival (death from study cancer)



No. at risk											
RT + ind.	174	157	128	116	104	96	88	76	69	61	52
RT + conc.	174	146	126	113	100	90	80	70	56	46	36
RT only	172	148	126	105	96	83	76	65	59	51	43

Survival (death not caused by study cancer)



No. at risk											
RT + ind.	174	117	88	76	70	66	60	52	46	38	30
RT + conc.	174	124	107	91	79	73	64	54	45	38	30
RT only	172	102	78	66	59	49	42	34	31	26	24

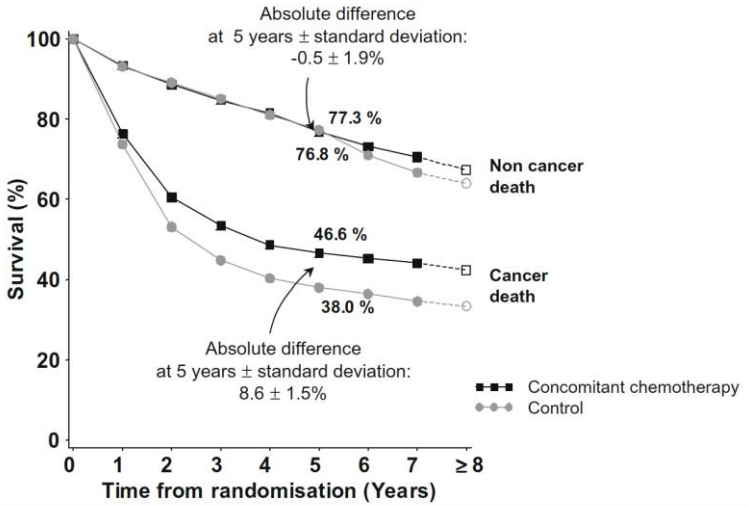
5yr OS: 58% vs, 55% vs. 54%
10yr OS: 39% vs. 28% vs. 32%

Death unrelated to cancer or treatment:
20.8% vs. 30.8% vs. 16.9%

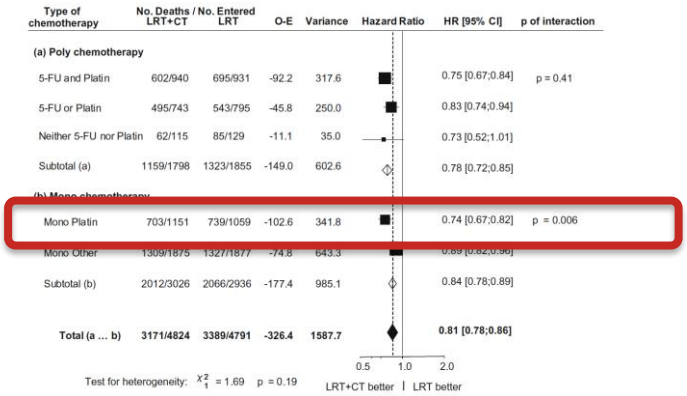
Forastiere AA, et al. NEJM 2003;349:2091-8

MACH Meta-Analyse

- 93 randomized studies
- >17’346 patients



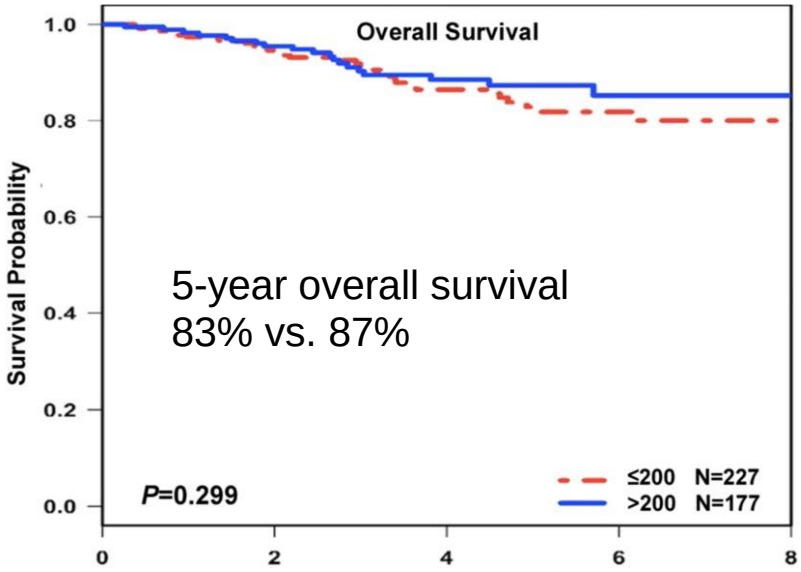
	Survival		
	HR	5yr OS benefit	p-value
Chemotherapy	0.90	4.4%	<0.0001
Concomittant chemotherapy	0.81	8%	<0.0001



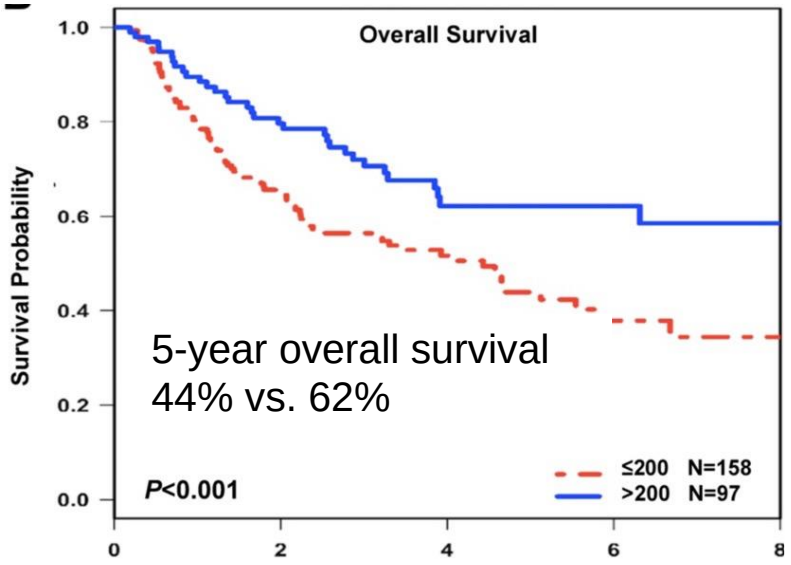
Pignon JP et al. Radiat Oncol 2009;92:4-14

Dosierung von Cisplatin

HPV positive



HPV negative



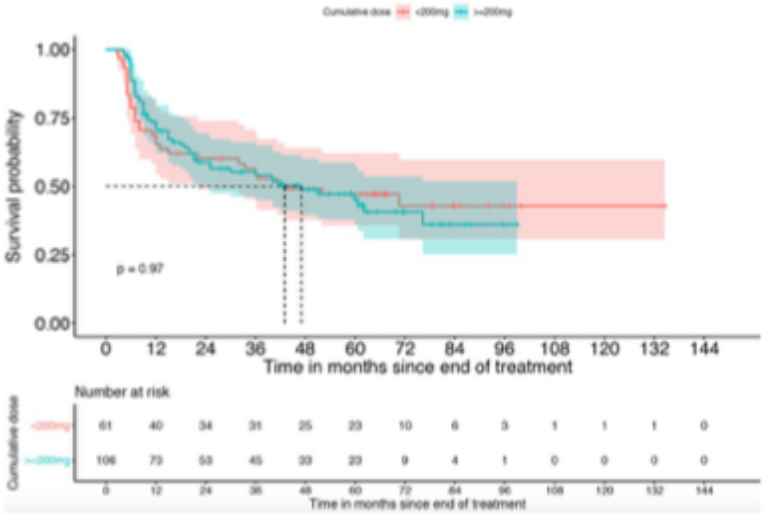
Results confirmed in multivariate analysis.

Cisplatin dose reduction ≤ 200 mg/m² has a detrimental impact on overall survival in HPV negative patients.

Spreafico A, et al. Eur J Cancer. 2016 Nov;67:174-182

3-wöchentliches vs. wöchentliches Cisplatin

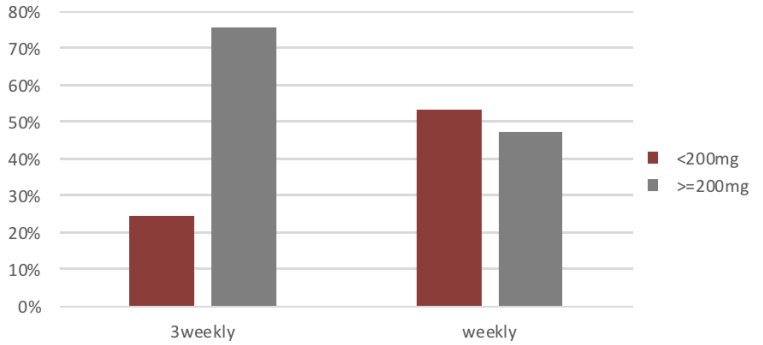
N=314 (127 pts. 3-weekly schedule; 187 pts. weekly schedule)



Cisplatin dose

- Median cumulative cisplatin dose was 200 mg/m2 (IQR 150-300) for pts treated with a 3-weekly schedule and 160 mg/m2 (120-240) for the weekly schedule
- More patients treated with a 3-weekly schedule reached a cumulative dose ≥ 200 mg/m^2 (75.6% vs. 47.1%, p<0.001)
- This association was also observed in multivariable analysis adjusted for age and sex (OR 3.46, 95% confidence interval [CI], 2.1 - 5.7)

Fig. 1 – Cumulative cisplatin dose



Helfenstein, Pless, Riesterer, Meier, Papachristofilou, Kasenda, Rothschild. Radiat Oncol 2019;14:32

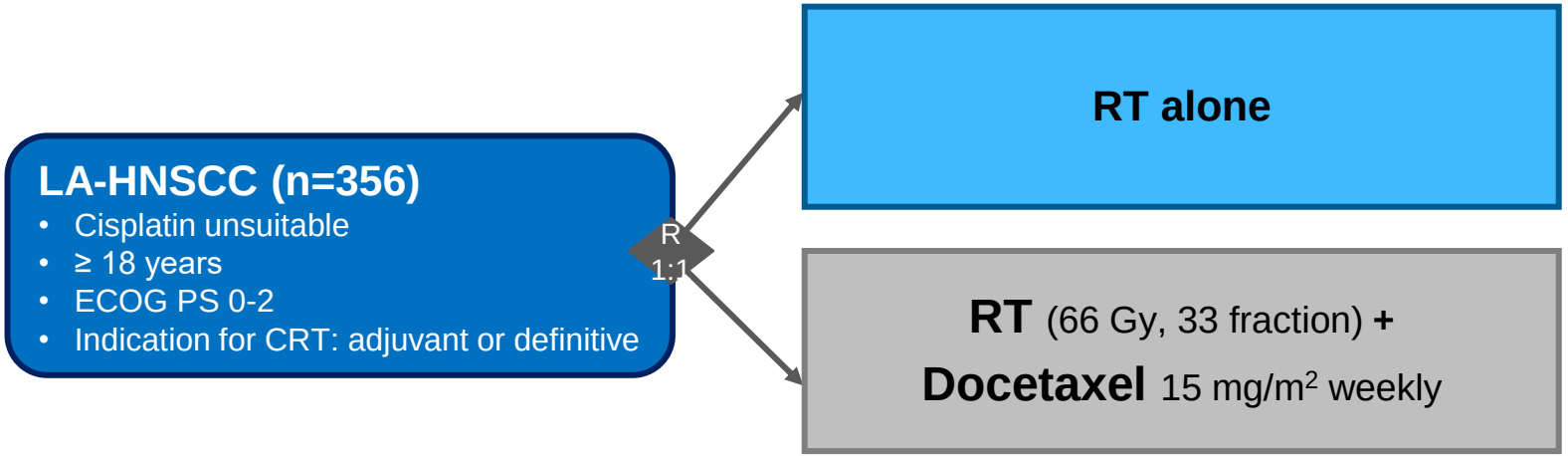
3-wöchentliches vs. wöchentliches Cisplatin

N=314 (127 pts. 3-weekly schedule; 187 pts. weekly schedule)

Toxicity	3-weekly (n=127)	Weekly (n=187)	Total (n=314)	p-value
Nephrotoxicity				0.022
- Yes	42 (33.1%)	39 (20.9%)	81 (25.8%)	
- No	85 (66.9%)	148 (79.1%)	233 (74.2%)	
Ototoxicity				0.711
- Yes	19 (15%)	24 (12.8%)	43 (13.7%)	
- No	108 (85%)	163 (87.2%)	271 (86.3%)	

Helfenstein, Pless, Riesterer, Meier, Papachristofilou, Kasenda, Rothschild. Radiat Oncol 2019;14:32

Docetaxel as a radiosensitizer in Cisplatin-ineligible patients – Trial Design



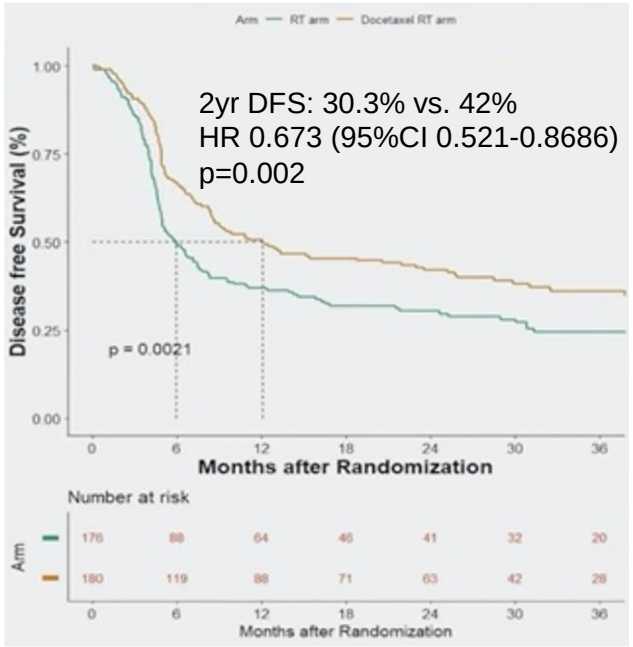
Primary endpoint: 2yr DFS

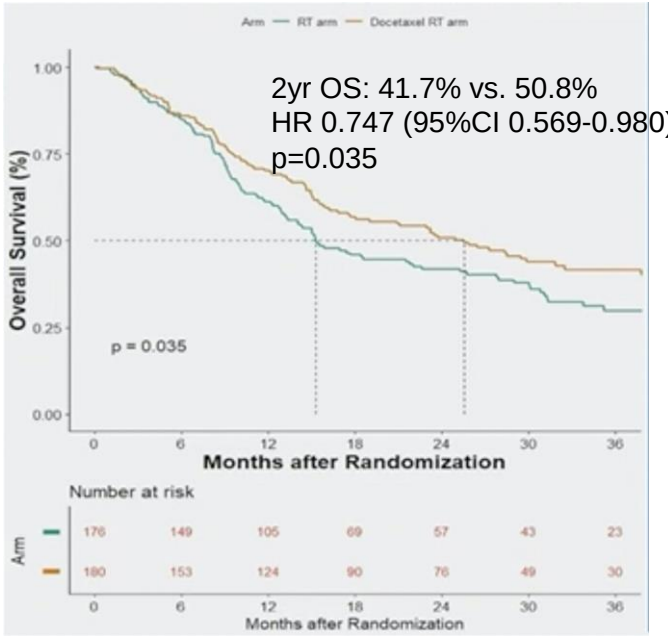
Secondary endpoints: 2yr OS, AEs, QoL

Stratification: Site of tumor; T-stage; N-stage; indication (adjuvant vs. definitive)

Noronha H, et al. ASCO 2022;Abstract 6003

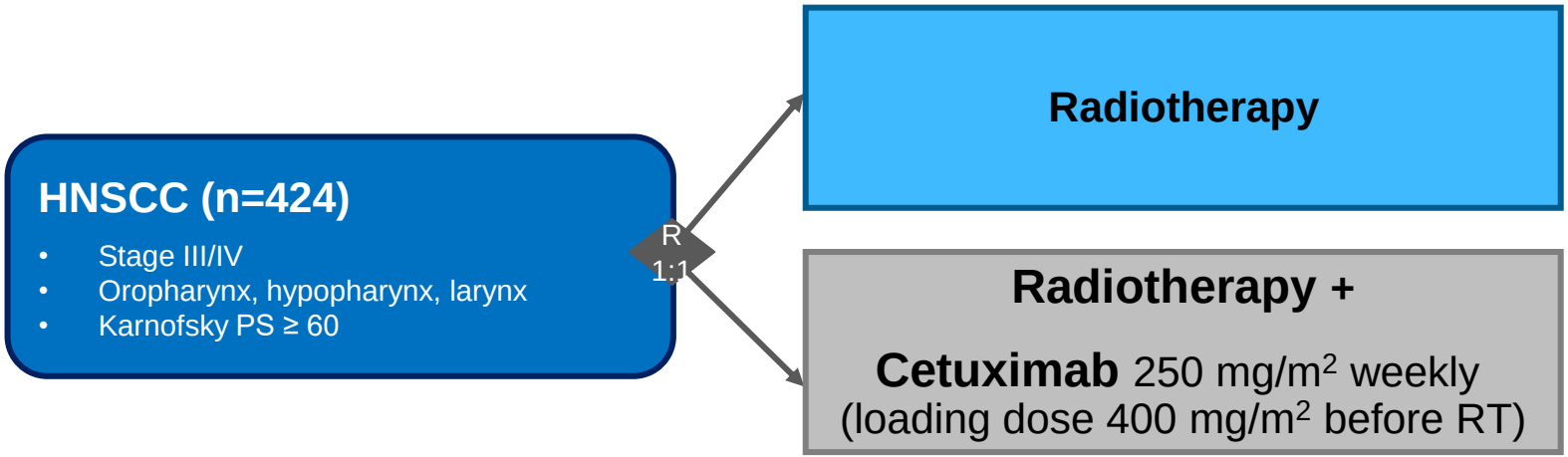
Docetaxel as a radiosensitizer in Cisplatin-ineligible patients – Study Design





Noronha H, et al. ASCO 2022;Abstract 6003

Radiotherapie + Cetuximab



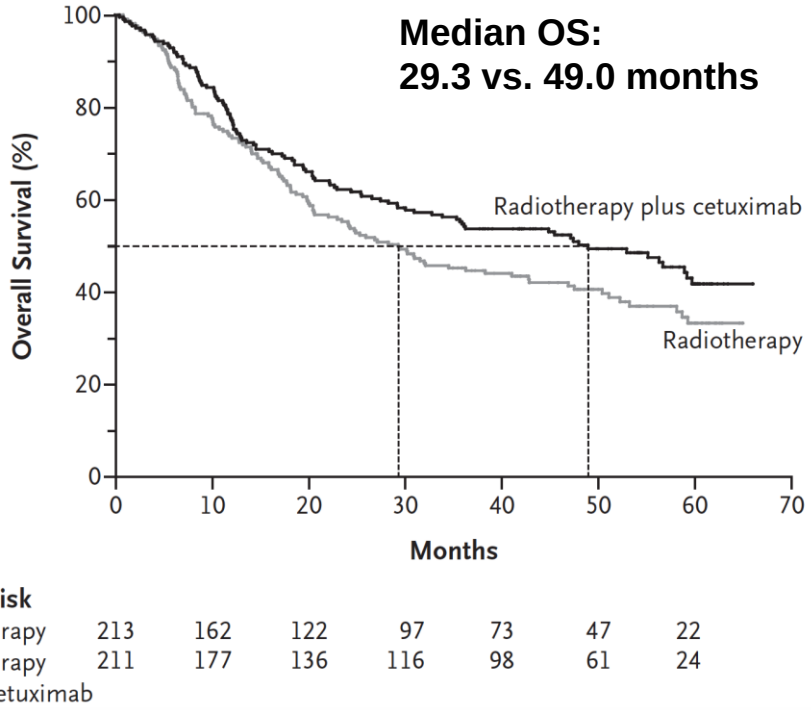
Primary endpoint: Locoregional control

Secondary endpoints: OS, PFS, ORR, Safety

Stratification: Karnofsky PS, nodal involvement, tumor stage, RT regimen

Bonner JA et al. NEJM 2006;354:567-78

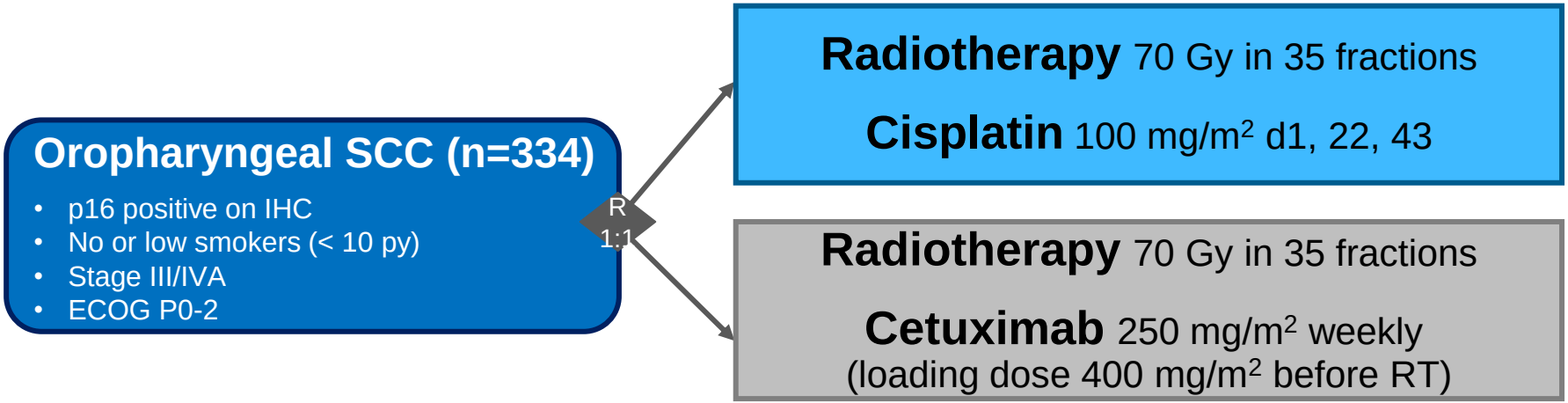
Radiotherapie + Cetuximab



- Similar severe toxicity to RT alone, except skin rash and infusion reactions[1]
- Improved OS 12% over RT alone[1]
- HR for death: 0.74, p=0.03
- HPV+ OPSCC: highest improvement in survival[2]
  - HR for death: 0.38, p=0.03
- Meta-analysis suggests cetuximab better tumor control than cisplatin in HPV+ disease[3]

[1]Bonner JA, et al. NEJM 2006;354:567-78; [2]Rosenthal DI, et al. J Clin Oncol. 2016;34(12):1300-8; [3]Huang J, et al. BMC Cancer 2016;16:689

De-ESCALaTE HPV – Trial Design



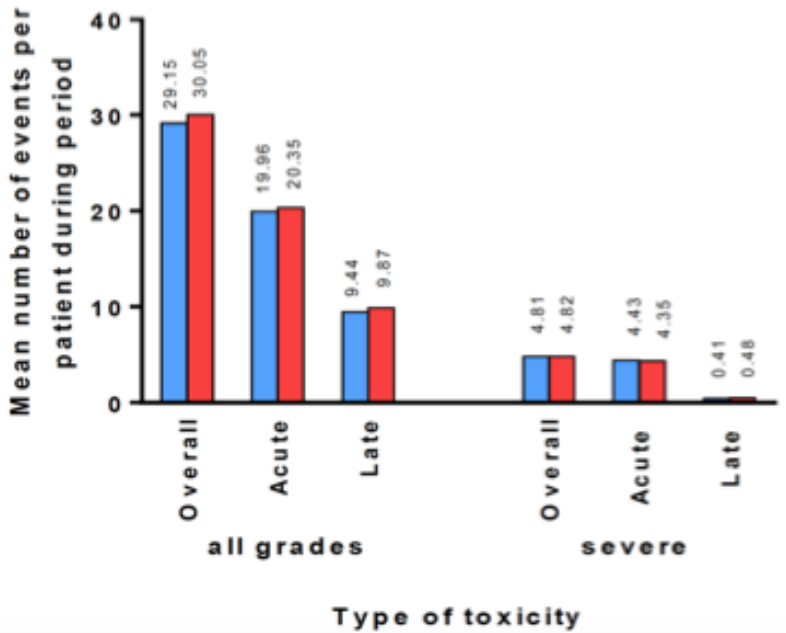
Primary endpoint: Overall severe (grade 3-5) toxicity at 24 months

Secondary endpoints: QoL, swallowing, OS, recurrence, cost effectiveness

Stratification: Centre, T stage, N stage, RT laterality, planned PEG use

Mehanna H, et al. Lancet 2019;393(10166):51-60.

De-ESCALaTE HPV – Toxicity



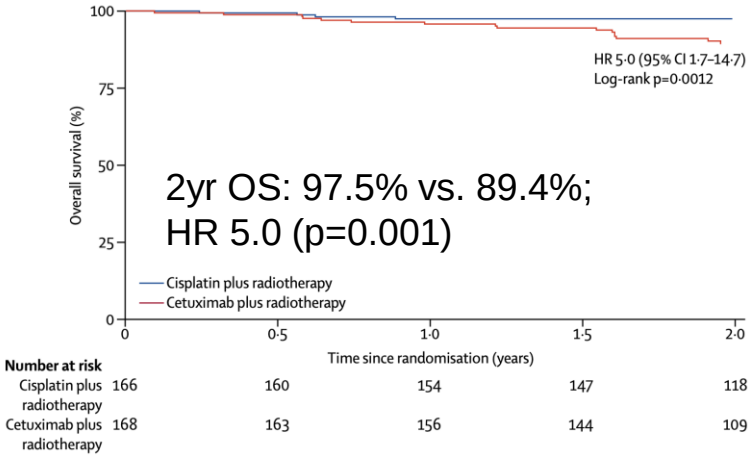
Overall severe toxicity events per patient:

- Cisplatin: 4.81 (95%CI 4.23-5.40)
- Cetuximab: 4.82 (95%CI 4.22-5.43)
- p=0.98

Mehanna H, et al. Lancet 2019;393(10166):51-60.

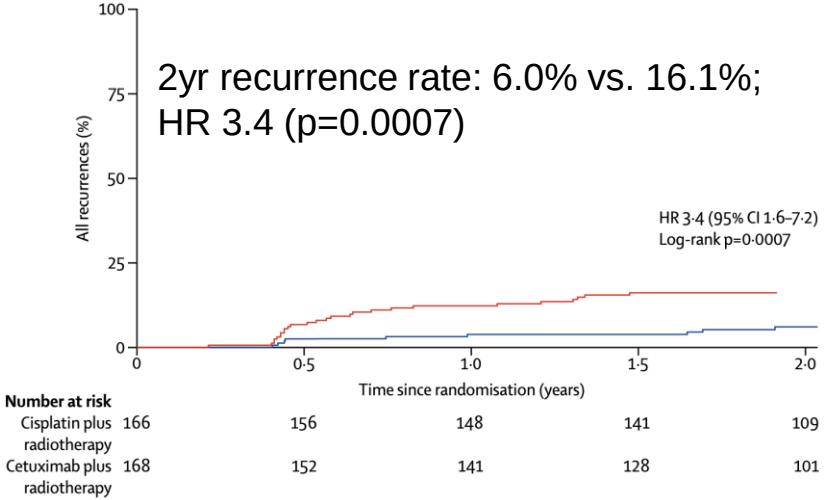
De-ESCALaTE HPV – Outcome

Overall Survival



2yr OS: 97.5% vs. 89.4%;
HR 5.0 (p=0.001)

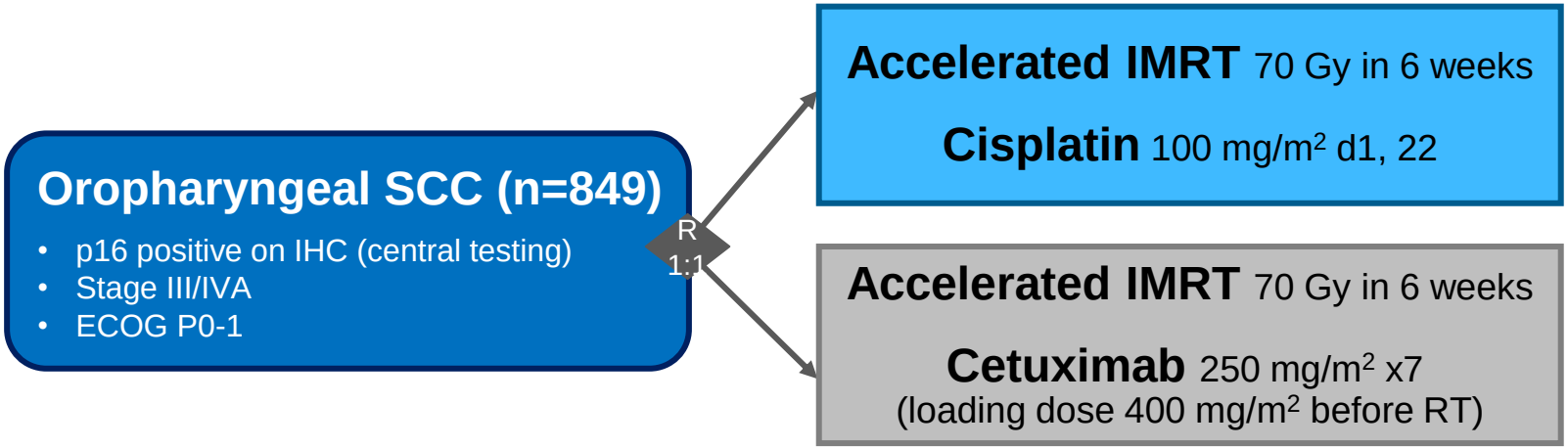
Recurrences



2yr recurrence rate: 6.0% vs. 16.1%;
HR 3.4 (p=0.0007)

Mehanna H, et al. Lancet 2019;393(10166):51-60.

RTOG 1016 – Randomized non-inferiority trial



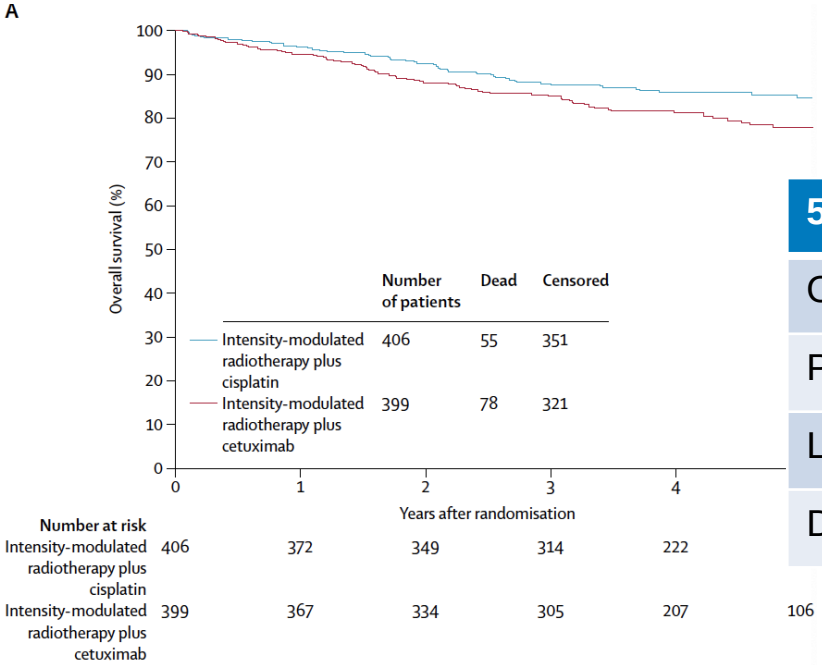
Primary endpoint: OS

Secondary endpoints: PFS, locoregional failure, distant metastases, Aes, feeding tube placement, dental health, QoL

Stratification: T stage; N stage; ECOG PS; smoking history

Gillison ML, et al. Lancet 2019; 393(10166):40-50

RTOG 1016 – Outcomes



5yr outcomes	Cisplatin	Cetuximab	p-value
OS	85%	78%	0.02
PFS	78%	67%	<0.001
Locoregional failure	10%	17%	<0.001
Distant metastasis	9%	12%	0.09

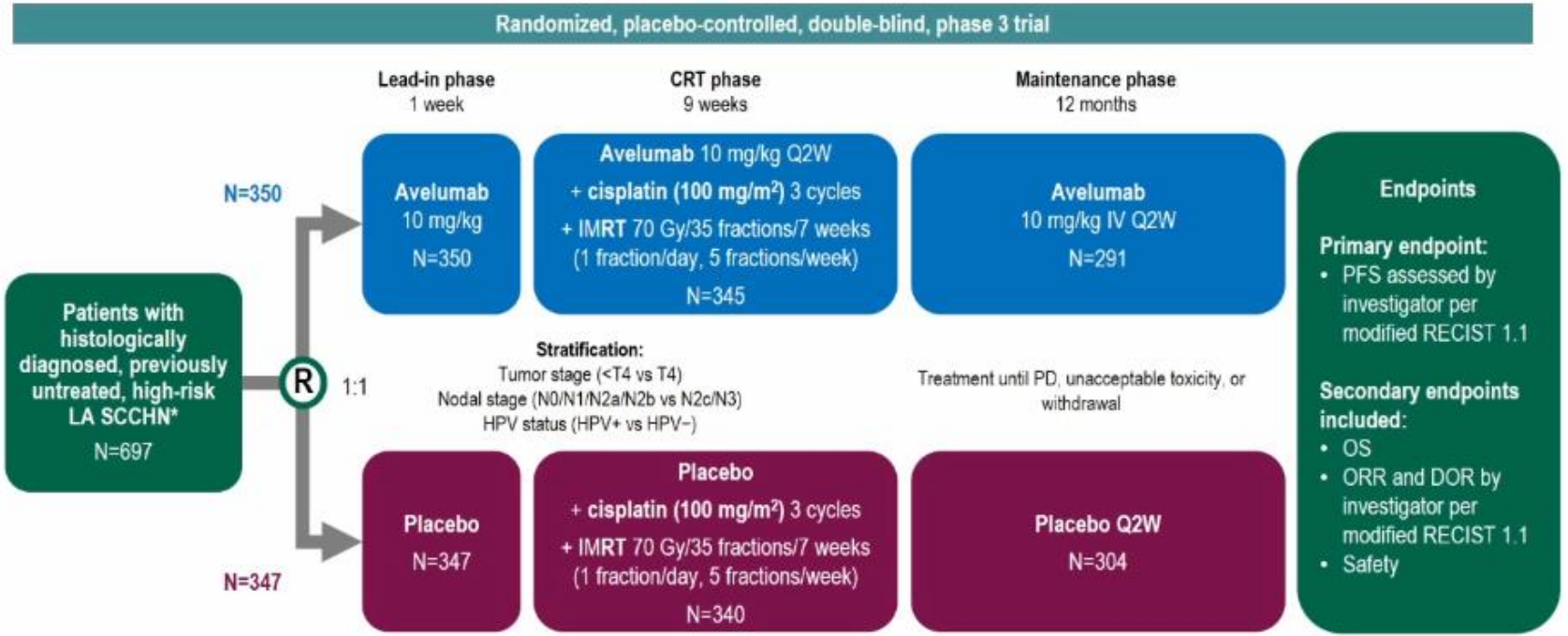
Gillison ML, et al. Lancet 2019; 393(10166):40-50

Radio-Chemotherapie + Immuncheckpoint-Inhibitoren

Study	Phase	Population	Arms	Adjuvant
CA-209-9TM (NCT03349710)	III	N=1046 Intermediate or high risk	CRT + CDDP +/- Nivo CRT + Nivo vs. Cetuximab	Nivo vs. Placebo Nivo vs. Placebo
KEYNOTE-412 (NCT03040999)	III	N=780 Intermediate or high risk	CRT + CDDP + Pembro CRT + CDDP + Placebo	Pembro Placebo
REACH (NCT02999087)	III	N=688 Stage III/IVA	CRT + Avelumab + Cetuximab CRT + CDDP + Cetuximab	Avelumab
JAVELIN HN100 (NCT02952586)	III	N=640 Intermediate or high risk	CRT + Avelumab + CDDP CRT + CDDP + Placebo	Avelumab Placebo
NRG-HN004 (NCT03258554)	II/III	N=533 CDDP unfit, intermediate / high risk	CRT + Durvalumab CRT + Cetuximab	Durvalumab
PembroRad (NCT02707588)	II	N=133 Stage III/IV, CDDP unfit	CRT + Pembro CRT + Cetuximab	
KEYCHAIN (NCT03383094)	II	N=122 p16+, high or intermediate risk	CRT + Pembro CRT + CDDP	Pembro
UPC 15-132 (NCT02777385)	II	N=44 Intermediate or high risk	CRT + CDDP CRT + CDDP + Pembro	Pembro Pembro

clinicaltrials.gov

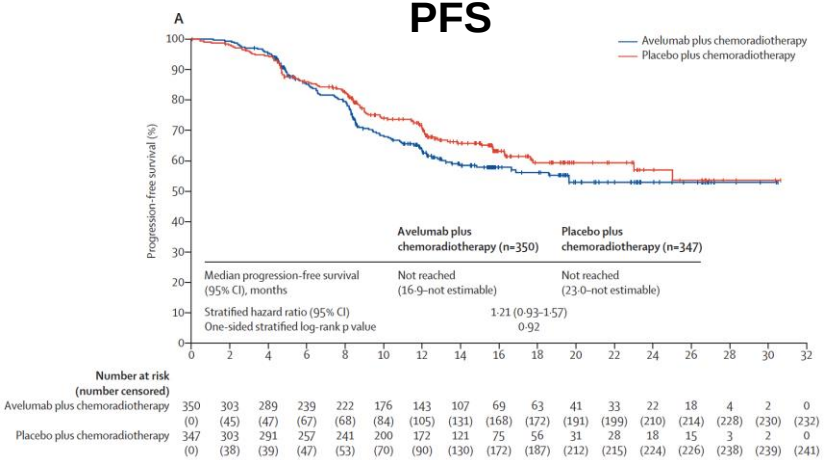
JAVELIN 100 – Trial Design



Lee NY, et al. Lancet Oncol 2021; 22: 450–62

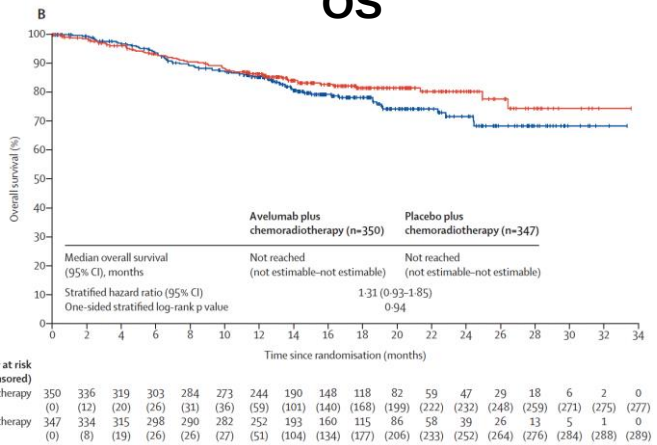
JAVELIN 100 – Outcome

PFS



HR 1.21 (95%CI 0.93-1.57), p=0.92

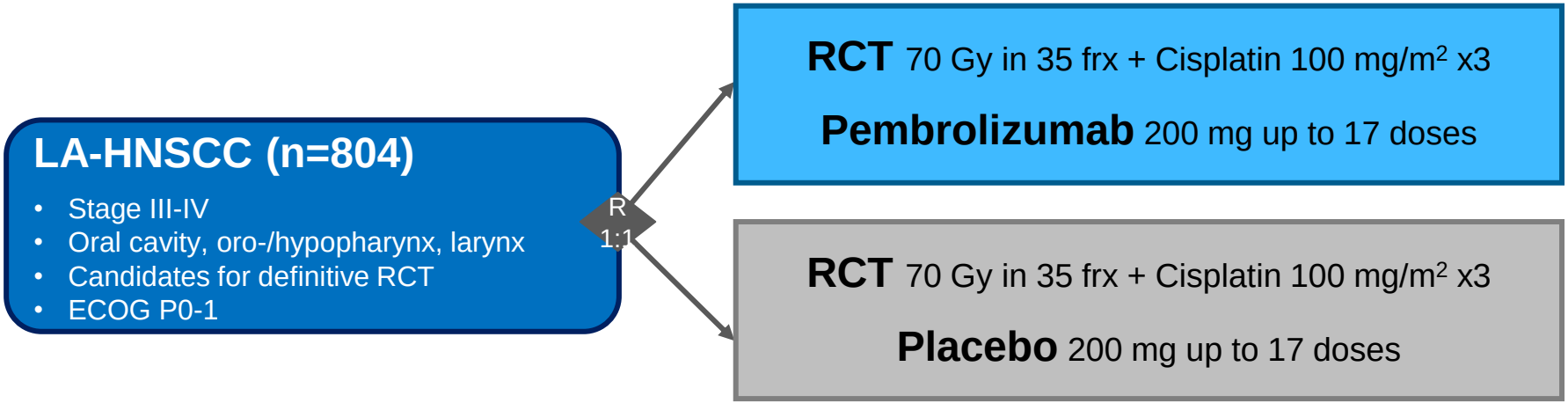
OS



HR 1.31 (95%CI 0.93-1.85), p=0.94

Lee NY, et al. Lancet Oncol 2021; 22: 450–62

KEYNOTE-412- Trial Design



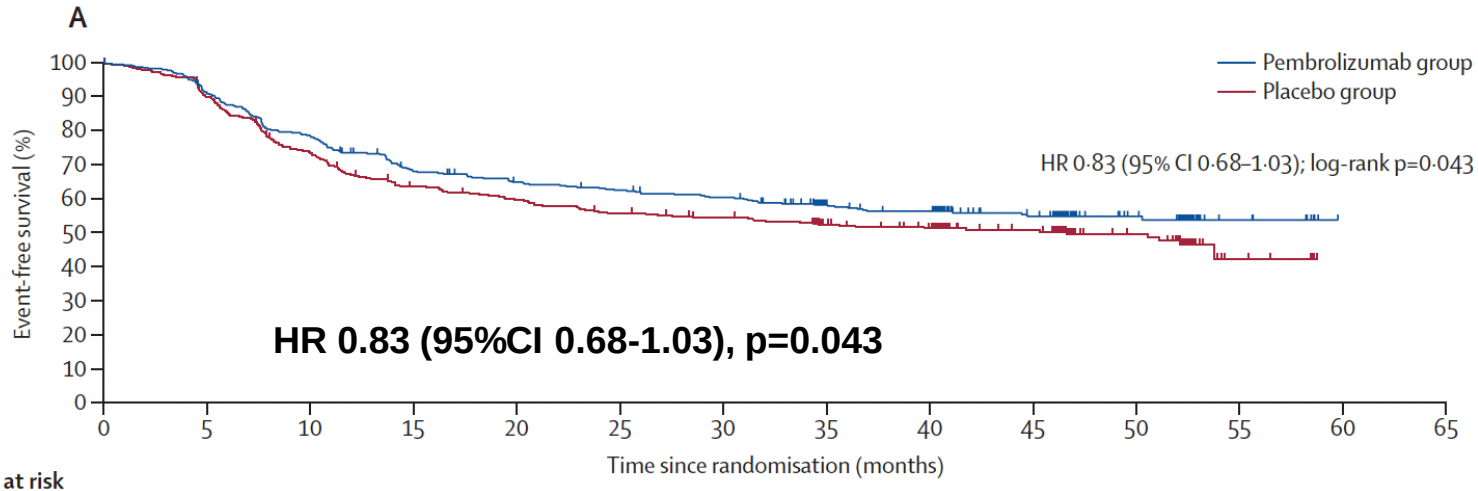
Primary endpoint: EFS

Secondary endpoints: OS, safetey, QoL, PROM

Stratification: RT regimen (accelerated vs. standard), tumor site, p16 status, stage

Machiels JP, et al. Lancet Oncol 2024;25:572-87

KEYNOTE-412 – Event-Free Survival

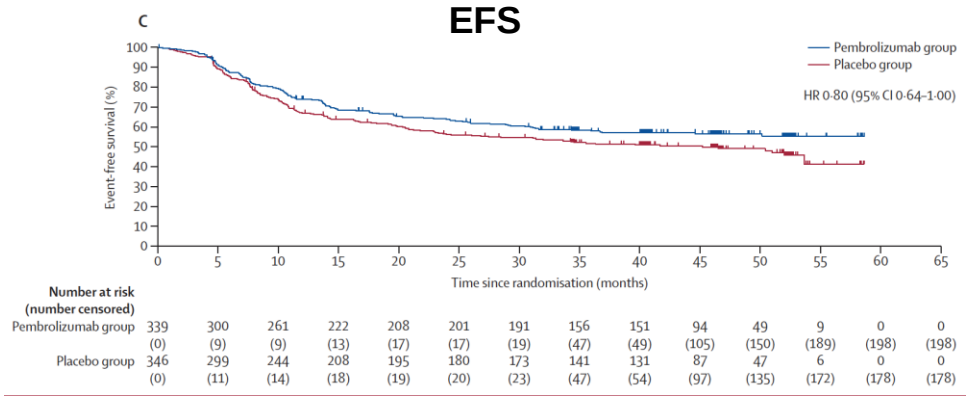


Number at risk (number censored)														
Pembrolizumab group	402	356	306	261	245	235	225	184	176	109	52	10	0	0
	(0)	(11)	(11)	(17)	(21)	(22)	(24)	(56)	(59)	(123)	(180)	(221)	(231)	(231)
Placebo group	402	349	282	240	224	209	200	162	149	99	51	7	0	0
	(0)	(15)	(18)	(22)	(23)	(24)	(28)	(58)	(68)	(117)	(163)	(203)	(210)	(210)

Machiels JP, et al. Lancet Oncol 2024;25:572-87

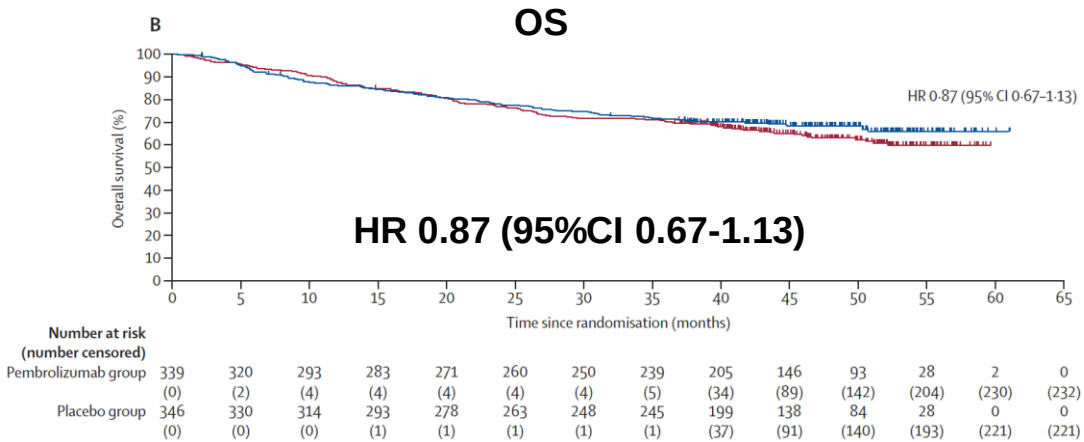
KEYNOTE-412 – EFS / OS PD-L1 CPS≥1

EFS



HR 0.80 (95%CI 0.64-1.00)

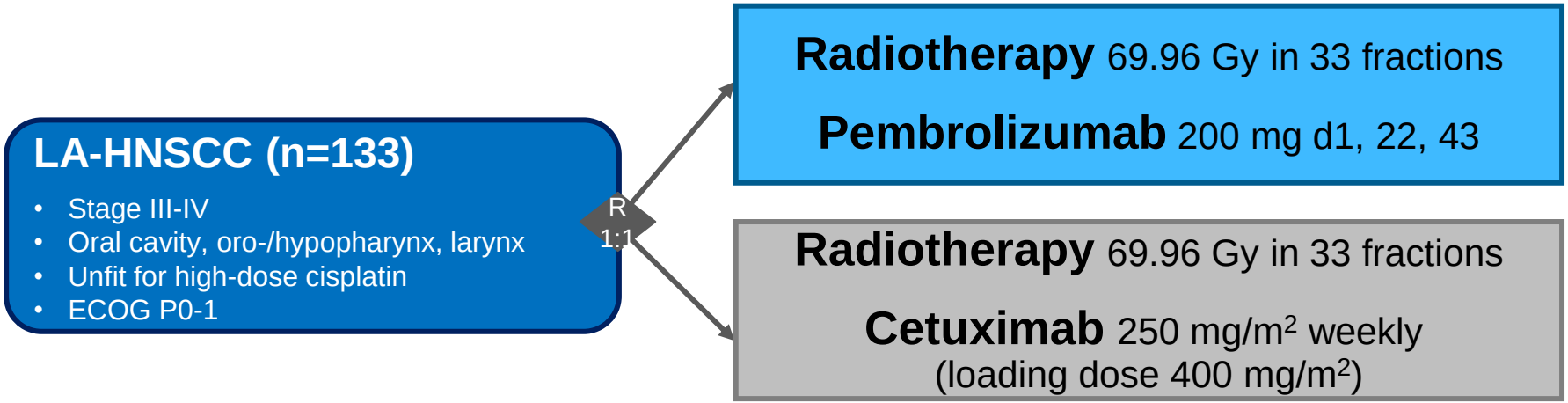
OS



HR 0.87 (95%CI 0.67-1.13)

Machiels JP, et al. Lancet Oncol 2024;25:572-87

PembroRad / GORTEC 2015 – Trial Design



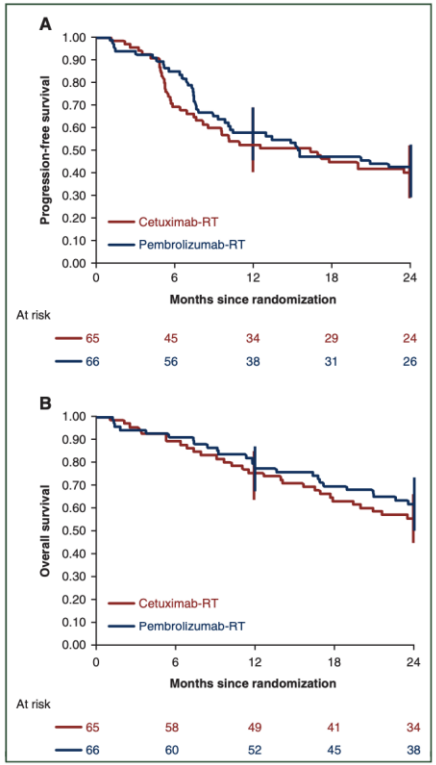
Primary endpoint: Loco-regional control (LRC) at 15 months

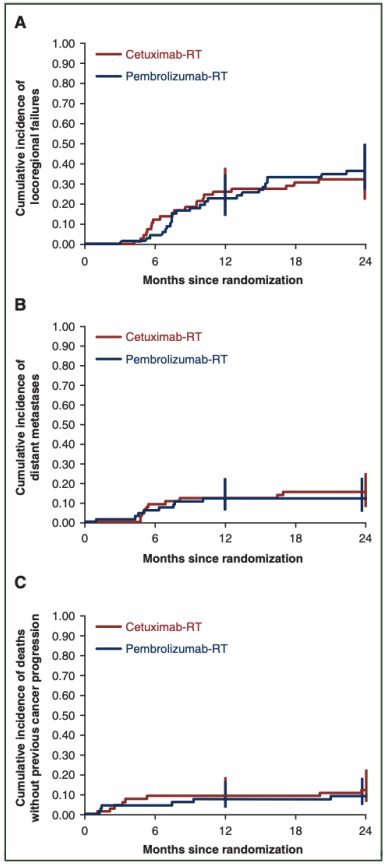
Secondary endpoints: PFS, locoreginal progression, distant metastases, OS, compliance, AEs

Stratification: N-stage (N0-1 vs. N2-3), p16 expression

Tao Y, et al. Ann Oncol 2023;34(1):101-10

PembroRad / GORTEC 2015 – Outcome

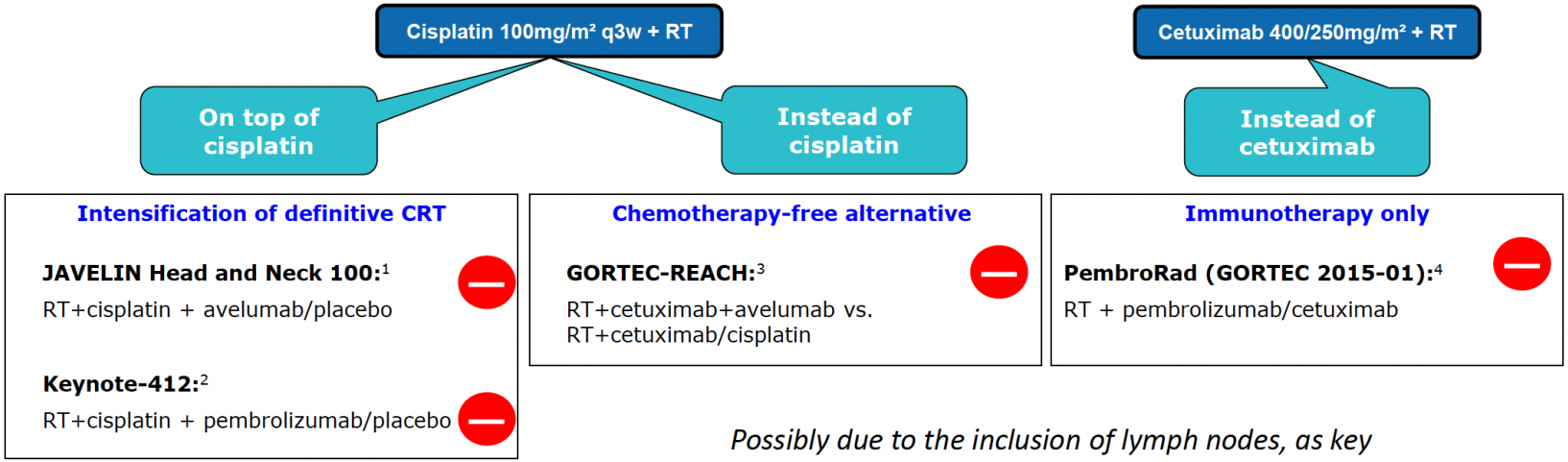




- 15-months LRC: 60% vs. 59% (p=0.91)
- HR PFS: 0.85 (95%CI 0.55-1.32), p=0.47
- HR OS: 0.83 (95%CI 0.49-1.40), p=0.49
- ≥G3 AEs: 74% vs. 92% (p=0.006)

Tao Y, et al. Ann Oncol 2023;34(1):101-10

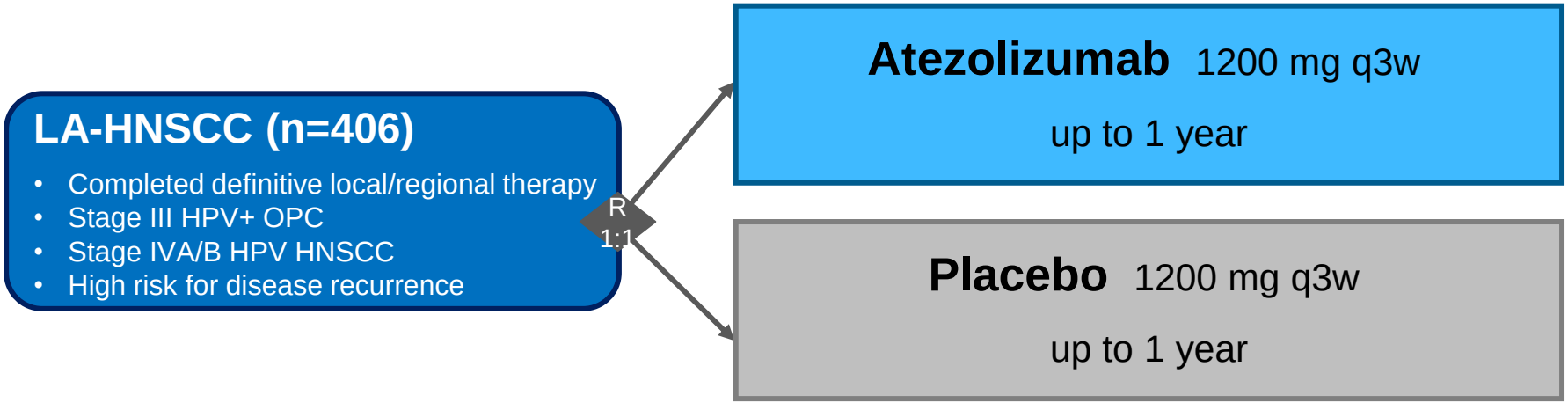
Immuntherapie beim LA-HNSCC – Negative Studien!



Possibly due to the inclusion of lymph nodes, as key organs of immunogenesis, in radiation fields.

[1]Lee NY et al. Lancet Oncol 2021;22:450-462. 2Machiels JP et al. Lancet Oncol 2024;25:572-587. [3]Bourhis J et al. Ann Oncol 2021;32:S1310 (abstract LBA 35).
[4]Tao Y et al. Ann Oncol 2023;34:101-110.

IMVOKE010 – Trial Design



Primary endpoint: EFS (BIRC) and OS

Secondary endpoints: EFS (investigator-assessed), safety, PRO

Stratification: HPV-status, response to definitive local therapy, surgery

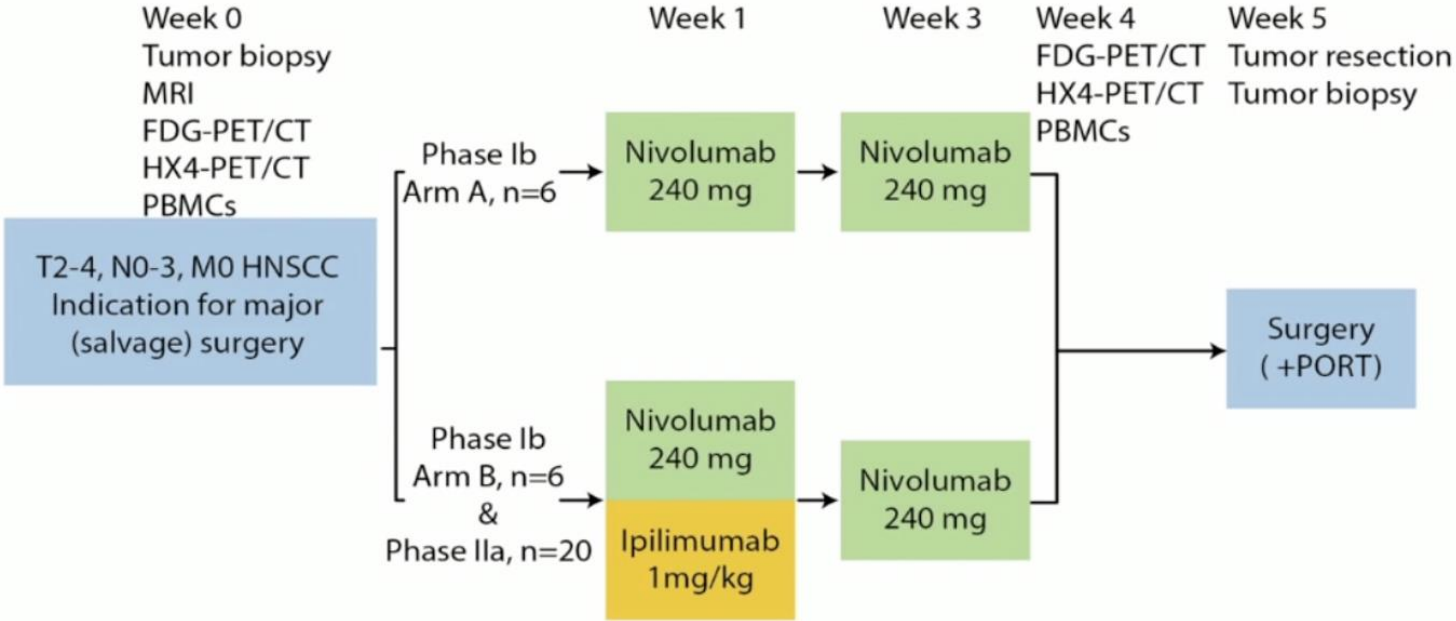
Wong DJ, et al. AACR 2024; abstract CT009

IMVOKE010 – Negative Studie!

Efficacy	Atezo (n=203)*	Placebo (n=203)
Median INV-EFS, mos	59.5	52.7
HR (95% CI)	0.94 (0.70-1.26)	
P-value	0.6804†	
Median OS, mos	NE	NE
HR (95% CI)	0.96 (0.68-1.36)	
Safety, n (%)		
Grade 3-4 AEs	55 (27.2)	43 (21.2)
TRAEs Grade 3-4	20 (9.9)	12 (5.9)
Grade 5 AEs	3 (1.5)	5 (2.5)
SAEs	32 (15.8)	32 (15.8)
AEs leading to tx discontinuation	18 (8.9)	9 (4.4)

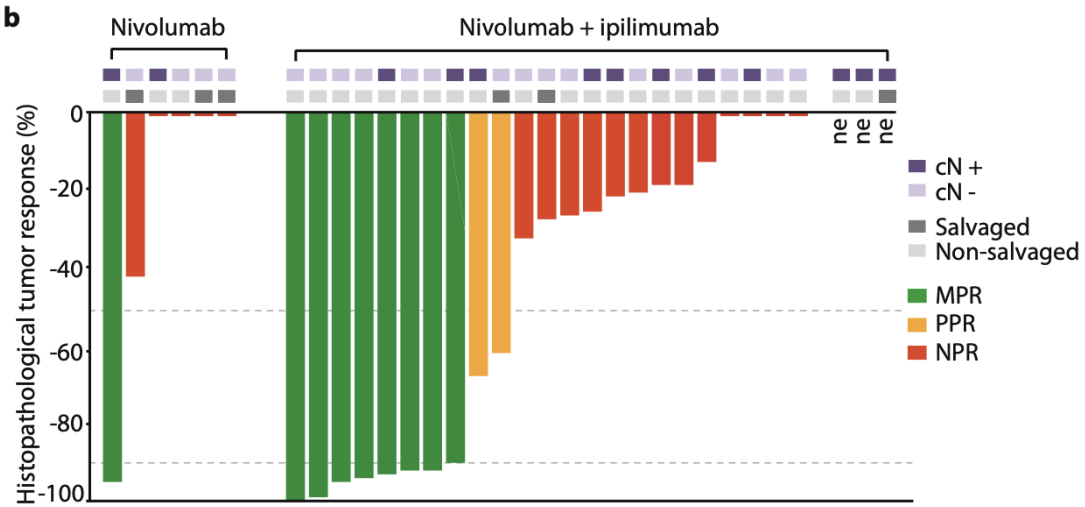
Wong DJ, et al. AACR 2024; abstract CT009

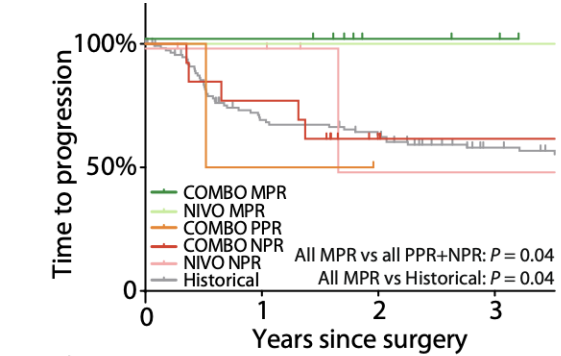
IMCISION – Neoadjuvante Immuntherapie



Vos JL, et al. Nat Commun 2021;12:7348

IMCISION – Neoadjuvante Immuntherapie





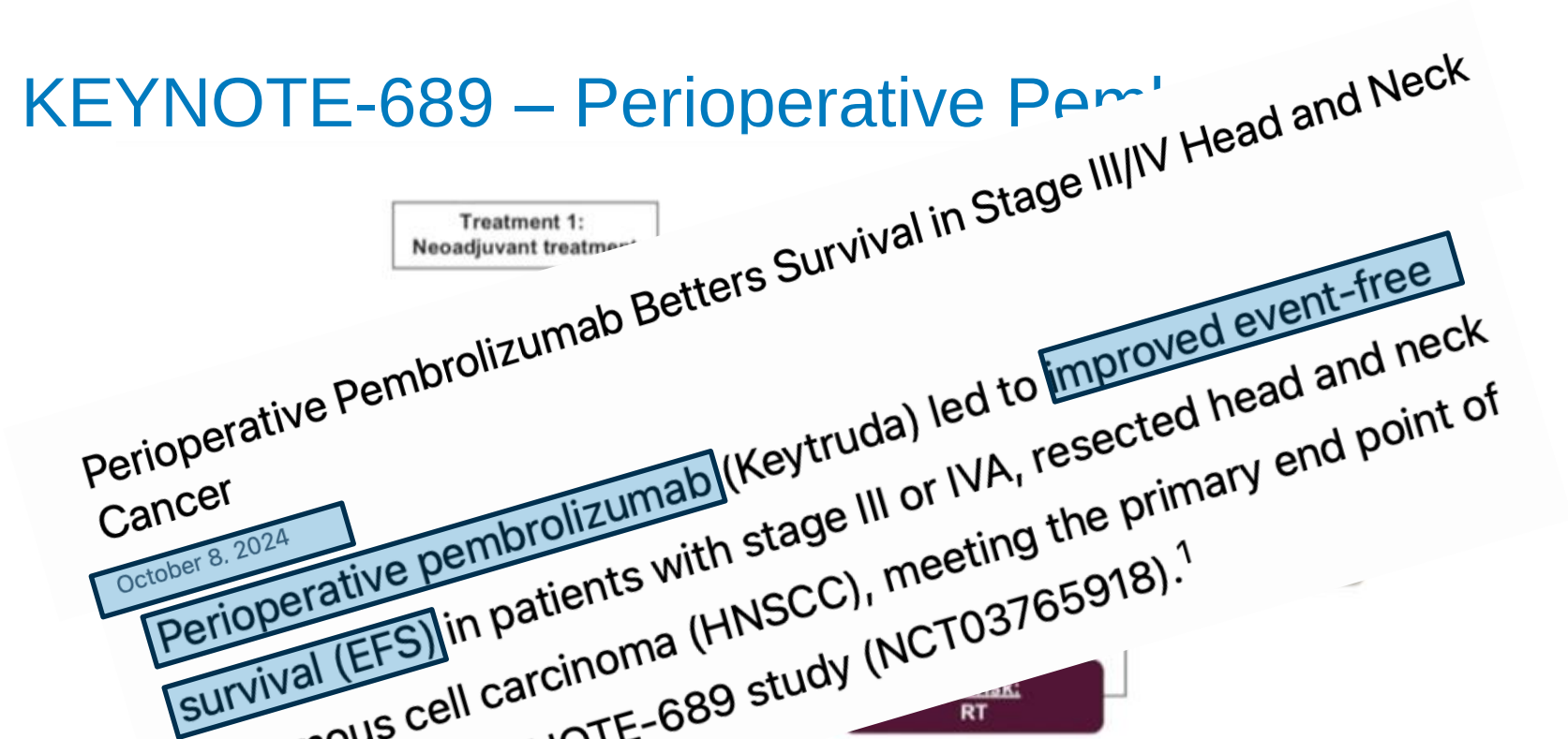
N at risk

COMBO MPR	8	8	8	7	3	3	2
NIVO MPR	1	1	1	1	1	1	1
COMBO PPR	2	2	1	1	0	0	0
COMBO NPR	13	11	10	8	2	1	1
NIVO NPR	5	4	4	2	1	1	1
Historical	114	92	71	69	63	52	44

- Surgery is not delayed or suspended for any patient in phase Ib, meeting the primary endpoint
- MPR: Nivo mono: 17%, Nivo/Ipi: 35%
- None of the MPR patients develop recurrent HSNCC during 24.0 months median postsurgical follow-up

Vos JL, et al. Nat Commun 2021;12:7348

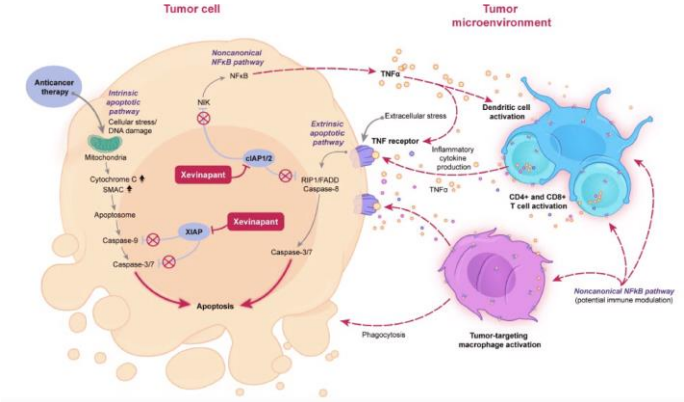
KEYNOTE-689 – Perioperative Pem

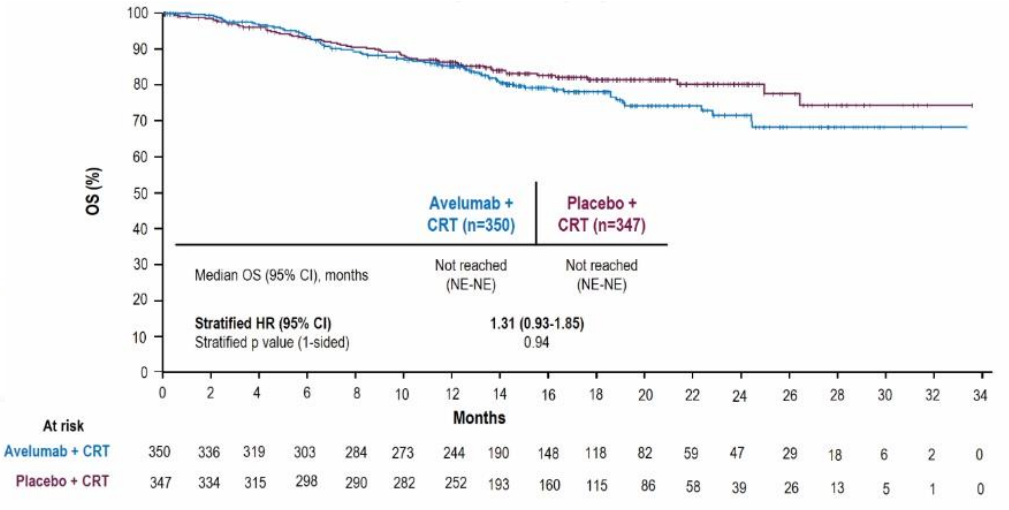


- N=6(
- Priary
- Secor . OS, pCR, safety

NCT03765918

Xevinapant – Randomized Phase II Trial





Ferris RL, et al. Cancer Treat Rev 2023;113:102492; Tao Y, et al. Eur J Cancer 2023;183:24-37

TRILYNX Trial - Xevinapant

LA-HNS

- Stage III-I
- Hypophary
- Oropharyn
- ECOG P0-1

Primary endp

Secondary en

n 100 mg/m^2 q3w x3

-14 q3w x3

0 mg/m^2 q3w x3

w x3

Merck, press release, 24 JUN 2024:

Trial **discontinued** due to a pre-planned **interim** analysis performed by the study's Independent Data Monitoring Committee, which found that the trial would be **unlikely** to meet its primary objective of prolonging event-free survival.

Other trials, incl. X-Ray Vision, RAVINA, discontinued as well.

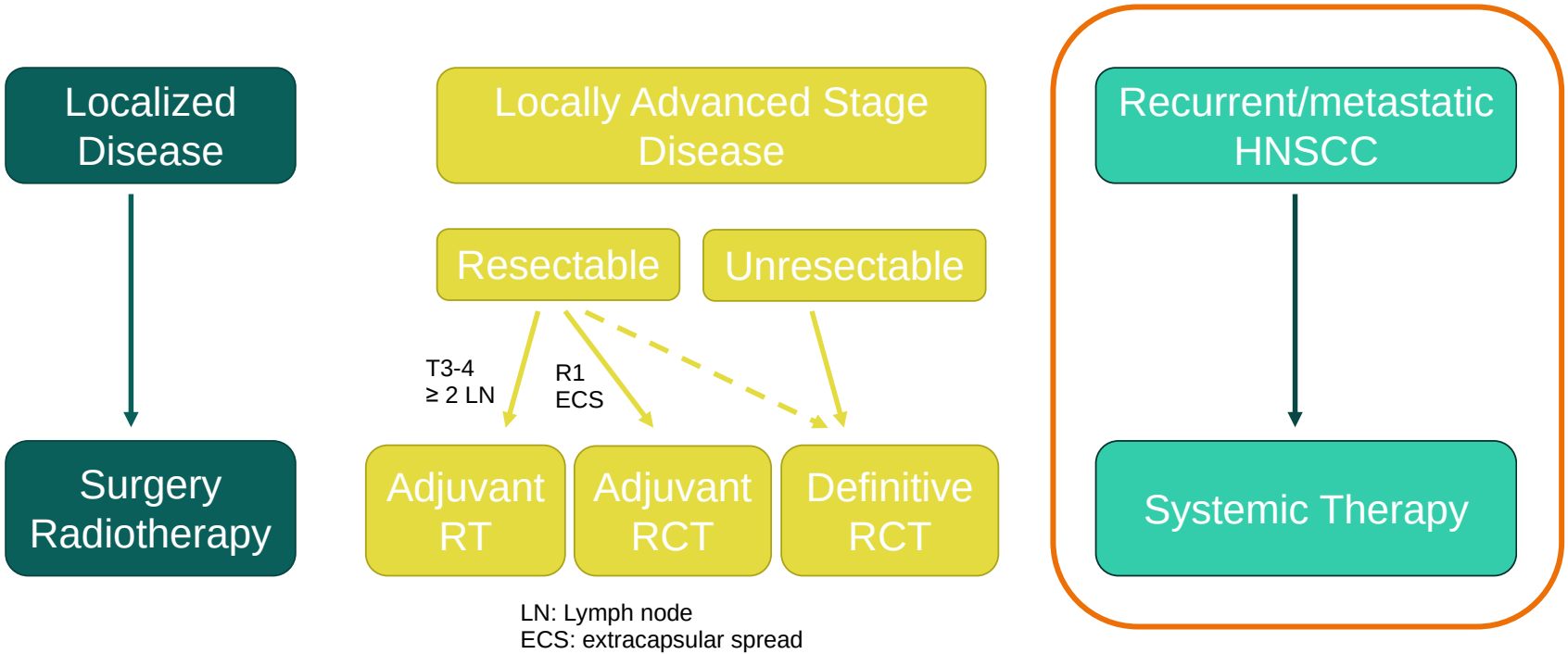
http://clinicaltrials.gov/show/NCT

Zusammenfassung – Lokal fortgeschrittene Stadien

- Kombinierte Radio-Chemotherapie mit Cisplatin ist der Standard
- Überlebensvorteil: 8% nach 5 Jahren[1]
- Cisplatin Dosierung ≥ 200 mg/m^2 sollte erreicht werden[2]
- HPV positive Oropharynxkarzinome: RT + Cisplatin ist / bleibt Standard[3,4]

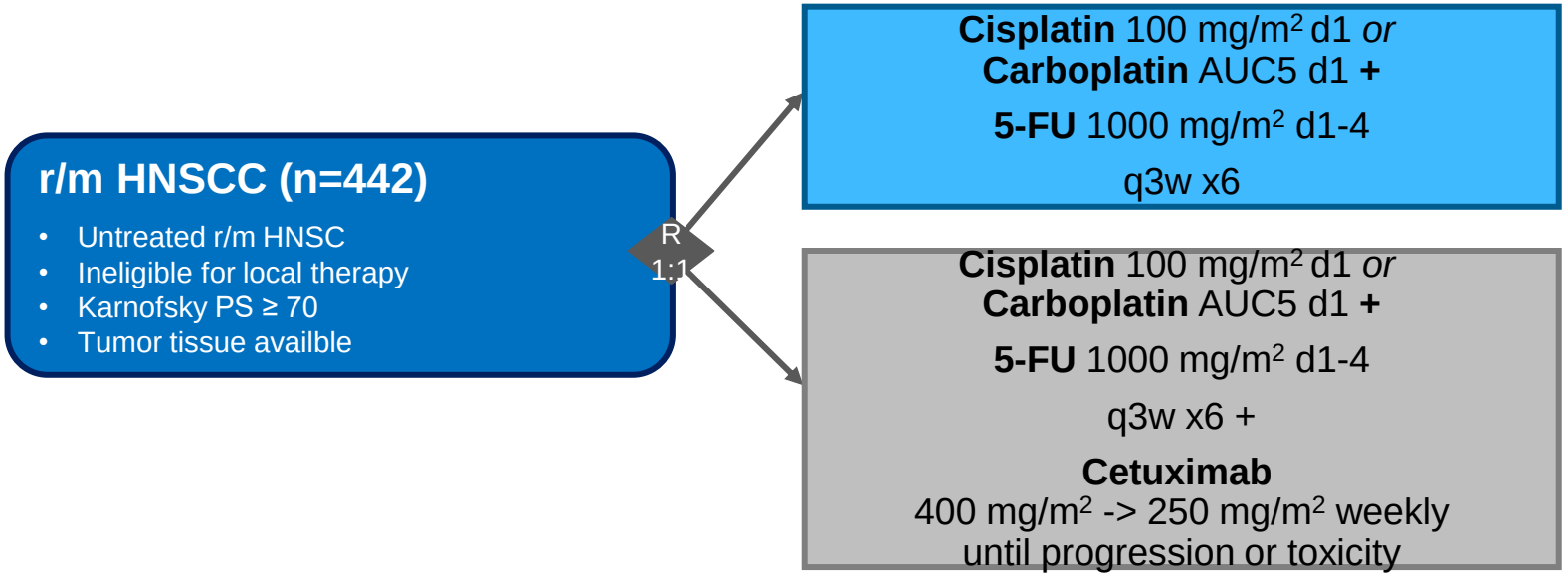
[1]Pignon JP et al. Lancet 2000;355:949-55; [2]Spreafico Eur J Cancer. 2016;67:174-182; [3]Mehanna H, et al. ESMO 2018; Abstract LBA9; [4]Trotti A, et al. ASTRO 2018

Behandlungskonzepte



LN: Lymph node
ECS: extracapsular spread

EXTREME – Trial Design



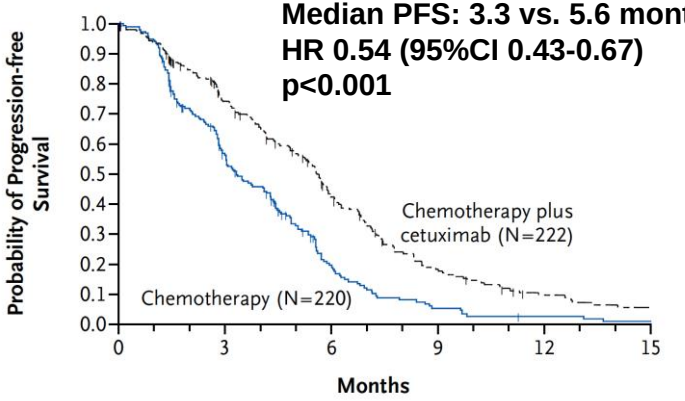
Primary endpoint: OS

Secondary endpoints: PFS, ORR, time to treatment failure, duration of response, safety

Vermorken JB et al. NEJM 2008;359:1116-27

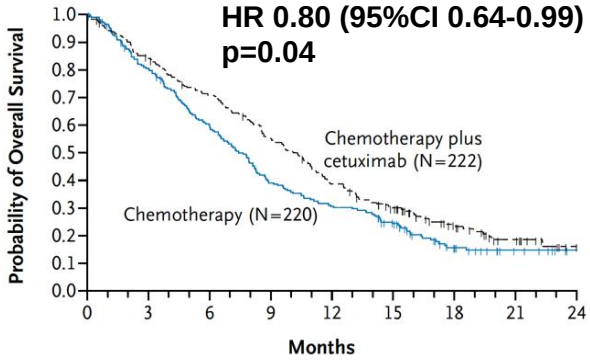
EXTREME-Studie

B



Median PFS: 3.3 vs. 5.6 months
HR 0.54 (95%CI 0.43-0.67)
p<0.001

No. at Risk						
Chemotherapy	220	103	29	8	3	1
Chemotherapy plus cetuximab	222	138	72	29	12	7

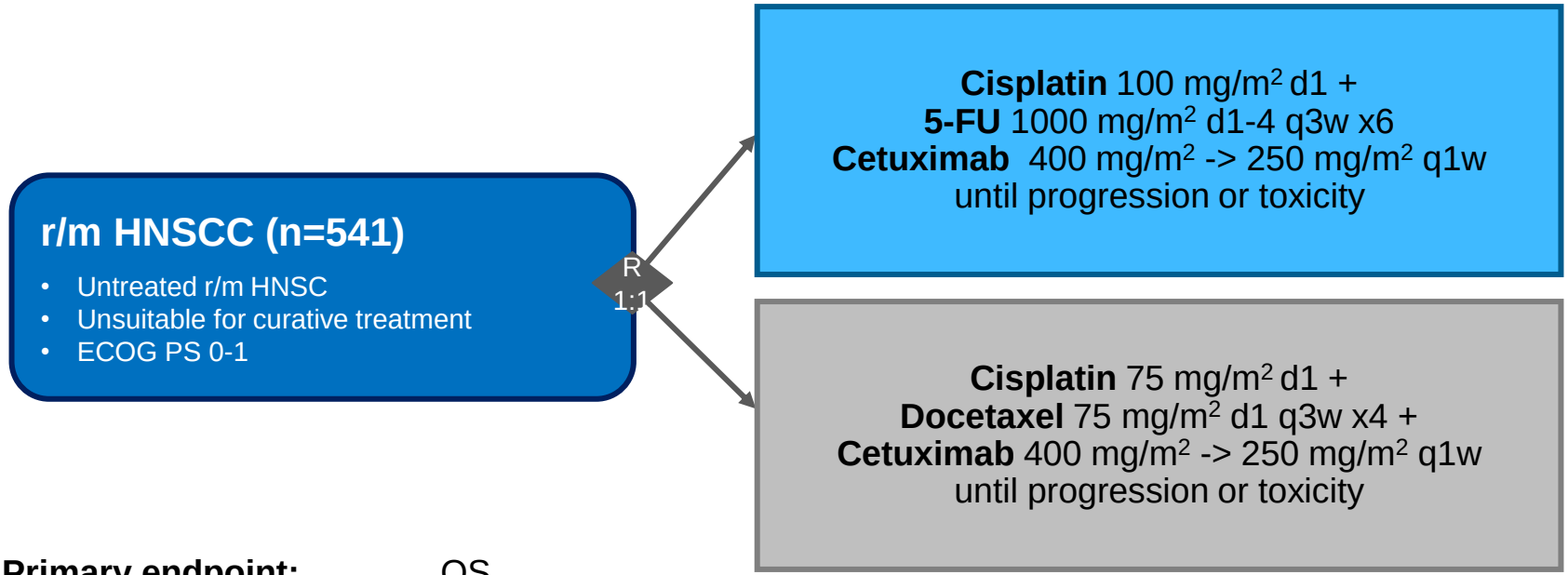


Median OS:
7.4 vs. 10.1 months
HR 0.80 (95%CI 0.64-0.99)
p=0.04

No. at Risk									
Chemotherapy	220	173	127	83	65	47	19	8	1
Chemotherapy plus cetuximab	222	184	153	118	82	57	30	15	3

Vermorken JB et al. NEJM 2008;359:1116-27

TPExtreme – Trial Design



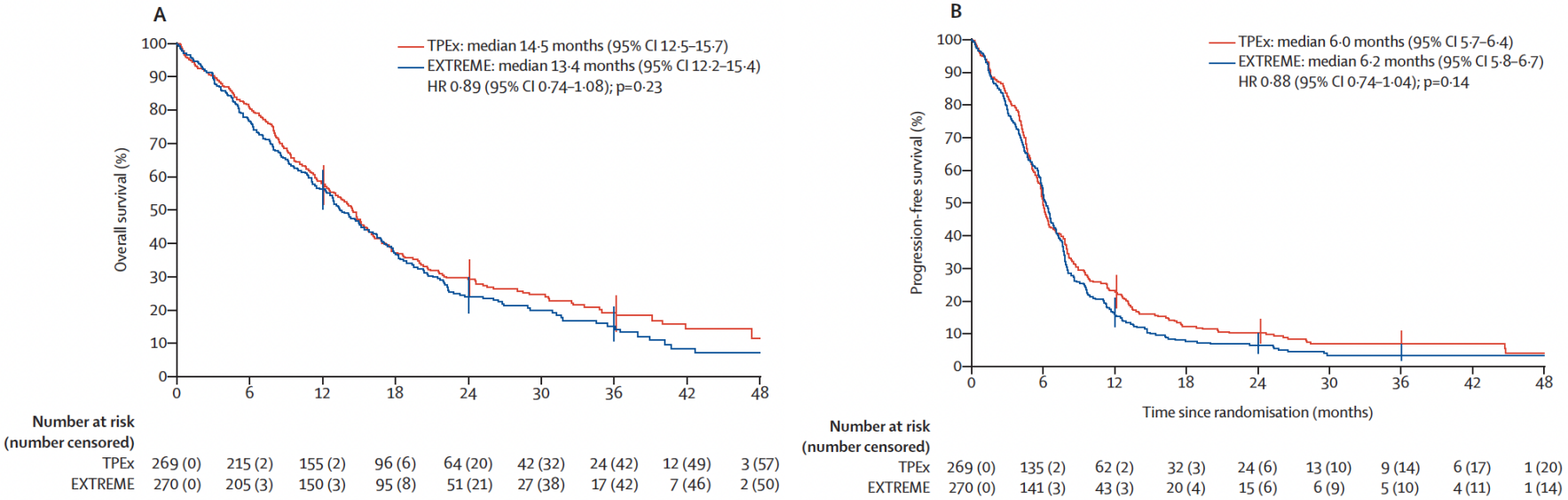
Primary endpoint: OS

Secondary endpoints: PFS, TTP, ORR, QoL

Stratification: ECOG PS, type of disease evolution, previous cetuximab therapy

Guigay J, et al. Lancet Oncol 2021;22:463-74

TPExtreme – Outcome



Guigay J, et al. Lancet Oncol 2021;22:463-74

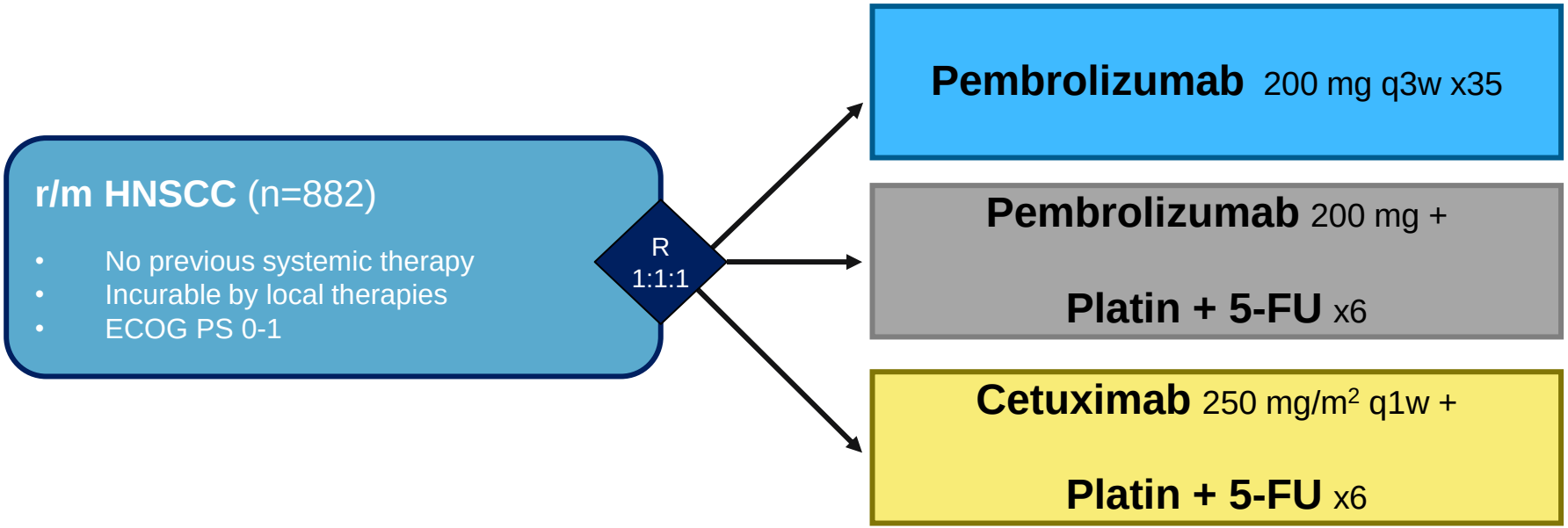
TPExtreme – Outcome

	TPEx regimen group (n=269)	EXTREME regimen group (n=270)
Number of chemotherapy cycles received		
0	8 (3%)	6 (2%)
1	23 (9%)	32 (12%)
2	27 (10%)	29 (11%)
3	16 (6%)	25 (9%)
4	194 (72%)	32 (12%)
5	1 (<1%)	27 (10%)
6	0 (<1%)	119 (44%)
Median	4 (3–4)	5 (3–6)
Reason for chemotherapy discontinuation*†		
End of chemotherapy period	191 (73%)	117 (44%)
Adverse event	31 (12%)	57 (22%)
Tumour progression	13 (5%)	35 (13%)
Death	10 (4%)	21 (8%)
Patient refusal or lost to follow-up	7 (3%)	19 (7%)
Other reason	8 (3%)	14 (5%)
Maintenance therapy with cetuximab†		
No	72 (28%)	126 (48%)
Yes	189 (72%)	138 (52%)
Best tumour response during treatment		
Complete response	25 (9%)	15 (6%)
Partial response	130 (48%)	139 (51%)
Stable disease	69 (26%)	62 (23%)
Progressive disease	21 (8%)	29 (11%)
Not evaluable or not evaluated	24 (9%)	25 (9%)

- SAEs: 54% vs. 45%
- G5 AE: 21 pts vs. 16 pts.

Guigay J, et al. Lancet Oncol 2021;22:463-74

KEYNOTE-048 – Trial Design

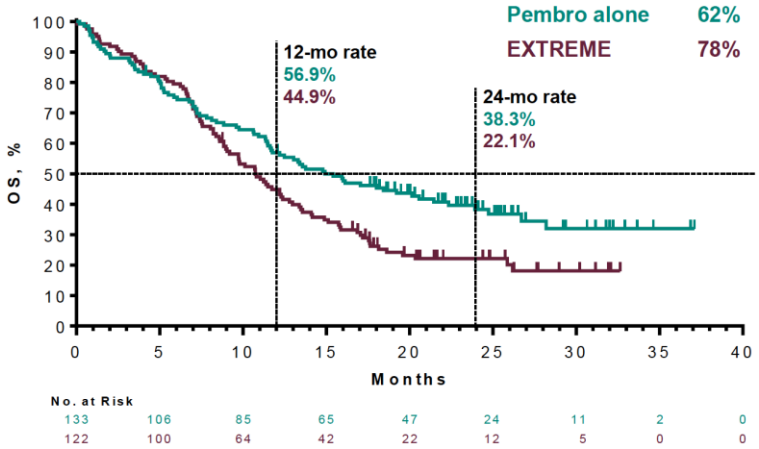


Primary endpoint:	OS, PFS (CPS ≥20%, CPS ≥1%, total population)
Secondary endpoints:	PFS at 6 and 12 months, ORR, QoL, safety
Stratification:	PD-L1 (TPS ≥50% vs. <50%), HPV status, ECOG PS

Burtness B, et al. Lancet 2019; 394(10212):1915-1928

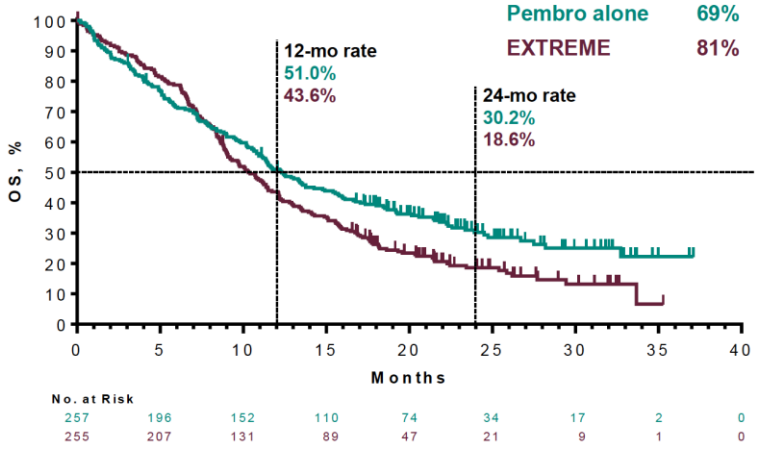
KEYNOTE-048 – Pembrolizumab vs. EXTREME

CPS ≥20% Population



Median OS: 14.9 vs. 10.7 months
HR 0.61 (95%CI 0.45-0.83)
p=0.0007

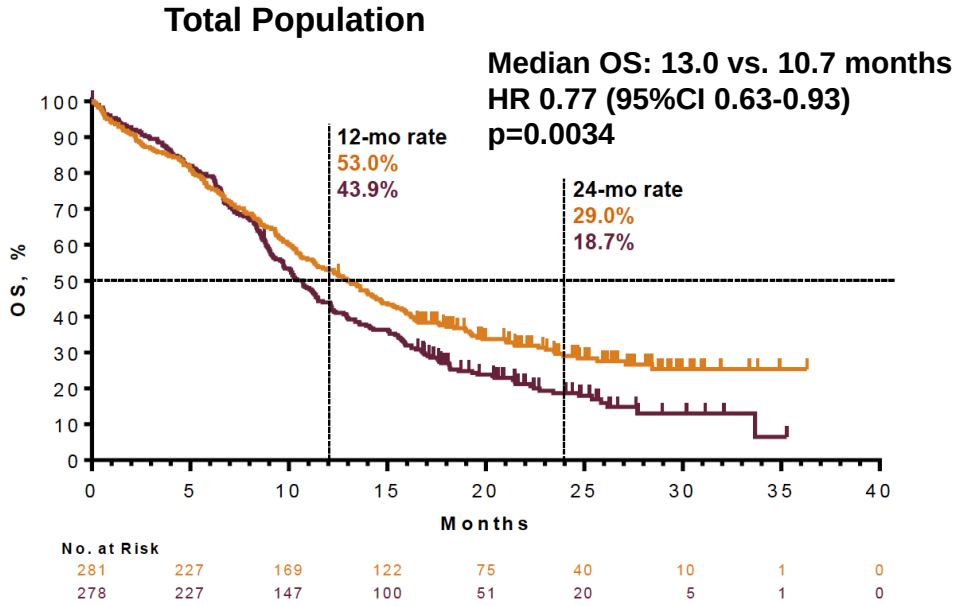
CPS ≥1% Population



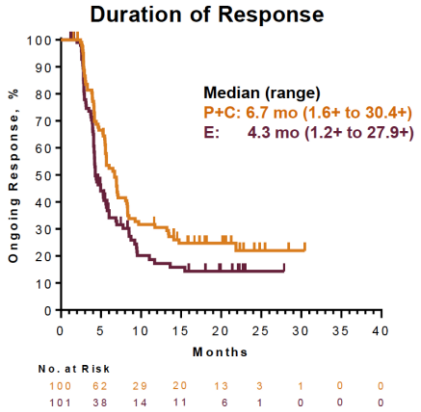
Median OS: 12.3 vs. 10.3 months
HR 0.78 (95%CI 0.64-0.96)
p=0.0086

Burtness B, et al. Lancet 2019; 394(10212):1915-1928

KEYNOTE-048 – Pembrolizumab + Chemotherapy vs. EXTREME

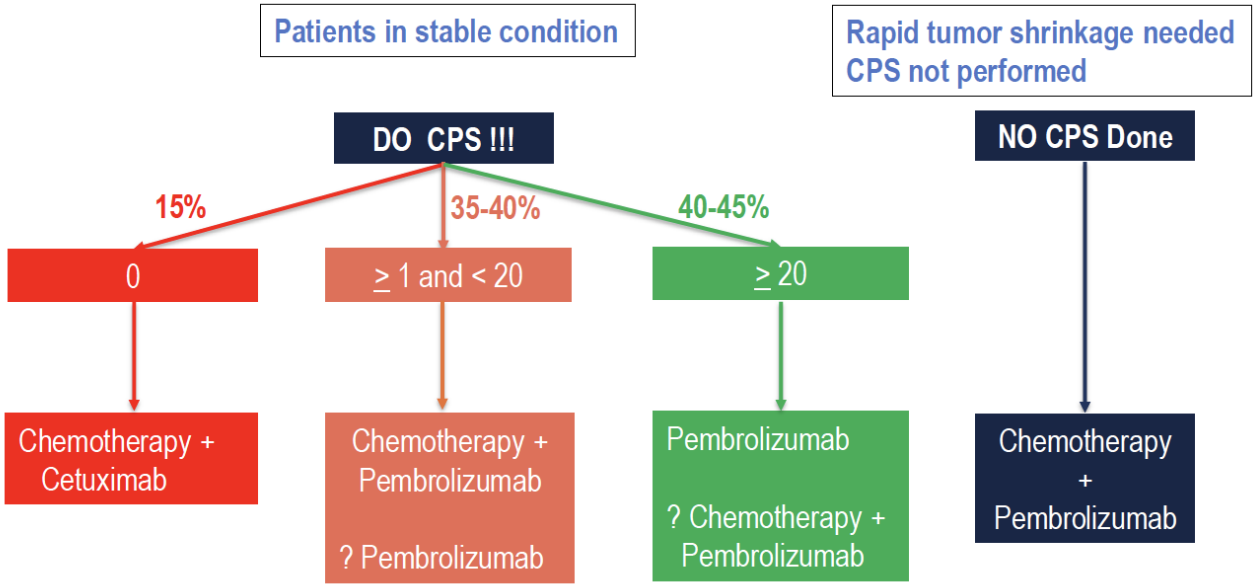


Response	Pembro + Chemo (n=281)	EXTREME (n=278)
ORR	35.6%	36.3%



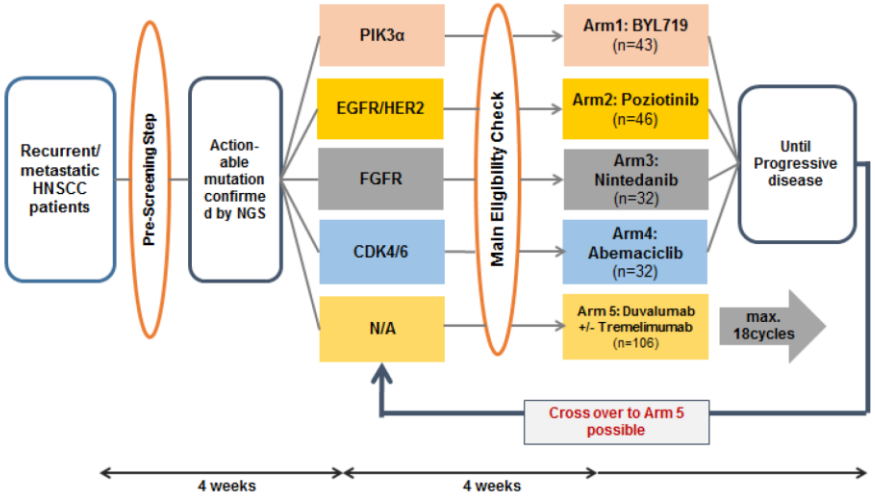
Burtness B, et al. Lancet 2019; 394(10212):1915-1928

Neuer Standard in der Erstlinientherapie



Machiels JP, et al. ESMO 2018; Discussion

TRIUMPH: TRanslational bIomarker-driven UMbrella Project



Primary endpoint: DCR arm 1 and ORR arm 2-5

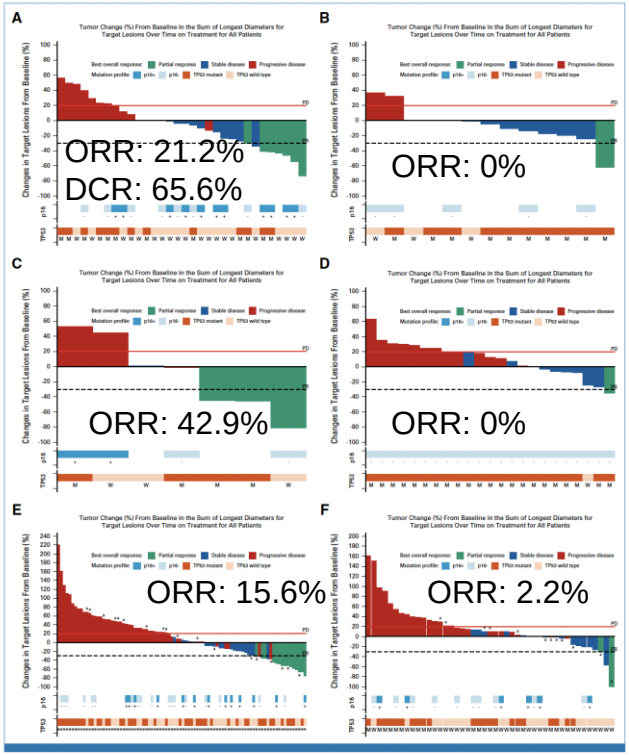


FIG 2. Waterfall plot of the maximum percent change in tumor size from baseline in each treatment arm (A) Arm 1: Alpelisib, (B), Arm 2: Poziotinib, (C) Arm 3: Nintedanib, (D) Arm 4: Abemaciclib, (E) Arm 5: Durvalumab, (F) Arm 5-1: Durvalumab + tremelimumab. *Represent crossover to arm 5; otherwise direct allocation to arm 5. PD, progressive disease; PR, partial response.

Keam B, et al. J Clin Oncol 2023;42:507-17

Vielen Dank!

Fragen?