[H/N Current Landscape]

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COMPREHENSIVE CANCER CENTER

H/N Current Landscape

- No disclosures

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Index

- Epidemiology, risk factors and pathways
- Adjuvant treatment
- Recurrent and metastatic disease
- Neoadjuvant / Induction chemotherapy
- New therapeutic options
- Conclusions

Objectives

- Discussion current adjuvant or recurrent/metastatic chemo/IO treatment options for patient with H/N cancers (excluding NPC and salivary gland tumors)
- Understanding high risk features that justify use adjuvant chemo/RT

Epidemiology

TABLE 1 Estimated new cancer

Cancer site	Estimated New Cases			Males	Females	Estimated New Cases		
All sites	Prostate	288,300	29%			Breast	297,790	31%
Oral cavity & pharynx	Lung & bronchus	117,550	12%			Lung & bronchus	120,790	13%
Tongue	Colon & rectum	81,860	8%			Colon & rectum	71,160	8%
Mouth	Urinary bladder	62,420	6%			Uterine corpus	66,200	7%
Pharynx	Melanoma of the skin	58,120	6%			Melanoma of the skin	39,490	4%
Other oral cavity	Kidney & renal pelvis	52,360	5%			Non-Hodgkin lymphoma	35,670	4%
Larynx	Non-Hodgkin lymphoma	44,880	4%			Thyroid	31,180	3%
Thyroid	Oral cavity & pharynx	39,290	4%			Pancreas	30,920	3%
	Leukemia	35,670	4%			Kidney & renal pelvis	29,440	3%
	Pancreas	33,130	3%			Leukemia	23,940	3%
	All Sites	**1,010,310**	**100%**			**All Sites**	**948,000**	**100%**

Siegel, RL, Miller, KD, Wagle, NS, Jemal, A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023; 73(1): 17-48.

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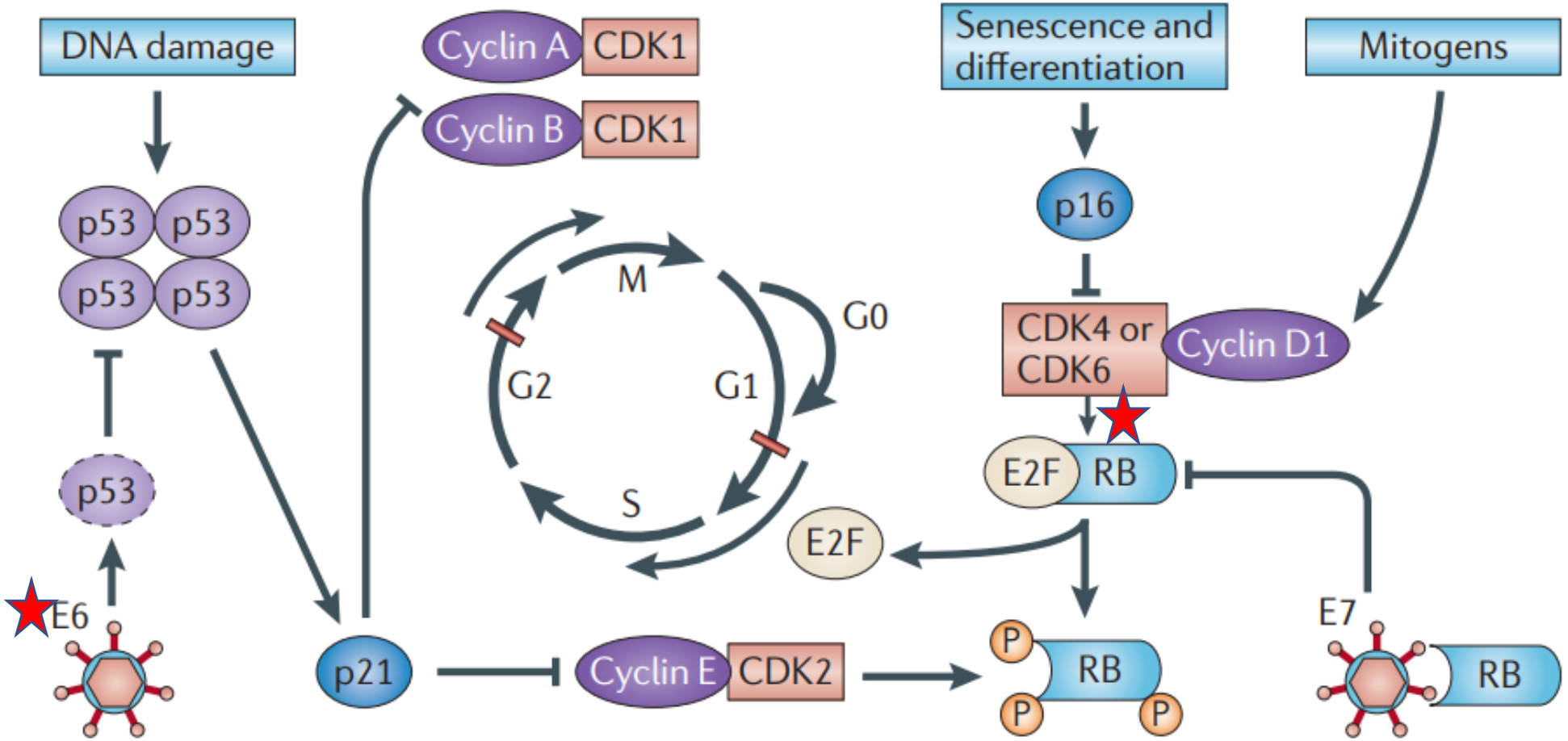
Cell cycle deregulation by HPV



Leemans et al. Molecular biology head and neck cancers. Nature 2011

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Risk factors / Molecular pathways

- HPV (+) – E6 oncoprotein targets p53, E7 inactivates RB
- Inhibition of TGFB – promotes cell survival (via activation SMAD and CDK's)
- Tyrosine Kinases (AKT/PIK3/PTEN)– increases proliferation & angiogenesis

- Smoking → mutations include TP53, CDKN2A, PTEN, PIK3.

Treatment plan

- Importance of multidisciplinary team discussion to address appropriate treatment plan

1. Staging scans (CT neck, PET/CT, facial MRI)?
2. Is tumor considered resectable? Vs definitive chemoradiation?
3. Pathology determine high risk factors (p16 status, PNI, LVI, ENE, margins and CPS score)
4. Consideration for adjuvant treatment.
5. Management of metastatic / recurrent H/N cancers.

Adjuvant Treatment (High Risk disease)

- RTOG 9501 (ECOG 9501 and SWOG 9515)

SCC arising from oral cavity, larynx and hypopharynx.

Macroscopic complete resection

High risk features – 2 or more LN, ECE, positive margins.

Endpoint= Local and regional tumor control.

Radiotherapy (60 Gy in 30 Fx) vs RT+concurrent Cisplatin (100 mg/m2 x3)

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Cooper, et al. NEJM 2004 Long term follow up RTOG 9501; Cooper et al,

Adjuvant Treatment (High Risk disease)

- RTOG 9501 (ECOG 9501 and SWOG 9515)

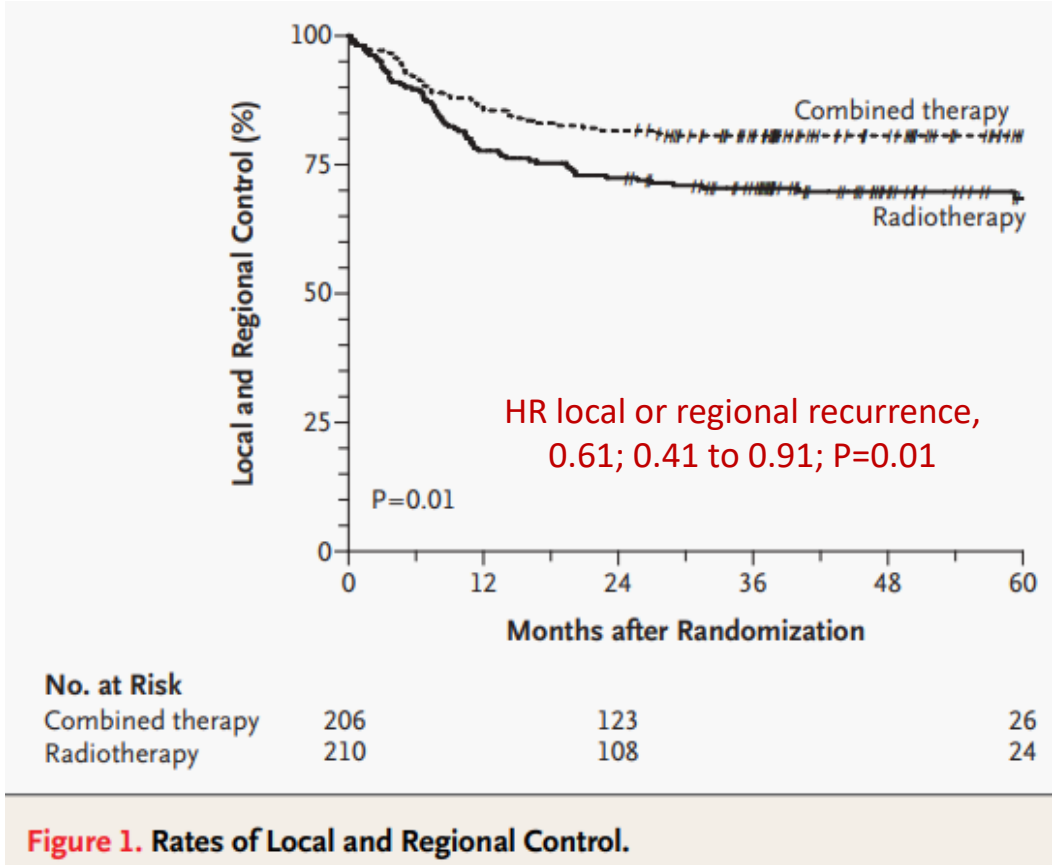

Figure 1. Rates of Local and Regional Control.

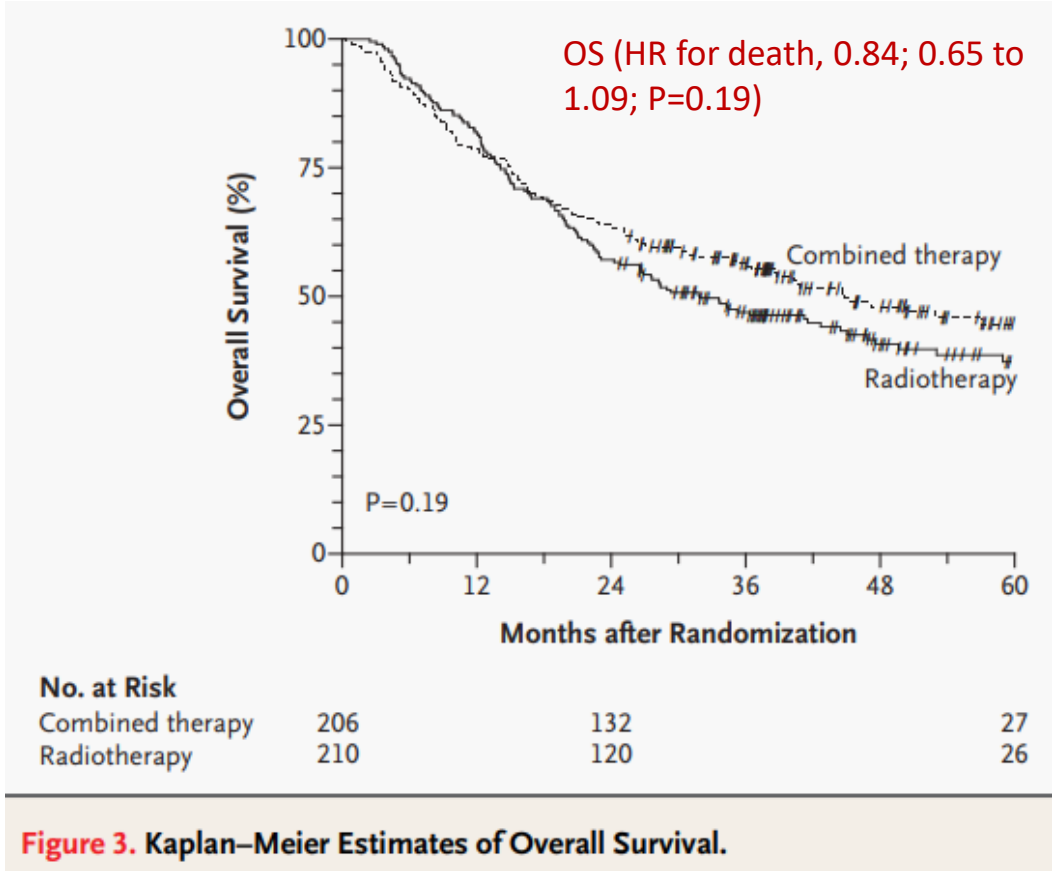

Figure 3. Kaplan–Meier Estimates of Overall Survival.

Cooper, et al. NEJM 2004

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Adjuvant Treatment (High Risk disease)

Table 1 Outcome of the entire group and 3 unplanned risk-related subsets

	RT	Combined	*P* value	HR
All patients				
10-year L-R recurrence	28.8	22.3	.10	0.73
95% CI	22.6-35.0	16.4-28.2		0.49-1.07
10-year DFS	19.1	20.1	.25	0.88
95% CI	13.1-25.0	14.2-26.0		0.71-1.09
10-year OS	27	29.1	.31	0.89
95% CI	20.5-33.5	22.3-35.8		0.70-1.12
ECE and/or Margin +				
10-year L-R recurrence	33.10	21.00	.02	0.56
95% CI	24.2-41.9	13.7-28.2		0.34-0.92
10-year DFS	12.3	18.4	.05	0.76
95% CI	5.2-19.4	11.3-25.5		0.57-1.00
10-year OS	19.6	27.1	.07	0.76
95% CI	11.5-27.7	18.9-35.4		0.57-1.03
No ECE and margin −				
10-year L-R recurrence	23.8	24.7	.92	1.03
95% CI	15.1-32.6	14.6-34.7		0.55-1.93
10-year DFS	26.3	22.4	.88	0.97
95% CI	16.7-36.0	11.6-33.1		0.68-1.39
10-year OS	35.90	32.20	.99	1.00
95% CI	25.6-46.1	20.5-43.9		0.68-1.46
Six + involved nodes				
5-Year L-R recurrence	19.2	28.6	.46	1.59

Table 3 Overall survival by cause of death

	Assigned treatment	Failures	5-year estimate (95% CI)	10-year estimate (95% CI)	Hazard ratio (95% CI)
		All patients			
Death from any cause*	RT	148	37.1 (30.4-43.8)	27.0 (20.5-33.5)	-
	RT + CT	141	45.8 (38.8-52.7)	29.1 (22.3-35.8)	0.89 (0.70-1.12)
Death from study cancer	RT	121	43.0 (35.8-50.2)	35.1 (27.7-42.5)	-
	RT + CT	100	56.9 (49.6-64.1)	42.7 (34.6-50.7)	0.78 (0.60-1.02)
Death not from study cancer	RT	27	83.7 (76.5-90.9)	74.1 (64.5-83.8)	-
	RT + CT	41	78.5 (71.3-85.7)	65.6 (55.9-75.3)	1.30 (0.80-2.11)
Patients who had involved margin(s) and/or extracapsular extension					
Death from any cause	RT	89	30.7 (22.0-39.4)	19.6 (11.5-27.7)	-
	RT + CT	91	42.5 (33.8-51.2)	27.1 (18.9-35.4)	0.76 (0.57-1.03)
Death from study cancer	RT	77	35.7 (26.4-45.1)	26.7 (17.1-36.2)	-
	RT + CT	67	53.4 (44.1-62.7)	37.4 (27.4-47.5)	0.66 (0.47-0.91)
Death not from study cancer	RT	12	82.7 (71.5-94.0)	69.8 (53.2-86.3)	-
	RT + CT	24	77.7 (68.5-87.0)	70.3 (59.5-81.2)	1.30 (0.65-2.61)

Abbreviation: CI = confidence interval.
* Overall survival.

Cooper, et al. Int Rad Oncology 2012

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Adjuvant treatment (High risk disease)

- EORTC 22931

SCC, T3-4NO with negative margins, T1-2 N2-3 or high risk features (ENE, PNI, positive margins, vascular tumor embolism)

Radiotherapy (66 Gy in 30 Fx) vs RT+ concurrent Cisplatin (100 mg/m2 x3)

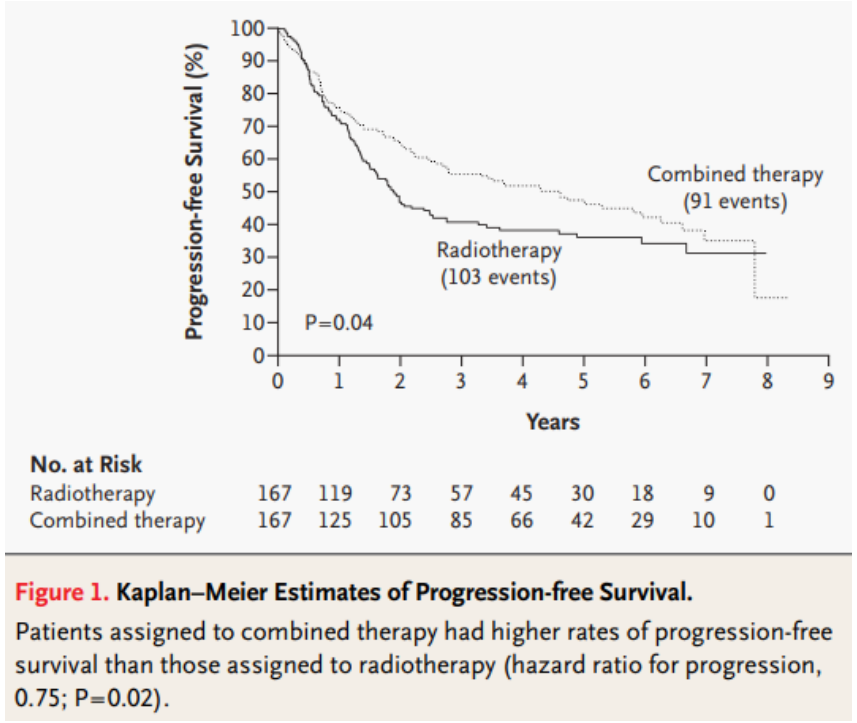

Figure 1. Kaplan–Meier Estimates of Progression-free Survival.
Patients assigned to combined therapy had higher rates of progression-free survival than those assigned to radiotherapy (hazard ratio for progression, 0.75; P=0.02).

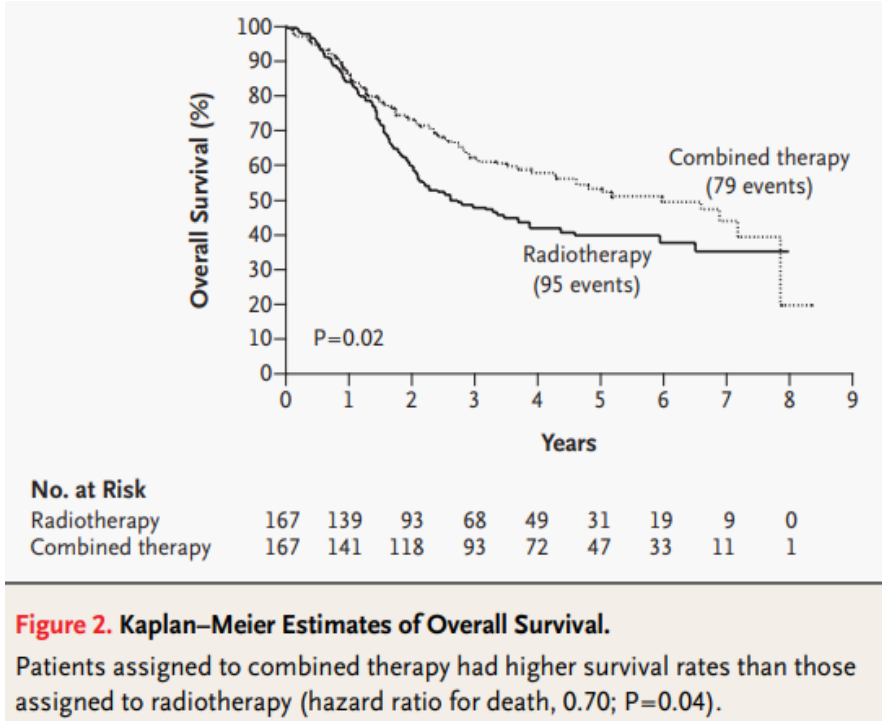

Figure 2. Kaplan–Meier Estimates of Overall Survival.
Patients assigned to combined therapy had higher survival rates than those assigned to radiotherapy (hazard ratio for death, 0.70; P=0.04).

Bernier et al. NEJM 2004

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Adjuvant treatment (High risk disease)

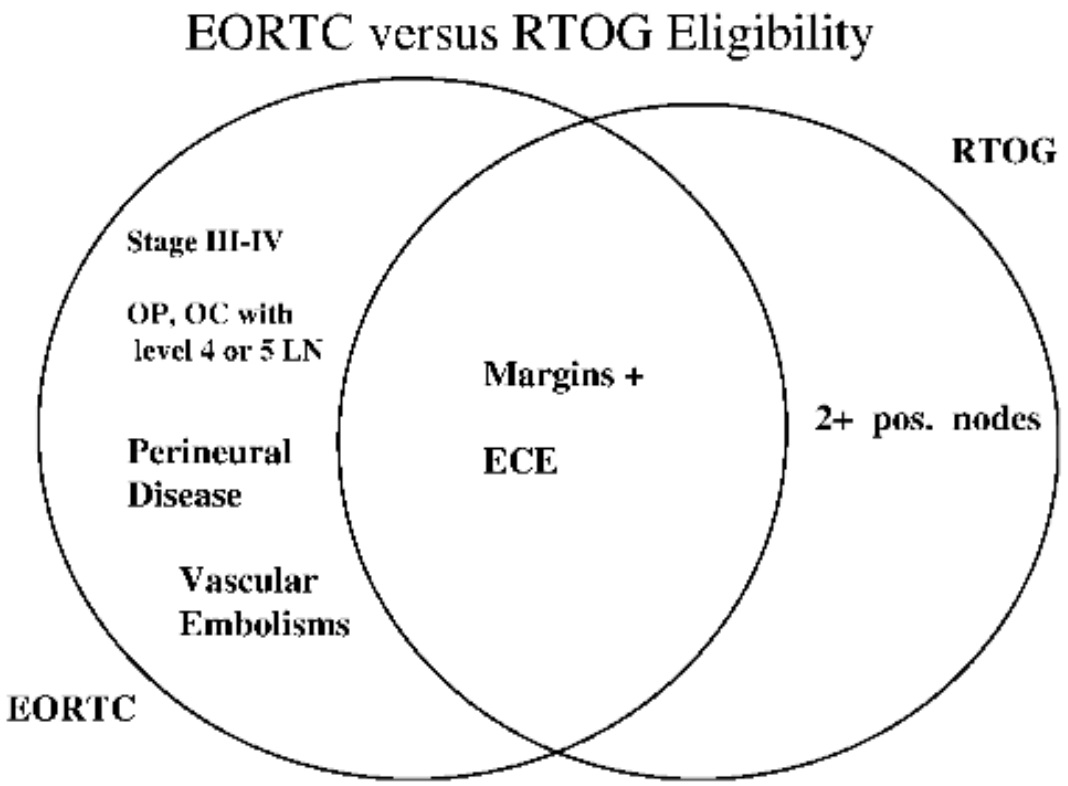

FIGURE 1. Eligibility criteria in EORTC 22931 and RTOG 9501 trials. OP, oropharynx; OC, oral cavity; LN, lymph node; ECE, extracapsular extension.

Adjuvant Chemo RT

✓ ECE and positive surgical margins

Favor – III-IV, PNI, Level 4/5 LAD

✖ NO benefit – 2+ LAD with NO ECE

Bernier et al. Head and neck 2006

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Adjuvant treatment / Cisplatin

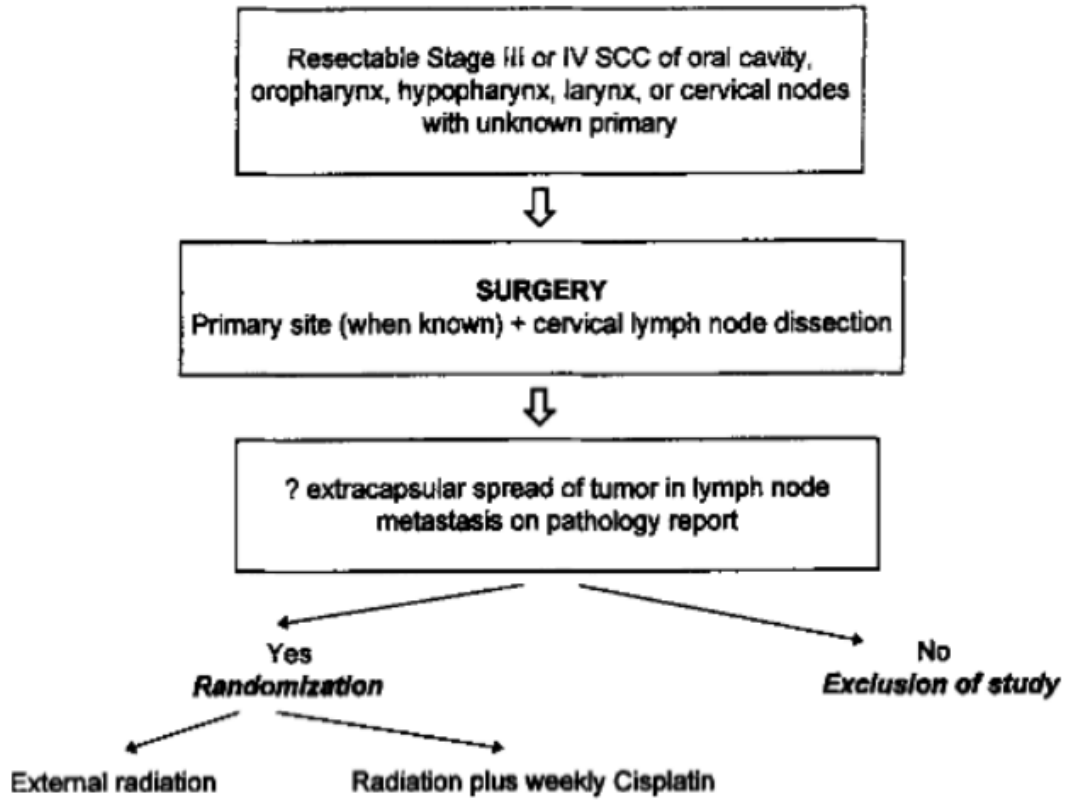


Fig. 1. The treatment protocol.

Bachaud et al. J Radiation Oncology 1996

Adjuvant treatment / Cisplatin

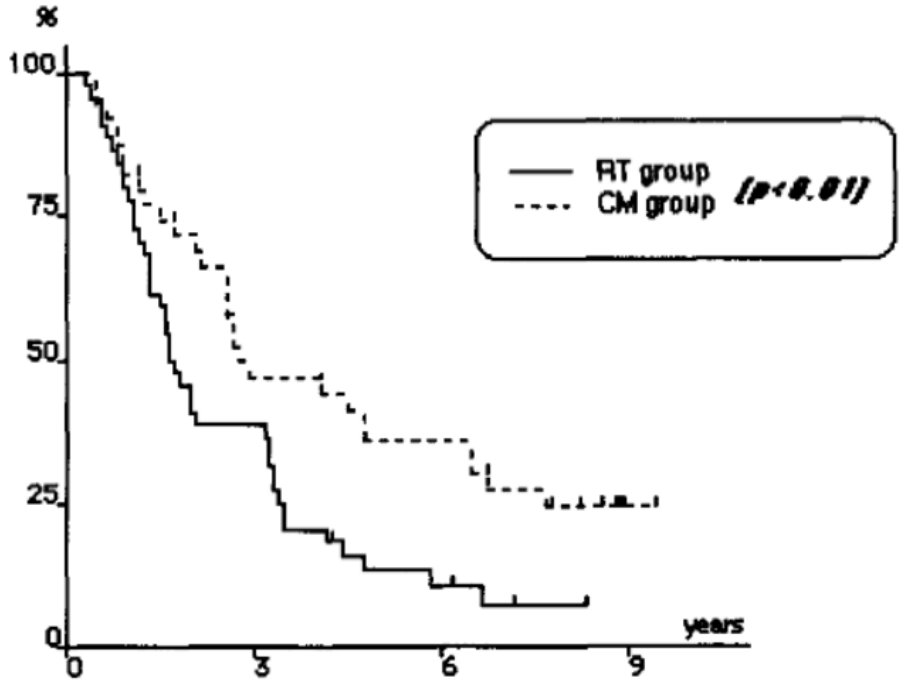


Fig. 2. Overall survival.

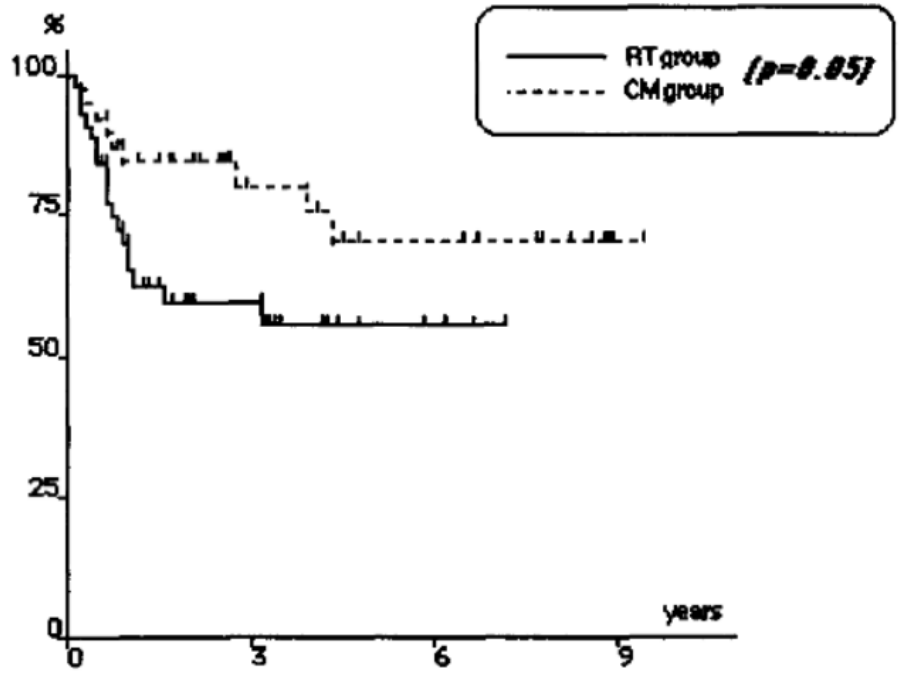


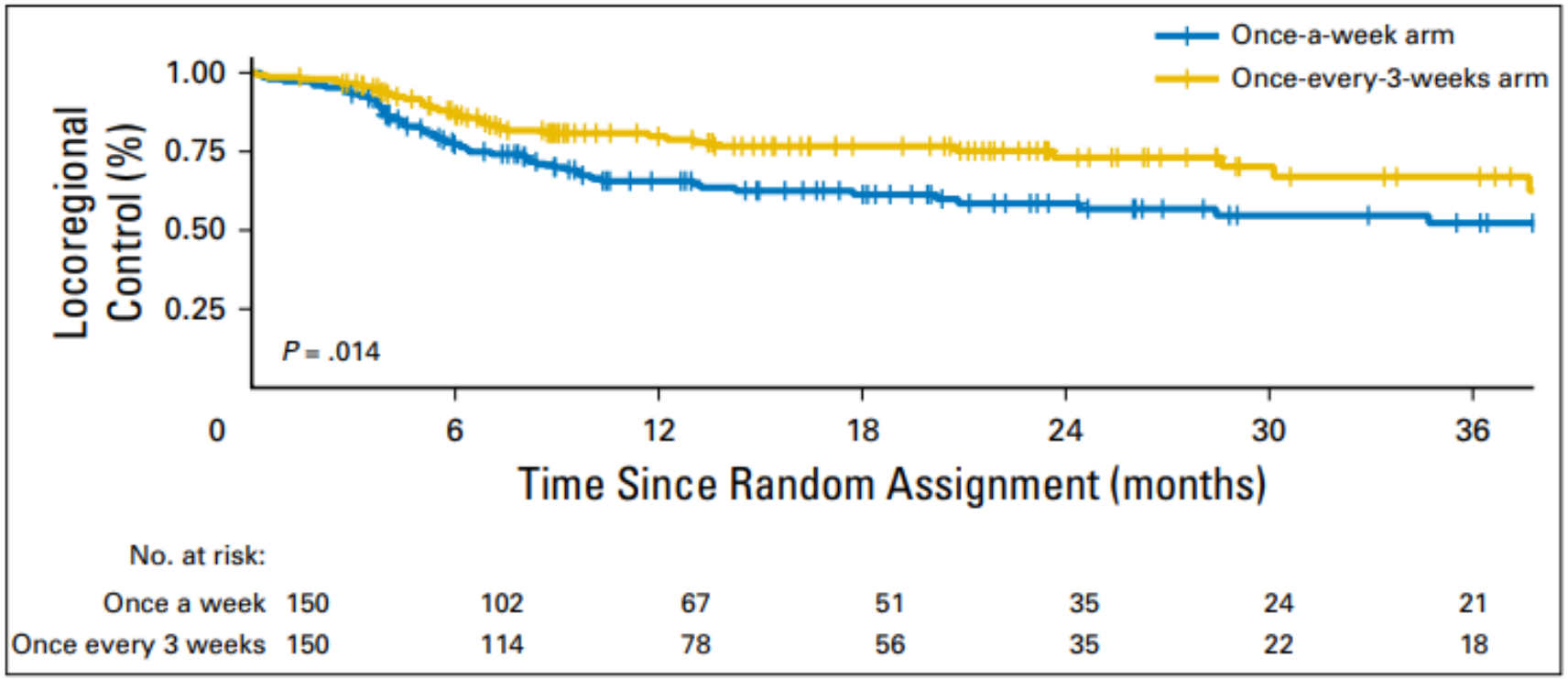
Fig. 4. Survival without locoregional recurrence.

Cisplatin became standard of care

Bachaud et al. J Radiation Oncology 1996

Weekly vs 3 week Cisplatin

- 2 year loco-regional → cisplatin once every 3 weeks (73.1%) vs receive weekly cisplatin (58.5%) (HR, 1.76; 95% CI, 1.11–2.79; P = .014).
- 3 weeks developed more severe acute toxicities, compared to patients randomized to receive weekly cisplatin (84.6% vs. 71.6%, respectively, P = .006). Hyponatremia, leukopenia, neutropenia



Noronha et al, JCO 2018

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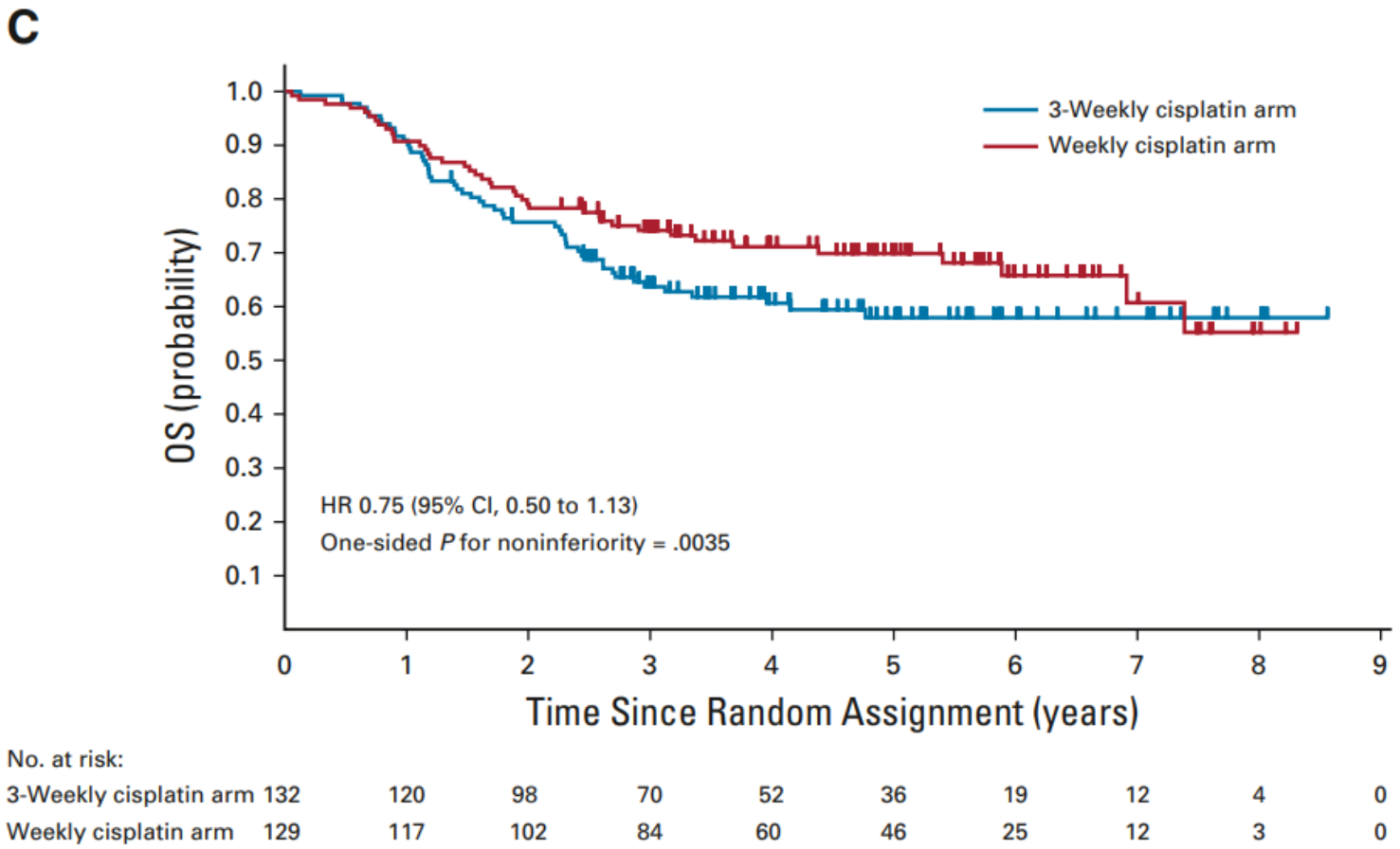
Weekly vs 3 week Cisplatin



Kiyota et al, JCO 2022

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Weekly vs 3 week Cisplatin

- 52 studies → 4,209 patients
- RT doses 60-66 Gy post op and definitive 66-70 Gy
- Cisplatin 100 mg/m2 vs weekly 40 mg/m2 at least 6 doses.
- Insufficient data to demonstrate meaningful survival difference

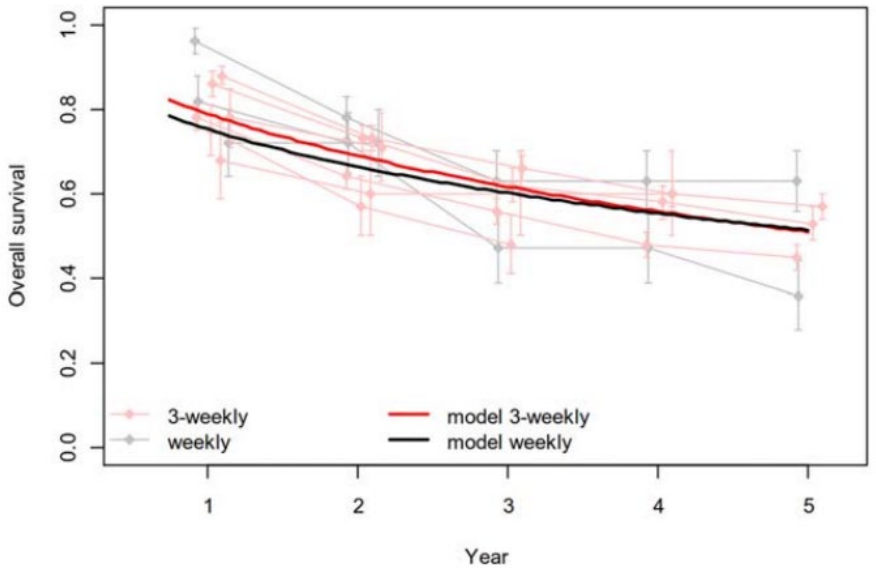

Figure 2. Overall survival analysis comparing weekly and three-weekly cisplatin given concurrently with postoperative radiotherapy.

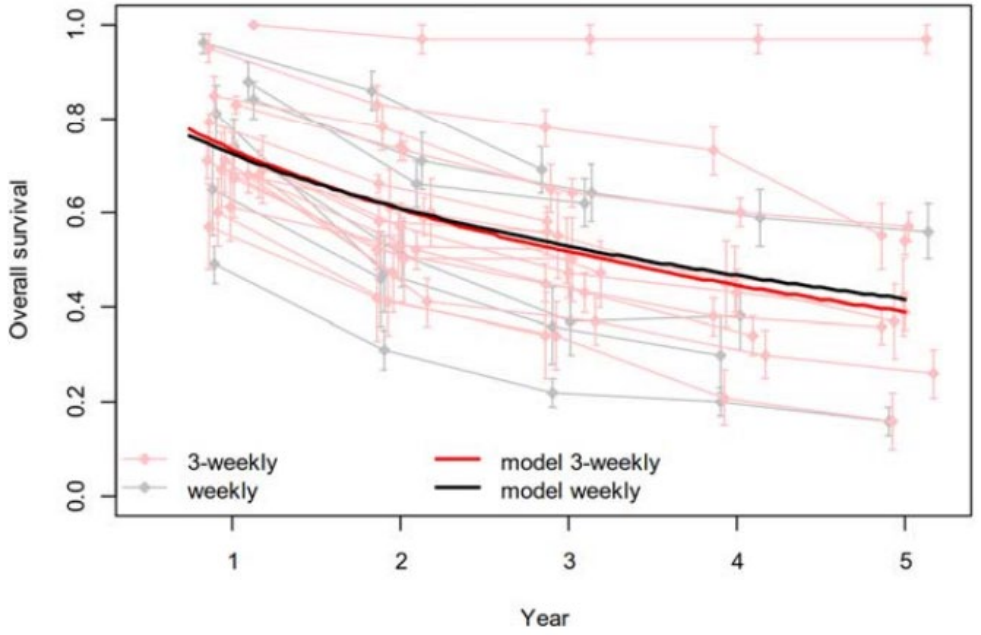

Figure 3. Overall survival analysis comparing weekly and three-weekly cisplatin given concurrently with definitive radiotherapy.

Szturz et al. The Oncologist 2017

Weekly vs 3 week Cisplatin

- Concert Trial – Phase III non-inferiority RCT – ORAL abstract ASCO 2022
- 278 patients → 59% comprising of oropharyngeal malignancy.
- 78.6% in 3-weekly and 81.6% patients in weekly arm received ≥200 mg/m2 of cisplatin.
- Toxicity was found to be significantly higher in 3-weekly arm.
- Noninferiority margin of 10%, locoregional control rates at 2 years were 57.69% in 3-weekly arm and 61.53%

Sharma et al. JCO 2022

Neoadjuvant / Induction (IC)

- TAX 324 trial – PF vs TPF (docetaxel, cisplatin, 5FU) = OS 30 months vs. 71 months, grade 3-4 neutropenia.
- TAX 323/EORTC 24971 – Lower doses of 5FU (1 g/m2/d), less neutropenia but 2.3% treatment related deaths.

<u>TPF standard of care for induction chemotherapy.</u>

TOXICITY as high as 6% related to treatment data from RTOG 91-11 and febrile neutropenia 11% requiring GCSF support.

RTOG 91-11. Forrastiere et al. JCO 2013
Posner et al. NEJM 2007
Vermoken et al. NEJM 2007

Neoadjuvant / Induction (IC)

- IC can also compromise completion of subsequent CRT as noted on Spanish phase III trial ➔ Cisplatin 100 mg/m2 = 49.5% vs 80.5%
- PARADIGM trial, did not show any difference in OS (HR 1.09; 95% CI 0.59–2.03), nor in PFS (HR 1.07; 95% CI 0.59–1.92) when comparing IC + CRT vs. CRT alone.
- DECIDE (limit N2 -N3 disease) – low power trial (47 patients) with uptrend to OS benefit.

**IC as effective treatment in resectable locally-advanced laryngeal and hypopharyngeal cancer, with the aim of organ preservation, patients less than stage T4a disease candidate to total laryngectomy
Px can be managed with sequential or concurrent CRT, with surgery as a secondary salvage option

Hitt et al, Ann Oncology 2014
Haddad et al. Lancet 2013
Cohen et al. JCO 2014

Recurrent / Metastatic disease

- Where is the recurrence? Is surgery vs re-irradiation an option? Second primary?
- NGS (NTRK fusions, CDKN2A, PIK3CA , EGFR amplification)
- Clinical trial enrollment
- CPS score
- Performance status
- Platinum-refractory? (<6 months since completion of chemo)
- Contraindications to immunotherapy?

KEYNOTE 048

- Phase 3, multicenter RCT – Pembrolizumab vs P/C/5FU vs Cetuximab/Platinum/5FU

	Pembrolizumab alone vs cetuximab with chemotherapy		Pembrolizumab with chemotherapy vs cetuximab with chemotherapy*	
	Pembrolizumab alone (n=301)	Cetuximab with chemotherapy (n=300)	Pembrolizumab with chemotherapy (n=281)	Cetuximab with chemotherapy (n=278)
Age (years)	62·0 (56·0–68·0)	61·0 (54·5–68·0)	61·0 (55·0–68·0)	61·0 (55·0–68·0)
Sex				
Female	51 (17%)	39 (13%)	57 (20%)	36 (13%)
Male	250 (83%)	261 (87%)	224 (80%)	242 (87%)
Region of enrolment				
Europe	87 (29%)	105 (35%)	88 (31%)	94 (34%)
North America	75 (25%)	62 (21%)	60 (21%)	59 (21%)
Rest of world	139 (46%)	133 (44%)	133 (47%)	125 (45%)
ECOG performance status score				
0	118 (39%)	117 (39%)	110 (39%)	108 (39%)
1	183 (61%)	183 (61%)	171 (61%)	170 (61%)
Smoking status				
Current or former	239 (79%)	234 (78%)	224 (80%)	215 (77%)
Never	62 (21%)	64 (21%)	57 (20%)	61 (22%)
Unknown	0	2 (<1%)	0	2 (<1%)
Oropharyngeal p16 positive	63 (21%)	67 (22%)	60 (21%)	61 (22%)
Tumour cells with PD-L1 expression				
≥50%	67 (22%)	66 (22%)	66 (23%)	62 (22%)
<50%	234 (78%)	234 (78%)	215 (77%)	216 (78%)
PD-L1 CPS				
≥1	257 (85%)	255 (85%)	242 (86%)	235 (85%)
≥20	133 (44%)	122 (41%)	126 (45%)	110 (40%)
Disease status				
Metastatic	216 (72%)	203 (68%)	201 (72%)	187 (67%)
Recurrent only†	82 (27%)	94 (31%)	76 (27%)	88 (32%)
Newly diagnosed, non-metastatic	3 (1%)	3 (1%)	4 (1%)	3 (1%)
Primary tumour location				
Hypopharynx	38 (13%)	39 (13%)	44 (16%)	36 (13%)
Larynx	74 (25%)	61 (20%)	46 (16%)	56 (20%)
Oral cavity	82 (27%)	91 (30%)	82 (29%)	84 (30%)
Oropharynx	113 (38%)	114 (38%)	113 (40%)	107 (38%)
Investigator's choice of platinum for study treatment‡				
Carboplatin	181 (60%)	170 (57%)	160 (57%)	156 (56%)
Cisplatin	120 (40%)	130 (43%)	121 (43%)	122 (44%)

Burtness et al. Lancet 2019

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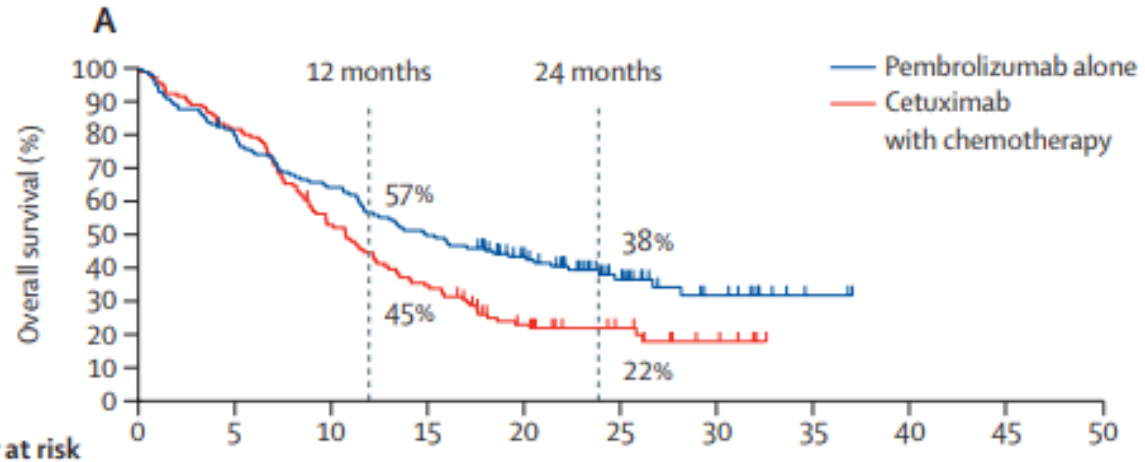
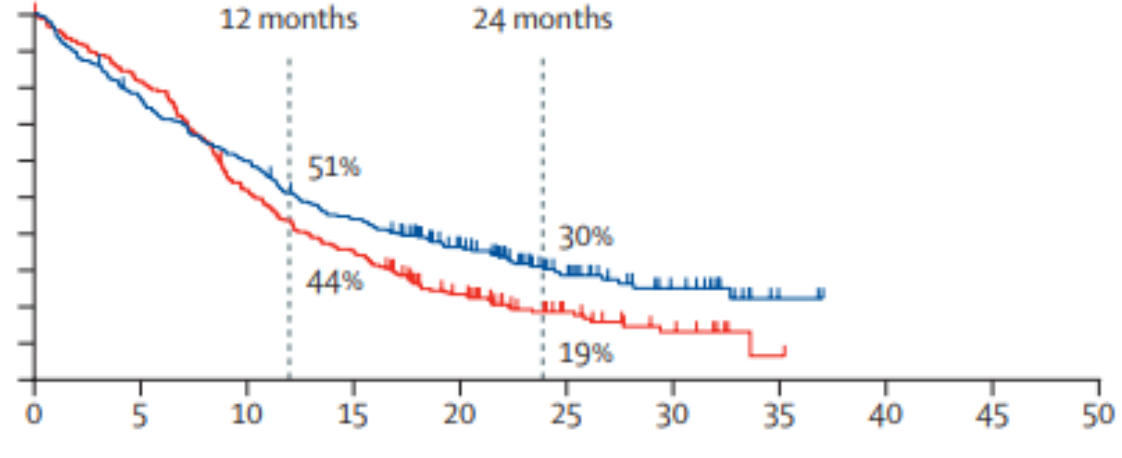
CPS >20



CPS >/=1



Number at risk (number censored)											
Pembrolizumab alone	133 (0)	106 (1)	85 (1)	65 (2)	47 (12)	24 (29)	11 (40)	2 (49)	0 (51)	0 (51)	0 (51)
Cetuximab with chemotherapy	122 (0)	100 (0)	64 (1)	42 (1)	22 (8)	12 (17)	5 (22)	0 (27)	0 (27)	0 (27)	0 (27)

Pembrolizumab alone	257 (0)	196 (2)	152 (2)	110 (4)	74 (22)	34 (50)	17 (64)	2 (78)	0 (80)	0 (80)	0 (80)
Cetuximab with chemotherapy	255 (0)	207 (1)	131 (2)	89 (2)	47 (16)	21 (34)	9 (41)	1 (48)	0 (49)	0 (49)	0 (49)

Burtness et al. Lancet 2019

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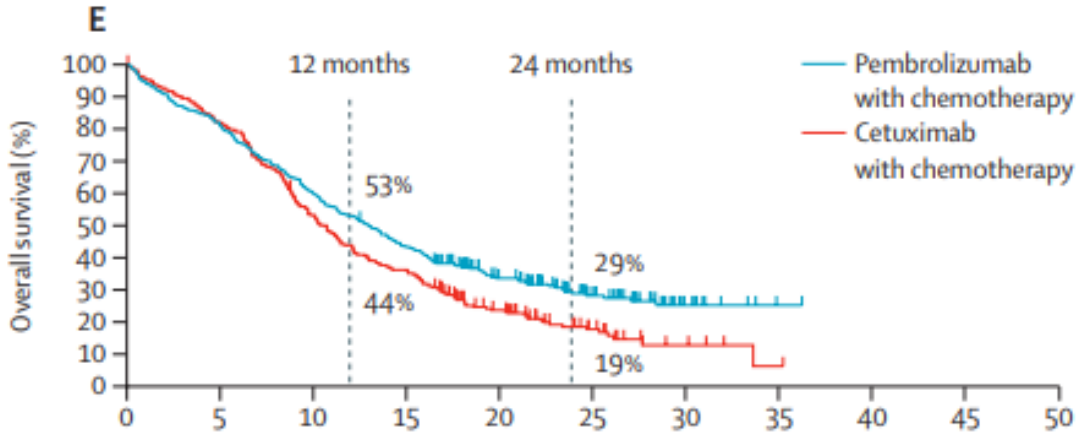
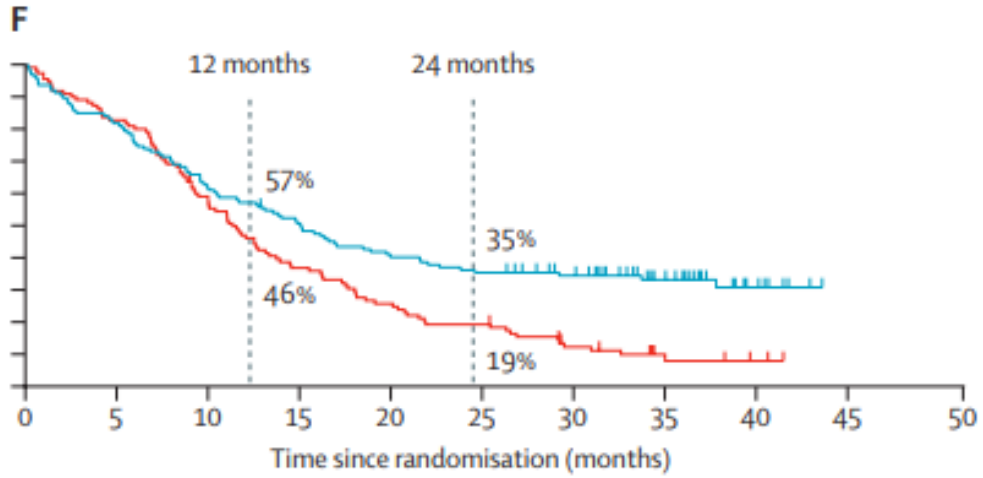
CPS >20



CPS >/=1



Number at risk (number censored)											
Pembrolizumab with chemotherapy	281 (0)	227 (0)	169 (0)	122 (1)	75 (22)	40 (47)	10 (74)	1 (83)	0 (84)	0 (84)	0 (84)
Cetuximab with chemotherapy	278 (0)	227 (1)	147 (2)	100 (2)	51 (19)	20 (40)	5 (51)	1 (54)	0 (55)	0 (55)	0 (55)

Pembrolizumab with chemotherapy	126 (0)	102 (0)	77 (0)	60 (1)	50 (1)	44 (1)	36 (8)	21 (22)	4 (38)	0 (42)	0 (42)
Cetuximab with chemotherapy	110 (0)	91 (0)	60 (1)	40 (1)	26 (1)	19 (2)	11 (4)	4 (8)	1 (11)	0 (12)	0 (12)

Burtness et al. Lancet 2019

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KEYNOTE 048

- Pembrolizumab vs P/P/5FU → first-line treatment for patients with recurrent or metastatic HNSCC with a CPS ≥ 1

~RR single agent Pembrolizumab 20%

- P/P/5FU → first-line treatment for patients with recurrent or metastatic HNSCC with a CPS < 1

- Clinical picture? Time to achieve response? Tumor burden?

Burtness et al. Lancet 2019

Treatment landscape R/M HNSCC

First Line →

PD1 Monotherapy	PD1 + Chemotherapy
- PDL1 + disease - CPS score 1 & >20	PDL1 – or unknown High tumor burden or rapid response is needed.

Second Line →

No standard of care
- Depends on first line therapy. - Performance status
1. No previous PDL1 → PD-1 therapy 2. Single agent vs doublet chemotherapy 3. EGFR naïve → Cetuximab/platinum

Third Line →

No standard of care
- Depends previous lines of therapy. Likely single agent chemotherapy

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ASCO 2023 – New treatments

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Abstract 6005 - BCA101 with pembrolizumab

Dose expansion results of the bifunctional EGFR/TGFβ inhibitor BCA101 with pembrolizumab.

- ✓ R/M HNSCC (oral cavity, oropharynx, hypopharynx and larynx)
- ✓ CPS > or equal 1.
- ✓ No prior systemic therapy.
- ✓ Stage 1 → 18 patients , >4 responses required to proceed stage 2.
- ✓ Stage 2 → 21 patients (total 39).

Abstract 6005 - BCA101 with pembrolizumab

- BCA101 mechanisms of actions:

TGF-b inhibitor (trap) to the tumor microenvironment through EGFR directed approach.

Increase antitumor activity via ADCC and increased NK cell activation.

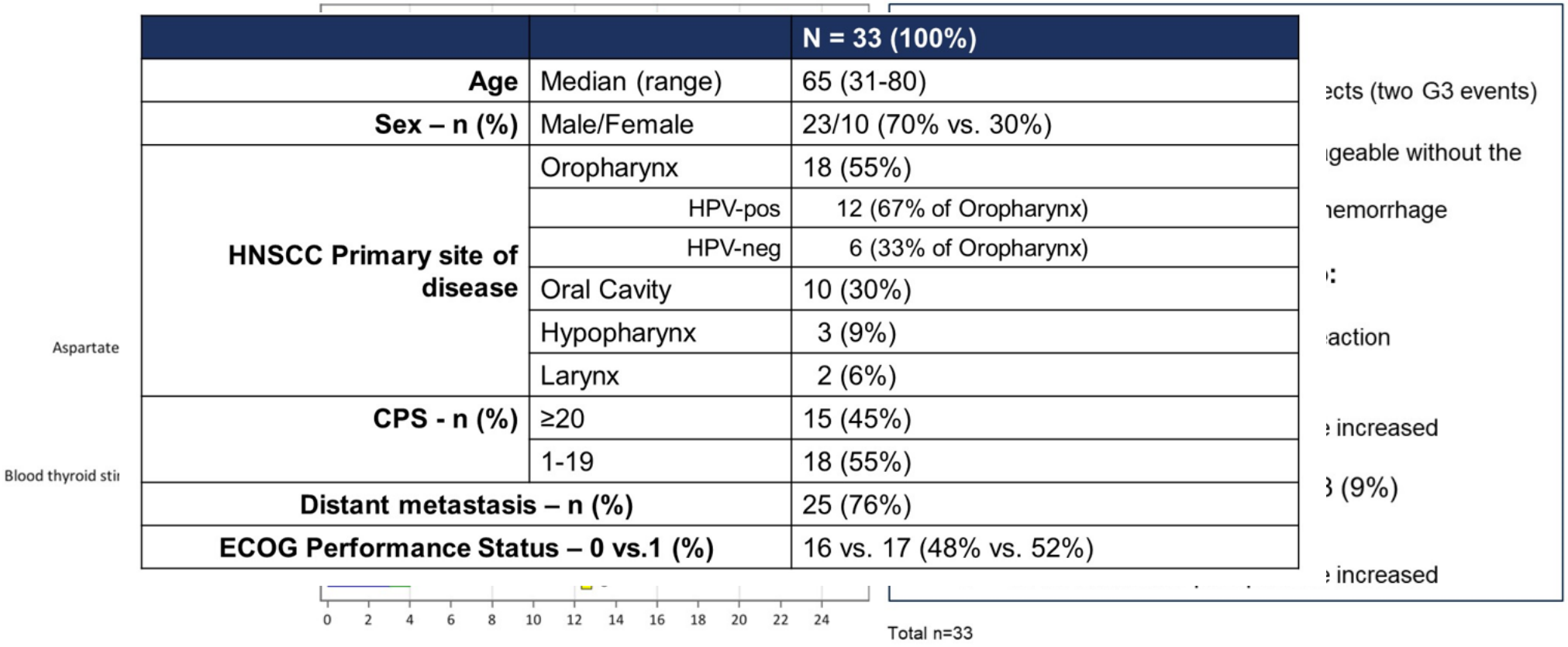
Dual inhibition of EGFR and TGF-B prevents epithelial-mesenchymal transition and metastasis.

Slides images from ASCO2023 Abstract presentation. Hanna et al.

Abstract 6005 - BCA101 with pembrolizumab

AEs, treatment-related, in ≥10% of subjects, preferred term & grade

		N = 33 (100%)
Age	Median (range)	65 (31-80)
Sex – n (%)	Male/Female	23/10 (70% vs. 30%)
HNSCC Primary site of disease	Oropharynx	18 (55%)
	HPV-pos	12 (67% of Oropharynx)
	HPV-neg	6 (33% of Oropharynx)
	Oral Cavity	10 (30%)
	Hypopharynx	3 (9%)
	Larynx	2 (6%)
CPS - n (%)	≥20	15 (45%)
	1-19	18 (55%)
Distant metastasis – n (%)		25 (76%)
ECOG Performance Status – 0 vs.1 (%)		16 vs. 17 (48% vs. 52%)



Slides images from ASCO2023 Abstract presentation. Hanna et al.

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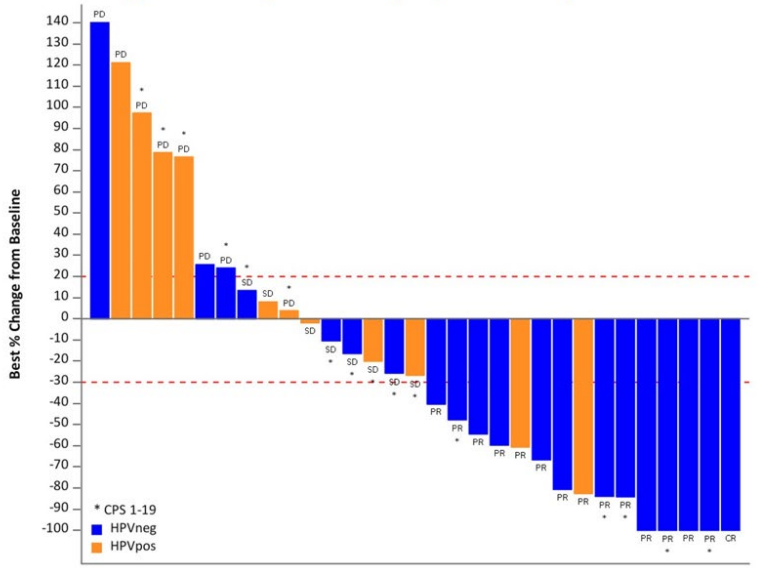
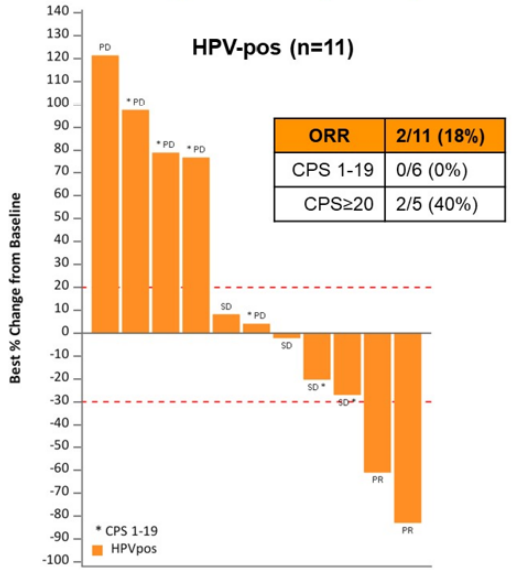
Abstract 6005 - BCA101 with pembrolizumab

Preliminary Efficacy – Total population (N=31 evaluable)

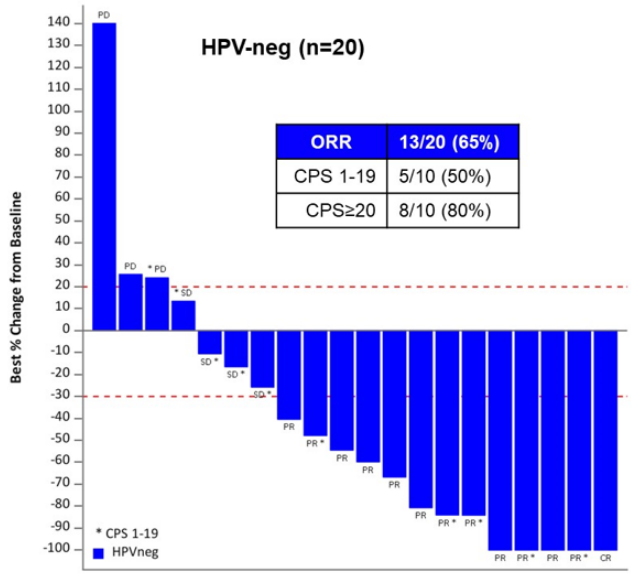


ORR	15/31 (48%)
CR	1 (3%)
PR	14 (45%)
SD	8 (26%)
PD	8 (26%)

Preliminary Efficacy – by HPV status



ORR	2/11 (18%)
CPS 1-19	0/6 (0%)
CPS≥20	2/5 (40%)



ORR	13/20 (65%)
CPS 1-19	5/10 (50%)
CPS≥20	8/10 (80%)

- ORR 65% in HPV-neg subjects with responses observed in both CPS subgroups

Slides images from ASCO2023 Abstract presentation. Hanna et al.

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Abstract 6005 - BCA101 with pembrolizumab

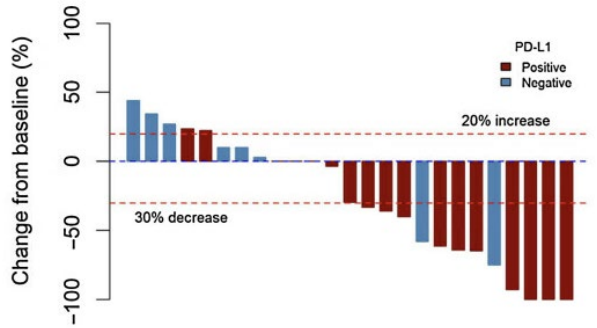
- <u>Discussion</u>

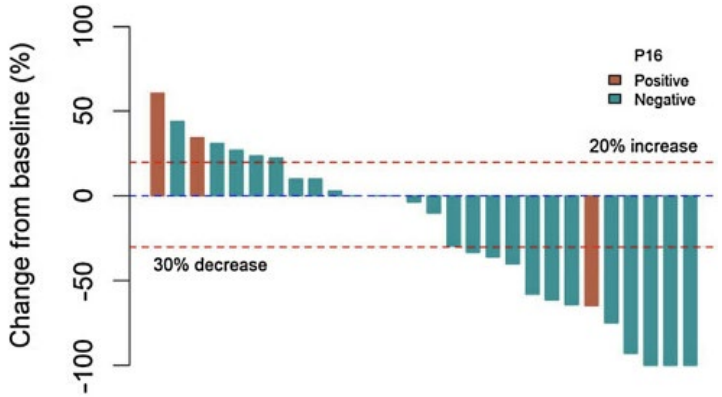
ORR 48%, HPV negative ORR 65%.

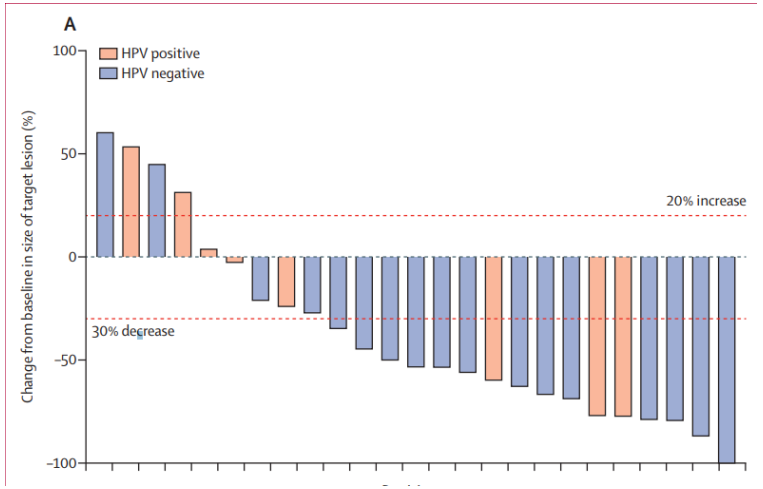
CPS 1-19 (5/10, 50%) & CPS >20 (8/10, 80%)

mPFS HPV negative NR (1.3-14.6, at least 6.6 months)

- Combination warrants larger analysis in randomized study specifically HPV negative population.
- Durvalumab/cetuximab (II) ORR 39% vs Pembrolizumab cetuximab (II) ORR 45%







1. Gulati et al. Durvalumab plus cetuximab in patients with recurrent or metastatic head and neck SCC: An open label, nonrandomized, phase II clinical trial. Clin Cancer Res (2023) 29 (10): 1906–1915.
2. Sacco et al. Pembrolizumab plus cetuximab in patients with recurrent or metastatic head and neck SCC: an open label, multi-arm, non-randomized, multicenter, phase 2 trial. Lancet Oncology June 2021, Volume 22, Issue 6, P 883-892

Abstract 6083 – Combined Pulse Radiotherapy + ICI

- Combination of “Quad shot” with ICI to enhance immune response for elderly patients ineligible for curative intent therapy.
- Advance cutaneous or mucosal SCC
- 33 patients → mean age of 81
- Pulse dose QUAD shot delivered to gross disease excluding elective nodal disease(45 – 59 Gy) spaced 3 weeks + Pembrolizumab or Cemiplimab.

Characteristic	n (%) or mean (SD)
Male, n (%)	20 (60.6%)
Age, mean (SD)	81.27 (8.57)
KPS, n (%)	
50	1 (3.0%)
60	12 (36.4%)
70	18 (54.5%)
80	2 (6.1%)
ECOG, n (%)	
1	3 (9.1%)
2	25 (75.8%)
3	5 (15.2%)

Pathology = SCC, n (%)	25 (75.8.%)
TNM, n (%)	
Recurrent	8 (24.2%)
T0N2M0	2 (6.1%)
T2N0M0	1 (3.0%)
T2N1M0	2 (6.1%)
T2N2M0	4 (12.1%)
T3N0M0	3 (9.1%)
T3N1M0	1 (3.0%)
T3N2M0	2 (6.1%)
T3N2M1	2 (6.1%)

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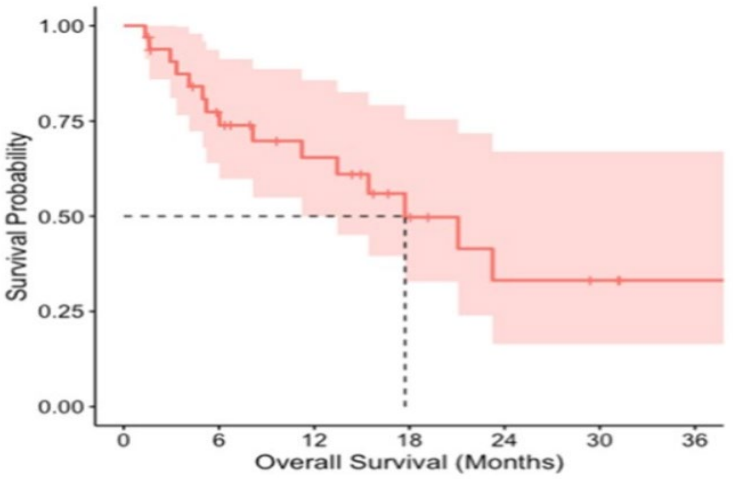
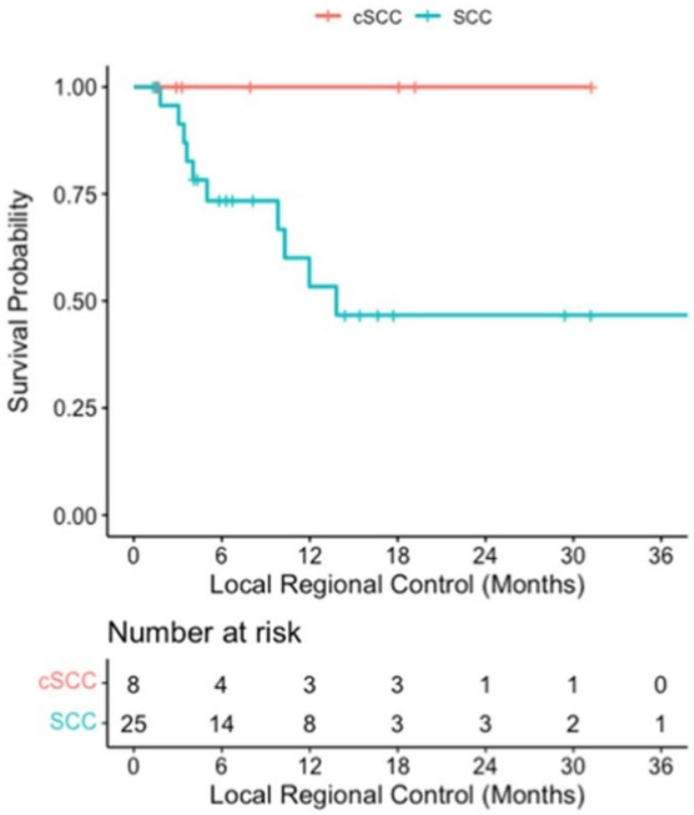
Abstract 6083 – Combined Pulse Radiotherapy + ICI

- Median OS with combination → 17 months vs 5.7 compared to previous series of QUAD
- DFS 1 year 59% , 2 years 37% LRC 61% 1 year and 55.5% 2 years.
- G3/4 = 9% (3/33) Colitis, fatigue, infusion

Figure 1. Kaplan-Meier Curve for Overall Survival (N= 33)



Month	0	6	12	18	24	30	36
Survival Rate	100%	74.40%	65.42%	49.75%	33.17%	33.17%	33.17%



Slides images from ASCO2023 Poster session. J. De Los Santos

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Abstract 6003 – Frail Immune

- Phase II FRAIL-IMMUNE trial evaluating the efficacy and safety of durvalumab combined with weekly paclitaxel carboplatin in first-line in patients with (R/M SCCHN). (GORTEC 2018-03)
- Objective : Efficacy and tolerance of PDL-1 inhibition (durvalumab) combined with weekly carboplatin (AUC2) + Paclitaxel as first line for patients R/M ineligible for cisplatin
- Prospective, multicenter, single arm phase II, N=64 patients
- Primary End Point: OS at 12 months
- Secondary End Points: PFS, ORR, DoR, QoL.

Abstract 6003 – Frail Immune

Patients and disease characteristics (N=64)			
Sex	Female	6	(9.4%)
	Male	58	(90.6%)
Age	Median (min; max)	69.5 (54.0; 90.0)	
ECOG	0	24	(37.5%)
	1	40	(62.5%)
Localization of the primary tumor	Oral cavity	9	(14.1%)
	Oropharynx	24	(37.5%)
	Hypopharynx	11	(17.2%)
	Larynx	18	(28.1%)
	Isolated cervical lymphnodes, unk primary site	2	(3.1%)
Status of the disease at inclusion	Primary metastatic	5	(7.8%)
	Metastatic only, recurrence	19	(29.7%)
	Locoregional only, recurrence	26	(40.6%)
	Primary locoregional and metastatic	1	(1.6%)
	Locoregional and metastatic recurrence	13	(20.3%)
PDL1	Missing	8	
	<1	13	(23.2%)
	>=1	43	(76.8%)
	>=20	17	(30.4%)
HPV (oropharynx)	Missing	4	
	Negative	11	(55.0%)
	Positive	9	(45.0%)

Criteria for Cisplatin ineligibility
Older than 70 years old (N=30)
Creatinine clearance: 40< Creat Cl <60ml/min (N=18)
Comorbidities (N=18)

Slides images from ASCO2023 Abstract presentation. Fayette MD, et al.

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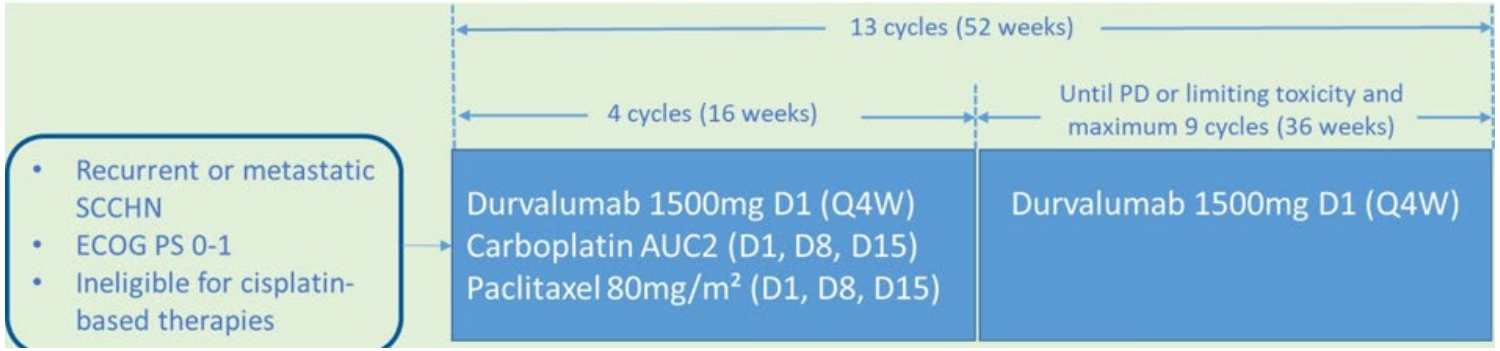
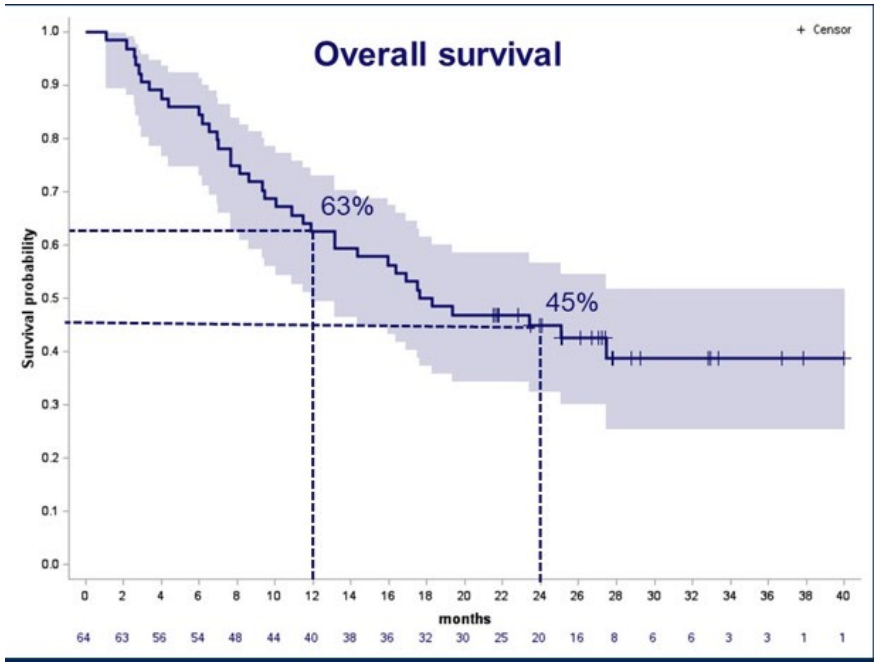
Abstract 6003 – Frail Immune trial





Analysis population N=64	
Number of deaths (%)	37 (57.8%)
Median OS, months [min-max]	18.0 [11.9-NR]
12-month OS-rate (95%CI)	63% [49-73]
24-month OS-rate (95%CI)	45% [32-57]

Median duration of follow-up was 27.1 months (21.5-40.1)

12 months OS 63%, mOS 18 months, PFS 7.0 months, ORR 71%

Slides images from ASCO2023 Abstract presentation. Fayette MD, et al.

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Abstract 6003 – Frail Immune trial

- Discussion

Durvalumab plus weekly Carboplatin (2AUC) + Paclitaxel (80 mg/m2) could serve as a potential option for cis-ineligible patients.

?KEYNOTE-B10 (ESMO 2022) → Pembrolizumab+Carboplatin + Paclitaxel (3 weekly). ORR 43%, PFS 5.6 months and OS 12.1.

Weekly schedule administration.

Not everything is chemo…

- Importance of psychosocial support during and after treatment.
- Nutritionist, Physical therapy, Speech pathologist.
- Pharmacist and Nurse navigators.
- Support groups.
- Smoking and alcohol cessation programs.
- Pain management.

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Take home points

- Highlight importance of H/N multidisciplinary team to provide best treatment modalities.
- Addition of adjuvant cisplatin on patients with positive margins and ENE. Consider with PNI, LVI.
- 3 week vs once a week Cisplatin efficacy is similar, decrease incidence of side effects.
- IC is not recommended due to side effects and lack of OS/PFS benefits.
- Pembrolizumab for R/M H/N based upon CPS score, if low or high tumor burden, add chemo/IO.

Questions?

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