Dana-Farber Cancer Institute

Squamous Cell Carcinoma of Head and Neck

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HEAD AND NECK CANCER

- Introduction: Epidemiology, Clinical Features, *HPV, New Staging System*, Treatment Modalities
- Concurrent Chemoradiotherapy
- Sequential Chemoradiotherapy
- Adjuvant Chemoradiotherapy
- Recurrent/Metastatic disease

HUMAN PAPILLOMAVIRUS (HPV)-POSITIVE HEAD AND NECK CANCER

- HPV 16 is the viral subtype in the vast majority of patients.
- Half of oropharynx cancers will have HPV 16 DNA.
- Often occurs in nonsmokers, nondrinkers
- Median age younger than HPV-negative patients; incidence increasing
- Associated with ↑ number of sexual partners and high-risk sexual practices
- Favorable prognosis
- In situ hybridization,p16 IHC, PCR

Fakhry C, et al. J Clin Oncol. 2006:24(17):2606-2617
Chaturvedi AK, et al. J Clin Oncol. 2008;26(4):612-619

PHASE III TRIAL OF RADIOTHERAPY PLUS CETUXIMAB VERSUS CHEMORADIOTHERAPY IN HPV-RELATED OROPHARYNX CANCER

REGISTER

Mandatory

p16

testing

STRATIFY

T Stage
1. T1-2
2. T3-4

N Stage
1. N0-2a
2. N2b-3

Zubrod Performance Status
1. 0
2. 1

Smoking History
1. ≤ 10 pack-years
2. > 10 pack-years

RANDOMIZE

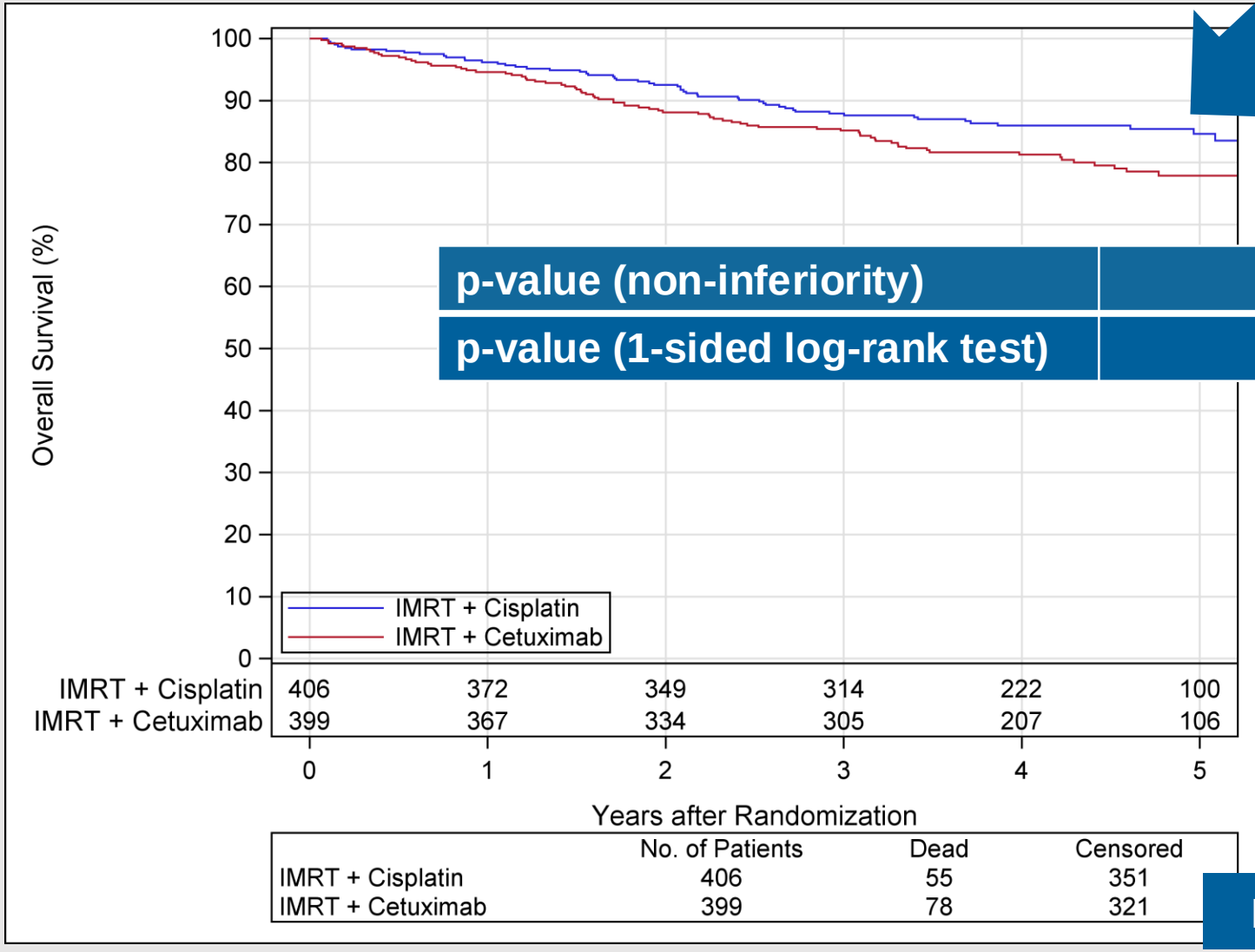
Arm 1 (Control):
Accelerated IMRT, 70 Gy for 6 weeks
+ high dose DDP (100 mg/m^2) Days 1 and 22
(Total: 200 mg/m^2)

Arm 2:
Accelerated IMRT, 70 Gy for 6 weeks
+ cetuximab (400 mg/m^2) loading dose pre-IMRT, then 250 mg/m^2 weekly during IMRT,
+ 1 week after IMRT for a total of 8 doses of cetuximab

RTOG 1016 HPV Trial

Gillison et al : Lancet . January 2019

OVERALL SURVIVAL



Cisplatin

85 vs 78% 5-yr

p-value (non-inferiority)	**0.51**
p-value (1-sided log-rank test)	**0.02**

RTOG 1016 HPV Trial

NRG ONCOLOGY

Advancing Research. Improving Lives.™

Interim Futility Results of NRG-HN005, A Randomized, Phase II/III Non-Inferiority Trial for Non-Smoking p16+ Oropharyngeal Cancer Patients

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Annual Meeting of the American Society for Radiation Oncology
September 30, 2024

@NRGOnc NRG Oncology

NCI National Clinical Trials Network — a National Cancer Institute program

NCI Community Oncology Research Program — A program of the National Cancer Institute of the National Institutes of Health

NRG-HN005 Phase II Schema

- **Oropharyngeal squamous cell carcinoma, p16-positive**
- **≤ 10 pack-year history of smoking**
- **8th ed. clinical stages T1-2N1M0 or T3N0-N1M0 (8th ed. stage I-II excluding T0, T1-2N0, or any N2)**

↓

STRATIFICATION
Zubrod Performance Status: 0 vs.1

RANDOMIZE 1:1:1

Arm 1	**Arm 2**	**Arm 3**
70 Gy radiation in 6 weeks using 6 fractions per week + Cisplatin x 2 cycles	**60 Gy radiation in 6 weeks using 5 fractions per week + Cisplatin x 2 cycles**	**60 Gy radiation in 5 weeks using 6 fractions per week + Nivolumab x 6 cycles**

NRG ONCOLOGY™

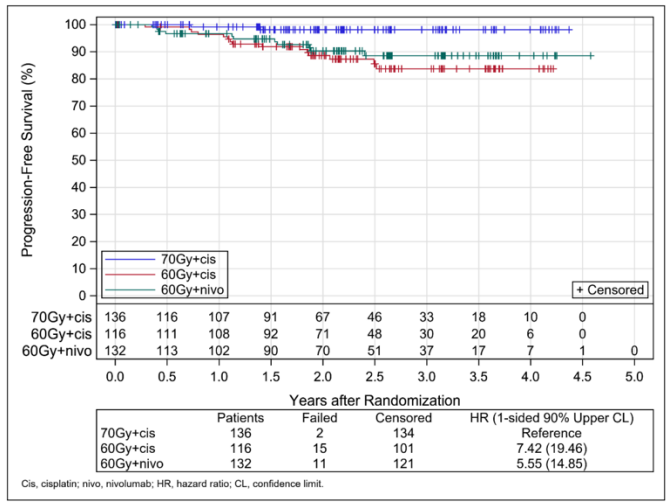
Stratified by Zubrod performance status and randomized (1:1:1) to 70 Gy IMRT over 6 weeks + Cisplatin at 100 mg/m^2 every 3 weeks (Arm 1) vs 60 Gy IMRT over 6 weeks + Cisplatin at 100 mg/m^2 every 3 weeks (Arm 2) vs 60 Gy IMRT over 5 weeks with nivolumab (Arm 3)

NRG-HN005 Phase II

2-Year Progression-Free Survival

At median follow-up of 2.2 years,
2-year PFS estimates are:

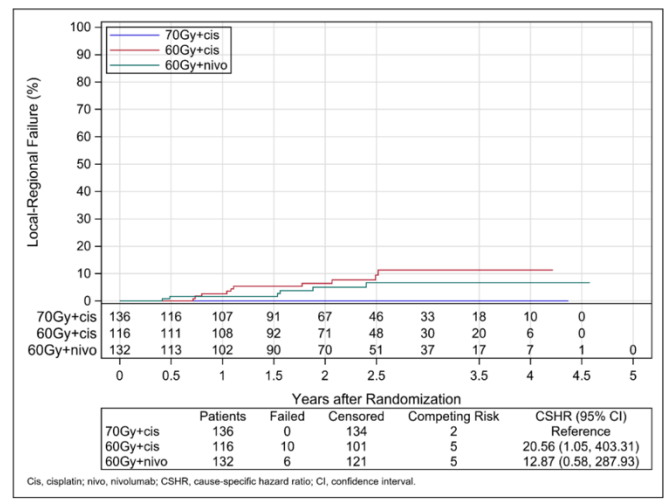
- Arm 1: 98.1% (95%CI 95.4, 100)
- Arm 2: 88.6% (95%CI 82.4, 94.7)
- Arm 3: 90.3% (95%CI 84.5, 96.1)



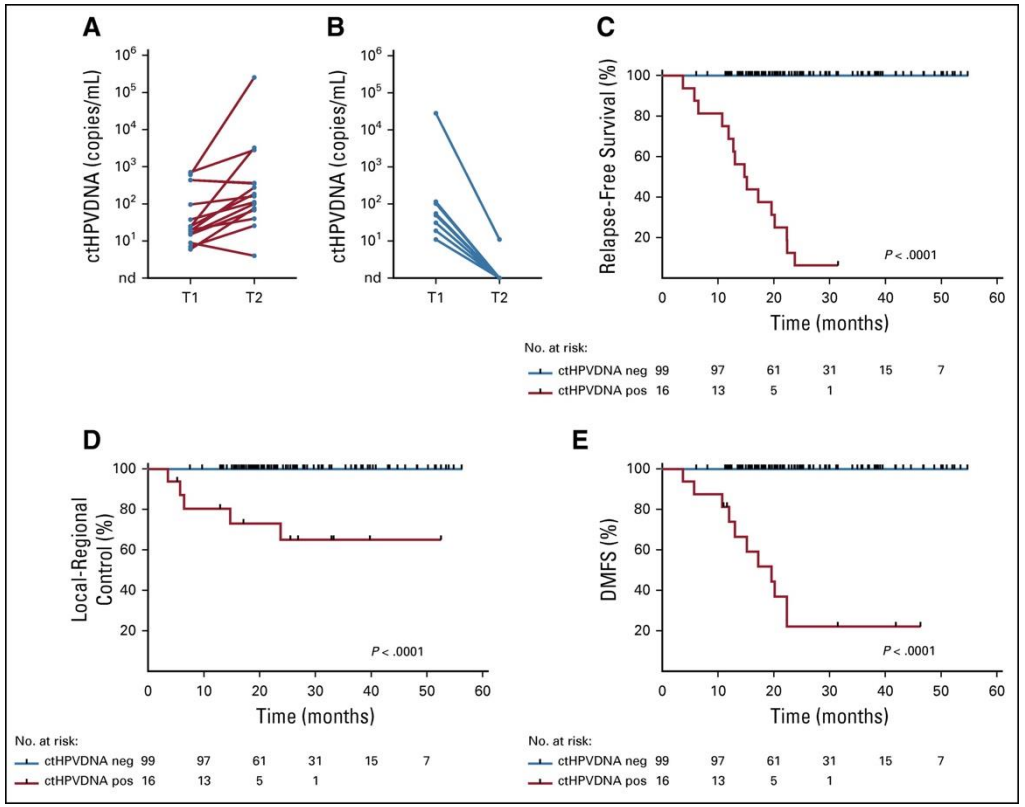
2-Year Locoregional Failure

2-year LRF estimates are:

- Arm 1: 0%
- Arm 2: 6.5% (95%CI 2.8, 12.2)
- Arm 3: 5.0% (95%CI 1.8, 10.6)



Plasma Circulating Tumor HPV DNA



Two consecutive positive tests for cfHPV had a PPV of 94% (95%CI, 70-90%) for disease recurrence

Consecutive negative tests NPV 100%

Median lead time between ctHPVDNA positivity and biopsy-proven recurrence was 3.9 month

Chera B et al, J Clin Oncol 2020 Apr 1;38(10)

TREATMENT APPROACH

Disease Extent	Treatment
T_1N_{0-1} or T_2N_0	Surgery or RT
T_2N_1 or T_{3-4} or N_{2-3}	Combined modality
Recurrent or M_1	Surgery and/or RT Combined modality Chemotherapy

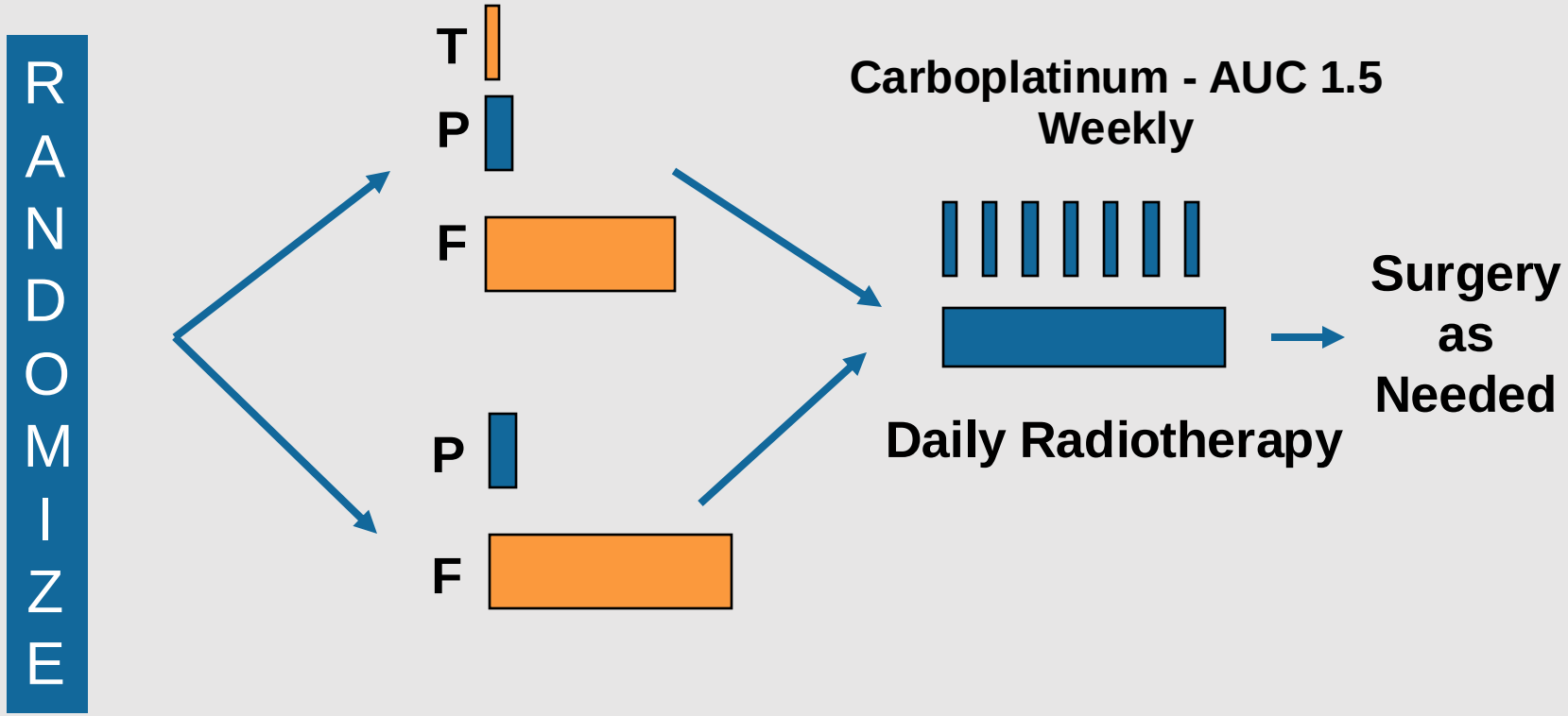
CONCURRENT CHEMORADIOTHERAPY

CONCURRENT THERAPY: STANDARD OF CARE

- Cisplatin 100 mg/m^2 days 1, 22, and 43 of RT
- RT standard fractionation, 70 Gy over 7 weeks (2-Gy fractions)
- Alternative Chemotherapy regimens:
  - 1- Weekly cisplatin 40mg/m^2
  - 2- Weekly Cetuximab
  - 3- Weekly carboplatin auc 1.5-2+Paclitaxel 30-45mg/m^2

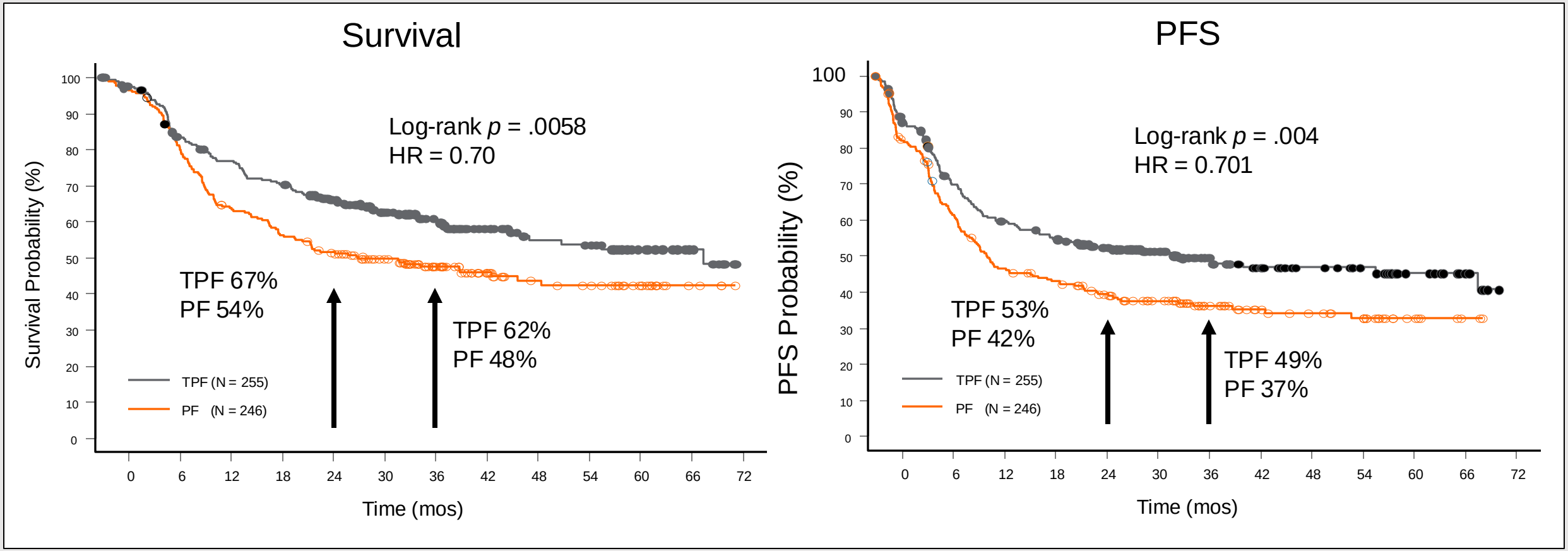
SEQUENTIAL CHEMORADIOTHERAPY

TAX 324: SEQUENTIAL COMBINED MODALITY THERAPY
TPF VS PF FOLLOWED BY CHEMORADIOTHERAPY



TPF: Docetaxel 75_{D1} + Cisplatin 100_{D1} + 5-FU $1000_{Cl\text{- }D1\text{-}4}$ Q 3 weeks x3
PF: Cisplatin 100_{D1} + 5-FU $1000_{Cl\text{-}D1\text{-}5}$ Q 3 weeks x 3

Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715



TPF significantly improves survival and PFS compared with PF in an ICT regimen followed by CRT

Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715

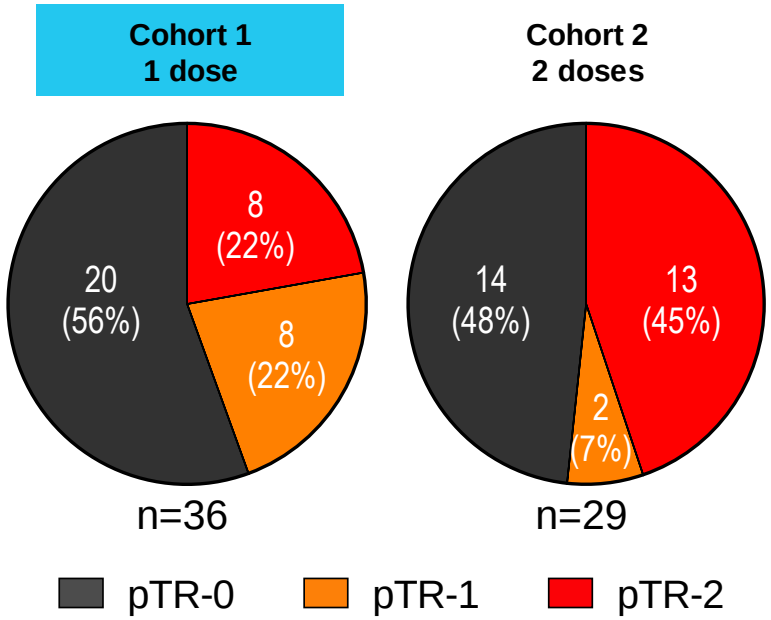
CLINICAL SCENARIOS TO CONSIDER INDUCTION THERAPY

1. Potential distant metastasis
2. Delay in radiation simulation
3. Impending local issue (eg, airway)
4. Markedly advanced disease (eg, bulky, N_{2c}, N_{2b}, N_3, low neck, dermal infiltration)
5. Organ preservation strategy in patients with markedly advanced disease

Rationale for Neoadjuvant Immunotherapy

- Need to Improve OS in High-Risk SCC (HPV neg, Larynx, Oral cavity, HP)
- Clear activity in R/M setting
- Neoadjuvant approach may help induce immune response to deliver durable benefit
- Neoadjuvant setting ideal : Untreated patients, lower burden of disease, intact tumor to allow for immune response
- “Immuno-reduction”- may alter surgery
- Reduced need for adjuvant approaches: Less RT, Less ChemoRT

Dose/ Timing in Neoadjuvant Pembrolizumab Studies



- Pathologic response scale
  - **pTR0** < 10%
  - **pTR1** ≥ 10% and <50%
  - **pTR2** ≥ 50%

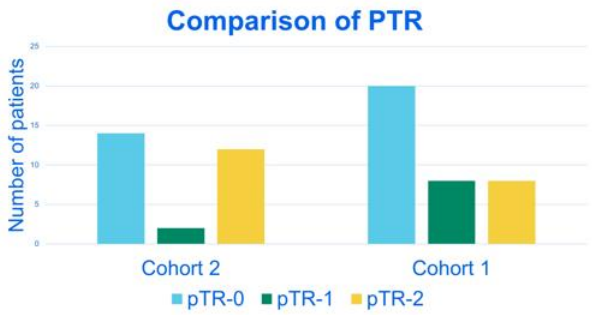
Cohort 1- pembrolizumab X 1 doses
Cohort 2- pembrolizumab X 2 doses

Exploratory analysis
- 1 dose pembro before surgery – 22% pTR2
- 2 doses pembro before surgery – 45% pTR2

% patients with any pTR similar Cohort 1 and 2

Uppaluri et al., CCR, 2020
Oliveira et al., Sci. Immunol, 2023

Cohort 1 versus 2



Characteristic	Cohort 2 (N=28)		Cohort 1 (N=36)		p-value	Diff (95% CI)
pTR Category						
pTR-0	14	50.0%	20	55.6%	0.11	-5.6 (-28.4 to 18.0)
pTR-1	2	7.1%	8	22.2%		-15.1 (-31.8 to 3.6)
pTR-2	12	42.9%	8	22.2%		20.6 (-2.1 to 41.5)
Pathologic risk category (positive margins/ENE)						
High risk	5	17.9%	18	50.0%	0.008	
Intermediate/low risk	23	82.1%	18	50.0%		32.1 (8.6 to 50.6)
Pathologic disease Stage, N (%)						
I-II	5	17.9%	3	8.3%	0.54	9.5 (-7.3 to 28.1)
III	5	17.9%	6	16.7%		1.2 (-17.0 to 21.0)
IVA-IVB	18	64.3%	27	75.0%		-10.7 (-32.3 to 11.3)

	Cohort 2 (N=28)		Cohort 1 (N=36)		p-value*	Diff (95% CI)
Downstaged (Clinical Stage > Pathologic Stage)	8	28.6%	7	19.4%	0.15	9.1 (-11.4 to 30.0)
Upstaged (Clinical Stage < Pathologic Stage)	2	7.1%	0	0.0%		7.1 (-3.8 to 22.6)
Stage unchanged (Clinical Stage = Pathologic Stage)	18	64.3%	29	80.6%		-16.3 (-37.1 to 5.4)

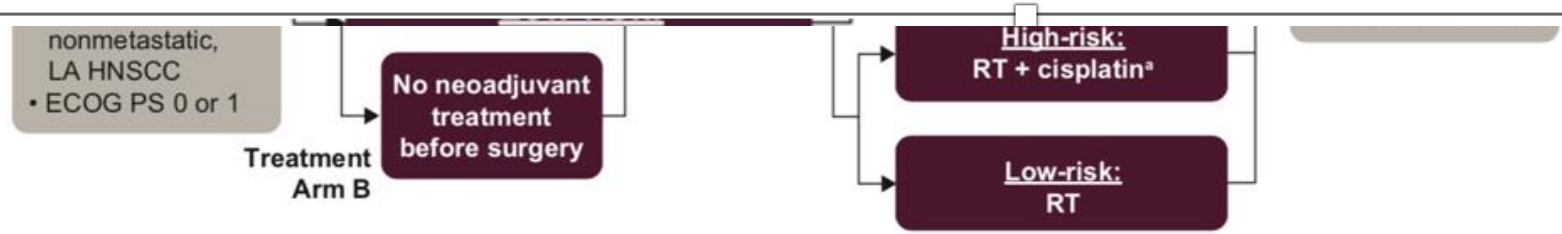
Uppaluri et al., CCR, 2020
Oliveira et al., Sci. Immunol, 2023

KEYNOTE-689: Phase 3 Study of Neoadjuvant and Adjuvant Pembrolizumab Combined With Standard of Care in Patients With Resectable, Locally Advanced Head and Neck Squamous Cell Carcinoma

2024-10-08

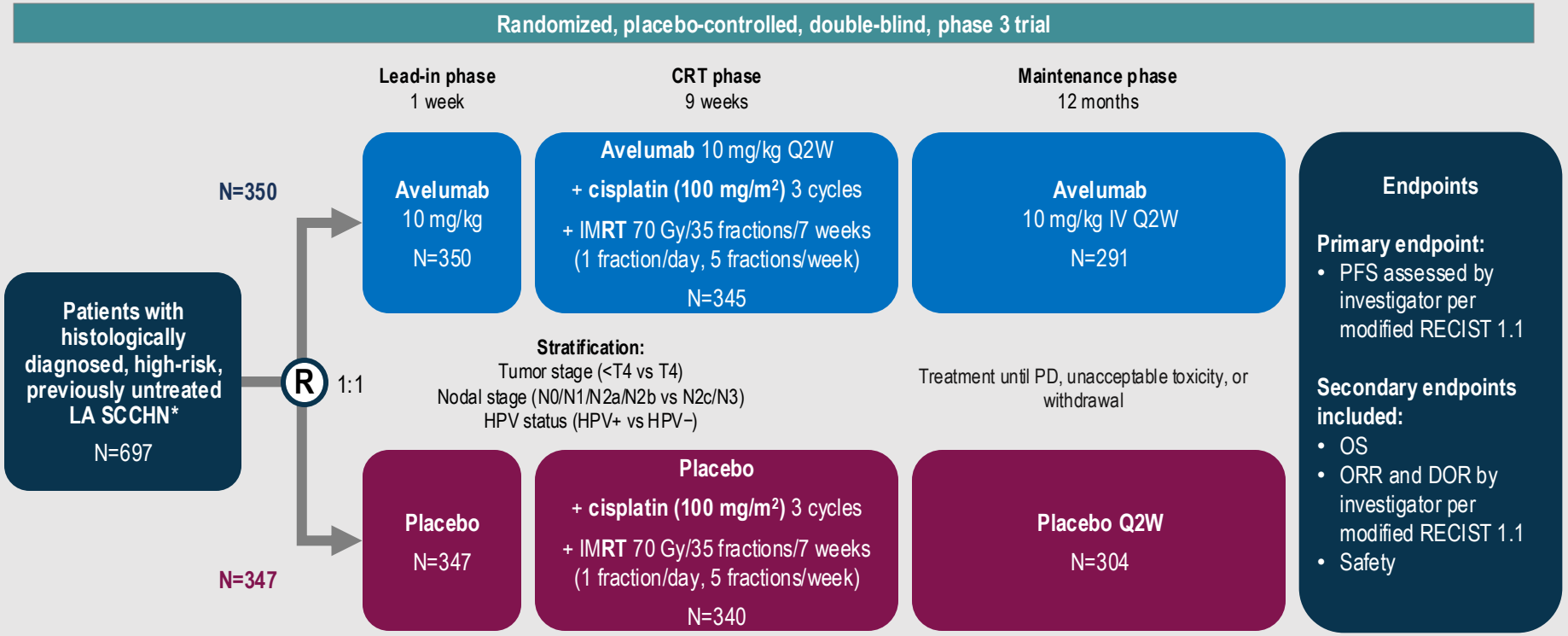
PRESS RELEASE

KEYNOTE-689 is the first Phase 3 trial to demonstrate statistically significant and clinically meaningful improvement in EFS in the intent-to-treat population in the neoadjuvant and adjuvant setting for an anti-PD-1 therapy in earlier stages of head and neck squamous cell carcinoma



NCT03765918

JAVELIN HEAD & NECK 100: STUDY DESIGN

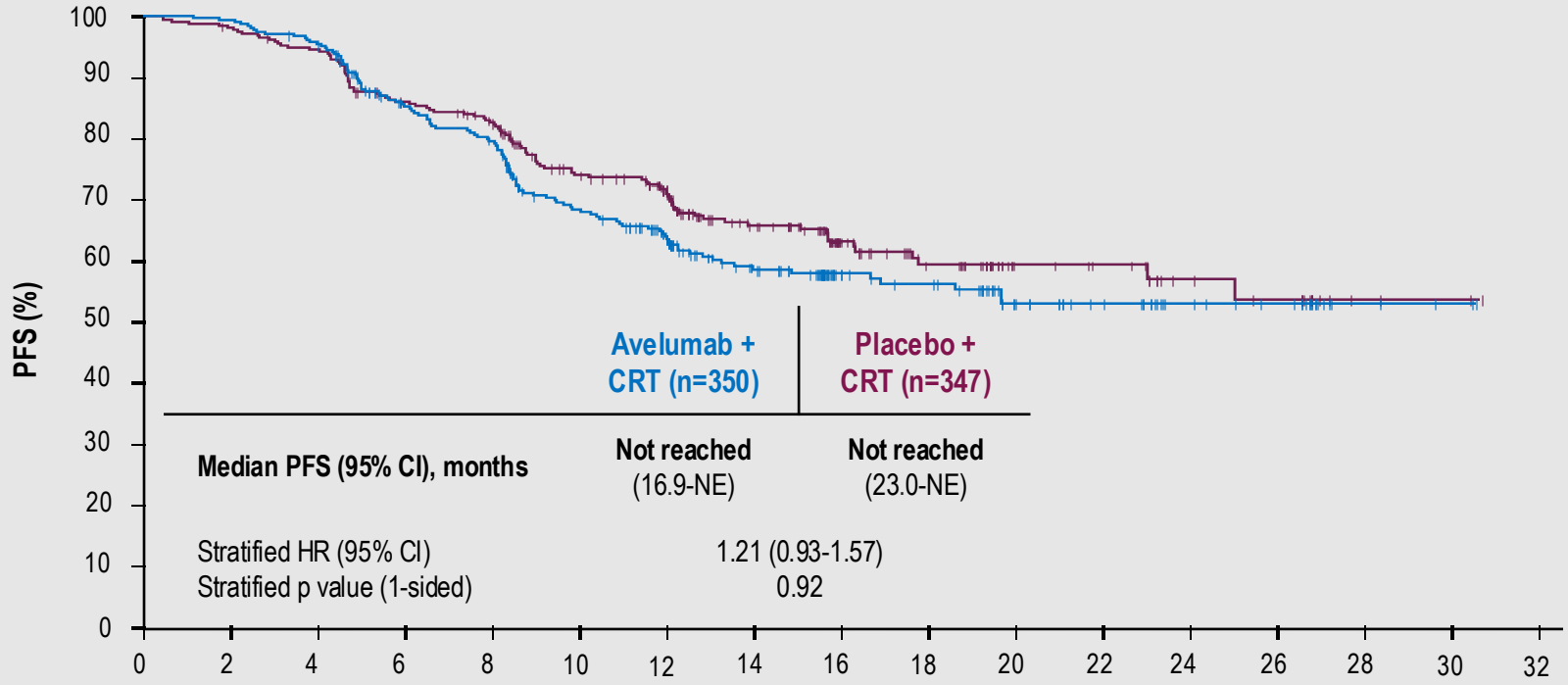


DOR, duration of response; **HPV**, human papillomavirus; **IMRT**, intensity-modulated radiation therapy; **IV**, intravenously; **ORR**, objective response rate; **OS**, overall survival; **PD**, progressive disease; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomized; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumors version 1.1.

* High-risk LA SCCHN (oral cavity, oropharynx, larynx, or hypopharynx): HPV-negative disease stage III, IVa, IVb; nonoropharyngeal HPV-positive disease stage III, IVa, IVb; HPV-positive oropharyngeal disease T4 or N2c or N3 (TNM staging per AJCC, 7th edition).

Lee N et al, Lancet Oncol 2021

PRIMARY ENDPOINT: PFS BY INVESTIGATOR PER MODIFIED RECIST 1.1



At risk																	
Avelumab + CRT	350	303	289	239	222	176	143	107	69	63	41	33	22	18	4	2	0
Placebo + CRT	347	303	291	257	241	200	172	121	75	56	31	28	18	15	3	2	0

NE, not estimable.

KEYNOTE-412 Study Design (NCT03040999)

Patients

- Newly diagnosed, pathologically proven, treatment-naive unresected LA HNSCC
  - T3–T4 [N0–N3] or any N2a–3 [T1–T4] larynx/hypopharynx/oral cavity/ p16-negative oropharynx cancers
  - T4 or N3 p16-positive oropharynx cancer
- Evaluable tumor burden per RECIST v1.1
- ECOG PS 0 or 1
- Candidates for definitive high-dose cisplatin-based CRT

R (1:1)
N=804

Pembrolizumab
200 mg IV Q3W
+
CRT[a]

Maintenance
Pembrolizumab
×14 cycles

Placebo
IV Q3W
+
CRT[a]

Maintenance
Placebo
×14 cycles

Treatment until

- PD or intolerable toxicity
- 17 cycles for pembrolizumab or placebo[b]
- Investigator/patient decision to withdraw

Stratification Factors

- Radiotherapy regimen (AFX vs SFX)
- Tumor site/p16 status (oropharynx [p16+ vs p16-] or larynx/hypopharynx/oral cavity)
- Disease stage (III vs IV)

Primary endpoint

- Event-free survival (EFS)

Secondary endpoints included:

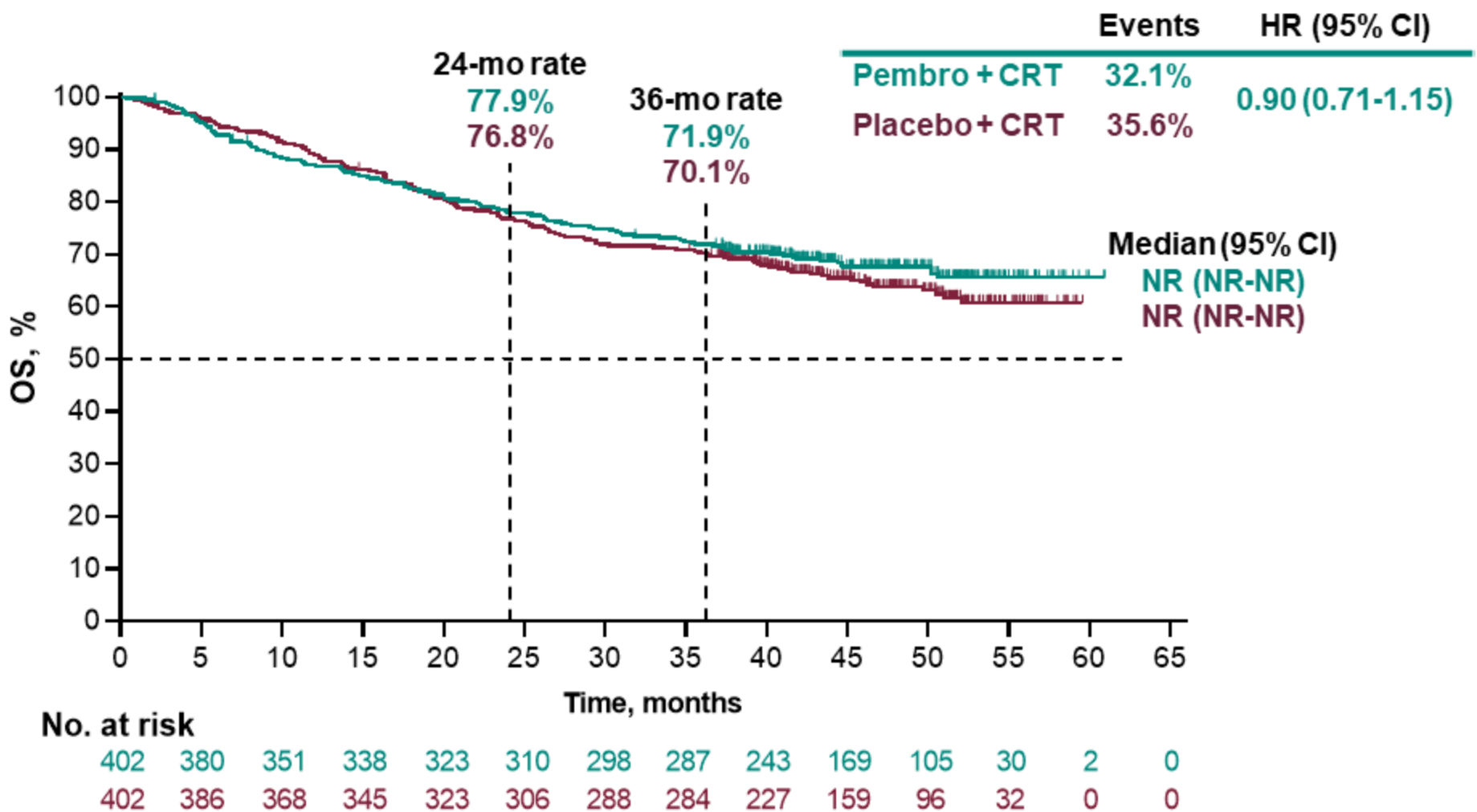
- OS
- Safety/tolerability

Post-treatment follow-up to assess

- Safety
- Disease status
- Survival

[a]CRT included cisplatin (100 mg/m^2, Q3W) and accelerated fractionation (AFX) (70 Gy, 6 fractions/week for 5 weeks and then 5 fractions for the 6th week, 35 fractions in total) or standard fractionation (SFX) (70 Gy, 5 fractions/week for 7 weeks, 35 fractions in total). [b]A pembrolizumab/placebo priming dose was given 1 week before CRT, followed by 2 doses during CRT and 14 doses of maintenance therapy after CRT, for a total of 17 doses.

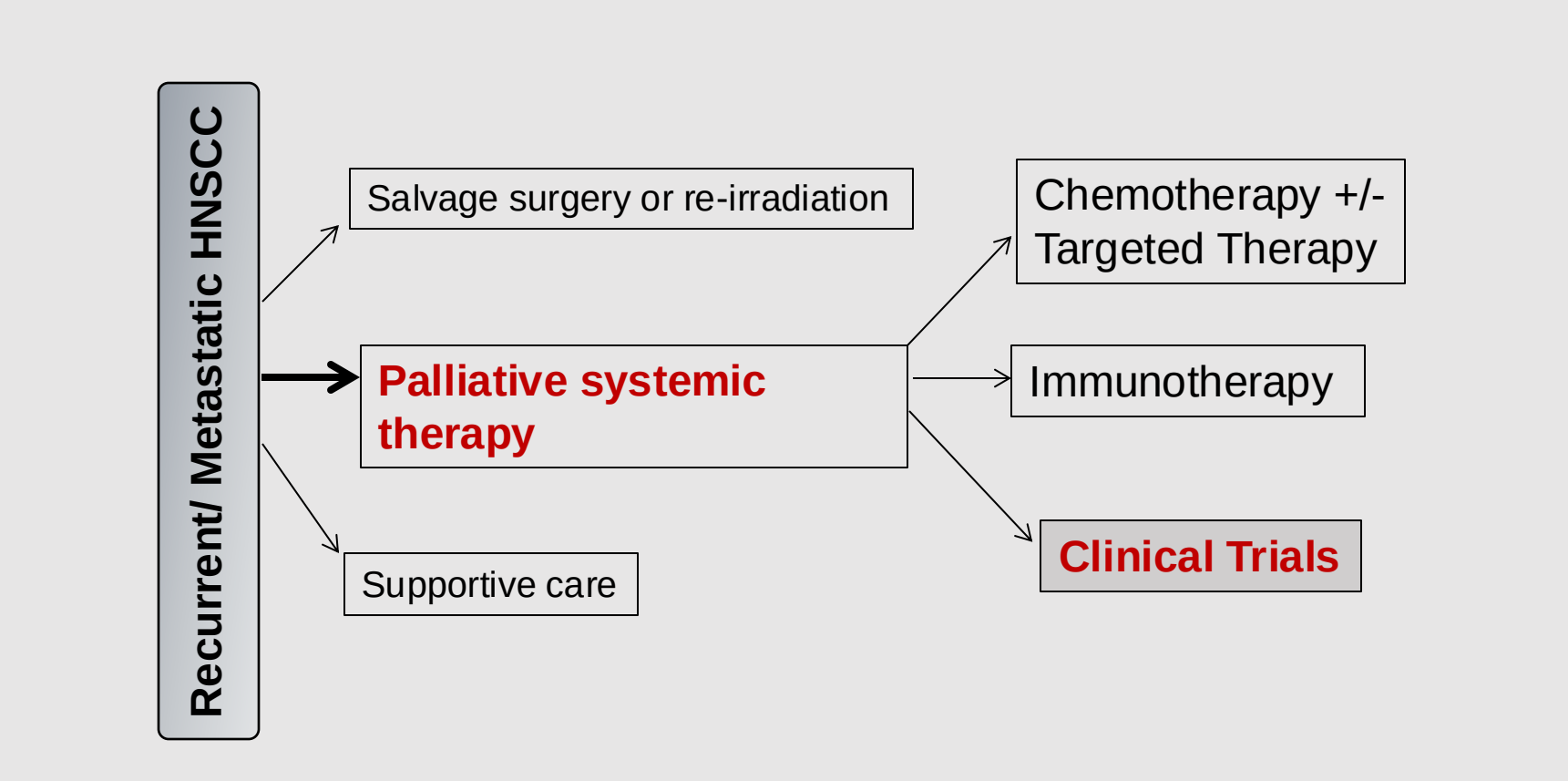
Overall Survival, ITT Population



Data cutoff date: May 31, 2022.

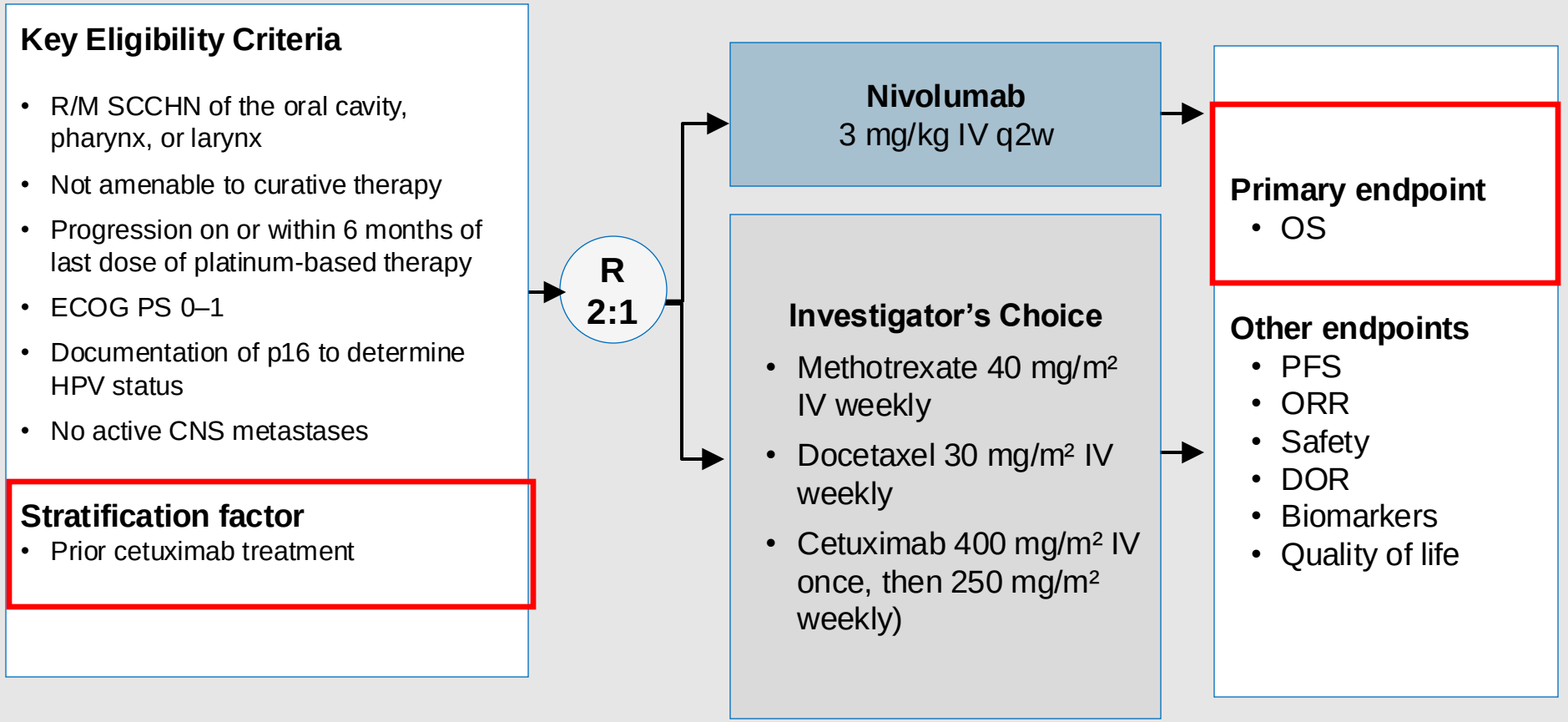
PALLIATIVE CHEMOTHERAPY

MANAGEMENT OF RECURRENT/METASTATIC SCCHN



CHECKMATE 141 STUDY DESIGN
NIVOLUMAB VS. CHEMOTHERAPY

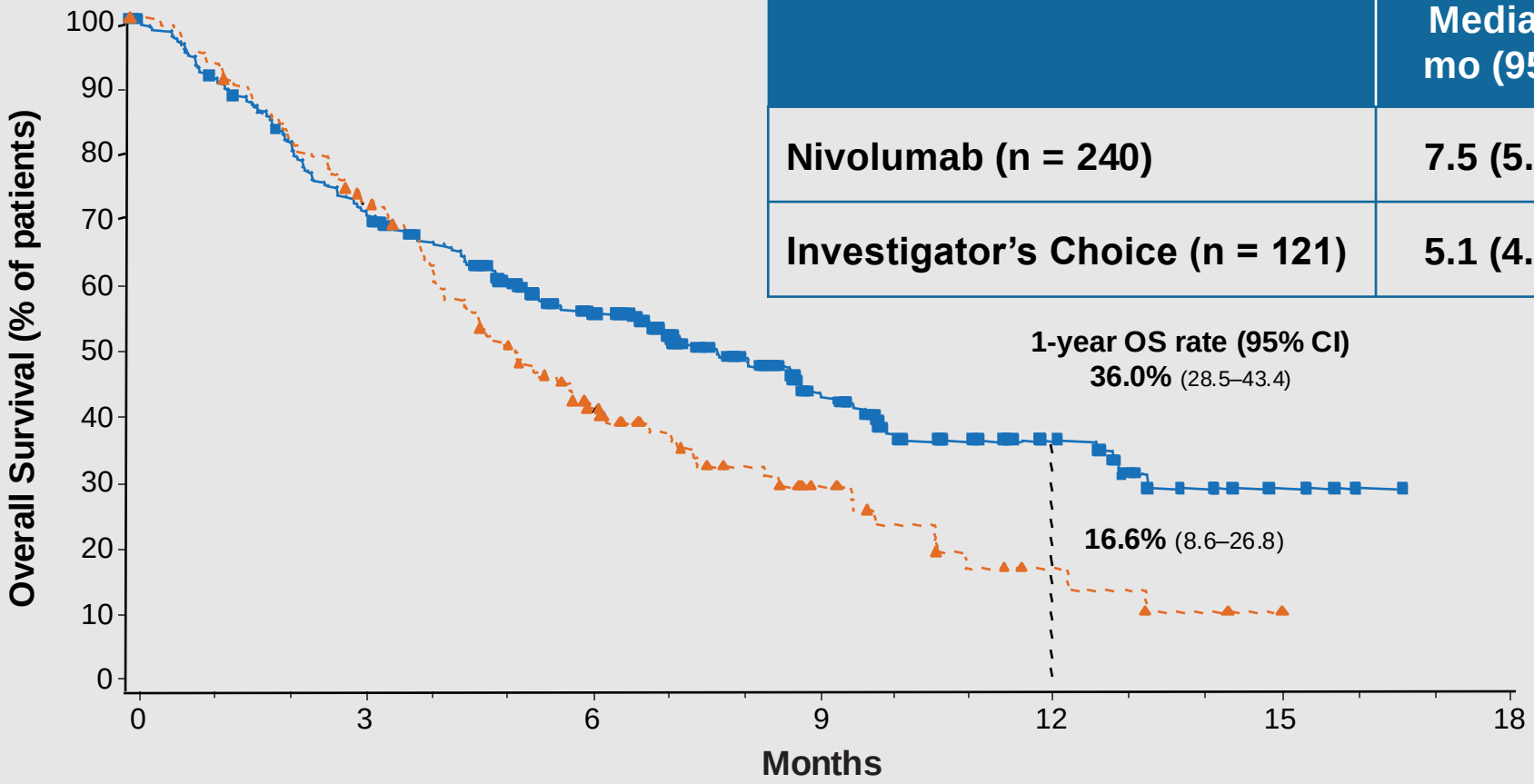
Randomized, global, phase 3 trial of the efficacy and safety of nivolumab versus investigator's choice in patients with R/M SCCHN



CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HPV, human papillomavirus; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomized; R/M, recurrent/metastatic; SCCHN, squamous cell carcinoma of the head and neck; Clinicaltrials.gov: NCT02105636.

OVERALL SURVIVAL

	Median OS, mo (95% CI)	HR (97.73% CI)	p-value
Nivolumab (n = 240)	7.5 (5.5–9.1)	0.70 (0.51–0.96)	0.0101
Investigator's Choice (n = 121)	5.1 (4.0–6.0)		



No. at Risk

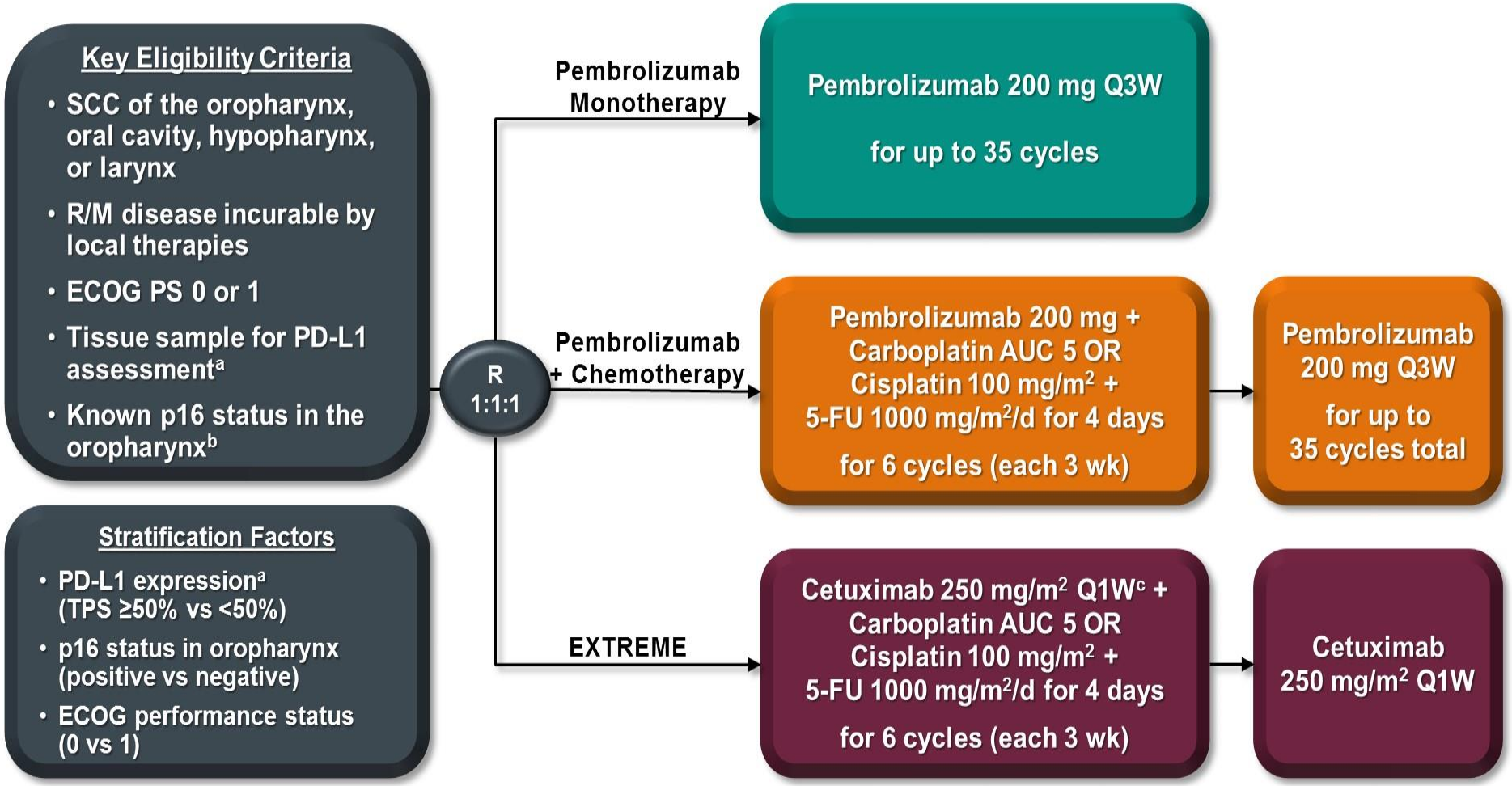
Nivolumab	240	167	109	52	24	7	0
Investigator's Choice	121	87	42	17	5	1	0

KEYNOTE-048

Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study

*Barbara Burtness, Kevin J Harrington, Richard Greil, Denis Soulières, Makoto Tahara, Gilberto de Castro Jr, Amanda Psyrri, Neus Basté, Prakash Neupane, Åse Bratland, Thorsten Fuereder, Brett G M Hughes, Ricard Mesía, Nuttapong Ngamphaiboon, Tamara Rordorf, Wan Zamaniah Wan Ishak, Ruey-Long Hong, René González Mendoza, Ananya Roy, Yayan Zhang, Burak Gumuscu, Jonathan D Cheng, Fan Jin, Danny Rischin, on behalf of the KEYNOTE-048 Investigators**

KEYNOTE-048 Study Design (NCT02358031)



[a]Assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent). TPS = tumor proportion score = % of tumor cells with membranous PD-L1 expression.
[b]Assessed using the CINtec p16 Histology assay (Ventana); cutpoint for positivity = 70%. [c]Following a loading dose of 400 mg/m².

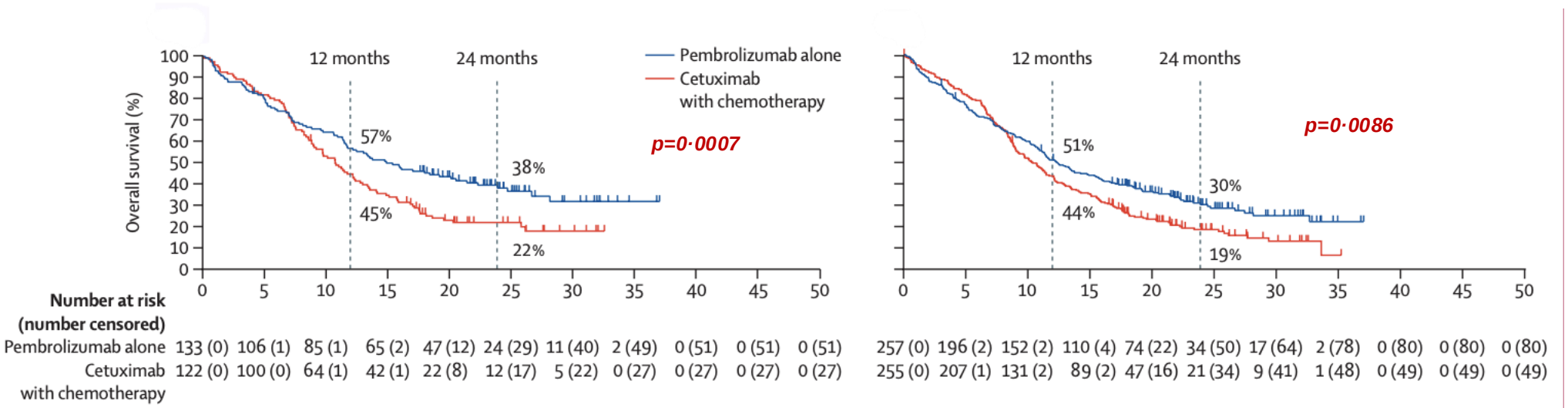
Burtness et al: Lancet 2019

Baseline Characteristics, ITT Population

Characteristic, n (%)	Pembro Alone vs EXTREME		Pembro + Chemo vs EXTREME	
	Pembro N = 301	EXTREME N = 300	Pembro + Chemo N = 281	EXTREME N = 278[a]
Age, median (range), yrs	62 (22-94)	61 (24-84)	61 (20-85)	61 (24-84)
Male	250 (83.1)	261 (87.0)	224 (79.7)	242 (87.1)
ECOG PS 1	183 (60.8)	183 (61.0)	171 (60.9)	170 (61.2)
Current/former smoker	239 (79.4)	234 (78.0)	224 (79.7)	215 (77.3)
p16 positive (oropharynx)	63 (20.9)	67 (22.3)	60 (21.4)	61 (21.9)
PD-L1 status				
TPS ≥50%	67 (22.3)	66 (22.0)	66 (23.5)	62 (22.3)
CPS ≥20	133 (44.2)	122 (40.7)	126 (44.8)	110 (39.6)
CPS ≥1	257 (85.4)	255 (85.0)	242 (86.1)	235 (84.5)
Disease status[b]				
Metastatic	216 (71.8)	203 (67.7)	201 (71.5)	187 (67.3)
Locoregional recurrence only	82 (27.2)	94 (31.3)	76 (27.0)	88 (31.7)

[a]Patients randomized to EXTREME during the pembro + chemo enrollment hold were excluded from all pembro + chemo vs EXTREME efficacy comparisons.
[b]3 patients in the pembro arm, 3 patients in the EXTREME arm, and 4 patients in the pembro + chemo arm had neither metastatic nor recurrent disease.
FA (data cutoff date: Feb 25, 2019).

Pembrolizumab vs Extreme



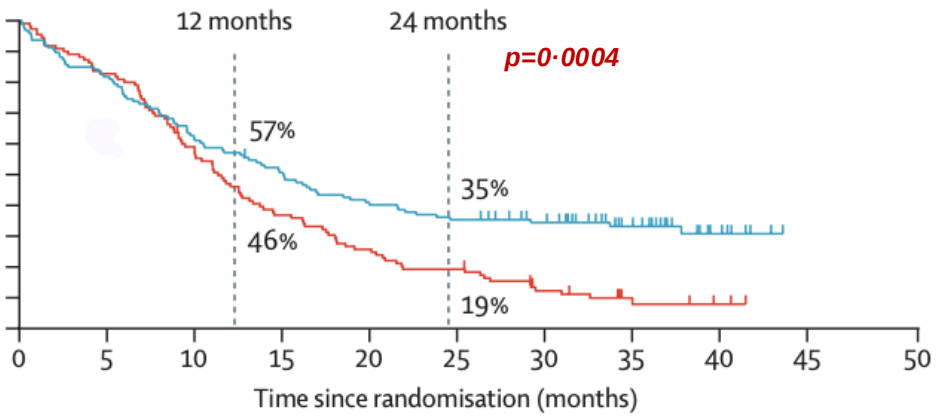
CPS 20

HR 0·61 (95% CI 0·45–0·83, p=0·0007)
Median OS 14·9 months versus 10·7 months

CPS 1

HR 0·78 (95% CI 0·64–0·96, p=0·0086);
Median OS 12·3 months versus 10·3 months

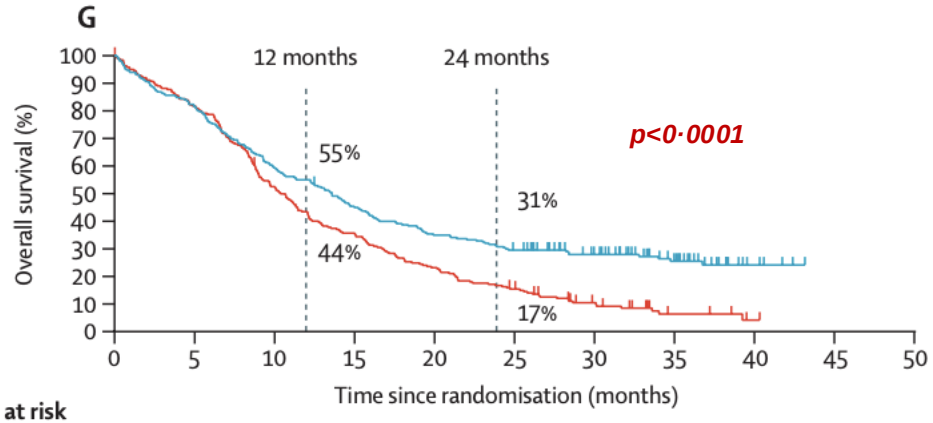
Pembrolizumab/Chemotherapy vs EXTREME



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

CPS 20

HR 0·60 (95% CI 0·45–0·82, p=0·0004)
Median OS 14·7 m versus 11·0 m

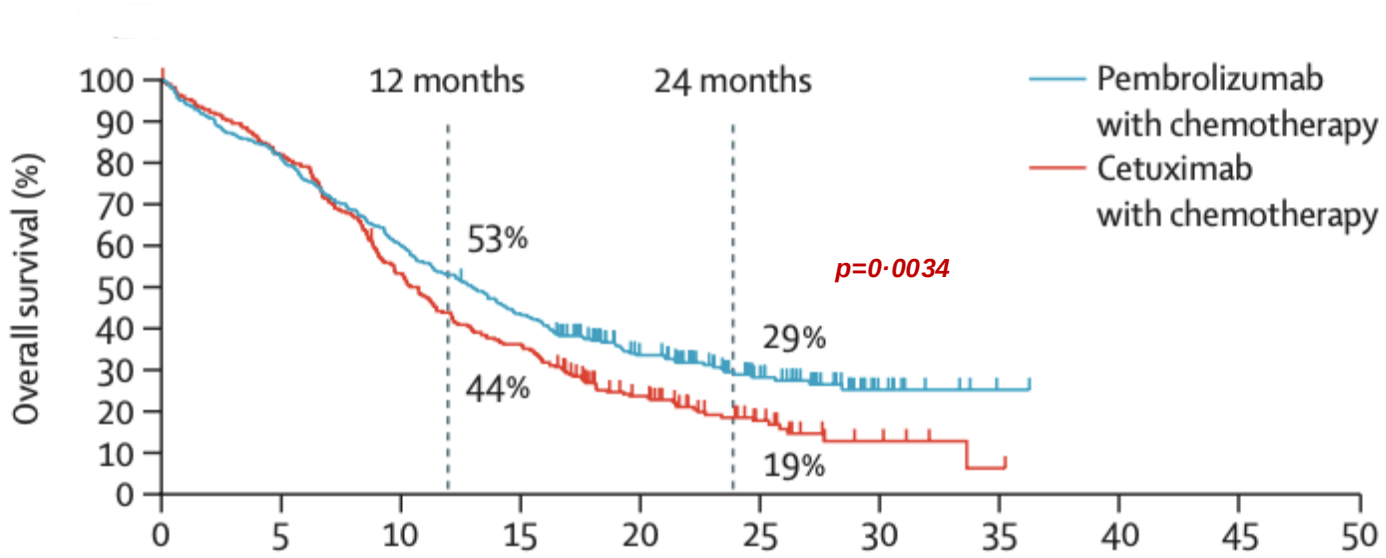


Number at risk (number censored)											
Pembrolizumab with chemotherapy	242 (0)	197 (0)	144 (0)	109 (1)	84 (1)	70 (2)	52 (17)	29 (37)	5 (60)	0 (65)	0 (65)
Cetuximab with chemotherapy	235 (0)	191 (1)	122 (2)	83 (2)	54 (2)	35 (3)	17 (11)	5 (18)	1 (21)	0 (22)	0 (22)

CPS 1

HR 0·65 (95% CI 0·53–0·80, p<0·0001),
Median OS 13·6 months versus 10·4 months

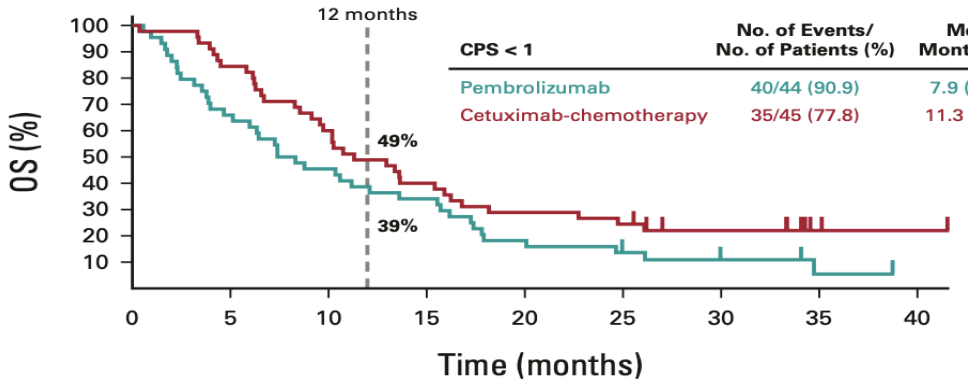
Total Population



HR 0·77 [95% CI 0·63−0·93], p=0·0034

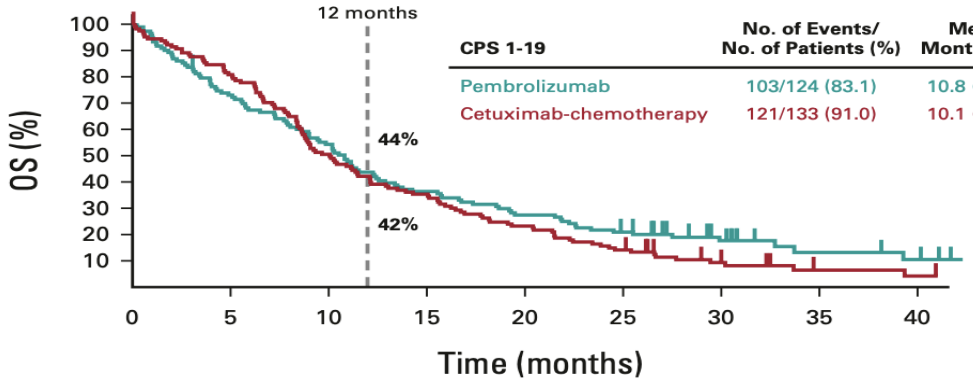
Median OS 13·0 months versus 10·7 months

KEYNOTE-048: Subgroup Analysis by CPS



CPS < 1	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)[a]	HR (95% CI)[b]	Nominal *P*[c]
Pembrolizumab	40/44 (90.9)	7.9 (4.7 to 13.6)	1.51 (0.96 to 2.37)	.96241
Cetuximab-chemotherapy	35/45 (77.8)	11.3 (9.1 to 15.9)		

No. at risk:									
Pembrolizumab	44	29	20	15	8	5	3	1	0
Cetuximab-chemotherapy	45	38	27	18	13	11	7	2	1

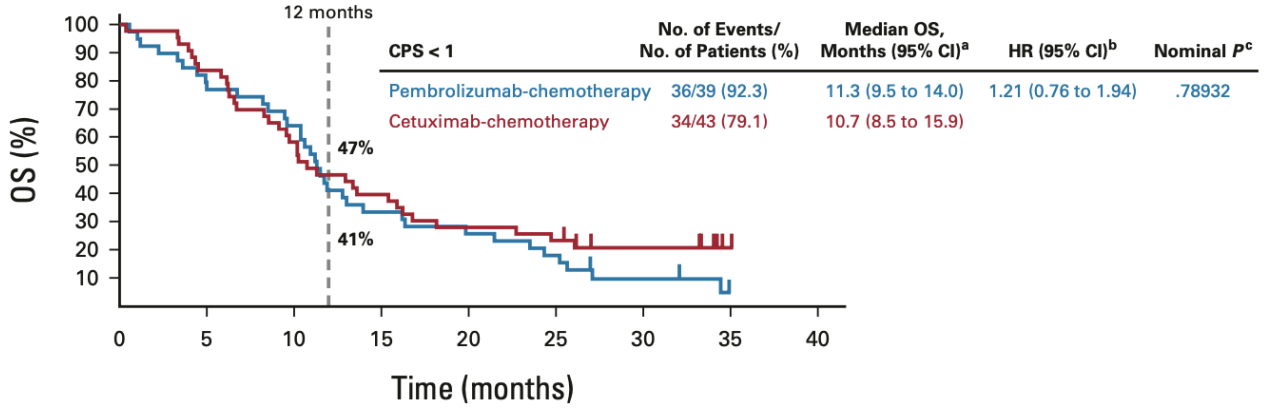


CPS 1-19	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)[a]	HR (95% CI)[b]	Nominal *P*[c]
Pembrolizumab	103/124 (83.1)	10.8 (9.0 to 12.6)	0.86 (0.66 to 1.12)	.12827
Cetuximab-chemotherapy	121/133 (91.0)	10.1 (8.7 to 12.1)		

No. at risk:									
Pembrolizumab	124	90	67	45	34	25	14	6	4
Cetuximab-chemotherapy	133	107	67	47	31	19	8	3	2

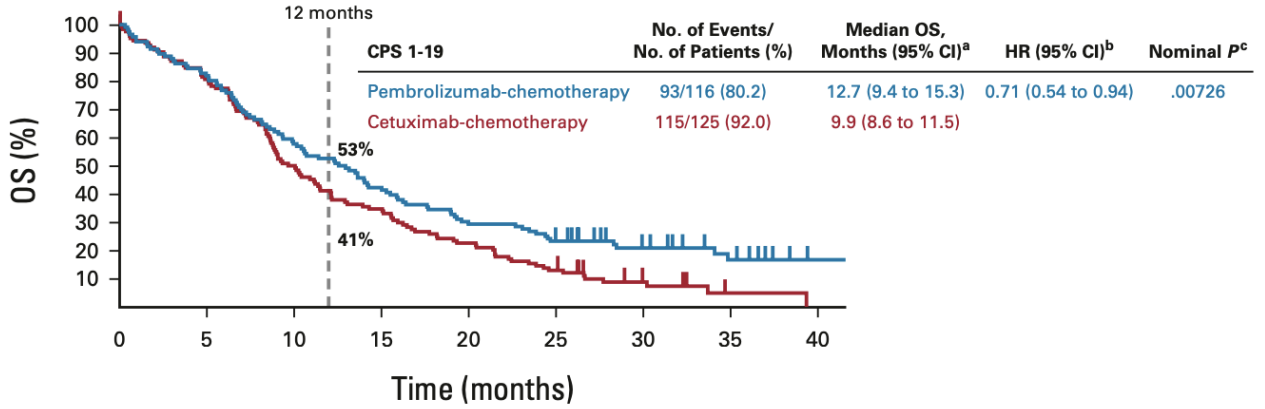
Burtness B et al: J Clin Oncol. 2022

KEYNOTE-048: Subgroup Analysis by CPS



CPS < 1	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)[a]	HR (95% CI)[b]	Nominal *P*[c]
Pembrolizumab-chemotherapy	36/39 (92.3)	11.3 (9.5 to 14.0)	1.21 (0.76 to 1.94)	.78932
Cetuximab-chemotherapy	34/43 (79.1)	10.7 (8.5 to 15.9)		

No. at risk:									
Pembrolizumab-chemotherapy	39	30	25	13	10	7	3	0	0
Cetuximab-chemotherapy	43	36	25	17	12	10	6	1	0



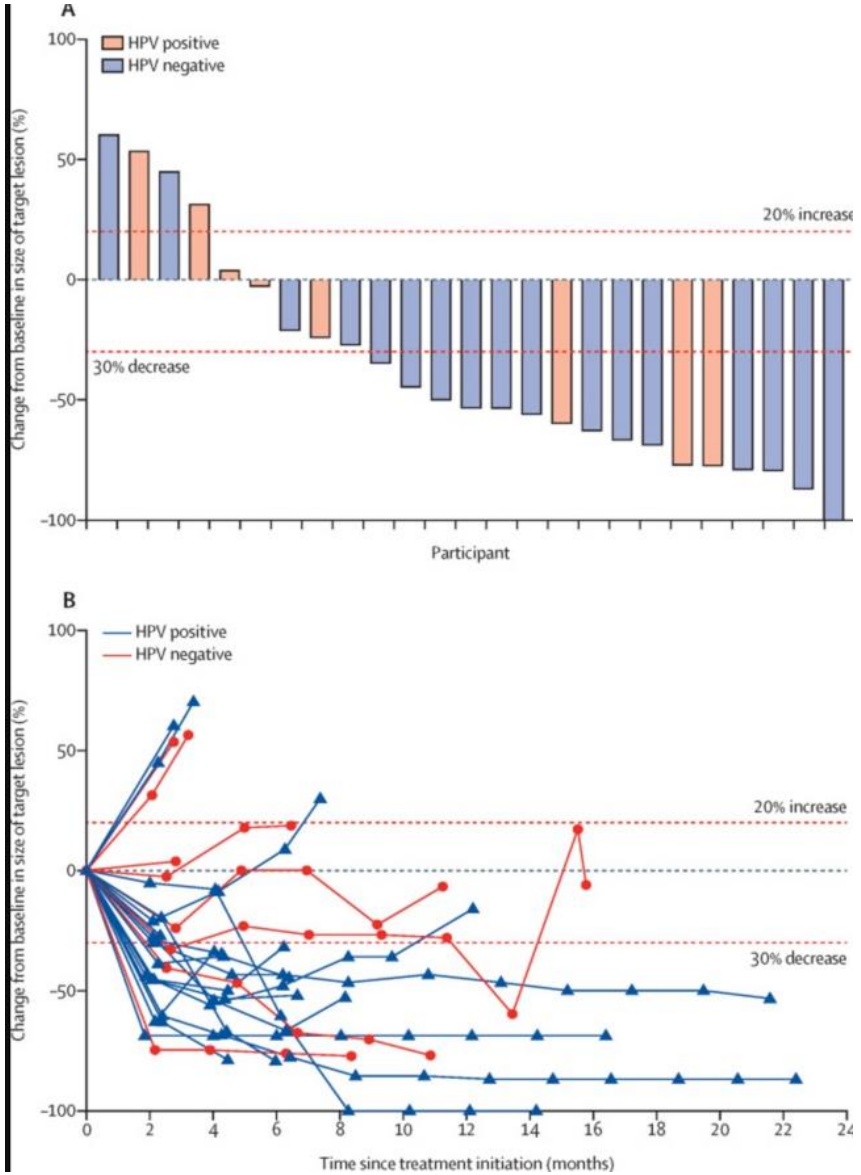
CPS 1-19	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)[a]	HR (95% CI)[b]	Nominal *P*[c]
Pembrolizumab-chemotherapy	93/116 (80.2)	12.7 (9.4 to 15.3)	0.71 (0.54 to 0.94)	.00726
Cetuximab-chemotherapy	115/125 (92.0)	9.9 (8.6 to 11.5)		

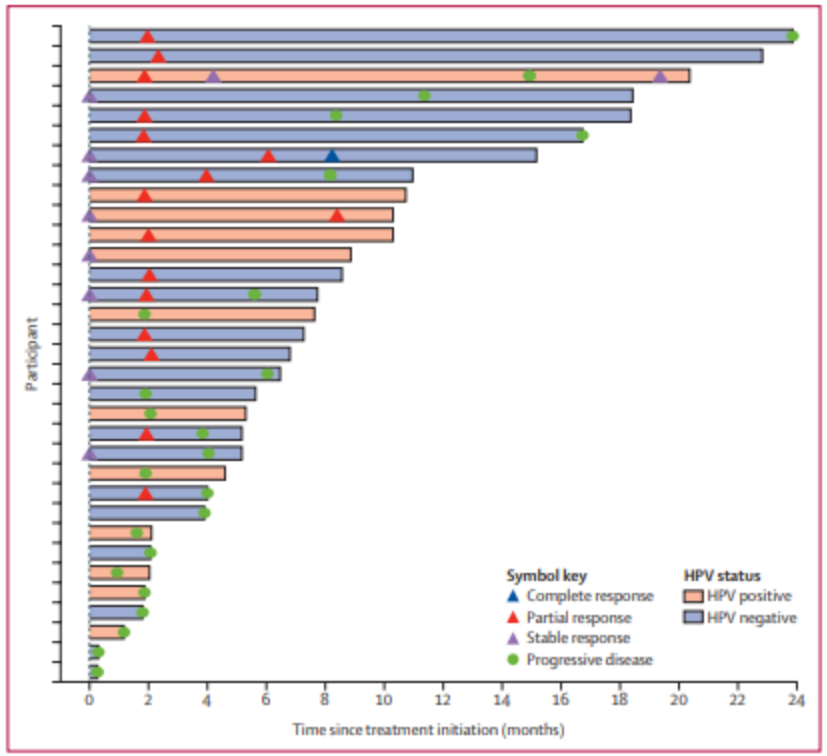
No. at risk:									
Pembrolizumab-chemotherapy	116	95	67	49	34	26	16	8	1
Cetuximab-chemotherapy	125	100	62	43	28	16	6	1	0

Burtness B et al: J Clin Oncol. 2022

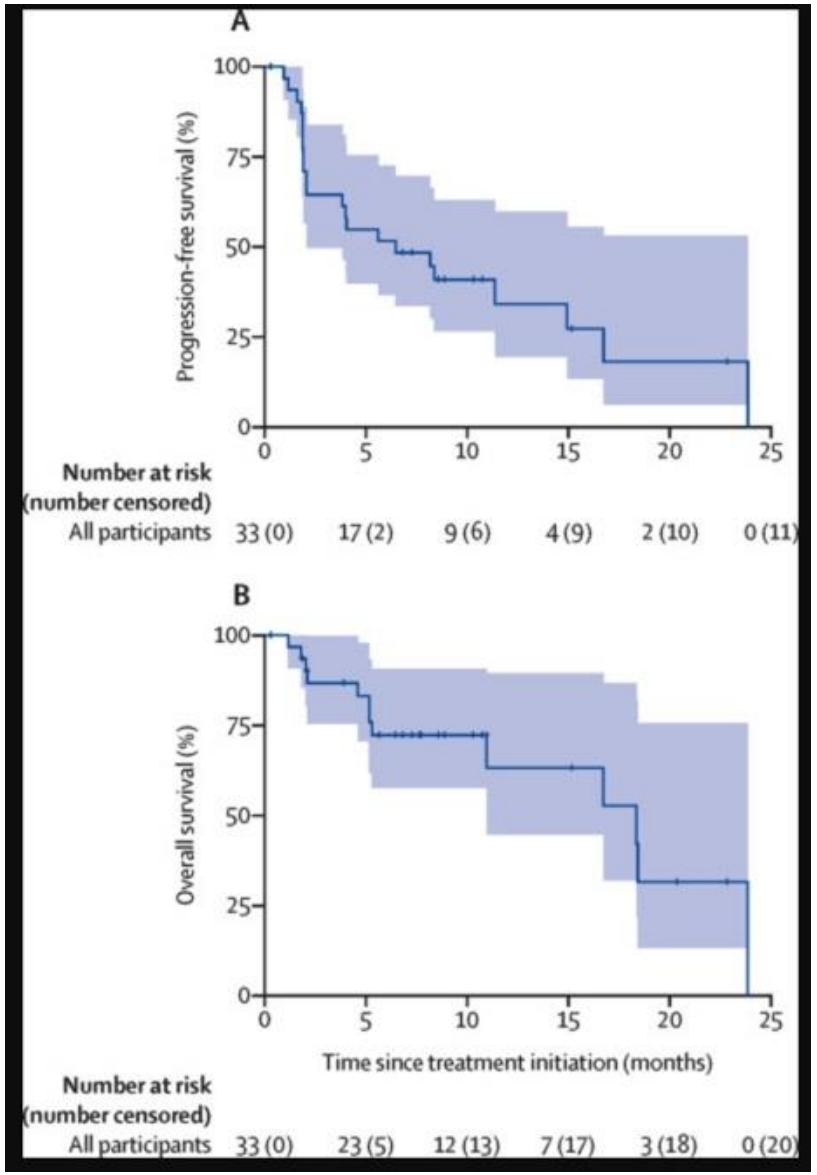
Pembrolizumab+Cetuximab Recurrent Head and Neck Cancer

Sacco et al June 2021 , Lancet Oncology





ORR 45 % (15/33 pts)



Sacco et al June 2021 ,
Lancet Oncology

2024 ASCO ANNUAL MEETING

Petosemtamab (MCLA-158) with pembrolizumab as first-line (1L) treatment of recurrent/metastatic (r/m) head and neck squamous cell carcinoma (HNSCC): Phase 2 study

Jérôme Fayette,[1] Florian Clatot,[2] Irene Braña,[3] Esma Saada,[4] Carla M. L. van Herpen,[5] Thibault Mazard,[6] Cesar A. Perez,[7] Josep Tabernero,[8] Christophe Le Tourneau,[9] Antoine Hollebecque,[10] Virginia Arrazubi,[11] Elisa Fontana,[12] Shumei Kato,[13] Assuntina G. Sacco,[13] Amir Harandi,[14] Jan Paul de Boer,[15] Jessica Ann Hellyer,[16] Eduardo Pennella,[17] Andrew K. Joe,[17] Amaury Daste[18]

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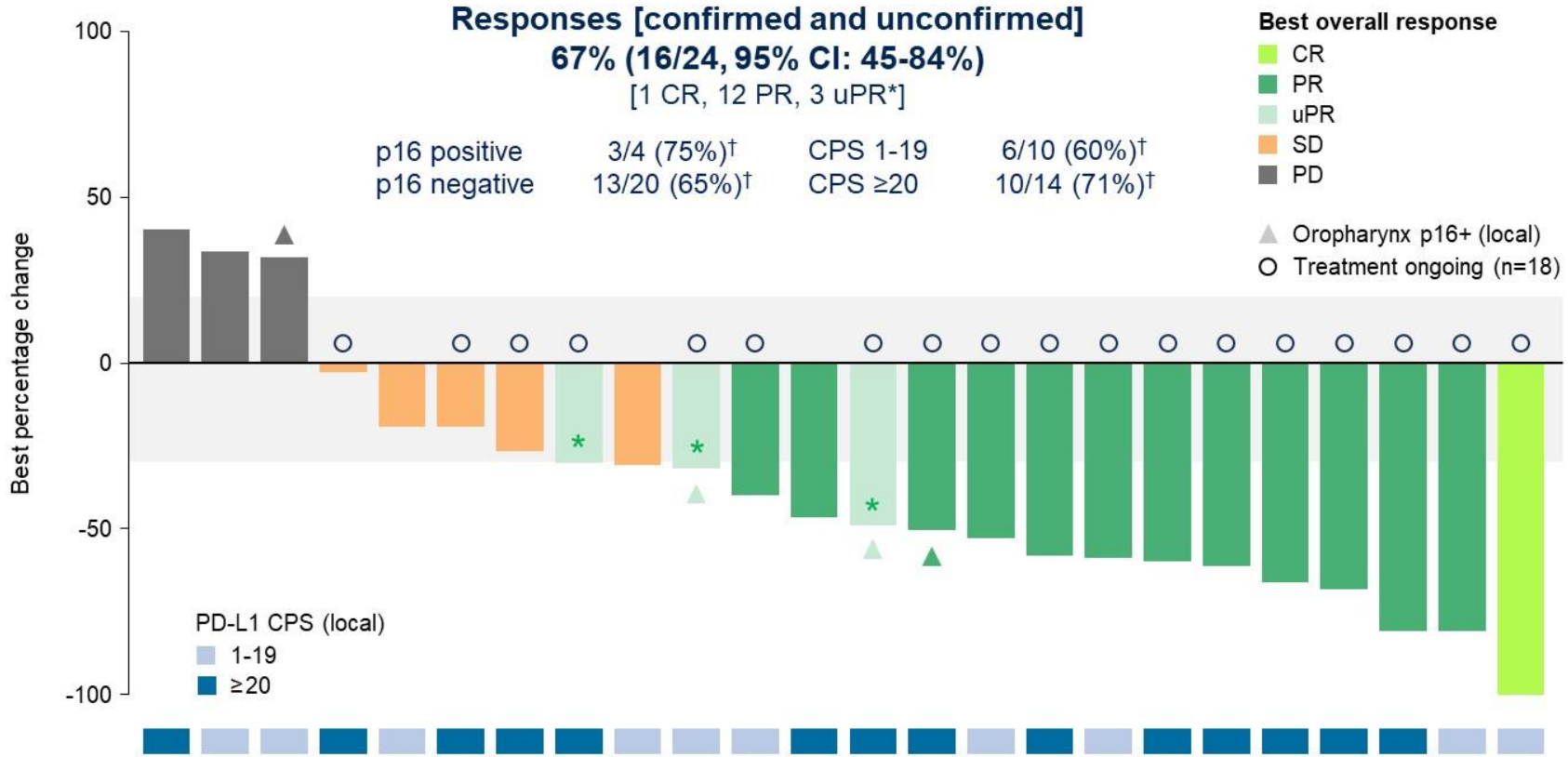
Overall response rate (RECIST 1.1, per investigator)

Best percent change in sum of target lesions from baseline (n=24)



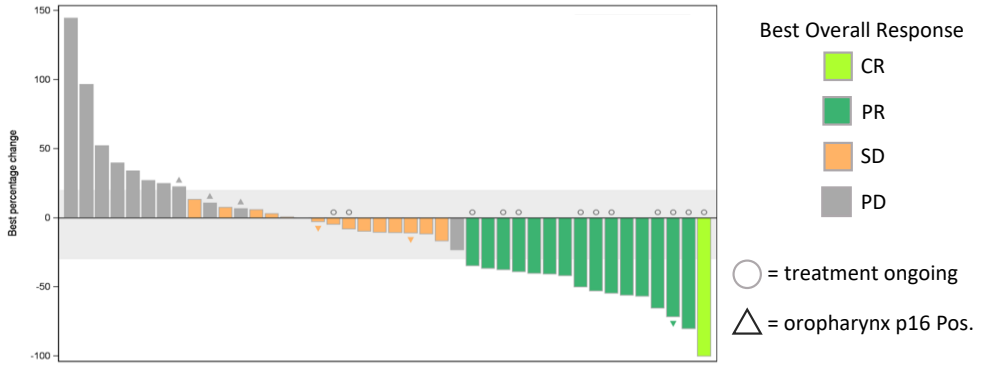
*All 3 uPR were confirmed as PR after data cutoff date; †Response values for p16 and PD-L1 CPS subgroups include CR, PR, and uPR.
CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; uPR, unconfirmed partial response.

PRESENTED BY: Dr. Jérôme Fayette

Overview of Results for Petosemtamab Monotherapy from the Phase 1/2 Trial

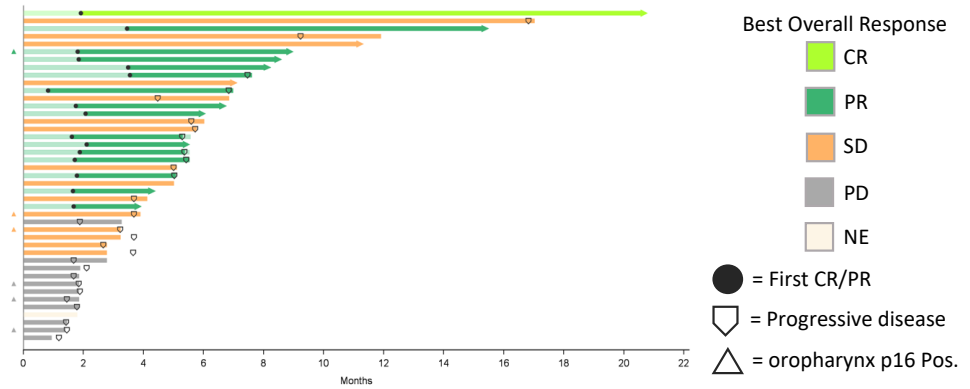
Overall Response Rate (RECIST 1.1, per Investigator)

Best Percent Change in Sum of Target Lesions From Baseline (N=43)



One patient with best overall response of not evaluable not included due to no post-baseline tumor assessment
p16 status was available in 9 of the 15 oropharynx patients (6 positive and 3 negative) in the efficacy evaluable population

Time to Response and Duration of Exposure



Arrows indicate treatment is ongoing at data cutoff date
p16 status was available in 9 of the 15 oropharynx patients (6 positive and 3 negative) in the efficacy evaluable population

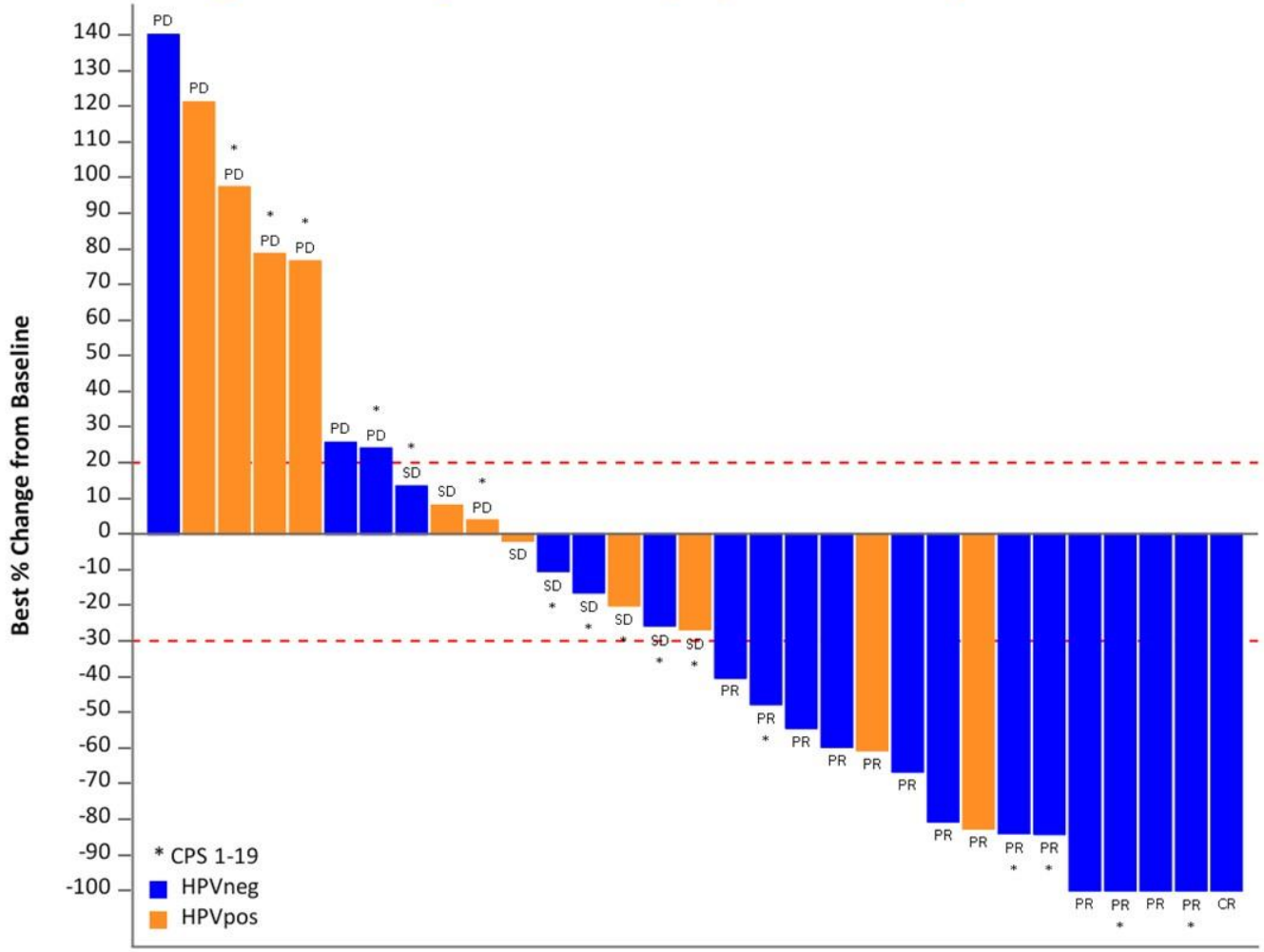
Overall Clinical Efficacy

ORR	**37.2%** [16/43; 95% CI: 23.0 - 53.3]
DCR (CR+PR+SD)	**72.1%** [31/43; 95% CI: 56.3 - 84.7]
Median time to response	**1.8 months** [range, 0.8 - 3.5]
On treatment at data cutoff date	**12/43 (28%) patients**
Median DOR	**6.0 months** [95% CI: 3.7 - NC] *10/16 (63%) responders had response ongoing at cutoff date*
Median PFS	**5.3 months** [95% CI: 3.7 - 6.8] *29/43 patients progressed, 14/43 censored*
Median OS	**11.5 months** [95% CI: 7.2 - 20.6] *29/49 patients still alive at data cutoff date*

Cohen E et al. AACR 2023

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L)

Preliminary Efficacy – Total population (N=31 evaluable)



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

PRESENTED BY: Glenn J. Hanna, MD

Source: Open clinical database, as of 22-May-2023

Cabozantinib and Pembrolizumab : Phase II

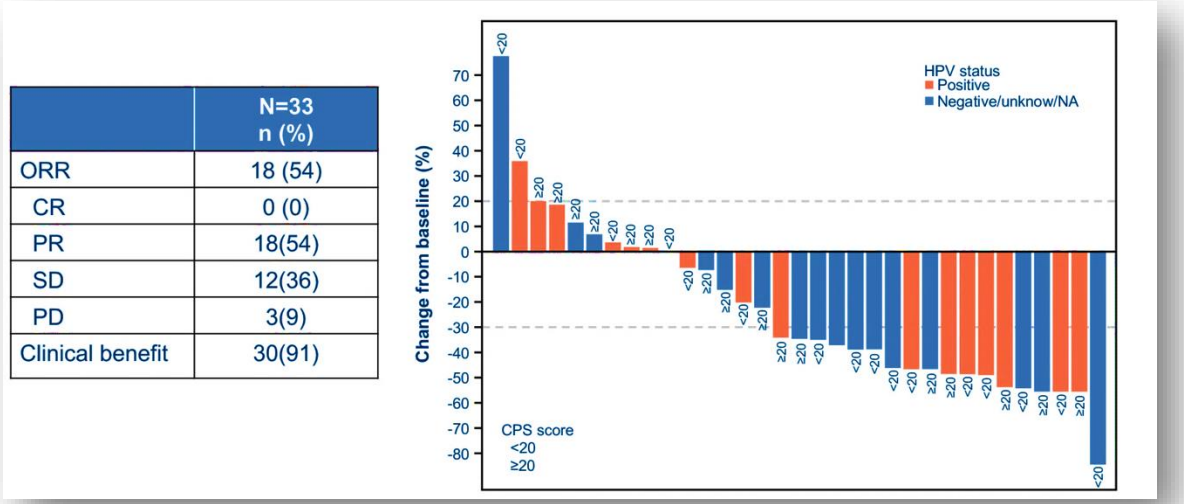
Patients with R/M HNSCC
Inclusion criteria
- Inoperable, refractory or metastatic R/M HNSCC
- RECIST v1.1 measurable disease
- ≤1 prior radiation therapy to the HN allowed
- Life expectancy >3 months
- ECOG performance status 0–1

Exclusion criteria
- HPV negative unknown primary disease
- Cavitating lesions or recent bleeding history

→ **Pembrolizumab 200 mg IV Q3W + Cabozantinib 40 mg PO QD** → Tumors were assessed by RECIST v1.1 criteria by CT/MRI every 9 weeks

Patient Characteristic		N=36 n (%)
Age, median (range), years		62 (54-67)
Gender	Male Female	30 (83) 6 (17)
ECOG performance status, %	0 1	18 (50) 18 (50)
Primary site	Oropharynx Oral cavity Hypopharynx Larynx Nasopharynx	22 (61) 2 (6) 2 (6) 4 (11) 6 (16)
HPV (p16)	Positive Negative Unknown	17 (47) 12 (33) 7 (20)
Prior therapy	Radiation Cisplatin Cetuximab	31 (89) 36 (100) 3 (8)
PD-L1 CPS score (total of 34)	CPS <1 CPS 1-19 CPS ≥20	2 (6) 15 (44) 17 (50)

	N=33 n (%)
ORR	18 (54)
CR	0 (0)
PR	18(54)
SD	12(36)
PD	3(9)
Clinical benefit	30(91)



Saba et al, Nat Med 2023

Head and Neck Cancer 2025 and Beyond

ChemoRT with or without surgery

HPV: New Staging, New treatment, New disease, De-escalation

Non-HPV: Is there room for Intensification?

Immunotherapy incorporated into all Phases of the treatment: Neo-adjuvant to palliative therapy

EGFR/IO and VEGF/IO in phase III

K689 likely practice changing

Head and Neck Cancer is a complex set of diseases with various nuances in treatment, treatment delivery and outcomes

ONE SIZE does not fit all patients: Multi-D care