Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy in the Treatment of Head and Neck Cancer

Cristina P. Rodriguez MD
Associate Professor

University of Washington

Seattle, WA USA

AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

Society for Immunotherapy of Cancer

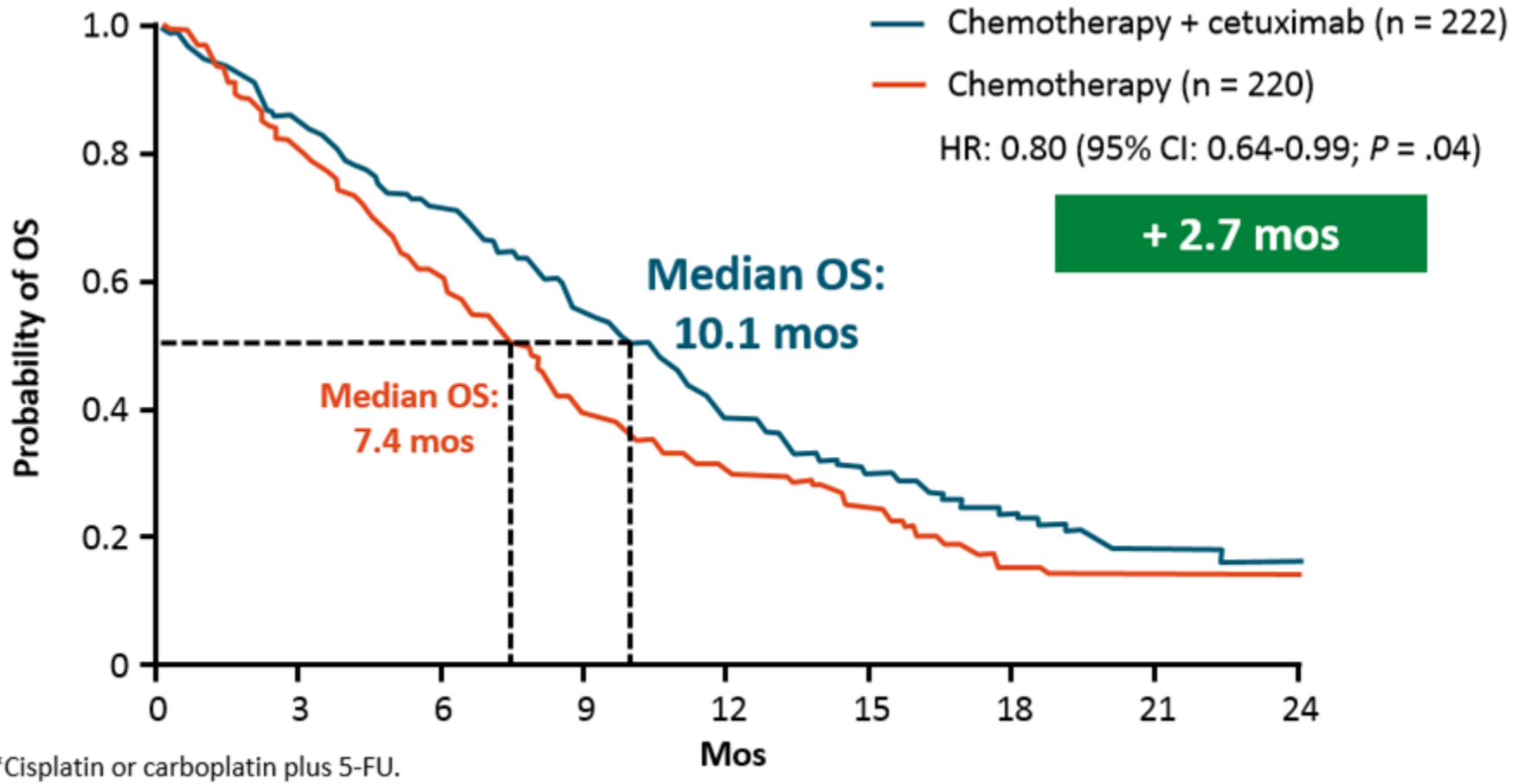
Disclosures

- **Consulting Fees:** Cue Biopharma
- **Contracted Research:** AstraZeneca, Ayala, Bristol Myers Squibb, CueBiopharma, GlaxoSmithKline, Kura, Merck
- **Partner Consulting Fees:** AstraZeneca, Merck
- **Partner Contracted Research:** Acerta, AstraZeneca, Genentech, Incyte, Merck, Pharmacyclics, Portola, Seagen

Background: Squamous cell carcinomas of the head and neck

- Mucosal squamous cell carcinomas
  - Originate from Oral Cavity, Larynx, Hypopharynx, Oropharynx
  - Tobacco related
  - Virally mediated
  - Most present with locally advanced disease
- Cutaneous squamous cell carcinomas
  - Elderly and/or immunocompromised
- Both have poor prognosis in the R/M setting
  - Immunotherapy with FDA indications in both

EXTREME trial



*Cisplatin or carboplatin plus 5-FU.

Vermorken. NEJM. 2008;359:1116.

Approved checkpoint inhibitors in Head and Neck Cancers

Drug	Approved	Indication	Dose
Pembrolizumab	2016	Recurrent/metastatic HNSCC, progression on/after chemotherapy	200 mg Q3W OR 400mg Q6W
Nivolumab	2016	Recurrent/metastatic HNSCC, progression on/after chemotherapy	240 mg Q2W OR 480 mg Q4W
Pembrolizumab + platinum + fluorouracil	2019	Recurrent/metastatic HNSCC 1st line – all patients	200 mg Q3W
Pembrolizumab	2019	Recurrent/metastatic HNSCC 1st line – PD-L1 CPS ≥ 1	200 mg Q3W OR 400mg Q6W
Cemiplimab	2018	Metastatic cutaneous squamous cell carcinoma, not candidate for curative therapies (any site)	350 mg Q3W
Pembrolizumab	2020	Metastatic cutaneous squamous cell carcinoma, not candidate for curative therapies (any site)	200 mg Q3W OR 400mg Q6W

CheckMate 141: Nivolumab vs Investigator's Choice in R/M HNSCC after Platinum Therapy

Phase III Randomized, Safety and Efficacy Trial

Key Eligibility Criteria

- R/M SCCHN of the oral cavity, pharynx, or larynx
- Progression on or within 6 months of last dose of platinum-based therapy
- Irrespective of no. of prior lines of therapy
- Documentation of p16 to determine HPV status (oropharyngeal)
- Regardless of PD-L1 status[a]

Stratification factor

- Prior cetuximab treatment

→ **R 2:1**

Nivolumab
3 mg/kg IV Q2W

Vs.

Investigator's Choice

- Methotrexate 40 mg/m² IV weekly
- Docetaxel 30 mg/m² IV weekly
- Cetuximab 400 mg/m² IV once, then 250 mg/m² weekly

Primary endpoint

- OS

Other endpoints

- PFS
- ORR
- Safety
- DOR
- Biomarkers
- Quality of life

DOR = duration of response; IV = intravenous; ORR = objective response rate; PFS = progression-free survival; Q2W = once every 2 weeks; R = randomized. Clinicaltrials.gov NCT02105636.

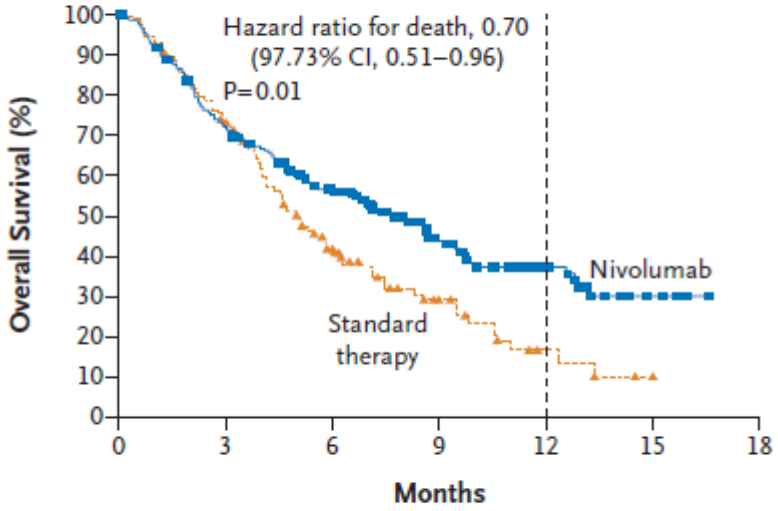
[a]Tissue required for testing

Ferris & Gillison, NEJM 2016.

Checkmate 141: Nivolumab vs Investigator's Choice in R/M HNSCC after Platinum Therapy

A Overall Survival

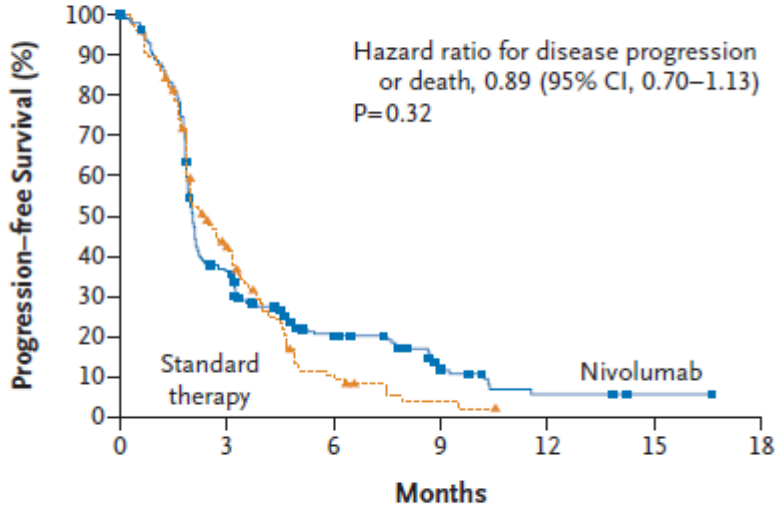
	No. of Patients	No. of Deaths	1–Yr Overall Survival Rate % (95% CI)	Median Overall Survival mo (95% CI)
Nivolumab	240	133	36.0 (28.5–43.4)	7.5 (5.5–9.1)
Standard Therapy	121	85	16.6 (8.6–26.8)	5.1 (4.0–6.0)



No. at Risk							
Nivolumab	240	167	109	52	24	7	0
Standard therapy	121	87	42	17	5	1	0

B Progression-free Survival

	No. of Patients	No. of Events	Median Progression-free Survival (95% CI) mo
Nivolumab	240	190	2.0 (1.9–2.1)
Standard Therapy	121	103	2.3 (1.9–3.1)



No. at Risk							
Nivolumab	240	79	32	12	4	1	0
Standard therapy	121	43	9	2	0	0	0

Ferris & Gillison, NEJM 2016.

CheckMate 141: AEs for Nivolumab vs Investigator's Choice in Recurrent/Metastatic HNSCC

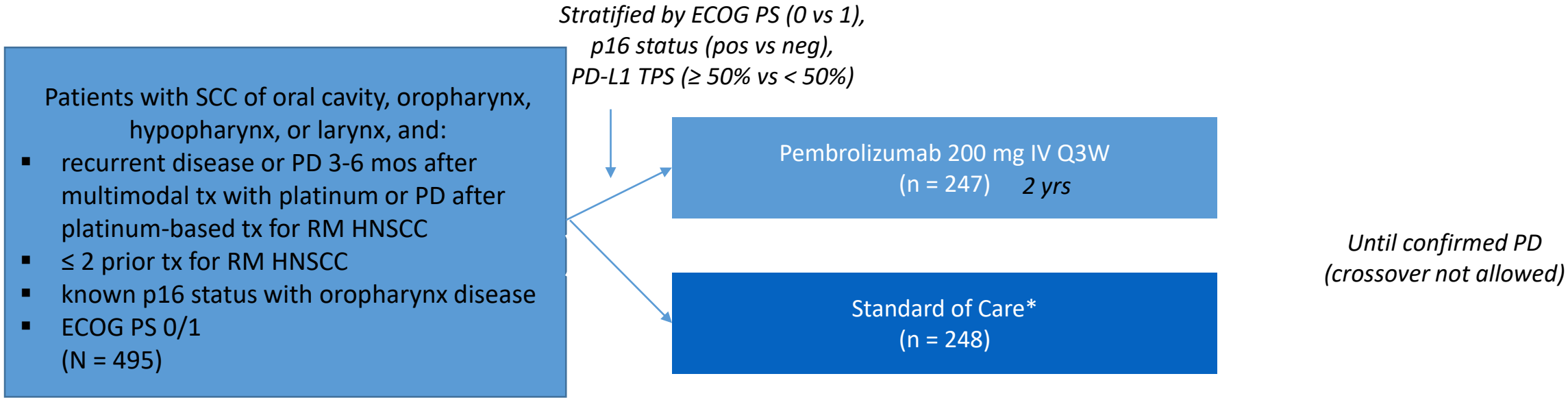
TRAEs, n (%) (≥ 15% Either Arm)	Nivolumab (n = 236)		Investigator's Choice (n = 111)	
	Any Grade*	Grade 3/4	Any Grade†	Grade 3/4
Any TRAE	146 (61.9)	36 (15.3)	88 (79.3)	41 (36.9)
Fatigue	37 (15.7)	5 (2.1)	20 (18.0)	3 (2.7)
Nausea	22 (9.3)	0	23 (20.7)	1 (0.9)
Anemia	12 (5.1)	3 (1.3)	19 (17.1)	6 (5.4)
Asthenia	10 (4.2)	1 (0.4)	17 (15.3)	2 (1.8)

Data include 1 patient with a grade 5 event of hypercalcemia and 1 patient with grade 3 pneumonitis who subsequently died of a grade 5 pulmonary embolism.

†Data include 1 patient with a grade 5 event of lung infection.

Ferris. NEJM. 2016;375:1856.

KEYNOTE-040: Pembrolizumab vs Standard of Care in R/M HNSCC



*Investigator's choice of methotrexate 40 mg/m^2/wk (in absence of toxicity could increase to 60 mg/m^2), docetaxel 75 mg/m^2 Q3W, or cetuximab loading dose of 400 mg/m^2 followed by 250 mg/m^2/wk.

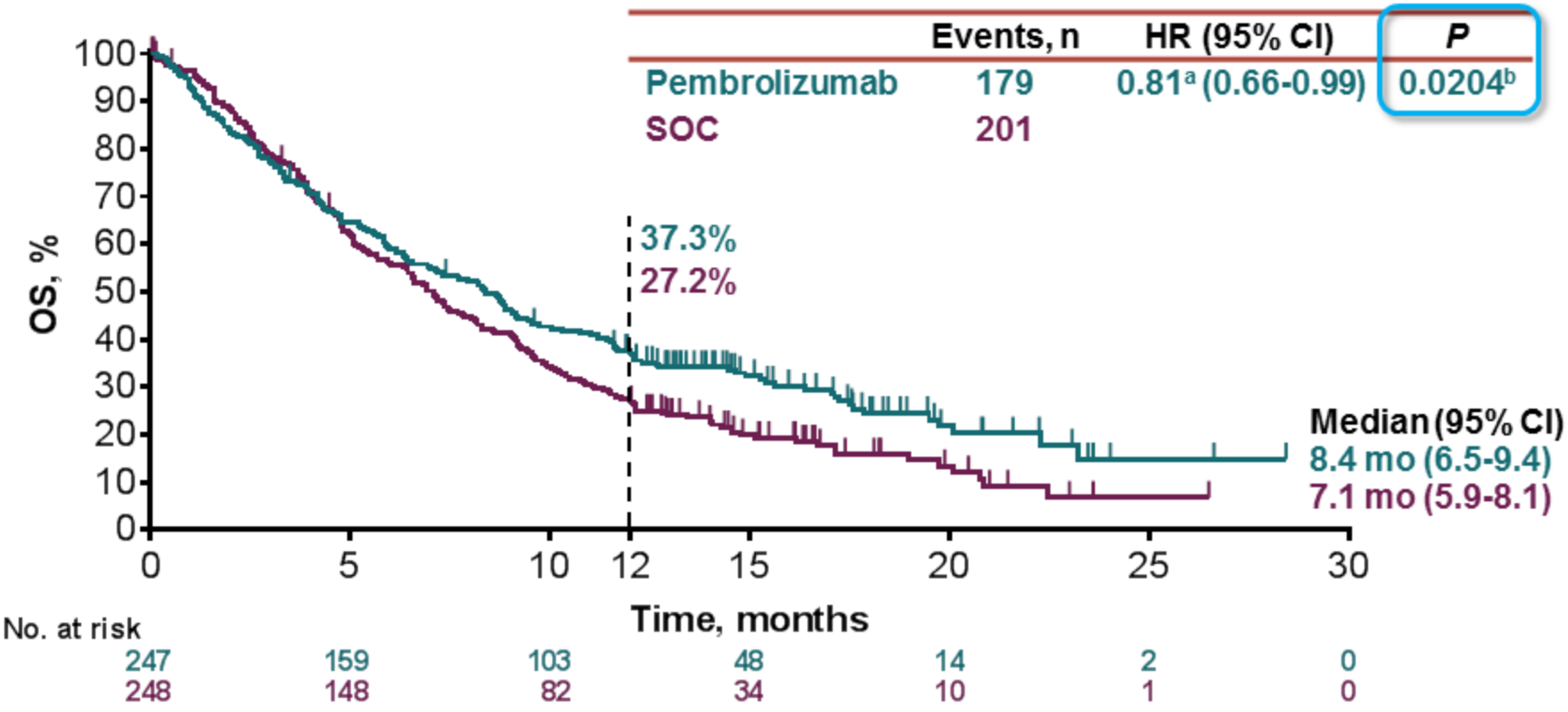
- Primary endpoint: OS in ITT population
- Secondary endpoints: OS in PD-L1–positive subgroups, PFS, ORR, DoR, safety, tolerability

Cohen. Lancet. 2019;393:156.

KEYNOTE-040

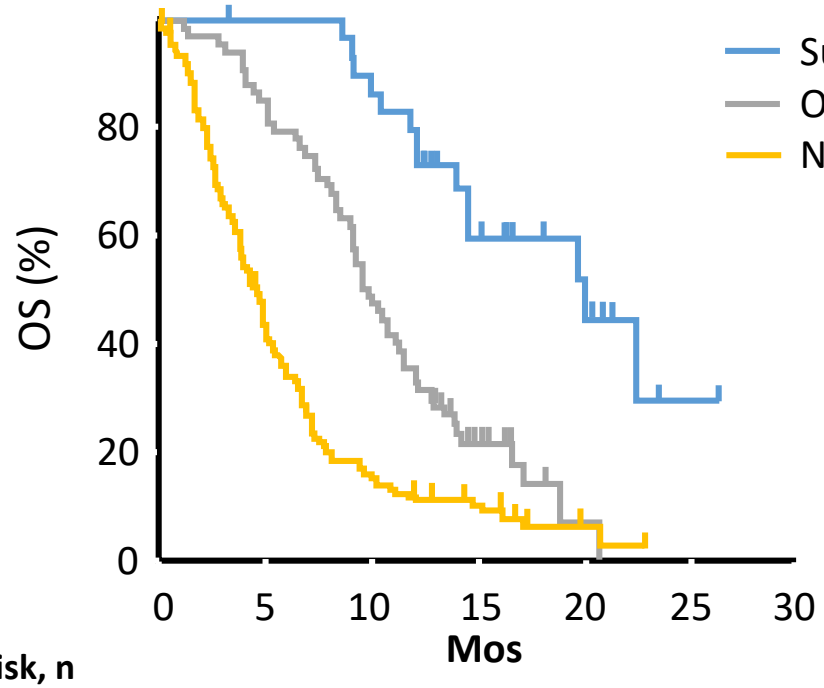
E Cohen_ESMO 2017

Overall Survival in ITT Population



[a]Cox proportional hazards model with treatment as a covariate stratified by the randomization stratification factors. Initially reported data: HR 0.82 (95% CI, 0.67-1.01), *P* = 0.0316. After the initial report, updated survival data were obtained for 4 patients. [b]One-sided *P* value based on the log-rank test stratified by the randomization stratification factors. Data cutoff date: May 15, 2017.

KEYNOTE-040: Subsequent Checkpoint Inhibitor Use

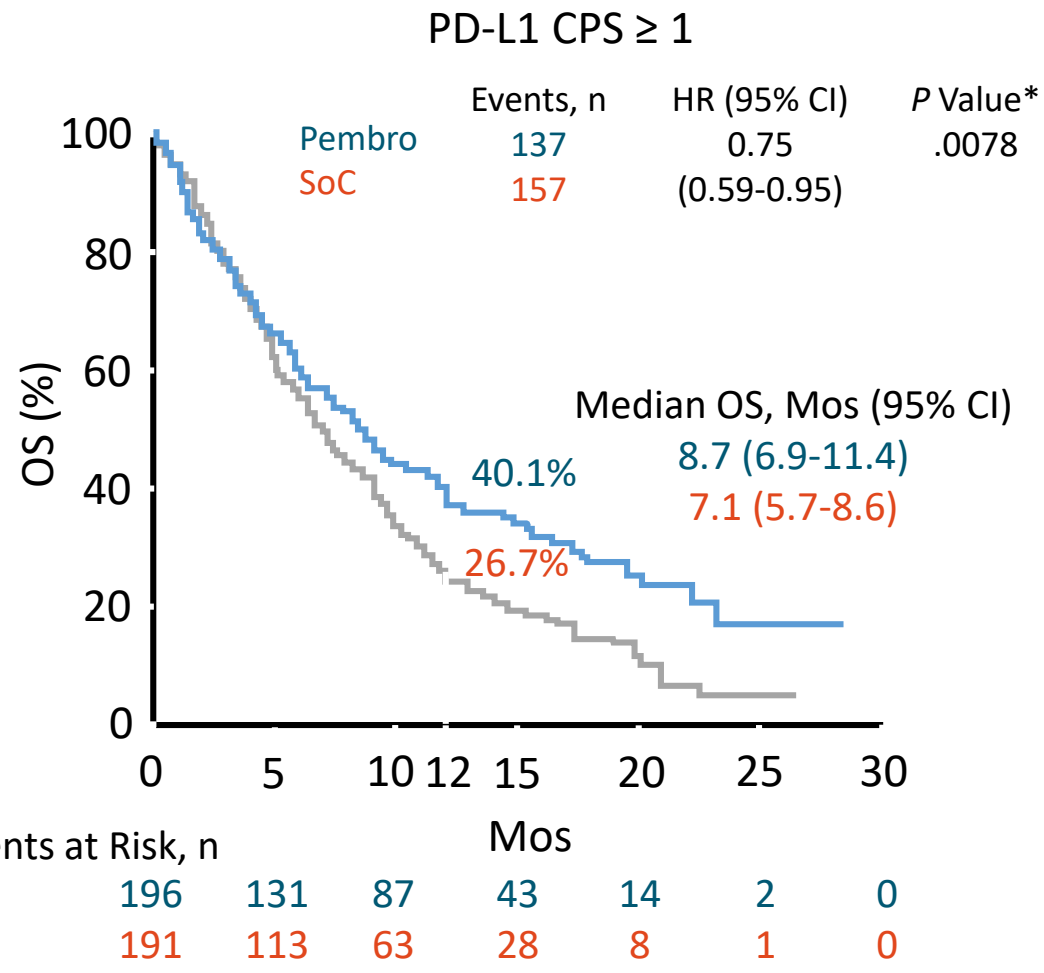


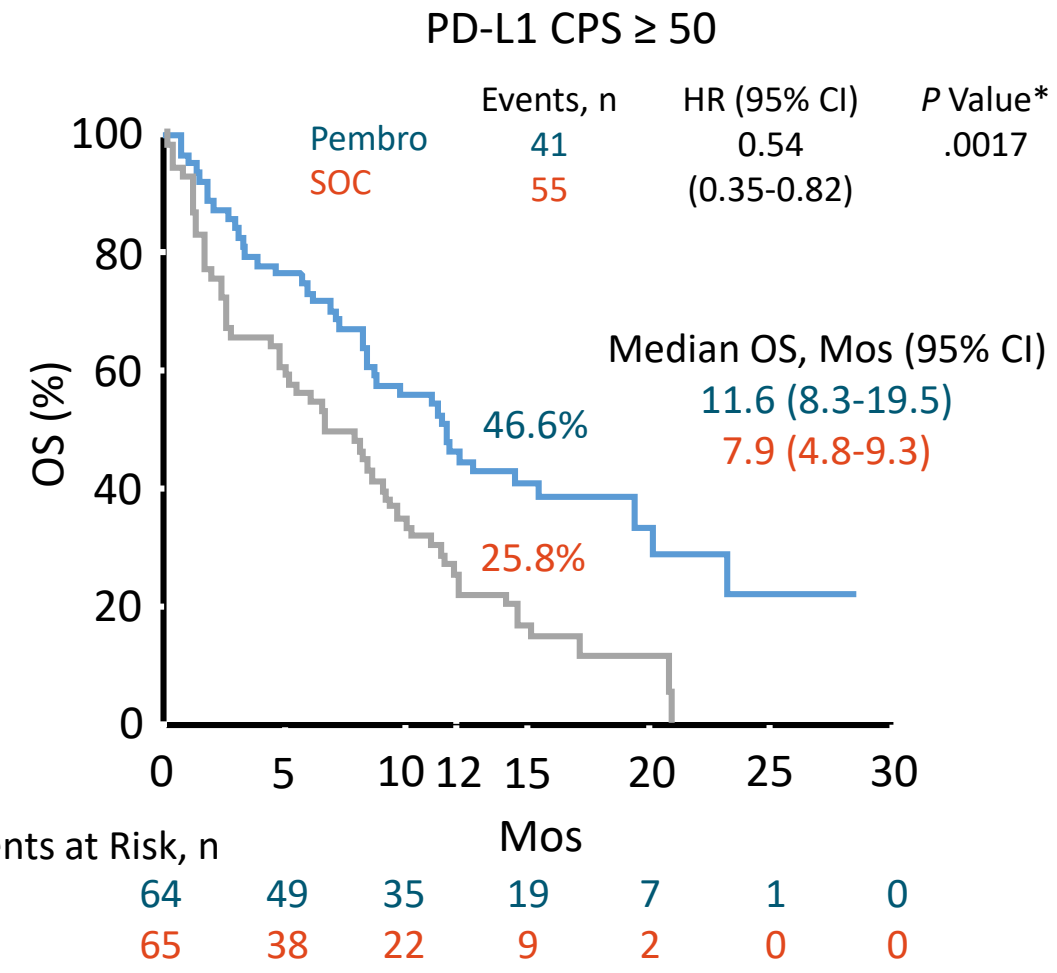
Patients **at Risk, n**							
Subsequent checkpoint inhibitor	31	30	26	13	7	1	0
Other subsequent therapy	69	59	34	10	1	0	0
No subsequent therapy	148	59	22	11	2	0	0

- Patients in the SoC group who received subsequent immune checkpoint inhibition had longer OS than the patients who received other or no subsequent therapy
- Median OS: 20.1 vs 9.7 vs 4.5 mos

Cohen. Lancet 2019;393:156.

KEYNOTE-040: OS by PD-L1 Expression





*Nominal 1-sided *P* value from log-rank test, stratified by randomization stratification factors.

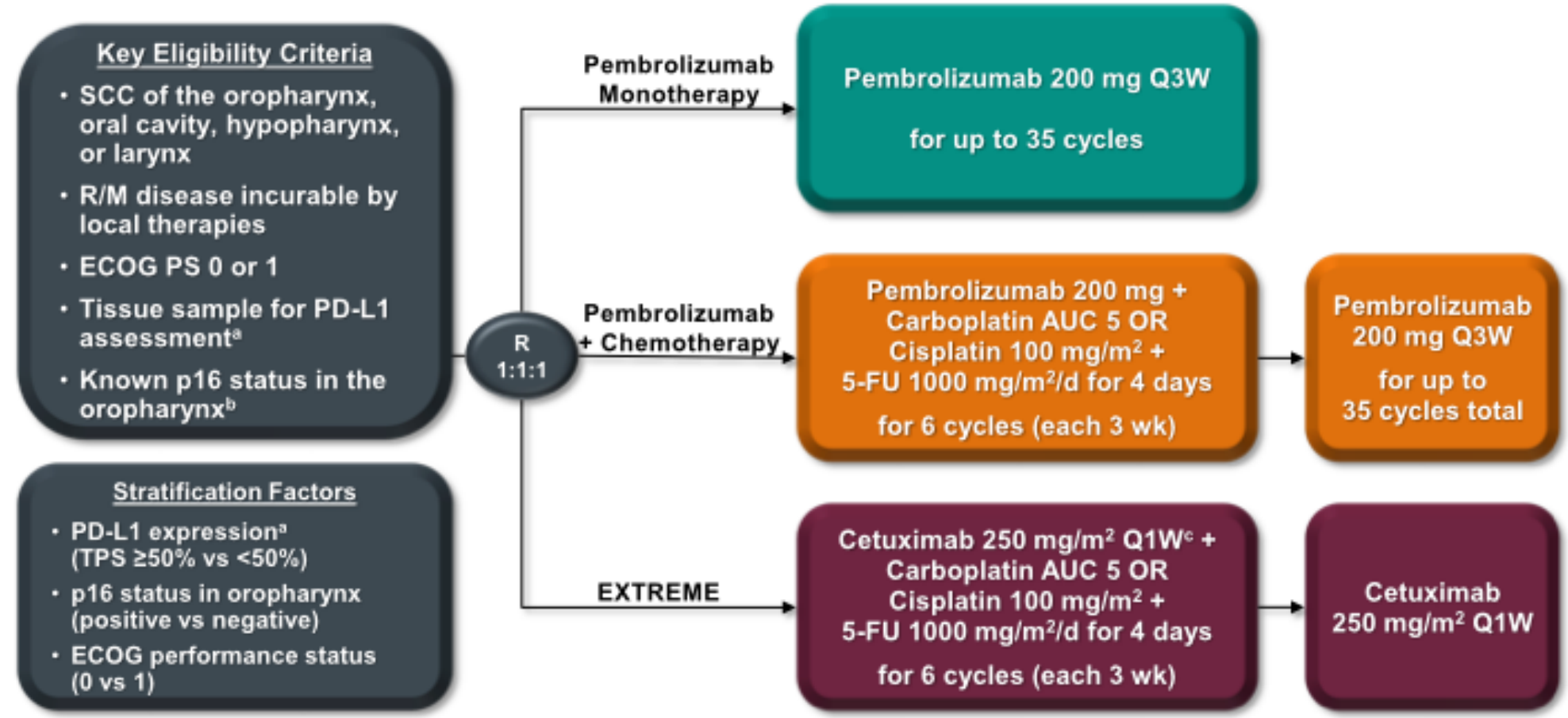
Cohen. Lancet. 2019;393:156.

KEYNOTE-040: TRAEs for Pembrolizumab vs Standard of Care in Recurrent/Metastatic HNSCC

TRAEs, n (%) (≥ 15% Either Arm)	Pembrolizumab (n = 246)		SoC (n = 234)	
	Any Grade	Grade 3-5	Any Grade	Grade 3-5
Any TRAE	155 (63)	33 (13)	196 (84)	85 (36)
TRAE leading to tx discontinuation	15 (6)	12 (5)	12 (5)	9 (4)
TRAE mortality	4 (2)	4 (2)	2 (1)	2 (1)

Cohen. Lancet. 2019;393:156.

KEYNOTE-048: Pembrolizumab +/- Chemotherapy in newly diagnosed R/M HNSCC



[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.

Rischin, ASCO 2019.

KEYNOTE-048: Baseline Characteristics, ITT Population

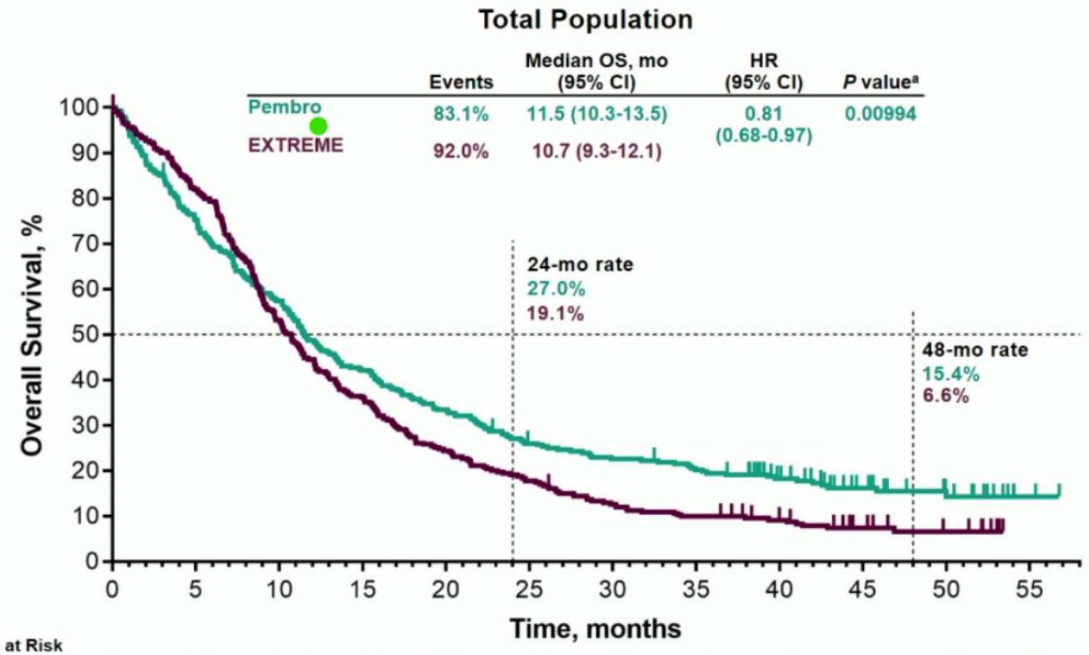
Characteristic	Pembrolizumab Alone vs EXTREME		Pembrolizumab + Chemo vs EXTREME	
	Pembrolizumab (n = 301)	EXTREME (n = 300)	Pembro + Chemo (n = 281)	EXTREME (n = 278*)
Age, median, yrs (range)	62 (22-94)	61 (24-84)	61 (20-85)	61 (24-84)
Male, n (%)	250 (83.1)	261 (87.0)	224 (79.7)	242 (87.1)
ECOG PS 1, n (%)	183 (60.8)	183 (61.0)	171 (60.9)	170 (61.2)
Current/former smoker, n (%)	239 (79.4)	234 (78.0)	224 (79.7)	215 (77.3)
p16 positive (oropharynx) , n (%)	63 (20.9)	67 (22.3)	60 (21.4)	61 (21.9)
PD-L1 status, n (%)				
▪ 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,† n (%)				
▪ Metastatic	216 (71.8)	203 (67.7)	201 (71.5)	187 (67.3)
▪ Recurrent only‡	82 (27.2)	94 (31.3)	76 (27.0)	88 (31.7)

*Patients randomized to EXTREME during pembro + chemo enrollment hold excluded from pembro + chemo vs EXTREME efficacy comparisons.
†3 patients in pembro arm, 3 patients in EXTREME arm, and 4 patients in pembro + chemo arm had neither metastatic nor recurrent disease.
‡Includes locally recurrent disease and disease that spread to cervical lymph nodes. Data cutoff date: June 13, 2018.

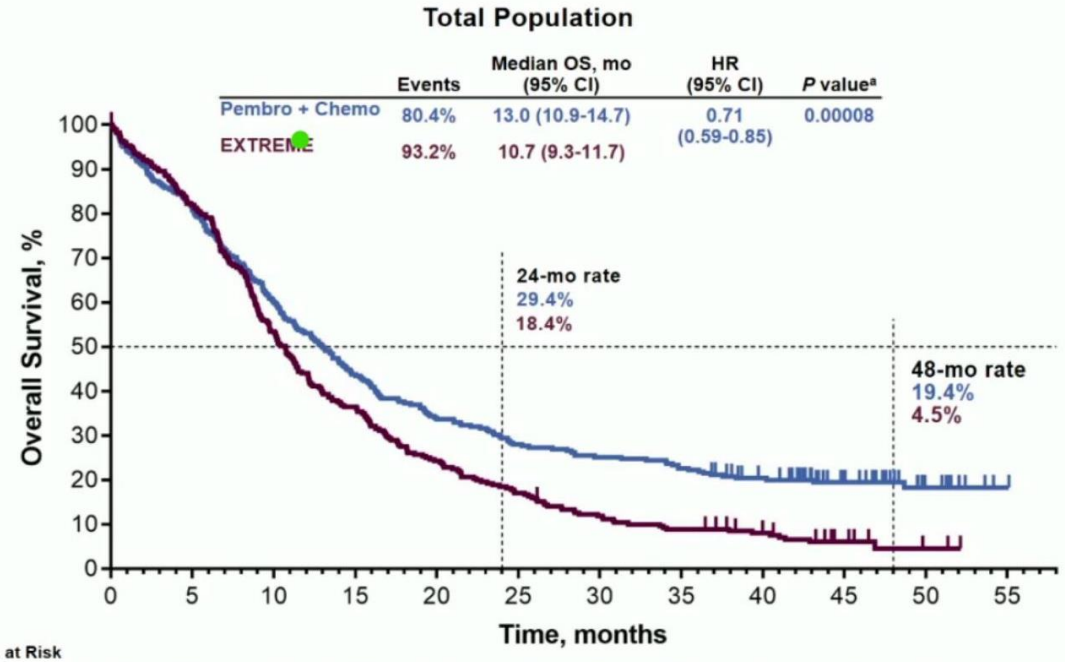
Burtness. Lancet. 2019;394:1915.

KEYNOTE-048: Updated Results ESMO 2020

OS: Pembrolizumab vs EXTREME



OS: Pembrolizumab + Chemo vs EXTREME

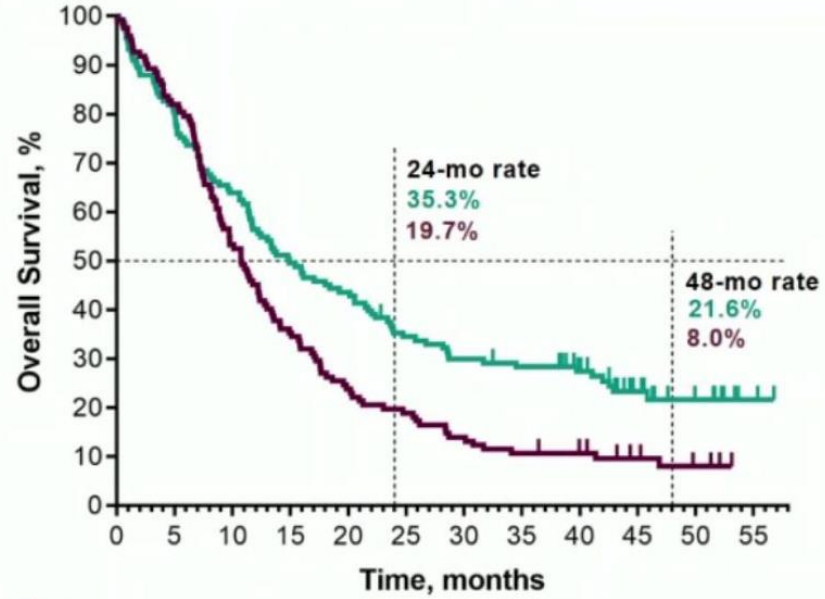


KEYNOTE-048: Updated Results ESMO 2020

OS: Pembrolizumab vs EXTREME

PD-L1 CPS ≥20

	Events	Median OS, mo (95% CI)	HR (95% CI)	*P* value[a]
Pembrolizumab	75.9%	14.9 (11.5-20.6)	0.61 (0.46-0.81)	0.00034
EXTREME	91.0%	10.8 (8.8-12.8)		

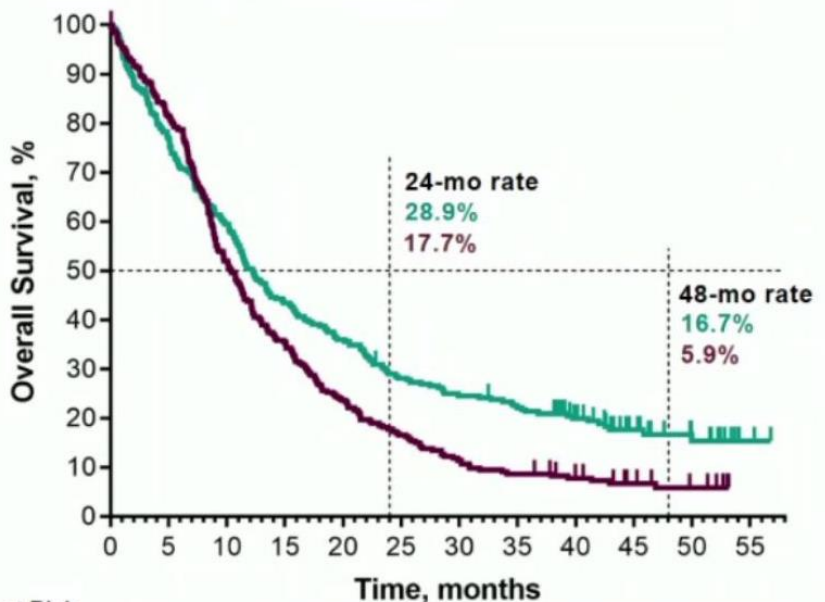


No. at Risk

Pembro	133	107	85	66	58	45	39	36	30	17	9	2
EXTREME	122	100	65	43	29	23	17	13	11	7	4	0

PD-L1 CPS ≥1

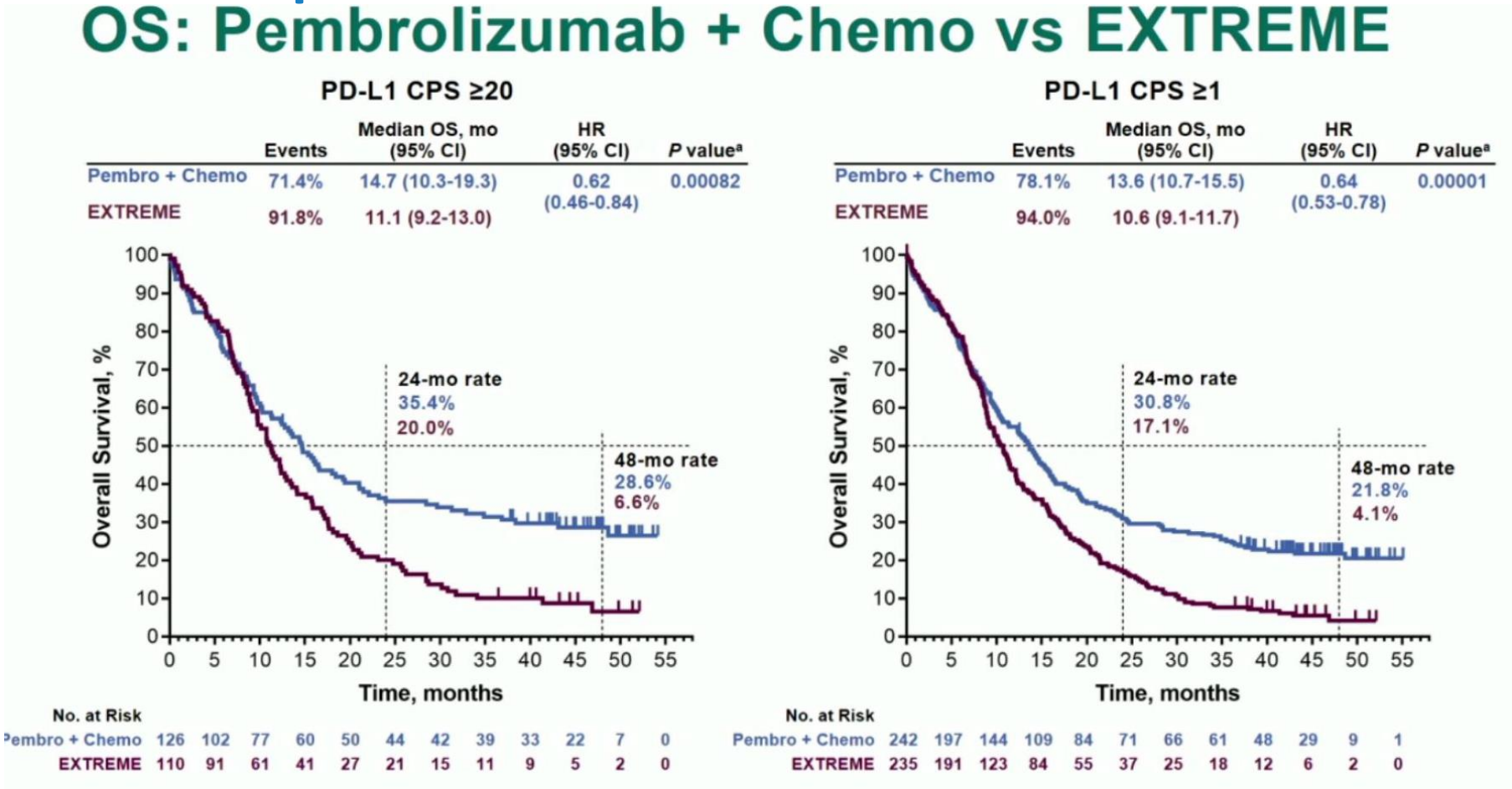
	Events	Median OS, mo (95% CI)	HR (95% CI)	*P* value[a]
Pembrolizumab	81.7%	12.3 (10.8-14.8)	0.71 (0.61-0.89)	0.00080
EXTREME	92.9%	10.4 (9.0-11.7)		



No. at Risk

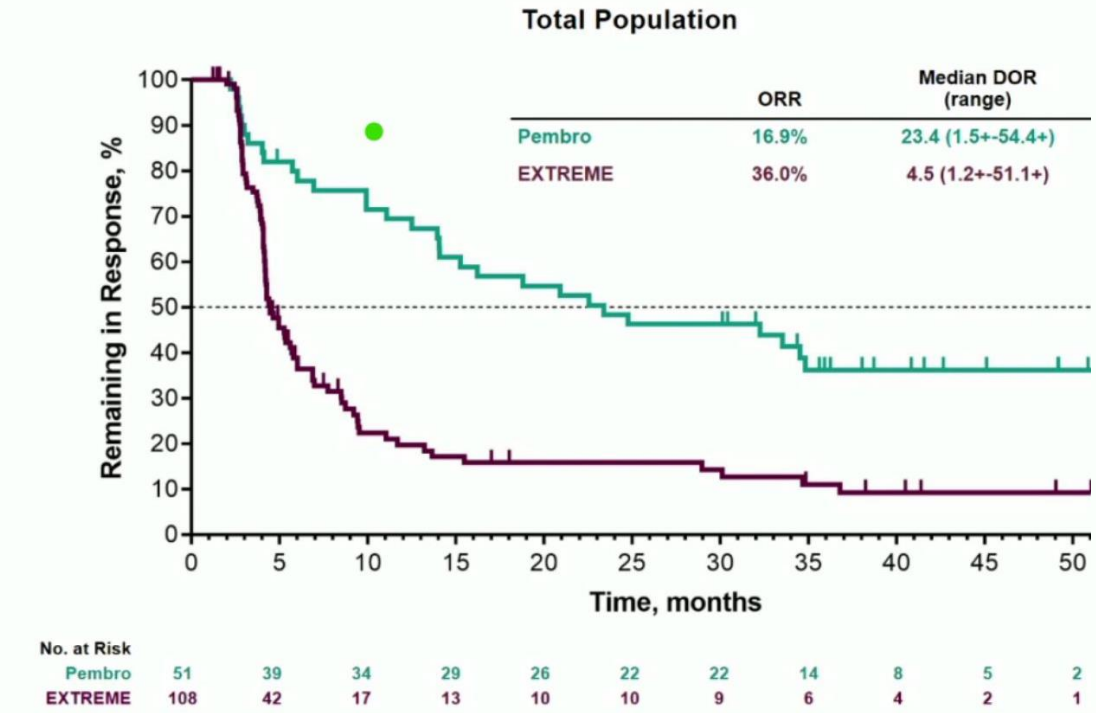
Pembro	257	197	152	111	92	71	62	55	40	22	12	2
EXTREME	255	207	132	90	60	42	29	22	16	10	6	0

KEYNOTE-048: Updated Results ESMO 2020

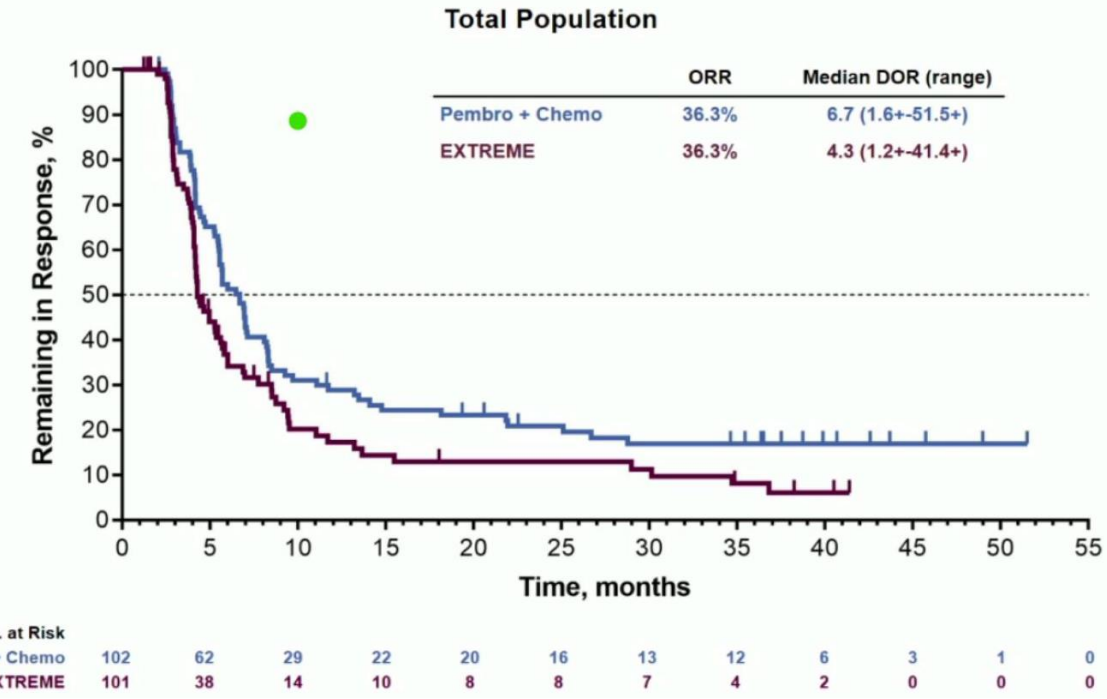


KEYNOTE-048: Updated Results ESMO 2020

DOR: Pembrolizumab vs EXTREME



DOR: Pembrolizumab + Chemo vs EXTREME



KEYNOTE-048: AE Update ESMO 2020

Safety

TRAEs	Pembro (n = 300)	EXTREME (n = 287)
Any grade	58.3%	96.9%
Grades 3-5	17.0%	69.3%

TRAEs	Pembro + Chemo (n = 276)	EXTREME (n = 287)
Any grade	95.7%	96.9%
Grades 3-5	71.7%	69.3%

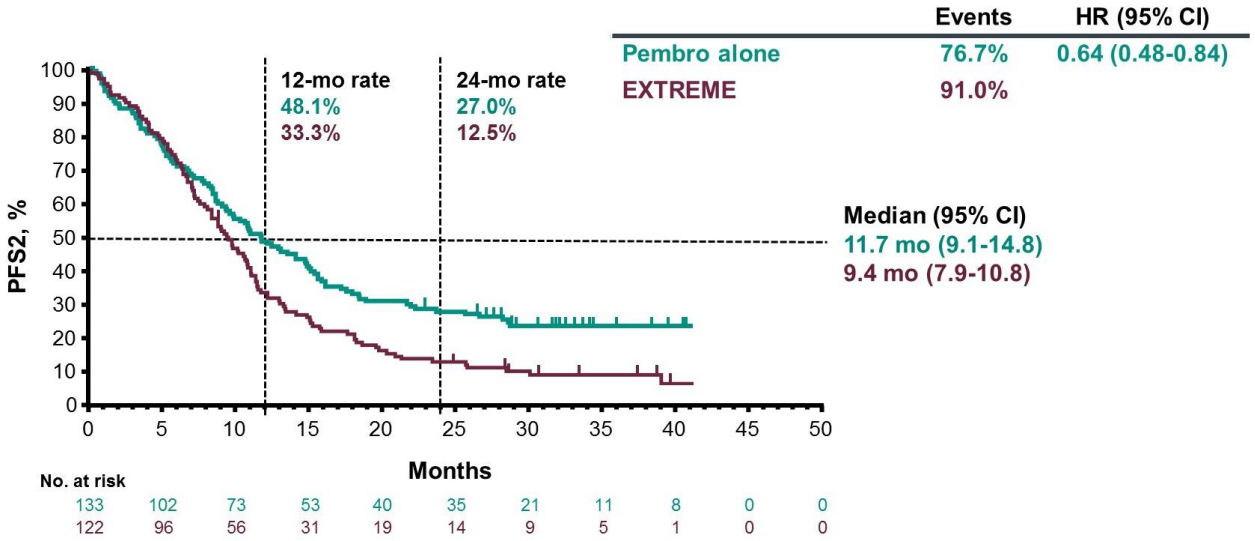
KEYNOTE-048: PFS2 ASCO 2020

First Subsequent Therapy

n (%)	Pembro Monotherapy n = 301	Pembro + Chemotherapy n = 281	EXTREME n = 300
Any new anticancer treatment[a]	148 (49.2)	115 (40.9)	159 (53.0)
Chemotherapy	135 (44.9)	88 (31.3)	102 (34.0)
EGFR inhibitor	59 (19.6)	37 (13.2)	19 (6.3)
Immune checkpoint inhibitor	6 (2.0)	12 (4.3)	50 (16.7)
Other immunotherapy	1 (0.3)	0 (0.0)	6 (2.0)
Kinase inhibitor	1 (0.3)	7 (2.5)	1 (0.3)
Other	2 (0.7)	1 (0.4)	2 (0.7)

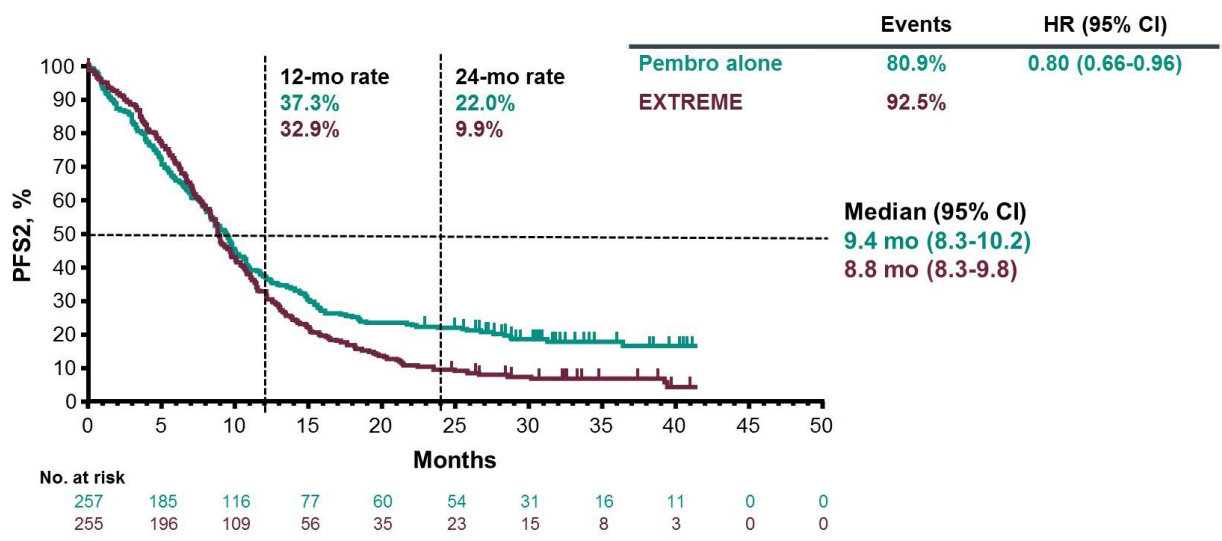
KEYNOTE-048: PFS2 ASCO 2020

PFS2: Initially Randomized, Pembro vs EXTREME, CPS ≥20 Population



PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro vs EXTREME)

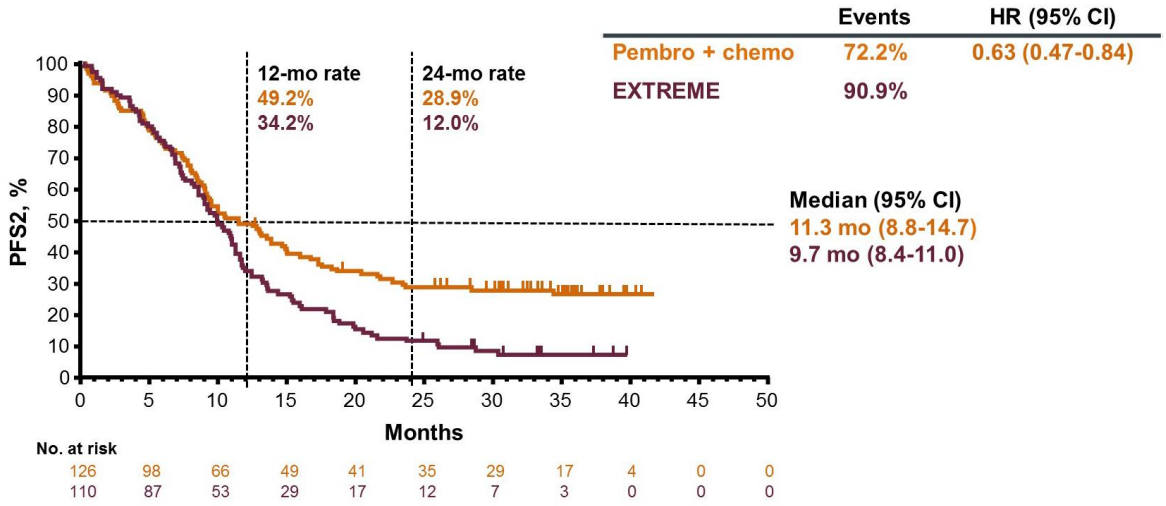
PFS2: Initially Randomized, Pembro vs EXTREME, CPS ≥1 Population



PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥1 (Pembro vs EXTREME)

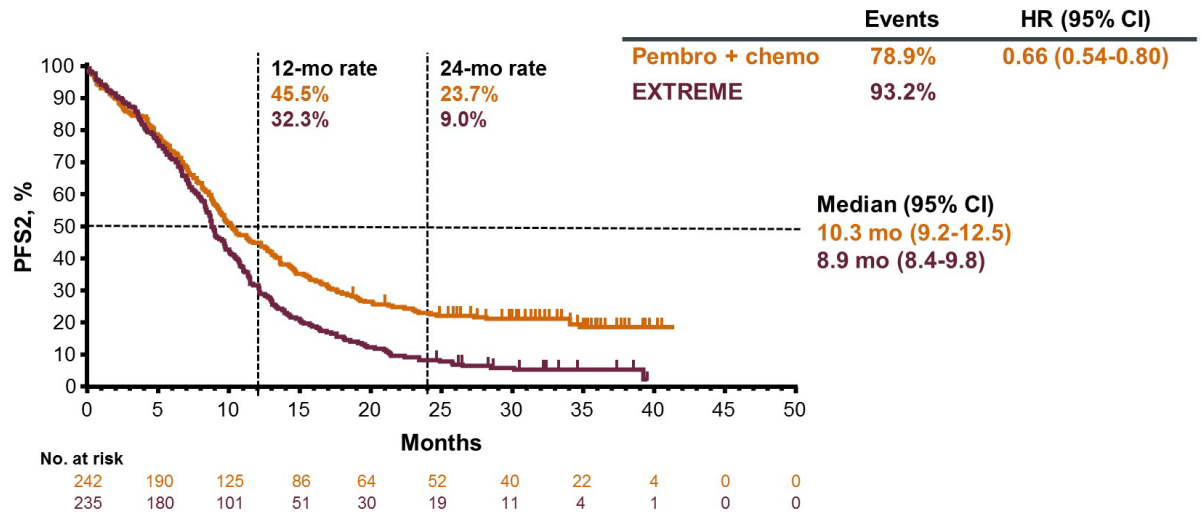
KEYNOTE-048: PFS2 ASCO 2020

PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥20 Population



PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro + Chemotherapy vs EXTREME)

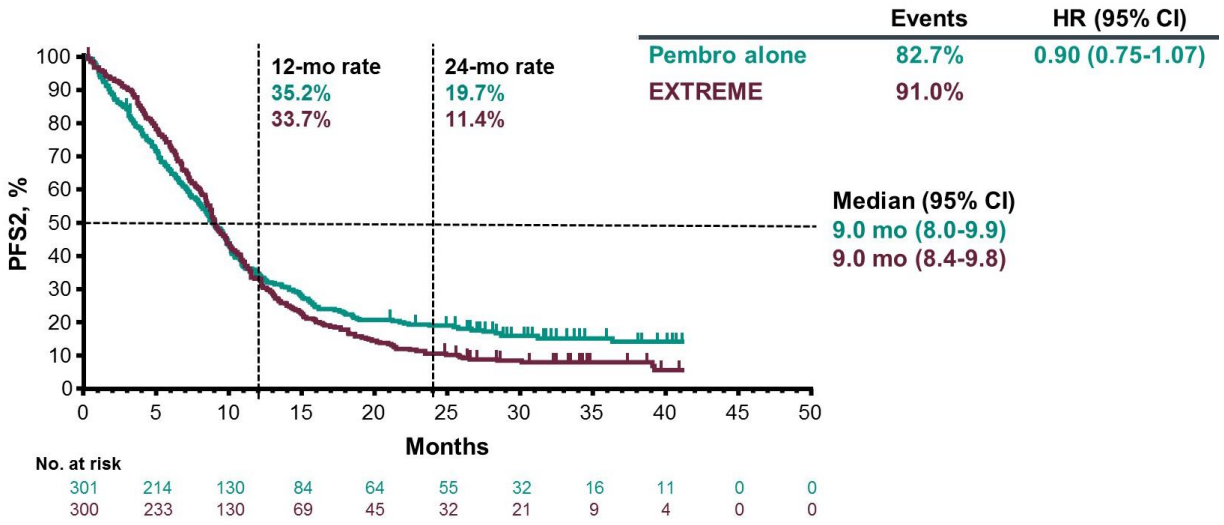
PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥1 Population



PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥1 (Pembro + Chemotherapy vs EXTREME)

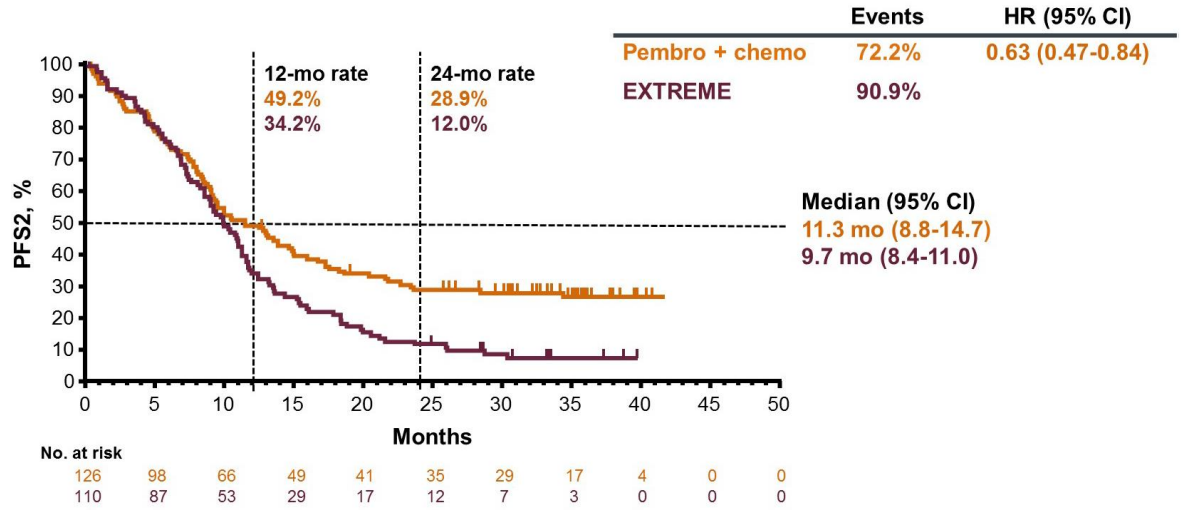
KEYNOTE-048: PFS2 ASCO 2020

PFS2: Initially Randomized, Pembro vs EXTREME, Total Population



PFS2 analysis involved patients in the ITT population (Pembro vs EXTREME)

PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥20 Population



PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro + Chemotherapy vs EXTREME)

Cemiplimab in advanced/metastatic cutaneous squamous-cell carcinoma

Key Eligibility Criteria
- Advanced cutaneous squamous-cell carcinoma (any site)
- Not eligible for surgery
- ECOG 0-1
- ≥1 assessable lesion

→

Cemiplimab
3 mg/kg IV Q2W

→

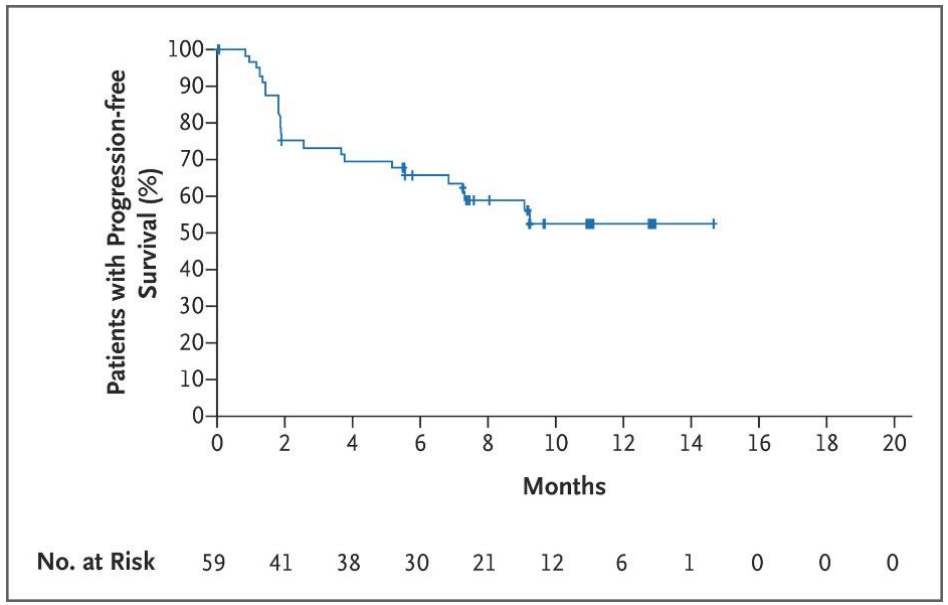
Primary endpoint
- Response rate

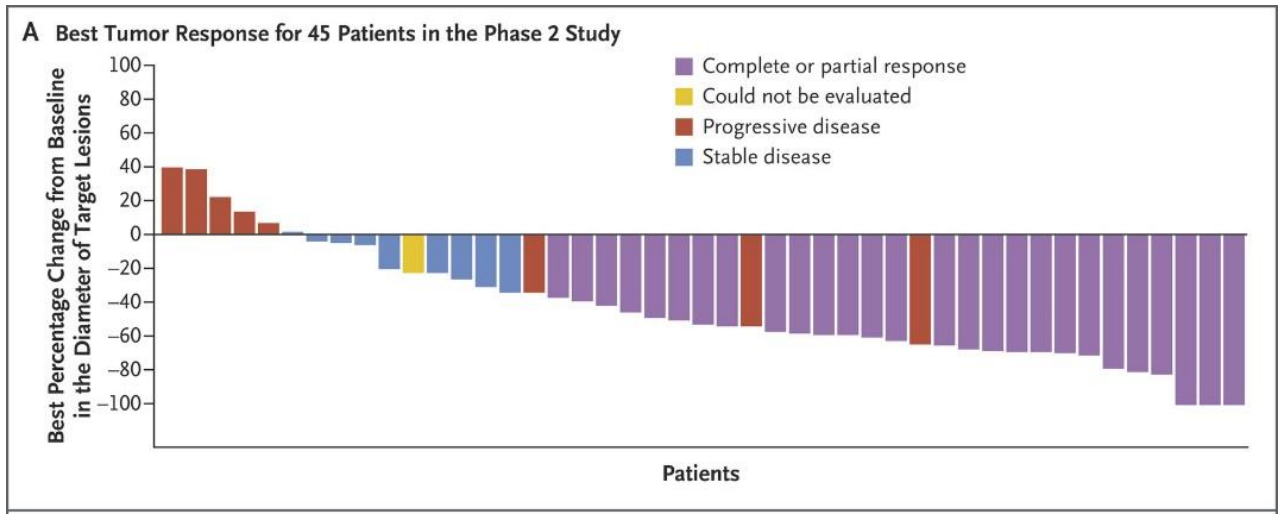
Other endpoints
- Duration of response
- PFS
- OS
- Side effects
- Durable disease control

Migden, NEJM 2018.

Cemiplimab in advanced/metastatic cutaneous squamous-cell carcinoma

- Cemiplimab 3 mg/kg Q2W
- 47% response rate in metastatic patients
- 60% of locally advanced had objective response





Migden, NEJM 2018.

Pembrolizumab in advanced/metastatic cutaneous squamous-cell carcinoma

Keynote-629

Phase II study
Primary endpoint: ORR

N=105

Pembrolizumab 200mg IV Q3 weeks

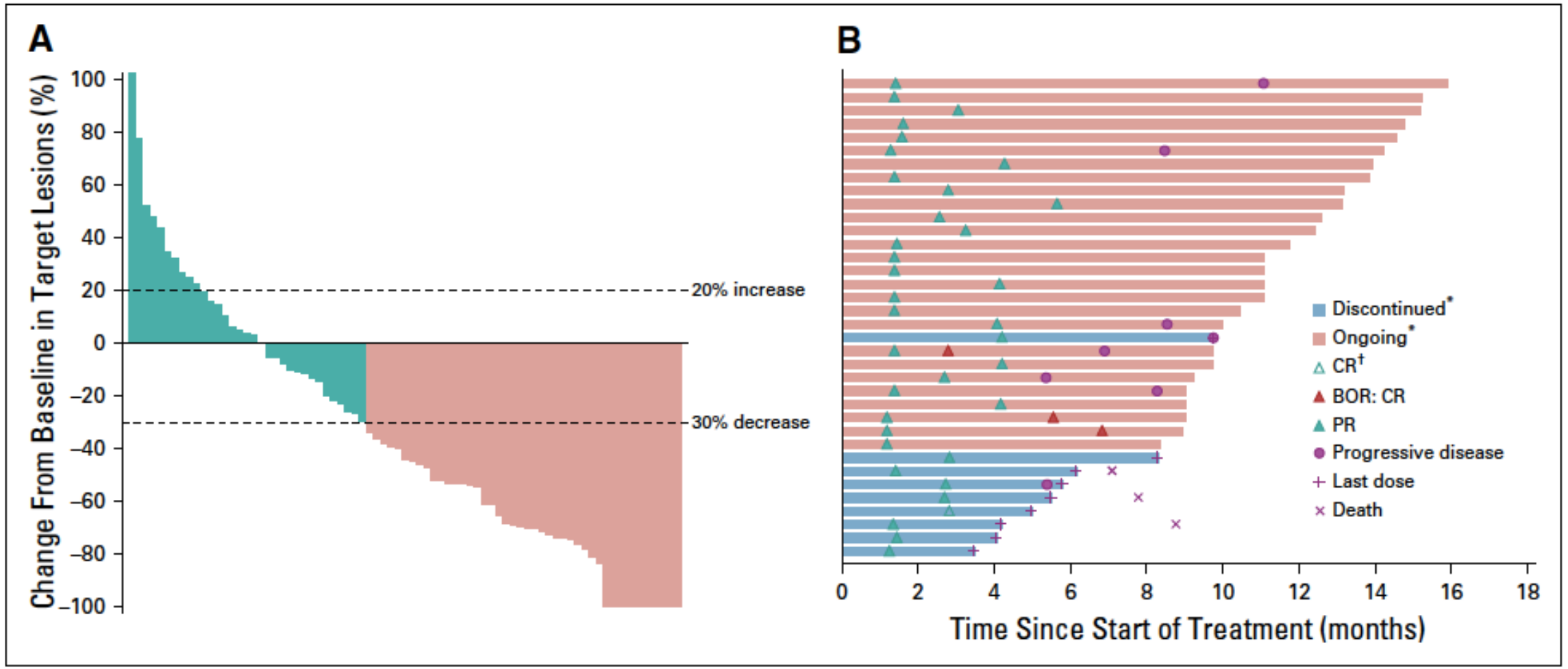
86% received one prior line of therapy

TABLE 2. Summary of Tumor Response in All Patients as Treated

Response	Pembrolizumab (N = 105)
Objective response rate, % (95% CI)[a]	34.3 (25.3 to 44.2)
Disease control rate, % (95% CI)[b]	52.4 (42.4 to 62.2)
Best overall response	
Complete response	4.0 (3.8)
Partial response	32.0 (30.5)
Stable disease	31.0 (29.5)
Stable disease ≥ 12 weeks	19.0 (18.1)
Progressive disease	28.0 (26.7)
Not evaluable[c]	2.0 (1.9)
Not assessed[d]	8.0 (7.6)

Grob JCO 2020.

Pembrolizumab in advanced/metastatic cutaneous squamous-cell carcinoma



Grob, JCO 2020.

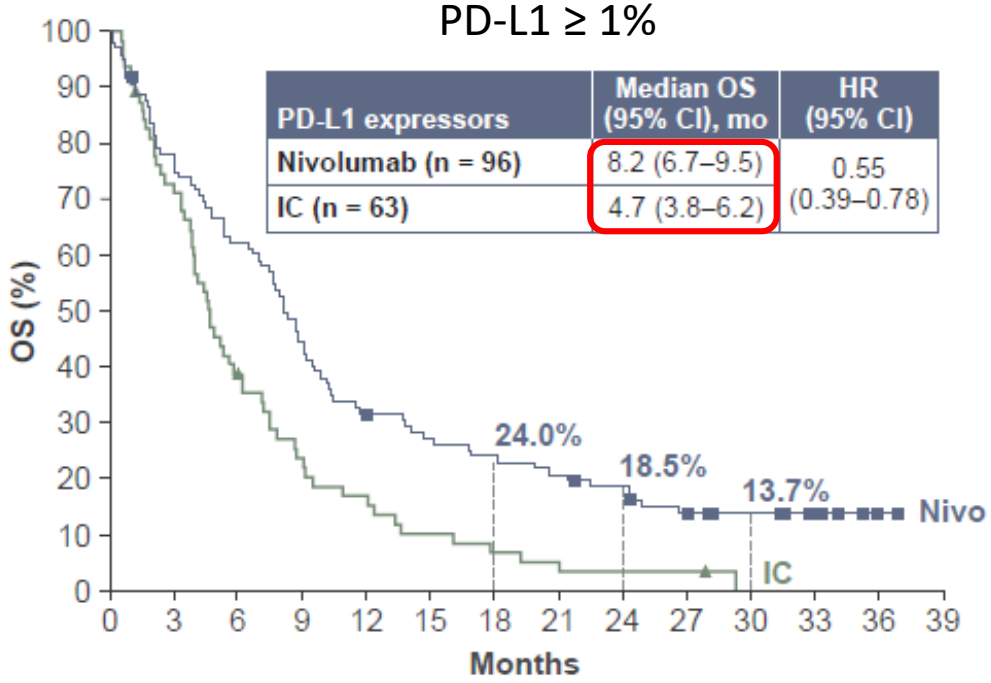
Evaluating Biomarkers in HNSCC

- Only indication that relies on PD-L1 expression: pembrolizumab monotherapy in 1st line HNSCC – CPS ≥ 1 (KEYNOTE-048)
- All other approvals not dependent on PD-L1 expression
  - KEYNOTE-012/055: Response rates not significantly different on the basis of tumor PD-L1 staining
  - Checkmate 141: Most benefit seen in PD-L1 positive tumors
  - KEYNOTE-040: pembrolizumab vs investigator's choice chemotherapy – did not meet survival endpoints in total population but improved outcomes in PD-L1-expressors

Evaluating Biomarkers in HNSCC

CheckMate 141: 2 year update

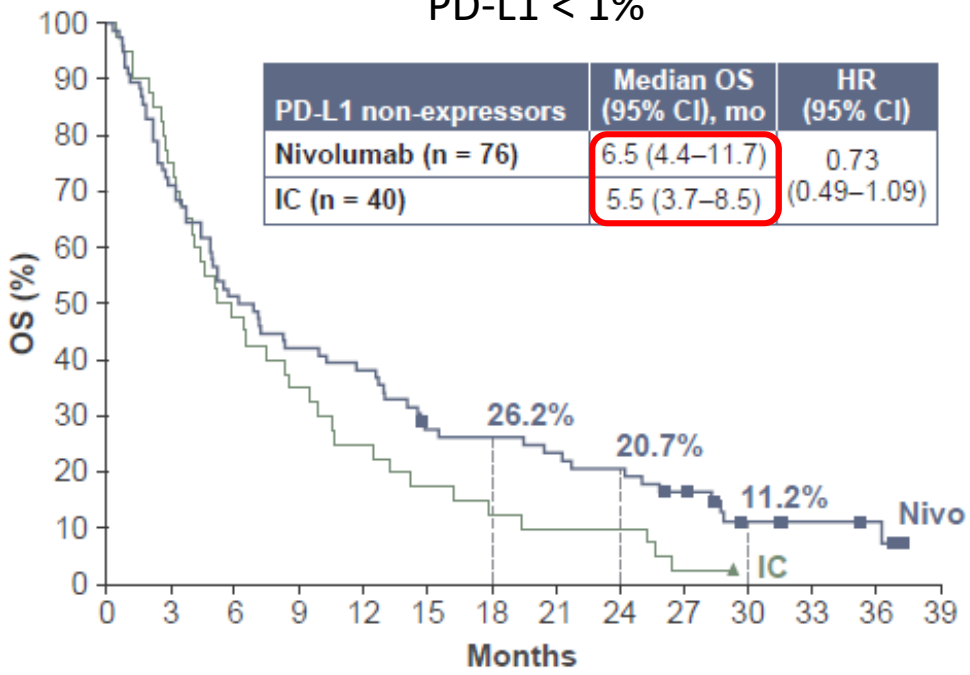
PD-L1 ≥ 1%



PD-L1 expressors	Median OS (95% CI), mo	HR (95% CI)
Nivolumab (n = 96)	8.2 (6.7–9.5)	0.55 (0.39–0.78)
IC (n = 63)	4.7 (3.8–6.2)	

No. at risk														
Nivo	96	74	59	42	30	25	22	19	16	11	8	5	1	0
IC	63	45	24	14	10	6	4	3	2	2	0	0	0	0

PD-L1 < 1%



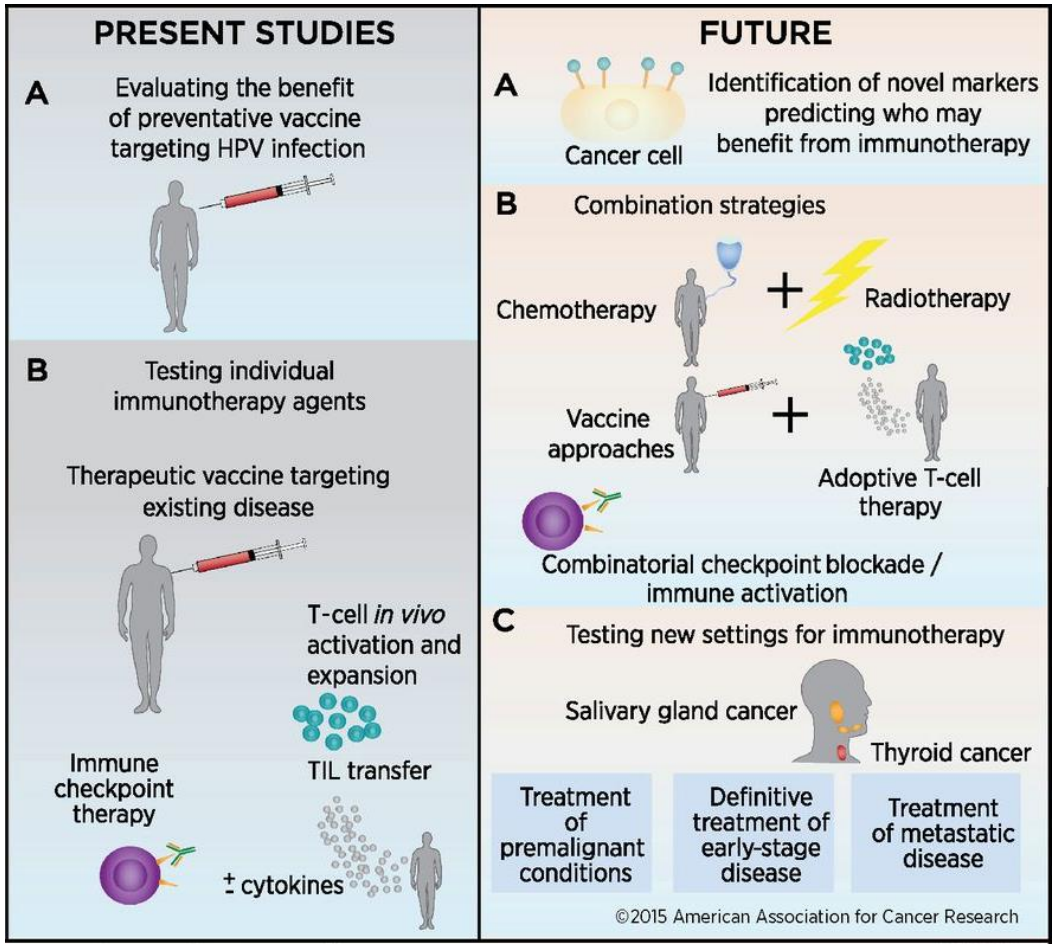
PD-L1 non-expressors	Median OS (95% CI), mo	HR (95% CI)
Nivolumab (n = 76)	6.5 (4.4–11.7)	0.73 (0.49–1.09)
IC (n = 40)	5.5 (3.7–8.5)	

No. at risk														
Nivo	76	54	39	32	29	20	19	17	15	11	5	4	3	0
IC	40	30	19	14	10	7	5	4	4	1	0	0	0	0

Ferris, Oral Oncol 2018.

Immunotherapy for the Treatment of Head and Neck Cancers

- Immuno-Oncology (I-O) frontiers in treatment of head and neck cancers
  - Expression of immunologic markers to guide treatment
  - Preventive vaccination against virally mediated cancers
  - Therapeutic vaccines for established cancers
  - CAR-T and cell-mediated therapies
  - Combinations with immunotherapies



Schoenfeld, Cancer Immunol Res, 2015

Future directions in immunotherapy for head and neck cancer

1. Curative Intent therapy
    1. Incorporation into established treatment in newly diagnosed patients (PULA).
    2. Locally recurrence/salvage surgery or reirradiation

2. Recurrent/Metastatic HNSCC
    1. Combination strategies in first line setting
    2. Previously antiPD1 treated
    3. Cellular therapeutics

Schoenfeld, Cancer Immunol Res, 2015

PULA HNSCC: Safety data in neoadjuvant setting

Trial	Phase	N	IO	Local Tx	Outcomes
NCT02296684	II	24	Pembro x 1	Surgery	42% with path resp
CheckMate 358	I/II	29	Nivo x 2	Surgery	28.5% TEAEs, No surgical delays
NCT02274155	Ib	17	MEDI6469 (OX40 antibody) x 3	Surgery	No ≥ Grade 3 AEs, no surgical delays
NCT03247712	I	10	Nivo x 3 doses + SBRT	Surgery	No surgical delays Gr1/2 mucositis dermatitis 5 pt with Adrenal insuffiency Delayed healing

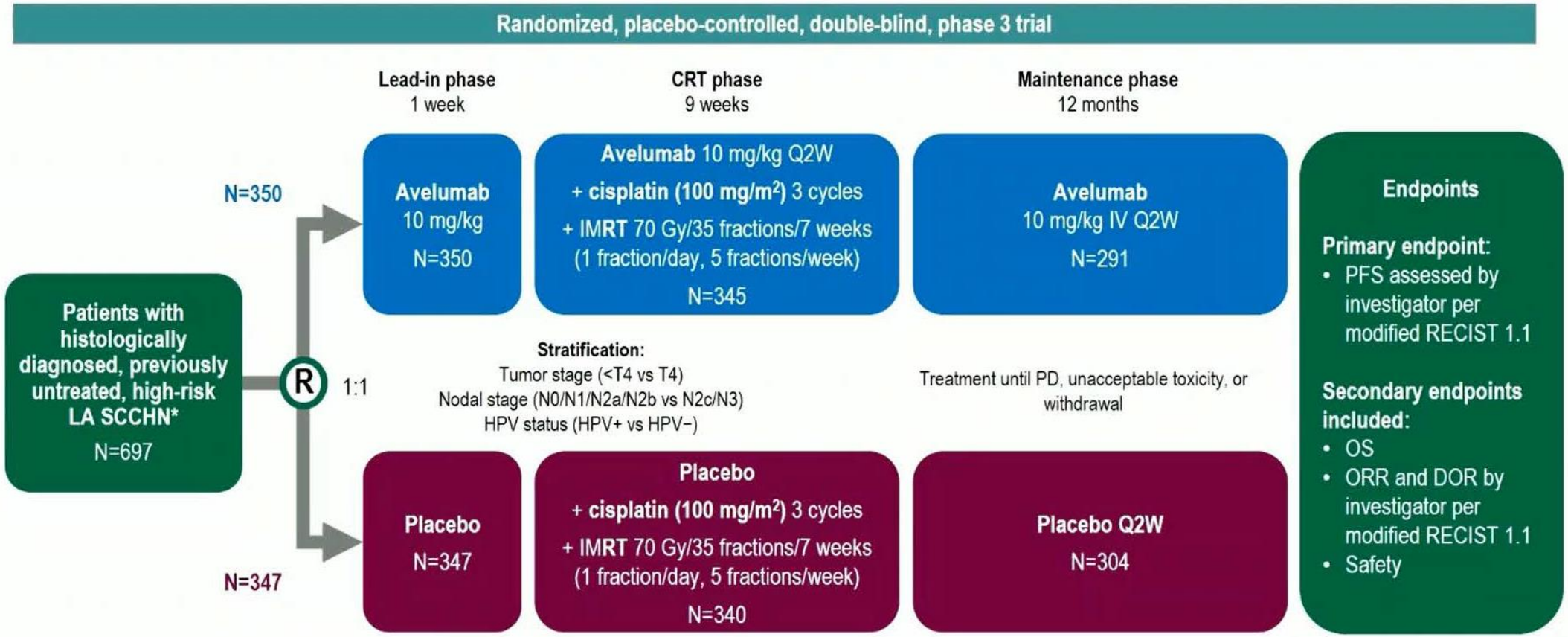
PULA HNSCC: Safety data in concurrent XRT setting

Trial	Phase	N	IO	Local Tx	Outcomes
NCT02586207	I	27	Pembro	Concurrent with cisXRT	CR in 78% ≤ Grade 3 irAEs in 3 pts 85% received cisplatin > 200 mg/m^2 All completed RT
NCT02641093	II	34 of planned 80	Pembro prior to surgery and concurrent with postop chemoXRT	Surgery and postop chemoXRT	Pathological response in > 50% of tumors after 1 dose No DLT in first 16 patients
RTOG 3504	I	10	Nivol + cetuximab + XRT		1 DLT (mucositis) 1 Grade 3 irAE

PULA HNSCC: Randomized studies

Trial	Treatment Population	N	Intervention
KEYNOTE-412	LAHNSCC (HPV+ for select stages/primary sites)	780	Pembro + cis + RT vs. placebo + cis + RT
JAVELIN HN100	LAHNSCC HPV- HNSCC (HPV+ for select stages/primary sites)	640	Avel + chemoRT vs chemoRT alone
PembroRAD GORTEC2015-01	LAHNSCC cisplatin unfit	133	Cetux + XRT vs Pembro XRT
REACH	Stage III/IVb HNSCC	688	Avel + cis + RT vs cis + RT and Avel + cetux + RT vs cis + RT
IMSTAR-HN	Stage III/IV p16- OPC, L, HP, OC	276	Neoadjuvant nivo, surgery, and adj chemoRT + adj nivo ± ipi vs SOC surgery + chemoRT
KEYNOTE-689	Resectable stage III/IVa L, HP, OC, p16-OPC Stage III p16+ OPC	600	Pembro prior to surgery/with adj chemoRT vs surgery

PULA HNSCC: JAVELIN ESMO 2020



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.

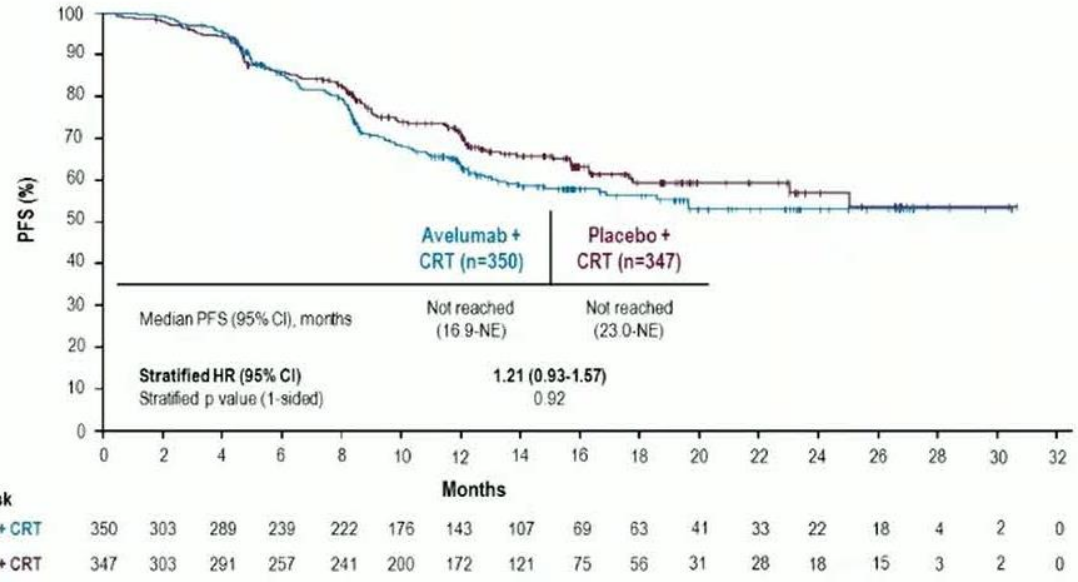
* High-risk LA SCCHN (oral cavity, oropharynx, larynx, or hypopharynx): HPV-negative disease stage III, IVa, IVb; nonoropharyngeal HPV-positive disease stage III, IVa, IVb; HPV-positive oropharyngeal disease T4 or N2c or N3 (TNM staging per AJCC, 7th edition)

PULA HNSCC: JAVELIN ESMO 2020

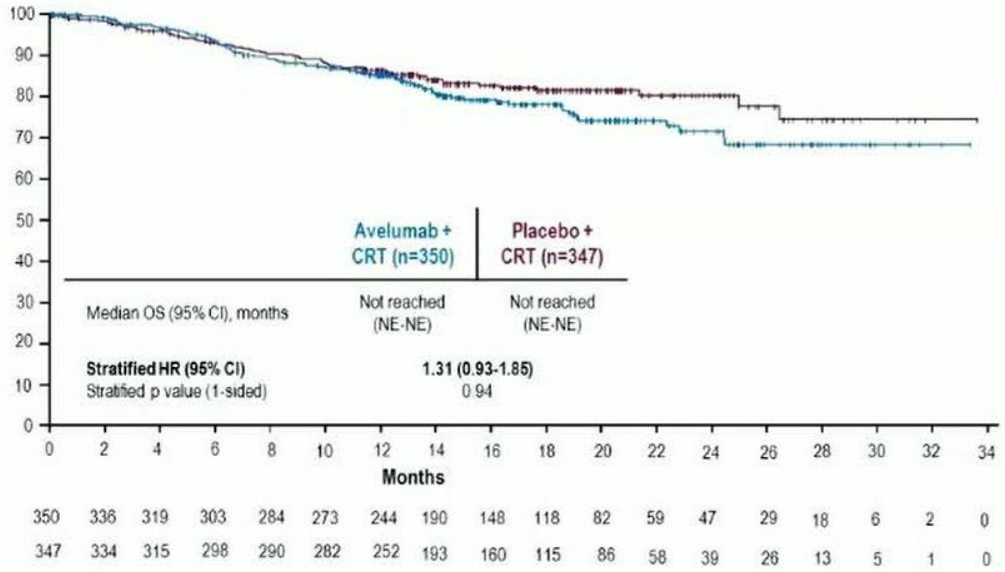
VIRTUAL 2020 ESMO congress

Addition of avelumab to CRT does not improve outcome

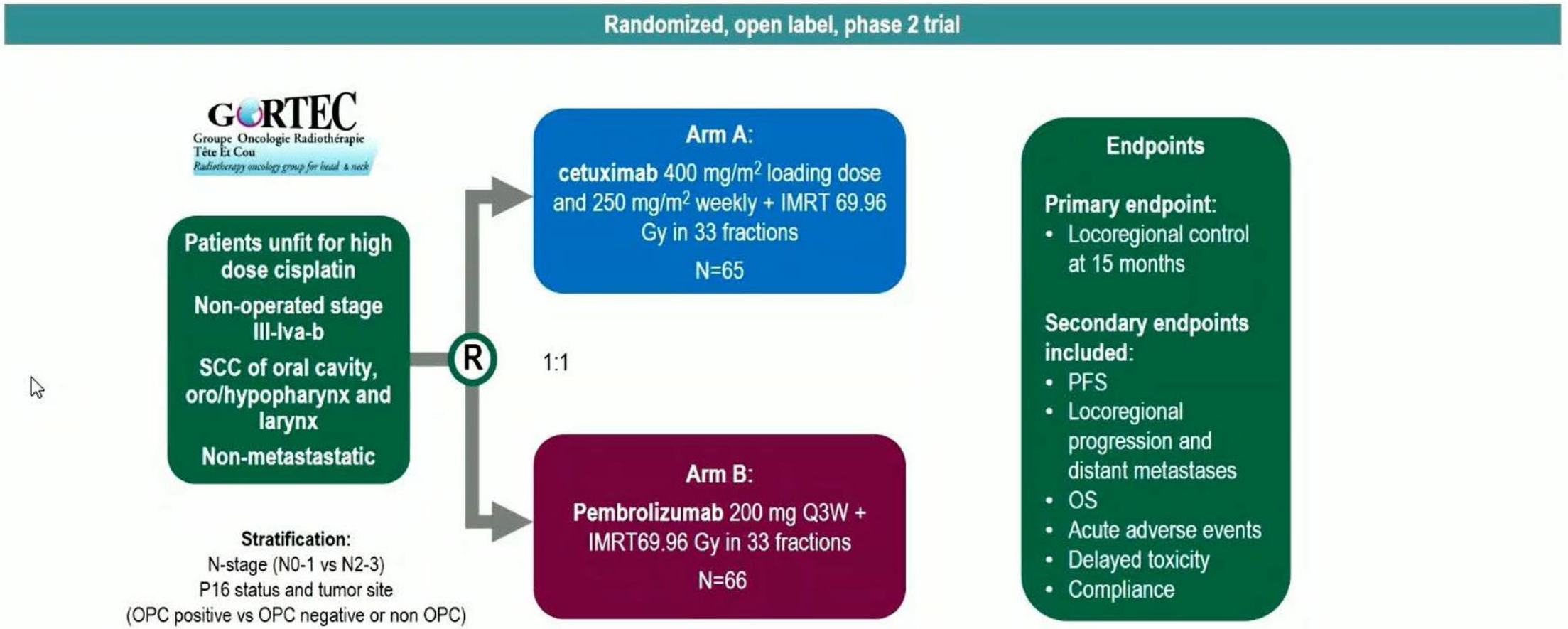
PFS



OS



PULA HNSCC: PembroRad ESMO 2020

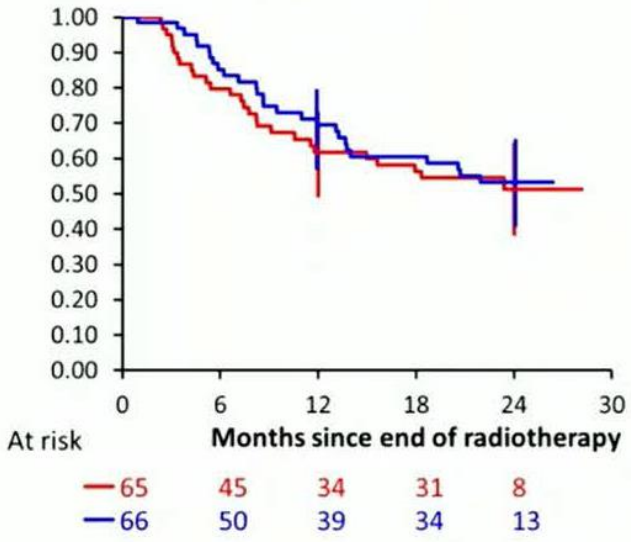


PULA HNSCC: PembroRad ESMO 2020

Pembro-RT does not improve outcome versus Cetux-RT

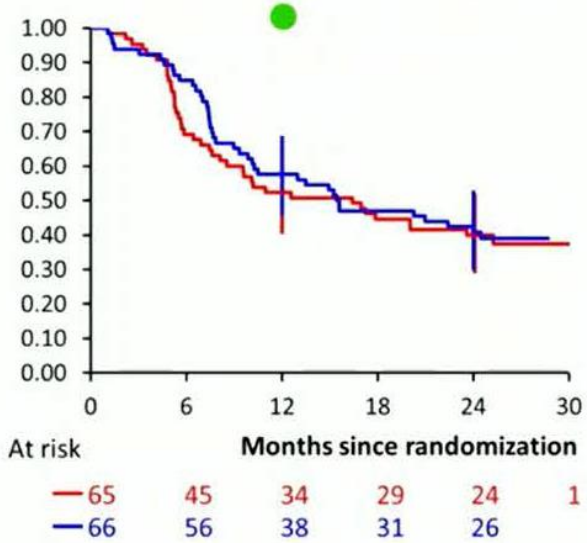
LRC

15 months:
Cetux-RT 59% (95% CI 45%-72%)
Pembro-RT 60% (95% CI 46%-72%)
OR = 1.05, p=0.91



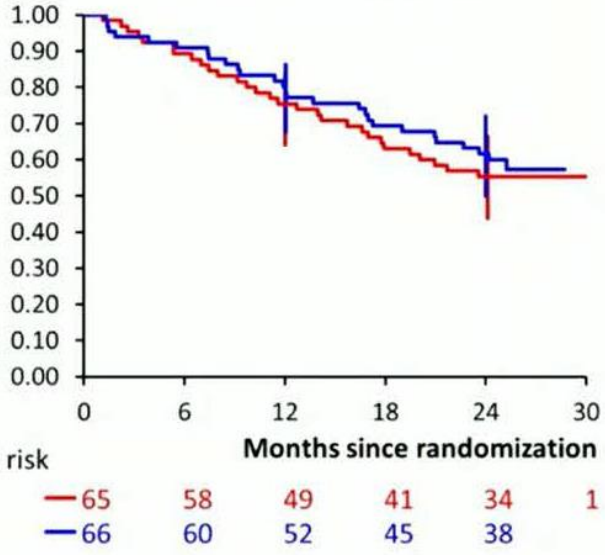
PFS

2 years:
Cetux-RT 40%
Pembro-RT 42%
HR = 0.83 (95% CI 0.53-1.29)



OS

2 years:
Cetux-RT 55%
Pembro-RT 62%
HR = 0.83 (95% CI 0.49-1.40)



PULA HNSCC: Randomized studies

Trial	Treatment Population	N	Intervention
IMvoke010	LAHNSCC treated with curative-intent therapy	400	Atezo vs placebo after chemoRT
EA3161	LAHNSCC p16+	744	Nivo vs. observation after chemoRT
NCT02841748 Pathway	High risk LAHNSCC	100	Pembro vs placebo after chemoxRT
KEYCHAIN	Int risk LAHNSCC p16+ OPC, L, OC	114	Cis + RT vs pembro + RT
HN005	Good risk LAHNSCC p16+	711	Cis XRT vs. cis deescRT vs nivo deesclRT
CompARE	Int and poor risk LAHNSCC	695	CisRT vs neoadjchemo cisXRT vs surg +cisRT vs durva cisXRT
HN004	Cisplatin-unfit LAHNSCC	523	Durva + RT vs cetux + RT in cis-ineligible pts

Ongoing Studies in Salvage Therapies for Locally Recurrent HNSCC

Trial	Intervention	Phase	N
NCT03317327	Re-irradiation + nivolumab	I/II	20
NCT02769520	Pembro in salvage surgery candidates	II	45
NCT03355560	Salvage resection followed by pembro	II	39
NCT02289209	Re-irradiation + pembrolizumab	II	48
RTOG 3507 KEYSTROKE	Stereotactic body radiation therapy ± pembrolizumab	II	102
ADJORL1	Adjuvant nivolumab or nivolumab + ipilimumab after salvage surgery	II	140

Randomized studies of combination therapies in Recurrent/Metastatic HNSCC

Trial	Combination	Phase	N	Results
EAGLE	Anti–PD-L1 + anti–CTLA-4	III	~700	No OS benefit vs second line systemic therapy
CheckMate 714	Nivolumab + ipilimumab vs nivolumab + Pbo	II	400	ORR/DOR in chemo-refractory subgroup
McBride 2018	Nivo vs Nivo+ SBRT	IIR	53	No ORR, OS, PFS benefit to Nivo + SBRT

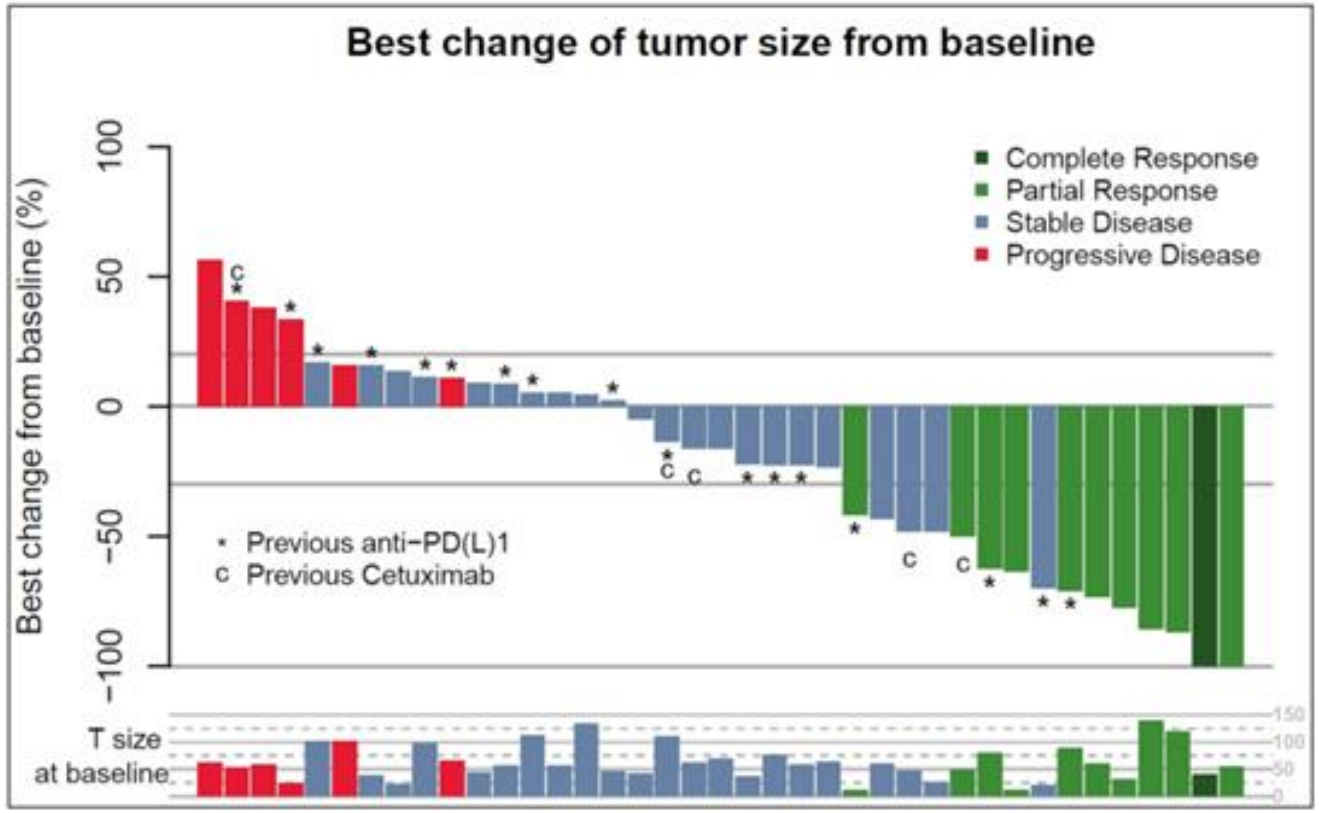
Ongoing IO Randomized Studies in 1L Recurrent/Metastatic HNSCC

Trial	Intervention	Phase	N	Primary Endpoint	Status
NCT02741570 CheckMate 651	Nivolumab + ipilimumab vs SOC (EXTREME study regimen)	III	930	OS/PFS in PD-L1+ subgroup	Accrual complete
NCT02551159 KESTREL	Durvalumab ± tremelimumab vs SOC (EXTREME study regimen)	III	823	OS	Accrual complete
NCT03669718	Cemiplimab vs cemiplimab + ISA101b	II	164	ORR/treatment-related AE rate	Accrual ongoing
NCT04128696 INDUCE-3	Pembrolizumab vs Pembrolizumab + GSK3359609	III	600	OS	Accrual ongoing
NCT04199104 LEAP-10	Pemrbo +/- Lenvatinib	III	500	ORR/OS/PFS	Accrual ongoing

Limited Reported Experience in Prior Immunotherapy-Treated Population

Drug	N	ORR, %
M7824, dual anti–PD-L1 (a TGFβ trap) Cho ESMO 2018	32 pts (75% had ≥ 2 prior lines of therapy)	21.9
Cetuximab + monalizumab* Fayette ESMO 2018	40	27.5

*Randomized study anticipated to open



Other avenues of early phase investigation

- Fusion proteins
- Tumor infiltrating lymphocytes
- Adoptive T cell tranfer
- CAR-T studies

Conclusions

- Cytotoxic chemotherapy achieves limited survival with unfavorable side effects.
- Checkpoint inhibitors that target the PD-1 axis, nivolumab and pembrolizumab, are approved in platinum-refractory/exposed recurrent/metastatic HNSCC.
- Nivolumab and pembrolizumab are in general better tolerated than cytotoxic chemotherapy.
- Robust areas of ongoing research in curative and palliative setting

Thank you! Resources

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POSITION ARTICLE AND GUIDELINES Open Access

The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of squamous cell carcinoma of the head and neck (HNSCC)

Ezra E. W. Cohen[1], R. Bryan Bell[2], Carlo B. Bifulco[2], Barbara Burtness[3], Maura L. Gillison[4], Kevin J. Harrington[5], Quynh-Thu Le[6], Nancy Y. Lee[7], Rom Leidner[2], Rebecca L. Lewis[8], Lisa Licitra[9], Hisham Mehanna[10], Loren K. Mell[1], Adam Raben[11], Andrew G. Sikora[12], Ravindra Uppaluri[13], Fernanda Whitworth[14], Dan P. Zandberg[8] and Robert L. Ferris[8*]