Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy for the Treatment of Head and Neck Cancer

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

sitc Society for Immunotherapy of Cancer

Disclosures

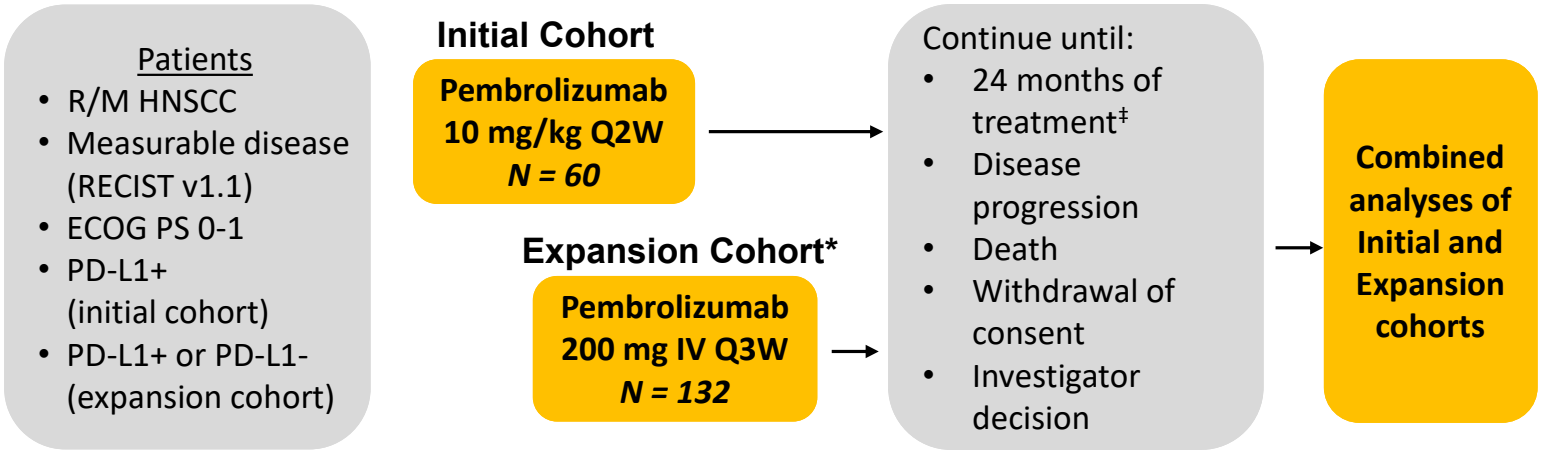
- Consulting Fees: Merck, Bayer

Approved checkpoint inhibitors in head and neck cancers

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

KEYNOTE-012: Pembrolizumab in R/M HNSCC

Nonrandomized, Phase 1b Trial, Cohorts† B, B2



Response assessment: Every 8 weeks until disease progression

Primary end points: ORR (RECIST v1.1, central imaging vendor review), safety

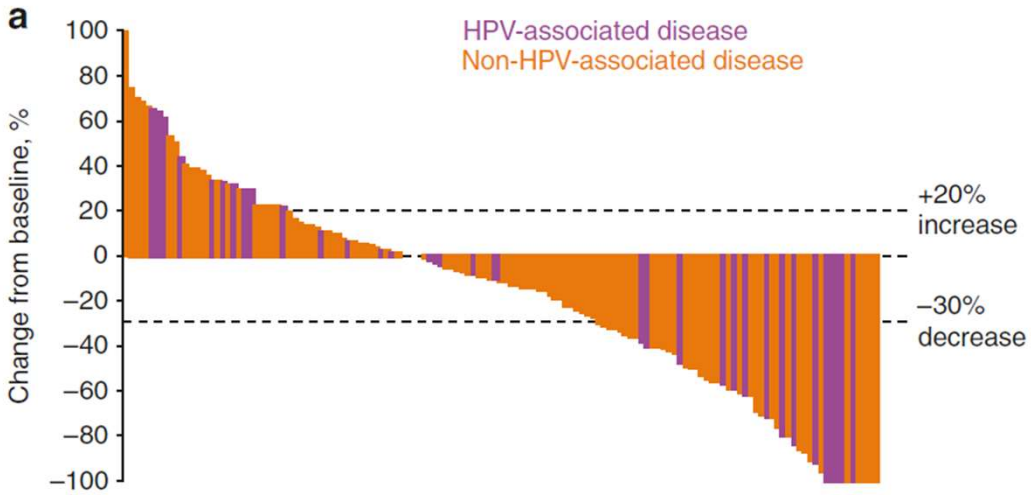
Secondary end points: ORR (investigator), PFS, OS, duration of response (DOR), ORR in HPV+ patients §

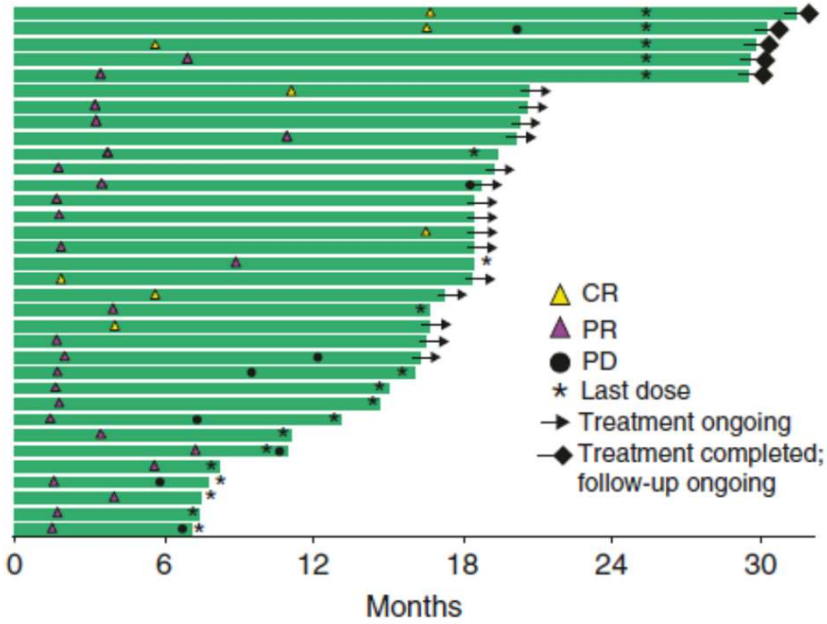
†Additional cohorts included bladder cancer, TN breast cancer, and gastric cancer.
‡Treatment beyond progression was allowed.
§ Initial cohort only.
*Median duration of disease not reached.

Seiwert, ASCO 2017.

KEYNOTE-012: Pembrolizumab in R/M HNSCC

Nonrandomized, Phase 1b Trial, Cohorts† B, B2





ORR 18% (13-24% CI)

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Mehra, Br J Can 2018.

KEYNOTE-040: Pembrolizumab vs Investigator's Choice in R/M HNSCC after Platinum Therapy

Phase III Randomized, Safety and Efficacy Trial

Key Eligibility Criteria

- SCC of the oral cavity, oropharynx, hypopharynx, or larynx
- PD after platinum regimen for R/M HNSCC or recurrence/PD within 3-6 months of multimodal therapy using platinum
- ECOG PS 0 or 1
- Known p16 status (oropharynx)
- Tissue sample for PD-L1 assessment

Stratification factor

- ECOG PS (0 vs 1)
- P16 status (positive vs negative)
- PD-L1 TPS (≥50% vs < 50%)

→ **R 1:1**

Pembrolizumab
200 mg IV Q3W for 2 yr

Vs.

Investigator's Choice

- Methotrexate 40 mg/m² IV QW
- Docetaxel 75 mg/m² IV Q3W
- Cetuximab 400 mg/m² IV once, then 250 mg/m² QW

Primary endpoint

- OS in total population

Secondary endpoints

- OS in PD-L1 CPS ≥ 1
- Total and PD-L1 CPS ≥ 1
  - Safety
  - PFS
  - ORR
  - DOR
  - Time to progression

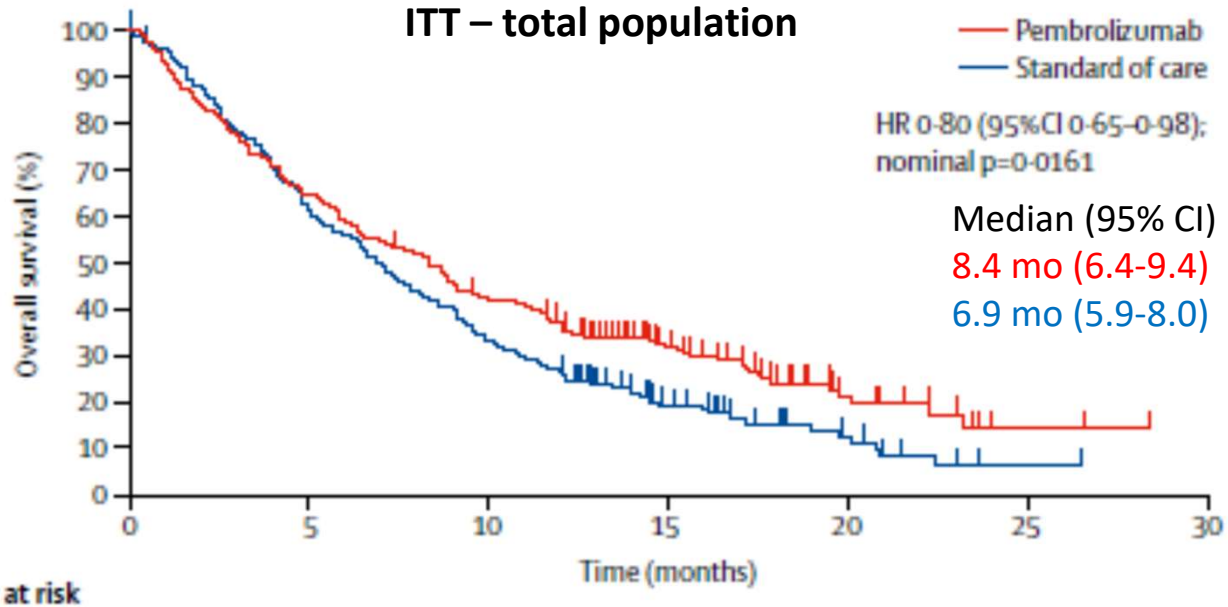
Exploratory end points

- OS and PFS in PD-L1 TPS ≥ 50 %

- Crossover not permitted

KEYNOTE-040: Pembrolizumab vs Investigator's Choice in R/M HNSCC after Platinum Therapy

Phase III Randomized, Safety and Efficacy Trial

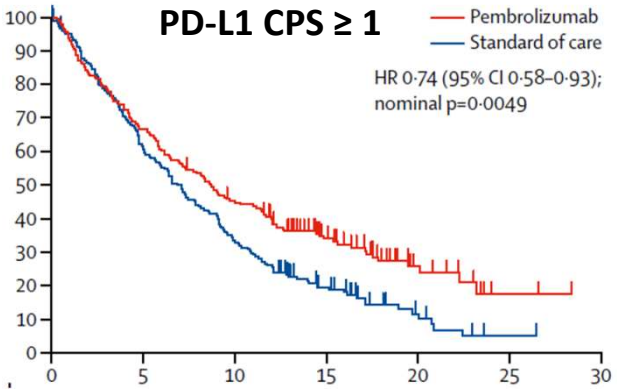


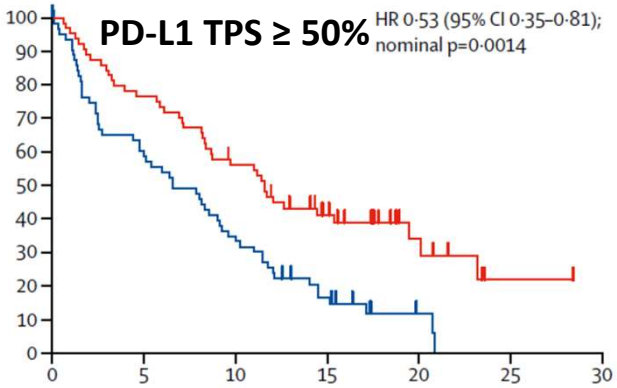
Number at risk (number censored)							
Pembrolizumab	247 (0)	160 (0)	103 (2)	48 (33)	14 (55)	2 (64)	0 (66)
Standard of care	248 (0)	151 (3)	82 (3)	34 (19)	10 (35)	1 (40)	0 (41)

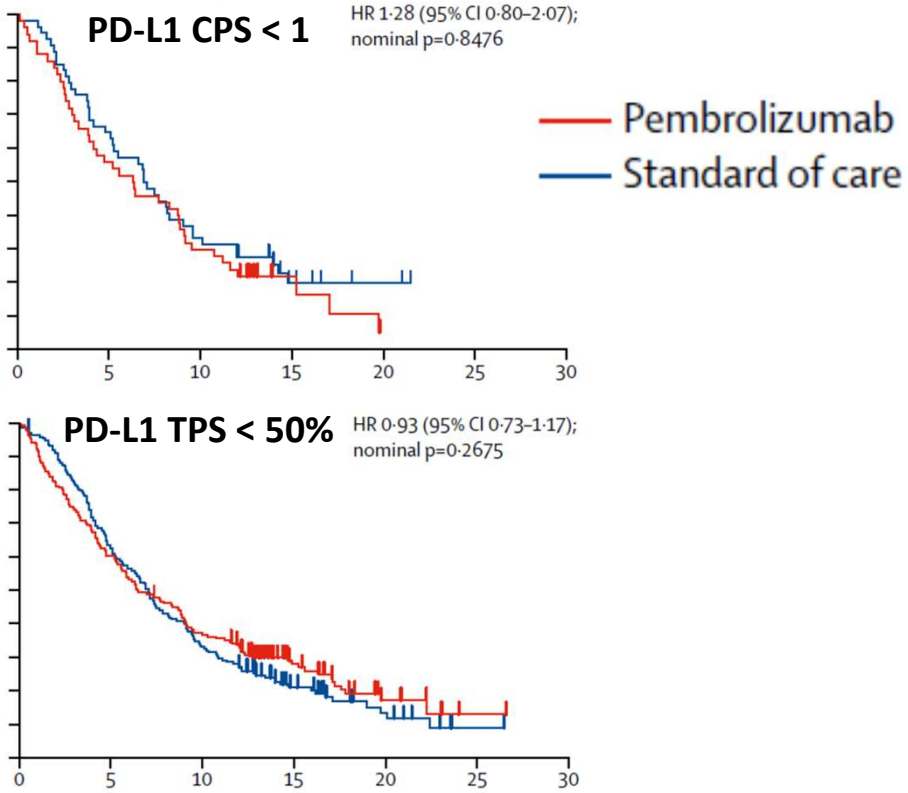
Cohen, Lancet 2019.

KEYNOTE-040: Pembrolizumab vs Investigator's Choice in R/M HNSCC after Platinum Therapy

Phase III Randomized, Safety and Efficacy Trial



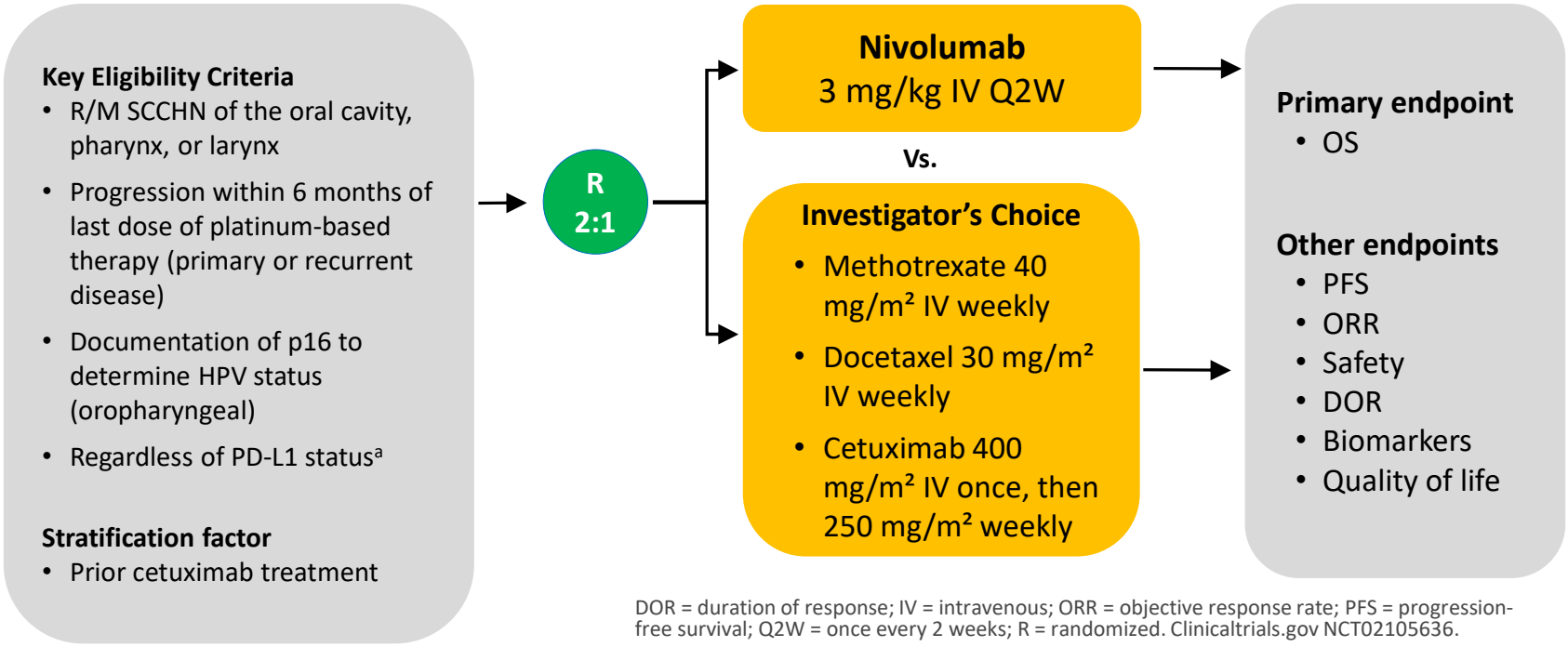




Cohen, Lancet 2019.

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

Phase III Randomized, Safety and Efficacy Trial



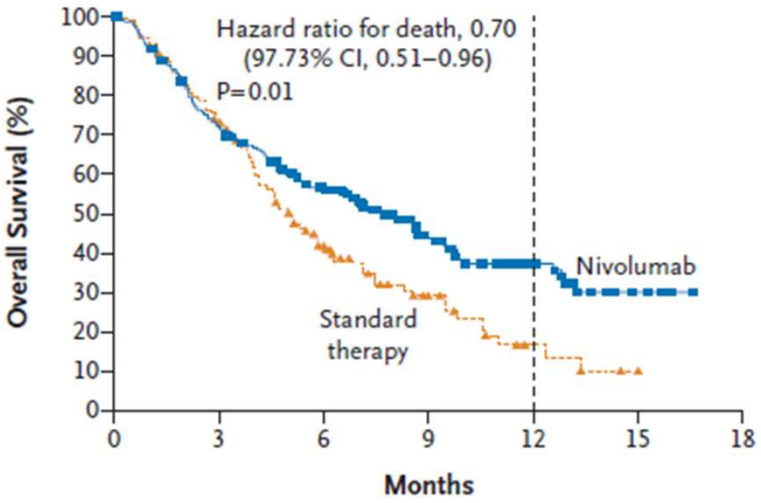
DOR = duration of response; IV = intravenous; ORR = objective response rate; PFS = progression-free survival; Q2W = once every 2 weeks; R = randomized. Clinicaltrials.gov NCT02105636.

[a]Tissue required for testing

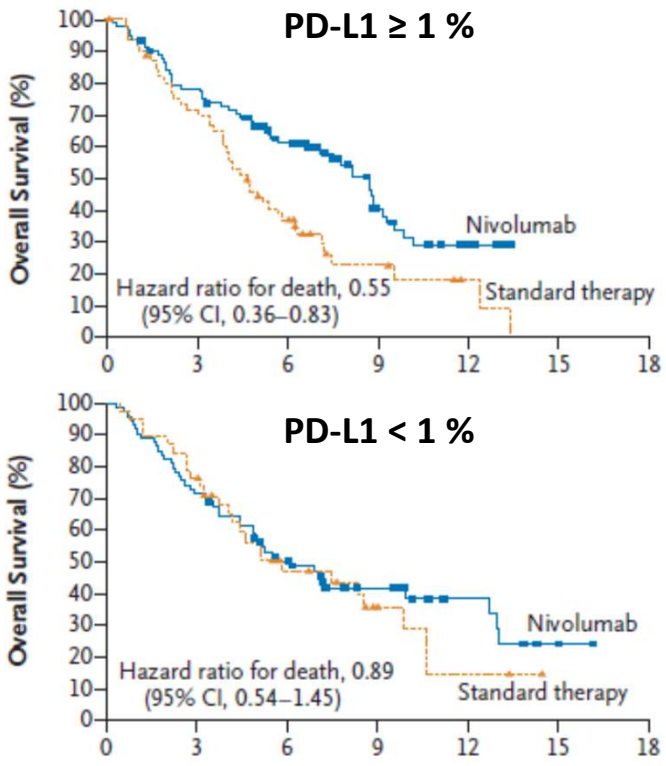
Ferris & Gillison, NEJM 2016.

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

	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)

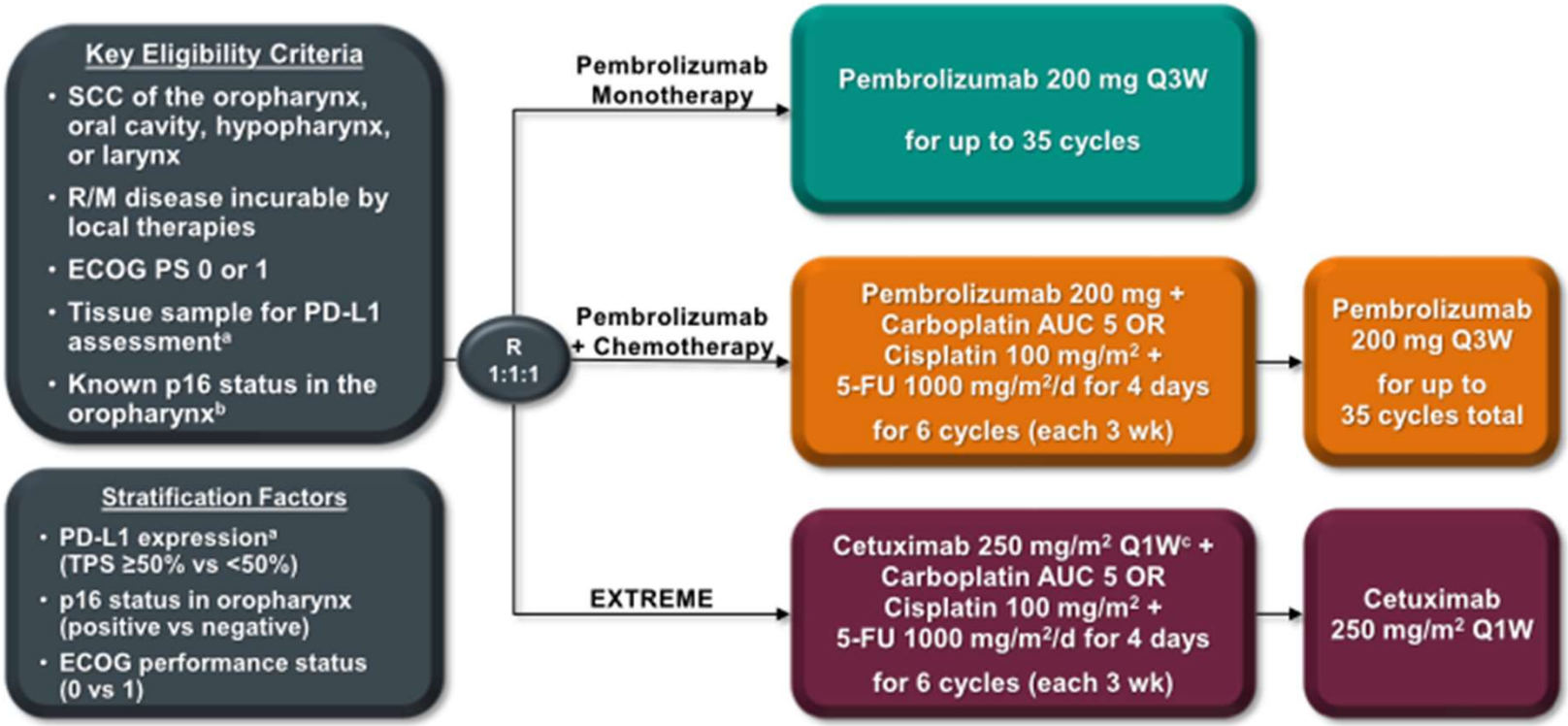


No. at Risk							
Nivolumab	240	167	109	52	24	7	0
Standard therapy	121	87	42	17	5	1	0



Ferris & Gillison, NEJM 2016.

KEYNOTE-048: Pembrolizumab +/- Chemotherapy in 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.

Burtness, Lancet 2019.

KEYNOTE-048: study end points

Primary

- CPS ≥20, CPS ≥1, and total populations
  - OS
  - PFS

Secondary

- CPS ≥20, CPS ≥1, and total populations
  - PFS rates at 6 and 12 months
  - ORR
  - QOL
- Total population
  - Safety and tolerability

Key exploratory

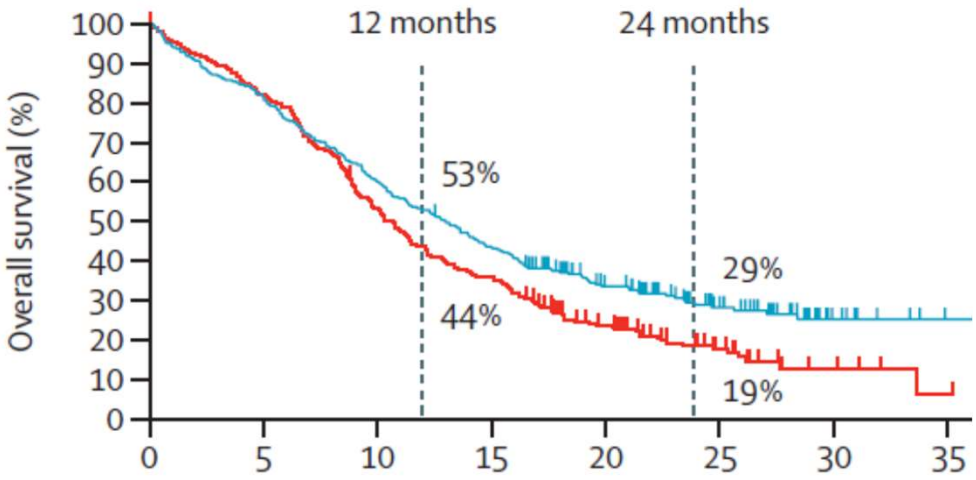
- CPS ≥20, CPS ≥1, and total populations
  - Duration of response

- Crossover not permitted

Burtness, Lancet 2019.

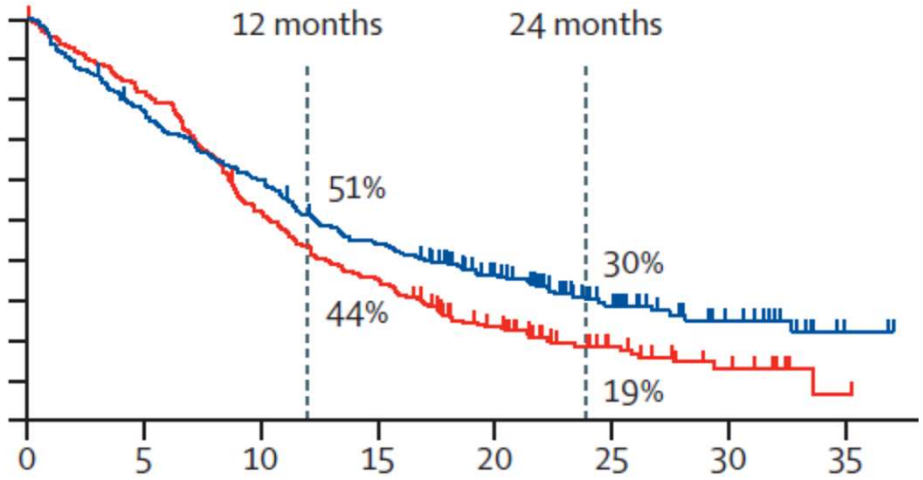
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in R/M HNSCC

OS, Pembro + chemo vs EXTREME, Total population



HR 0.77 (95% CI 0.63-0.93, p=0.0034)
Median (95% CI)
13.0 mo (10.9-14.7)
10.7 mo (9.3-11.7)

OS, Pembro vs EXTREME, PD-L1 CPS ≥ 1

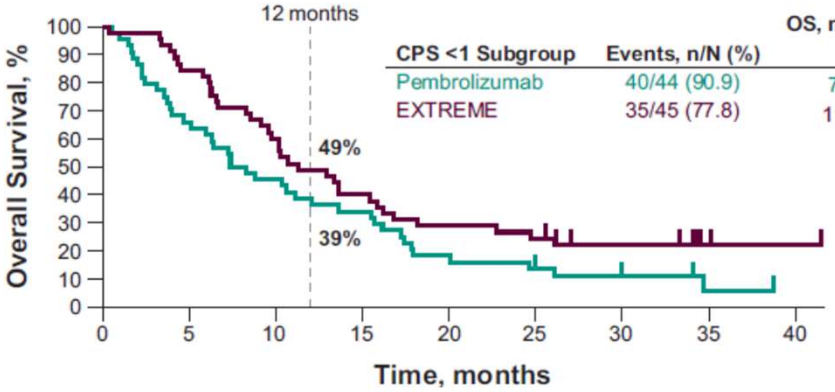


HR 0.78 (95% CI 0.64-0.96, p=0.0086)
Median (95% CI)
12.3 mo (10.8-14.9)
10.3 mo (9.0-11.5)

Burtness, Lancet 2019.

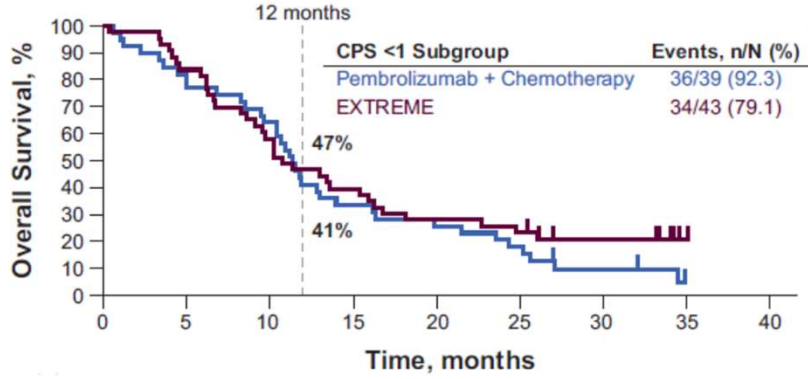
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in R/M HNSCC

Pembrolizumab vs EXTREME, PD-L1 CPS <1



CPS <1 Subgroup	Events, n/N (%)	OS, median (95% CI), months[b]	HR (95% CI)[c]
Pembrolizumab	40/44 (90.9)	7.9 (4.7-13.6)	1.51 (0.96-2.37)
EXTREME	35/45 (77.8)	11.3 (9.1-15.9)	

Pembrolizumab + Chemotherapy vs EXTREME, PD-L1 CPS <1

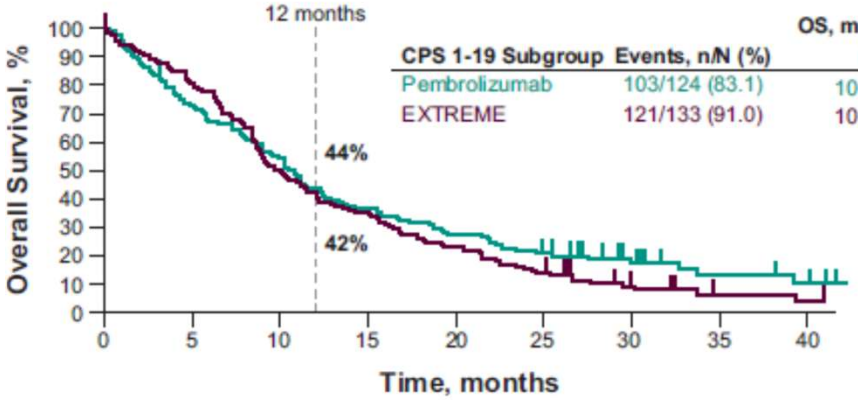


CPS <1 Subgroup	Events, n/N (%)	OS, median (95% CI), months[b]	HR (95% CI)[c]
Pembrolizumab + Chemotherapy	36/39 (92.3)	11.3 (9.5-14.0)	1.21 (0.76-1.94)
EXTREME	34/43 (79.1)	10.7 (8.5-15.9)	

Burtness, AACR 2020

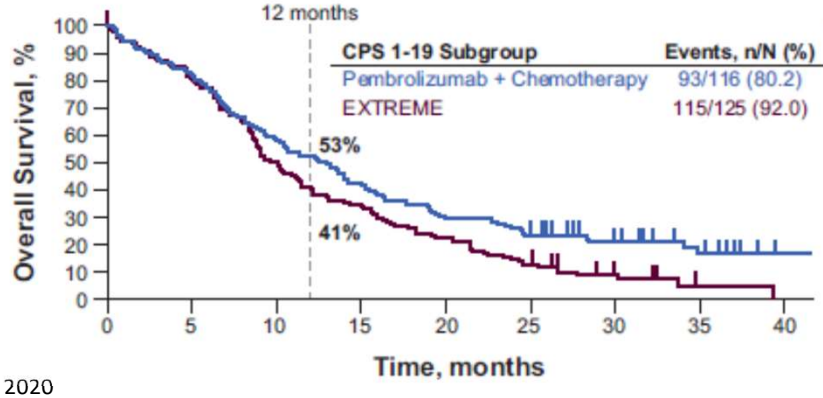
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in R/M HNSCC

Pembrolizumab vs EXTREME, PD-L1 CPS 1-19



CPS 1-19 Subgroup	Events, n/N (%)	OS, median (95% CI), months[b]	HR (95% CI)[c]
Pembrolizumab	103/124 (83.1)	10.8 (9.0-12.6)	0.86 (0.66-1.12)
EXTREME	121/133 (91.0)	10.1 (8.7-12.1)	

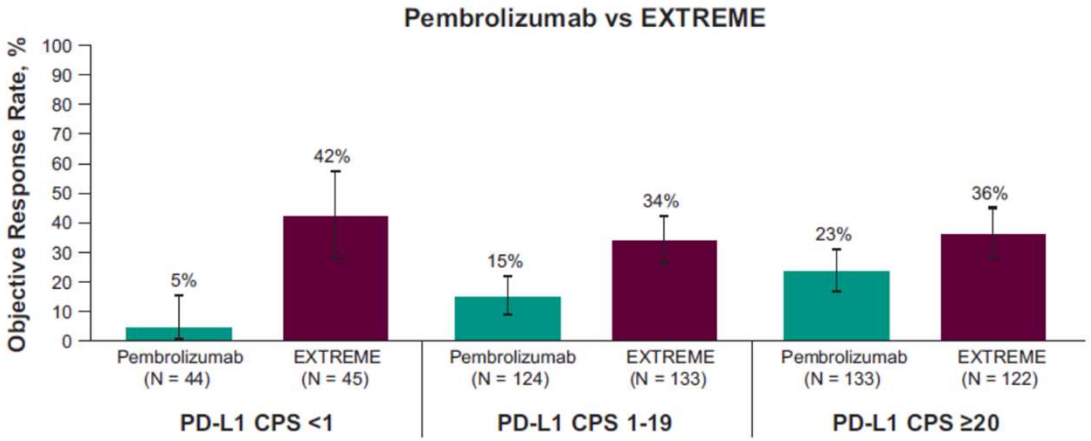
Pembrolizumab + Chemotherapy vs EXTREME, PD-L1 CPS 1-19

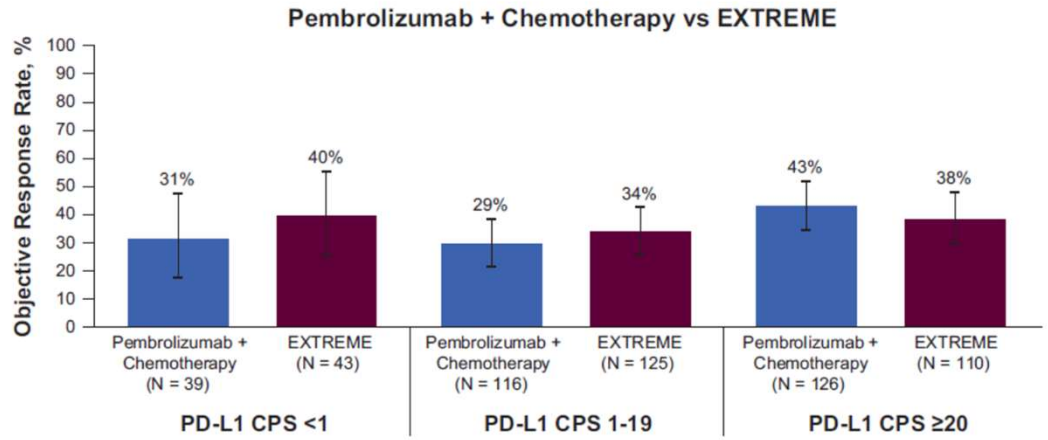


CPS 1-19 Subgroup	Events, n/N (%)	OS, median (95% CI), months[b]	HR (95% CI)[c]
Pembrolizumab + Chemotherapy	93/116 (80.2)	12.7 (9.4-15.3)	0.71 (0.54-0.94)
EXTREME	115/125 (92.0)	9.9 (8.6-11.5)	

Burtness, AACR 2020

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





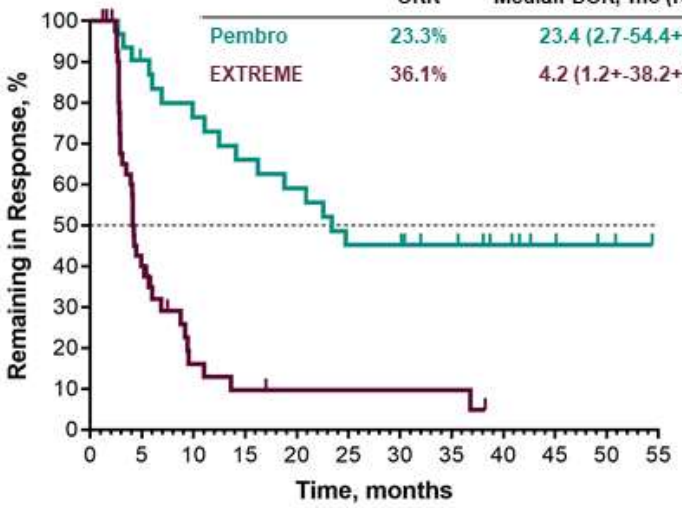
Burtness, AACR 2020

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

DOR: Pembrolizumab vs EXTREME

PD-L1 CPS ≥20

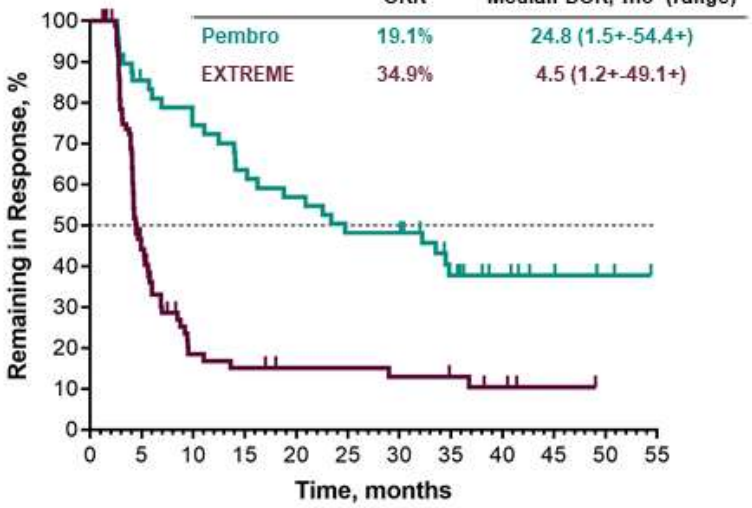
	ORR	Median DOR, mo (range
Pembro	23.3%	23.4 (2.7-54.4+)
EXTREME	36.1%	4.2 (1.2+-38.2+)



No. at Risk												
Pembro	31	26	22	19	17	13	13	10	7	4	2	0
EXTREME	44	16	5	3	2	2	2	2	0	0	0	0

PD-L1 CPS ≥1

	ORR	Median DOR, mo (range)
Pembro	19.1%	24.8 (1.5+-54.4+)
EXTREME	34.9%	4.5 (1.2+-49.1+)

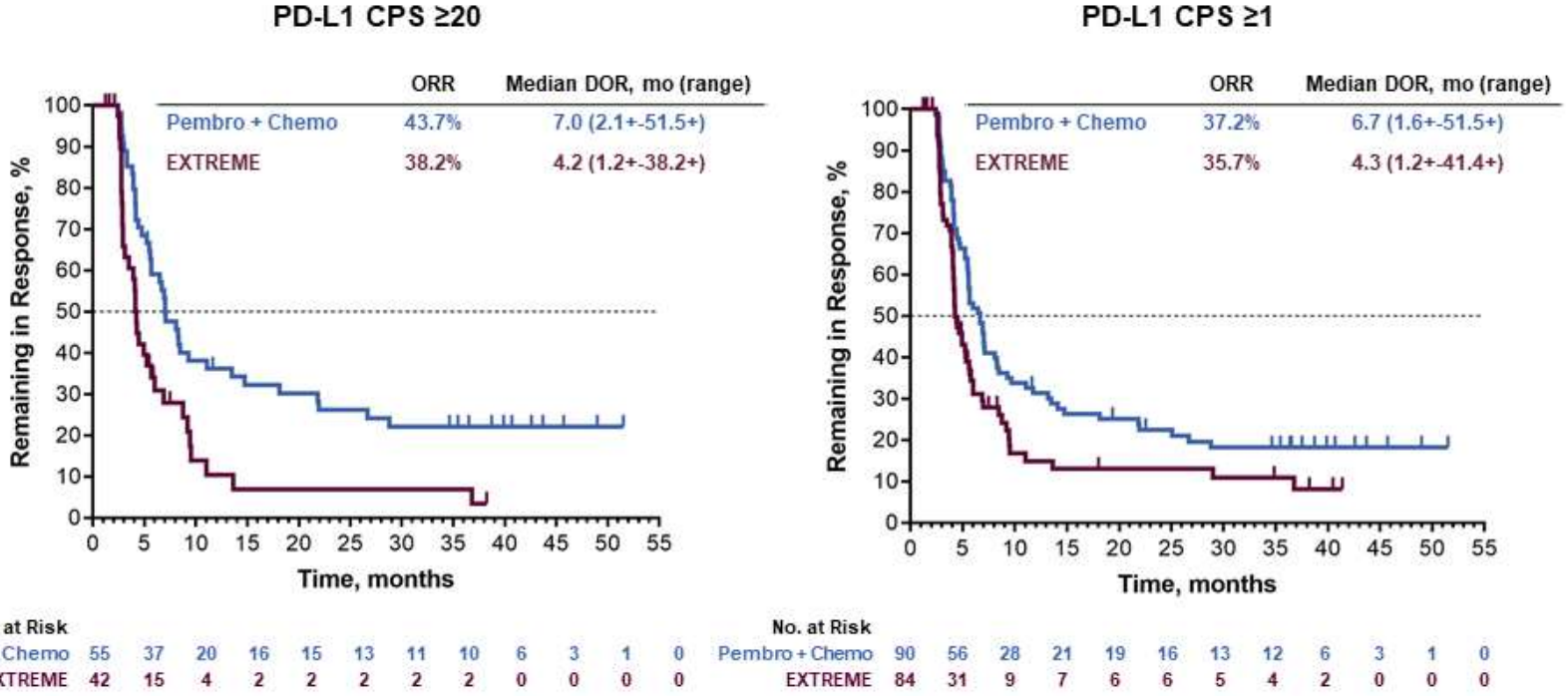


No. at Risk												
Pembro	49	39	34	29	26	22	22	14	8	5	2	0
EXTREME	89	34	11	9	7	7	6	5	3	1	0	0

Greil, ESMO 2020

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

DOR: Pembrolizumab + Chemo vs EXTREME



Greil, ESMO 2020

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

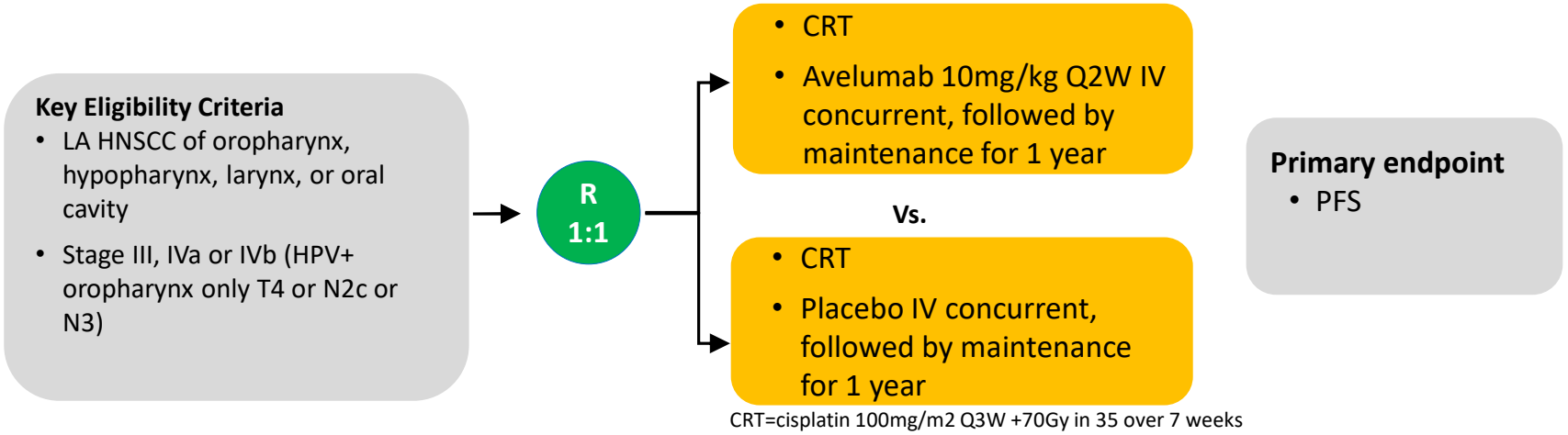
Safety

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%

Greil, ESMO 2020

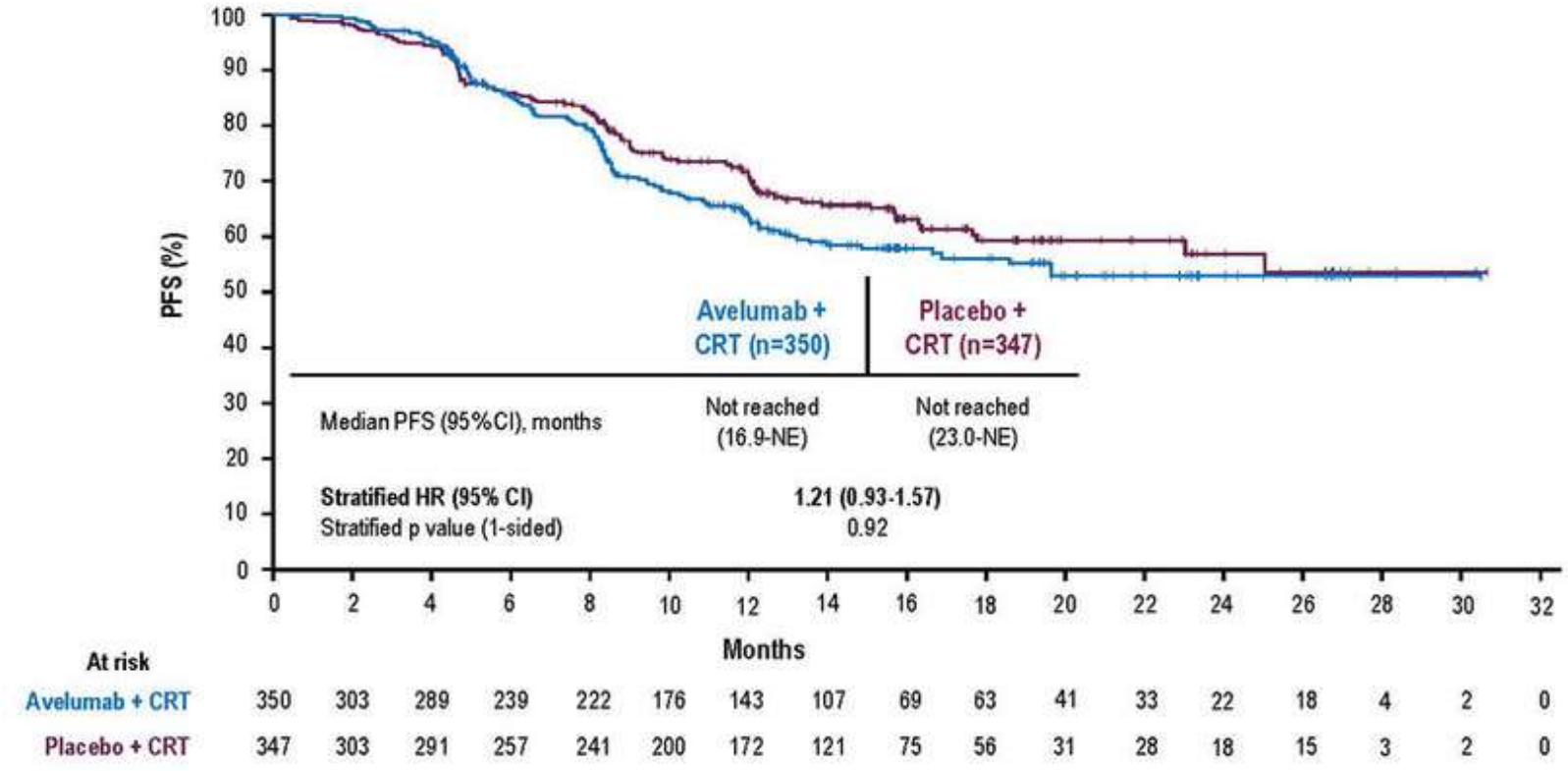
JAVELLIN Head & Neck 100



CRT=cisplatin 100mg/m2 Q3W +70Gy in 35 over 7 weeks

Cohen, ESMO 2020.

JAVELLIN Head & Neck 100



Cohen, ESMO 2020.

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 →

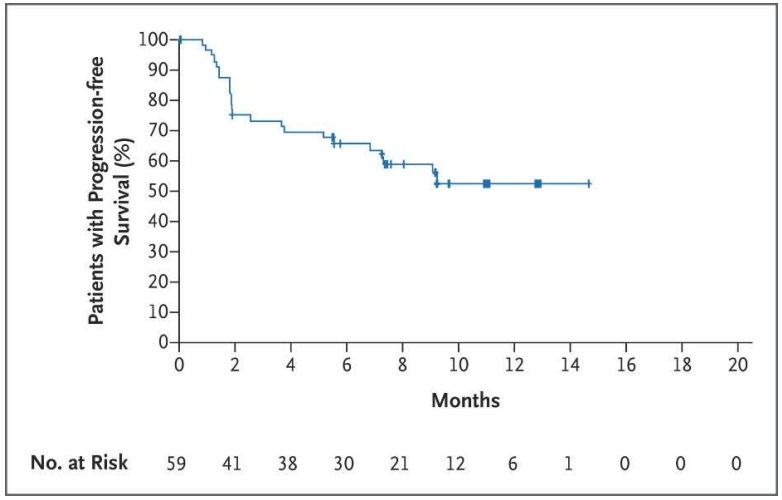
Primary endpoint
- Response rate

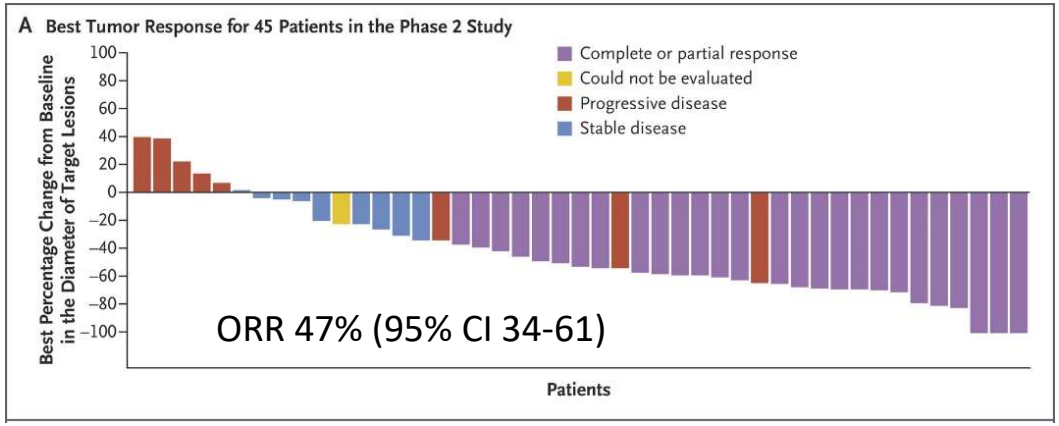
Other endpoints
- Duration of response
- PFS
- OS
- Side effects
- Durable disease control

Migden, NEJM 2018.

Cemiplimab in advanced/metastatic cutaneous squamous-cell carcinoma

Primary site of cutaneous squamous-cell carcinoma — no. (%)	Expansion Cohorts of the Phase 1 Study (N=26)	Metastatic-Disease Cohort of the Phase 2 Study (N=59)
Head or neck	18 (69)	38 (64)
Arm or leg	5 (19)	12 (20)
Trunk	2 (8)	9 (15)
Penis	1 (4)	0





Migden, NEJM 2018.

Conclusions

Drug	Approv	Indication
Pembrolizumab	2016	R/M HNSCC, progression on/after chemotherapy
Nivolumab	2016	R/M HNSCC, progression on/after chemotherapy
Cemiplimab	2018	Metastatic cutaneous squamous cell carcinoma, not candidate for curative therapies (any site)
Pembrolizumab + platinum + fluorouracil	2019	R/M HNSCC 1st line – all patients
Pembrolizumab	2019	R/M HNSCC 1st line – PD-L1 CPS ≥ 1

- Immunotherapy for H&N cancers
  - Indications in 1st and "2nd" line R/M HNSCC
  - Survival benefit
  - Better safety/tolerability than chemotherapy
- Ongoing areas of immunotherapy research include:
  - Neo-adjuvant/Adjuvant/CRT
  - PD-L1 negative populations?

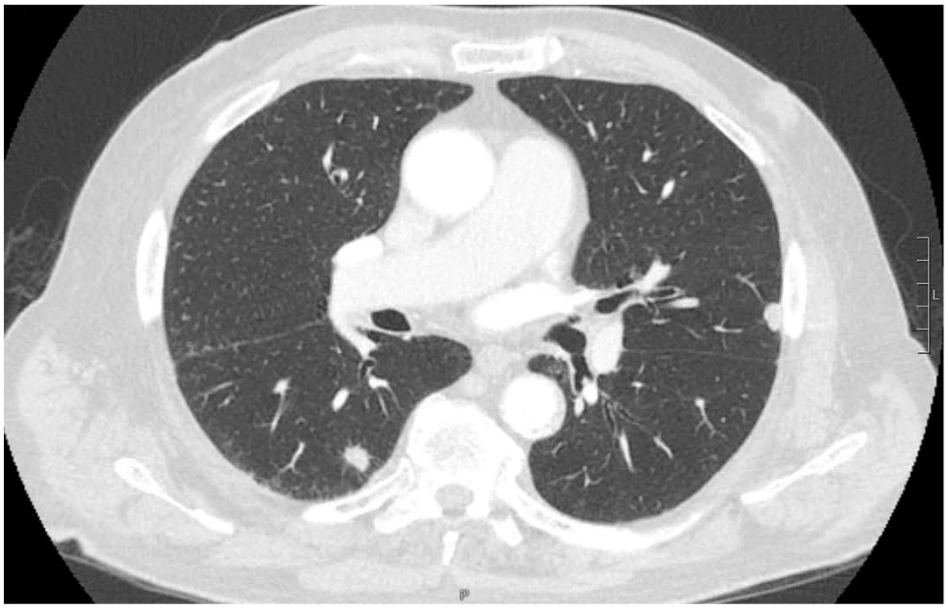
Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Case Study

Case Study

- 68M
- PmHx: COPD, HTN
- Social hx: 50 pack years, previous heavy ETOH use
- Oncologic hx:
  - November 2018: cT2N3b SCC of supraglottic larynx
  - January 2019: Definitive CRT with 3 high dose cisplatin, excellent response, surveillance follow-up
  - January 2020: 2 new lung nodules, 12mm and 17mm, not accessible for easy biopsy
  - April 2020: further growth of the 2 nodules, no other disease
  - July 2020: SBRT to lung nodules

October 2020: response in SBRT treated nodules, but multiple new lung nodules (7) and mediastinal adenopathy



Clinical status: grade 1 fatigue, dry cough, ECOG 1

Case Study

- What is the next step in the management of this patient?
  - A) Start chemotherapy
  - B) Obtain more information
  - C) Observation
  - D) More SBRT

Case Study

- Systemic treatment is discussed and the patient is interested in pursuing treatment
- Biopsy specimen from initial diagnosis is available (Nov 2018) and submitted for PD-L1 testing
  - CPS 1-19%

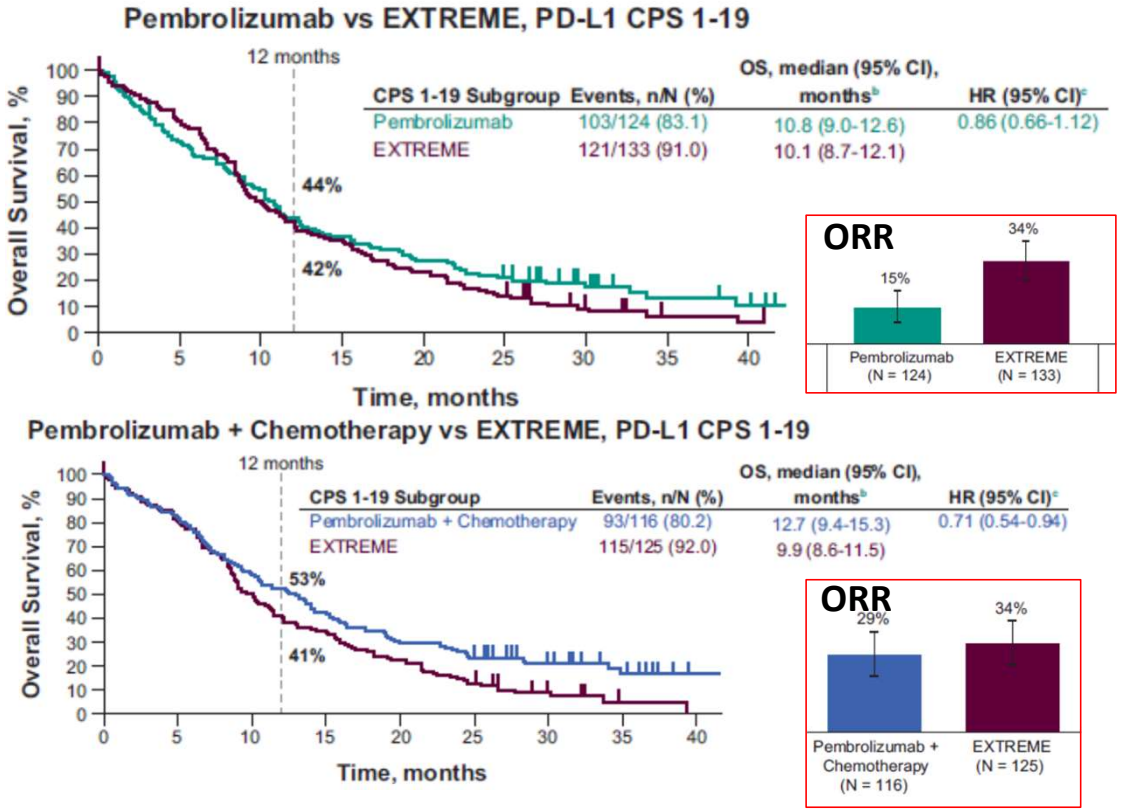
Case Study

- What systemic treatment would you start?
  - A) Chemotherapy alone (carbo/taxol in Canadian context)
  - B) Pembrolizumab alone
  - C) Pembrolizumab + platinum/5-Fu
  - D) Clinical trial

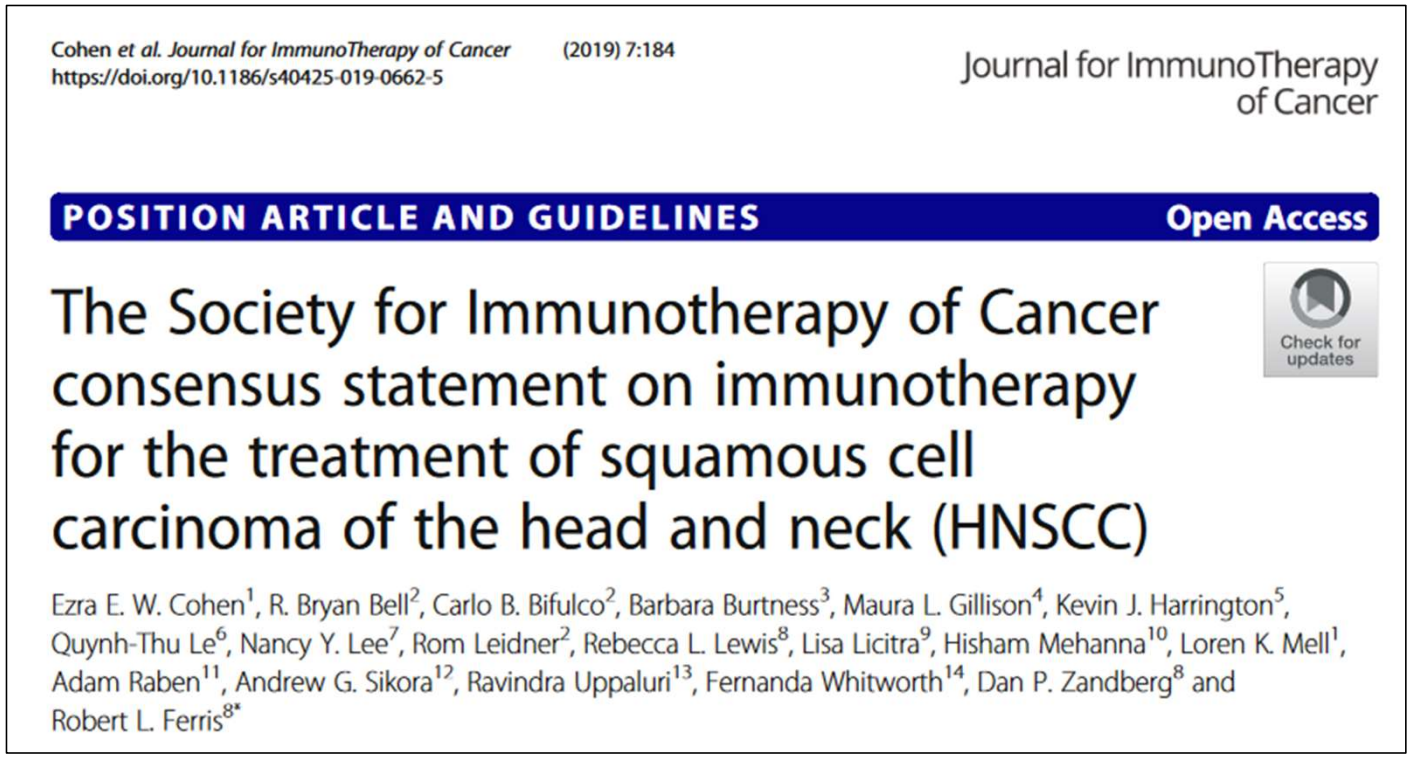
Case Study

	Pembrolizumab	Pembrolizumab + platinum/5-FU
Pro	1) Well tolerated 2) Once q3 weeks	1) Higher response rate 2) OS benefit?
Con	1) Lower response rate	1) Higher risk of AEs 2) 4 day 5-FU infusion

Patient elects to go onto a clinical trial



Resources



Cohen *et al. Journal for ImmunoTherapy of Cancer* (2019) 7:184
https://doi.org/10.1186/s40425-019-0662-5

Journal for ImmunoTherapy of Cancer

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*]