Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy for the Treatment of Head and Neck Cancer

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ACCC Association of Community Cancer Centers

Society for Immunotherapy of Cancer

Disclosures

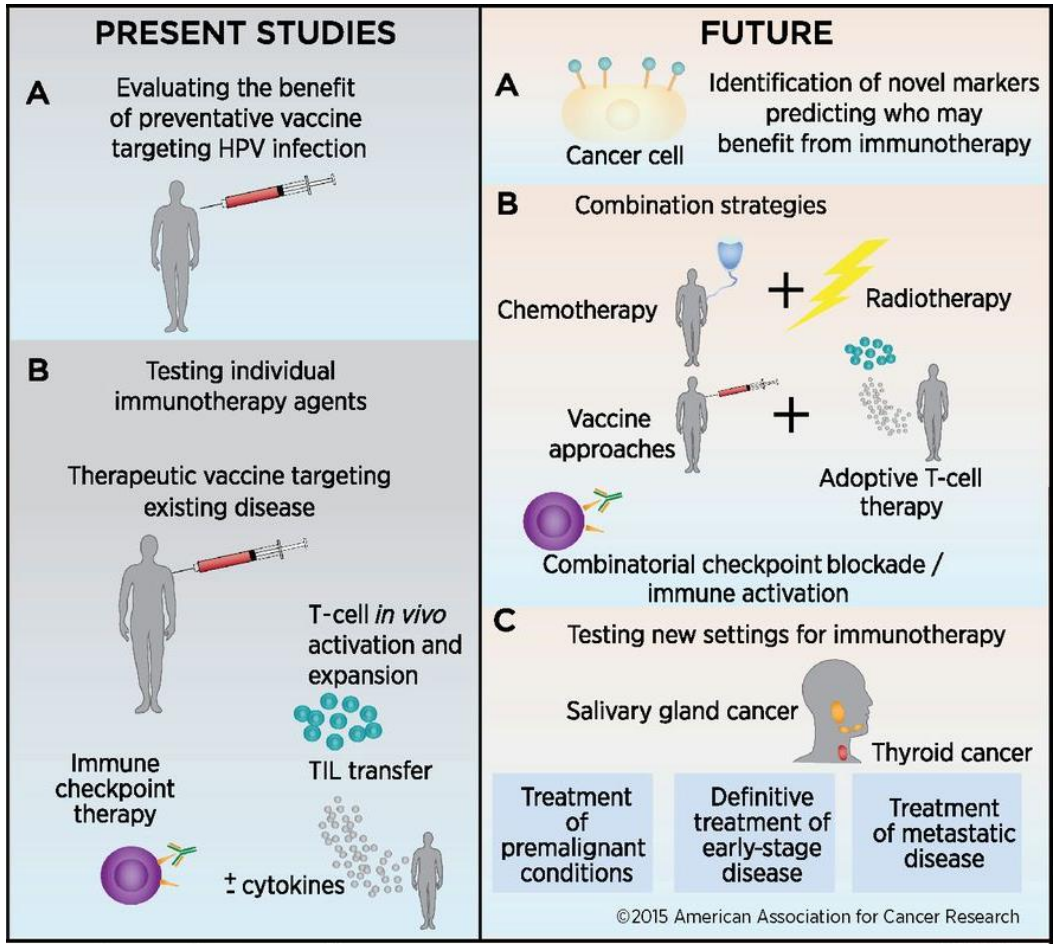
- Disclosures:

  Advisory board honoraria: MERCK, BAYER, EISAI

- I will not be discussing non-FDA approved indications during my presentation.

Immunotherapy for the Treatment of Head and Neck Cancers

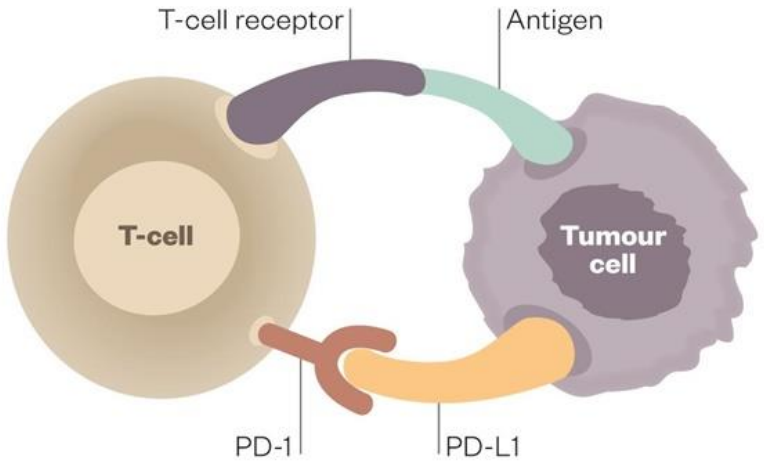
- Immuno-Oncology (I-O) developments in treatment of head and neck cancers
  - Expression of immunologic markers to guide treatment
  - Preventive vaccination against virally mediated cancers
  - PD-1 checkpoint inhibitors for the treatment of metastatic disease



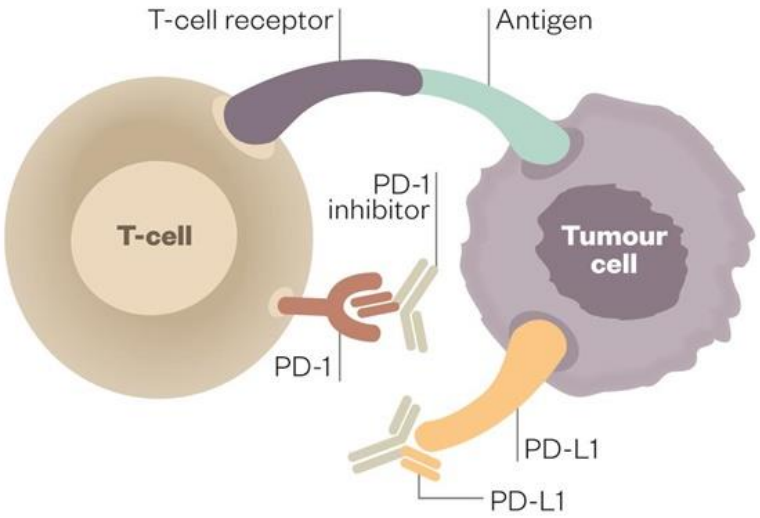
Schoenfeld JD, Cancer Immunol Res, 2015

Immunotherapy for the Treatment of Head and Neck Cancers

Immune Checkpoint Inhibitors (ICI)



PD-1 acts as “off-switch” for T cells, allowing cancer cells to evade immune attack



Antibodies against PD-1 and PD-L1 boost the immune response against cancer cells

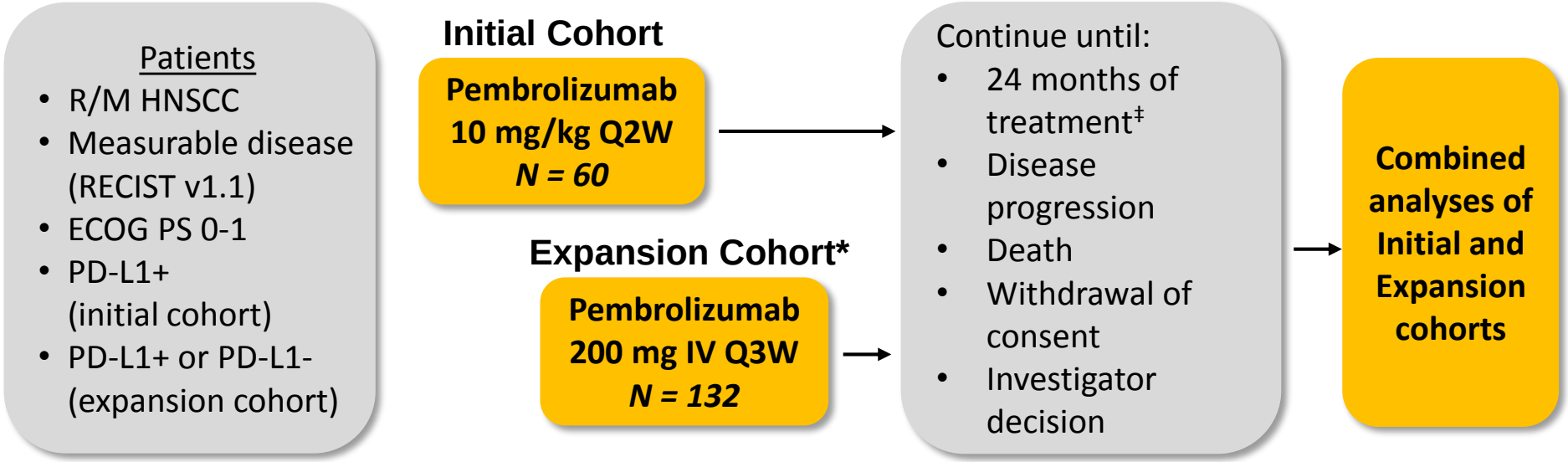
FDA-approved Checkpoint Inhibitors for Use in Head and Neck Cancers

- Pembrolizumab 200 mg IV Q3W(anti-PD-1)
  - KEYNOTE – 012/055: Patients with recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (HNSCC) with disease progression on or after platinum-containing chemotherapy
  - Accelerated Approval by FDA – August 5, 2016

- Nivolumab 240 mg IV Q2W or 480 mg IV Q4W (anti-PD-1)
  - CheckMate – 141: Patients with R/M HNSCC with disease progression on or after a platinum-based therapy
  - Breakthrough Therapy Designation by FDA – April, 2016
  - Approval – November 10, 2016

KEYNOTE-012: Pembrolizumab in R/M HNSCC

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



Response assessment: Every 8 weeks until disease progression

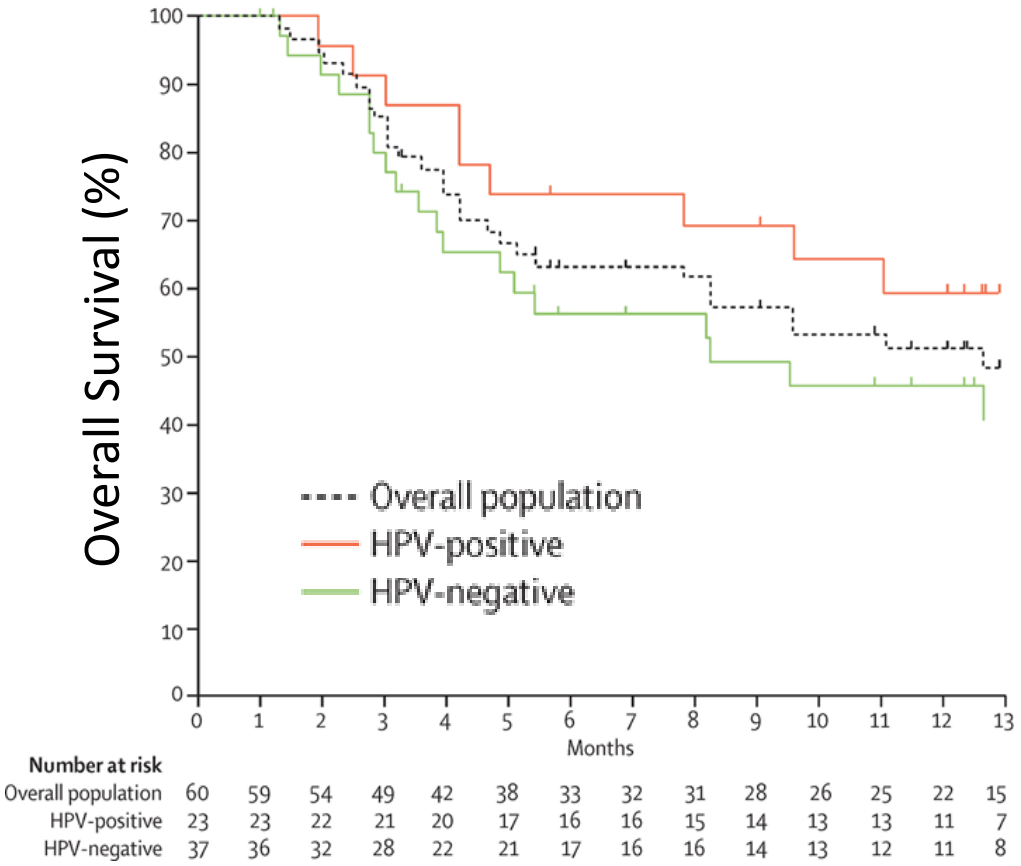
Primary end points: ORR (RECIST v1.1, central imaging vendor review), safety

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.

KEYNOTE-012: Pembrolizumab in R/M HNSCC

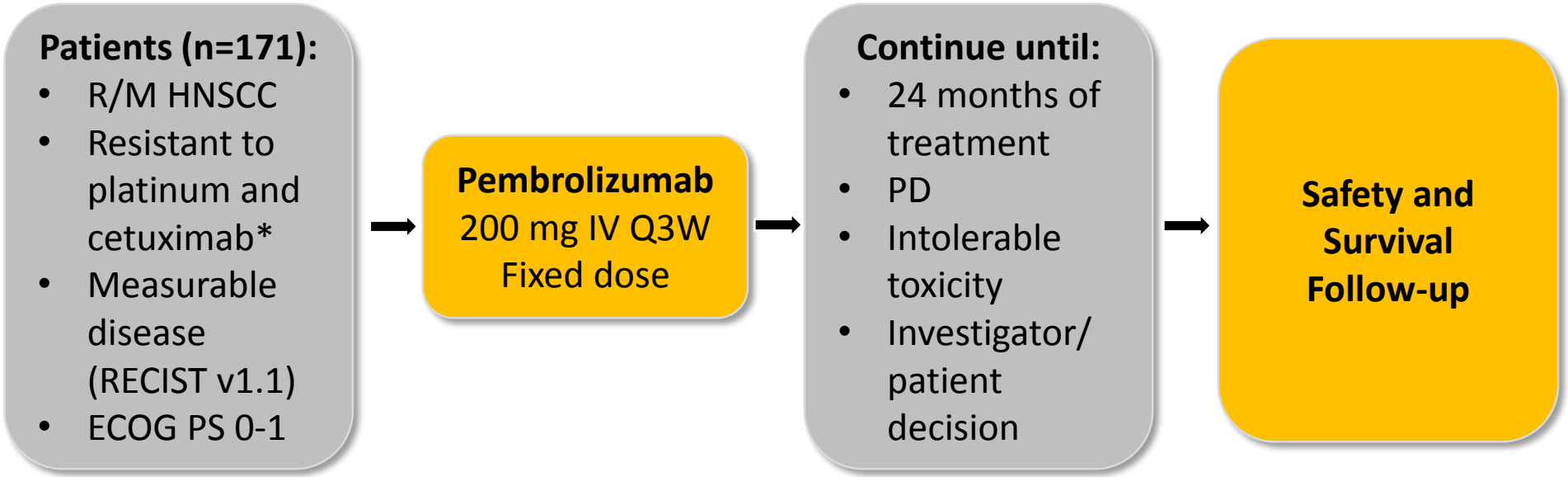
Nonrandomized, Phase 1b Trial, Cohorts† B, B2



- ORR = 18%
  - CR = 4%
  - PR = 14%
- mOS = 8.0 months
- mPFS = 2.2 months

KEYNOTE-055: Pembrolizumab in R/M HNSCC after Progression on Platinum/Cetuximab

Phase II Trial, Single Arm



Bauml J JCO 2017

Response assessment: Imaging every 6 to 9 weeks (central radiology review)

Primary end points: ORR (RECIST v1.1) by Response Evaluation Criteria in Solid Tumors and safety

Secondary end points: ORR (RECIST v1.1) in all dosed patients, ORR for HPV+, PD-L1+, DOR, PFS, OS

*75% of patients had ≥ 2 prior lines of therapy for metastatic disease

KEYNOTE-055: Pembrolizumab in R/M HNSCC after Progression on Platinum/Cetuximab

Phase II Trial, Single Arm

Outcome	All Patients	HPV Status		PD-L1 Status		
	N=171	Positive n=37	Negative n=131	≥1% n=140	<1% n=26	≥50% n=48
ORR, %	16	16	15	18	12	27
mPFS, mo	2.1					
6-mo PFS,%	23	25	21	24	20	31
6-mo OS, %	59	72	55	59	56	60

Bauml J, et al, J Clin Oncol. 2017

- Neither tumor PD-L1 expression or HPV status are sufficiently robust in guiding the use of pembrolizumab at this time.

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.

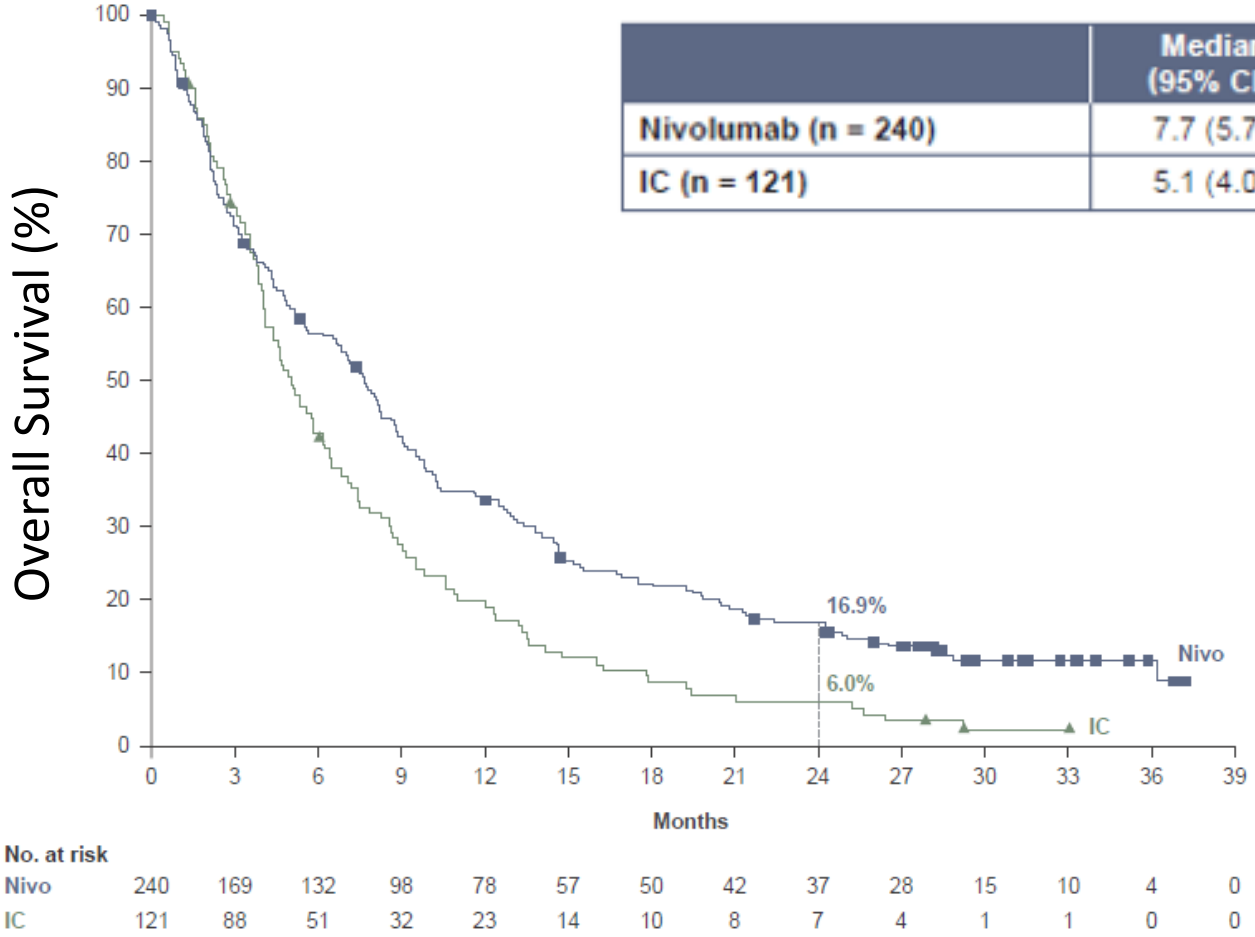
[a]Tissue required for testing

Ferris & Gillison, NEJM, 2016

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

Overall Survival: 2 year report

	Median OS (95% CI), mo	HR (95% CI)
Nivolumab (n = 240)	7.7 (5.7–8.8)	0.68 (0.54–0.86)
IC (n = 121)	5.1 (4.0–6.2)	

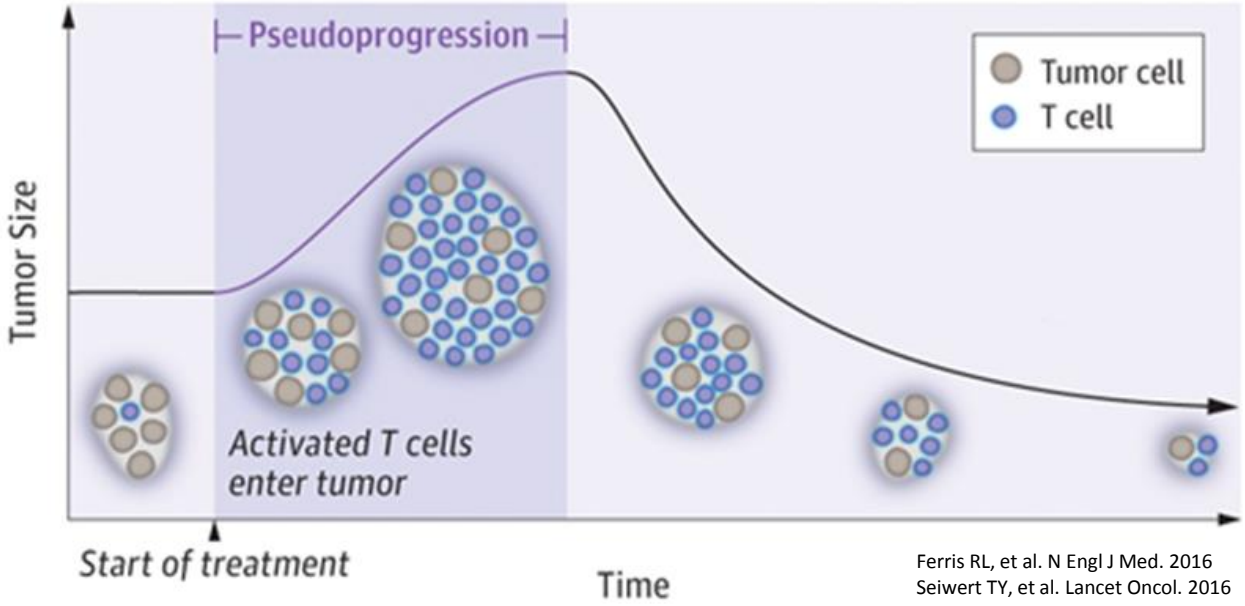


Ferris RL. Oral Oncology, 2018

Response to Immune Checkpoint Inhibitor Treatment with Brief Increase in Tumor Size

Pseudoprogression

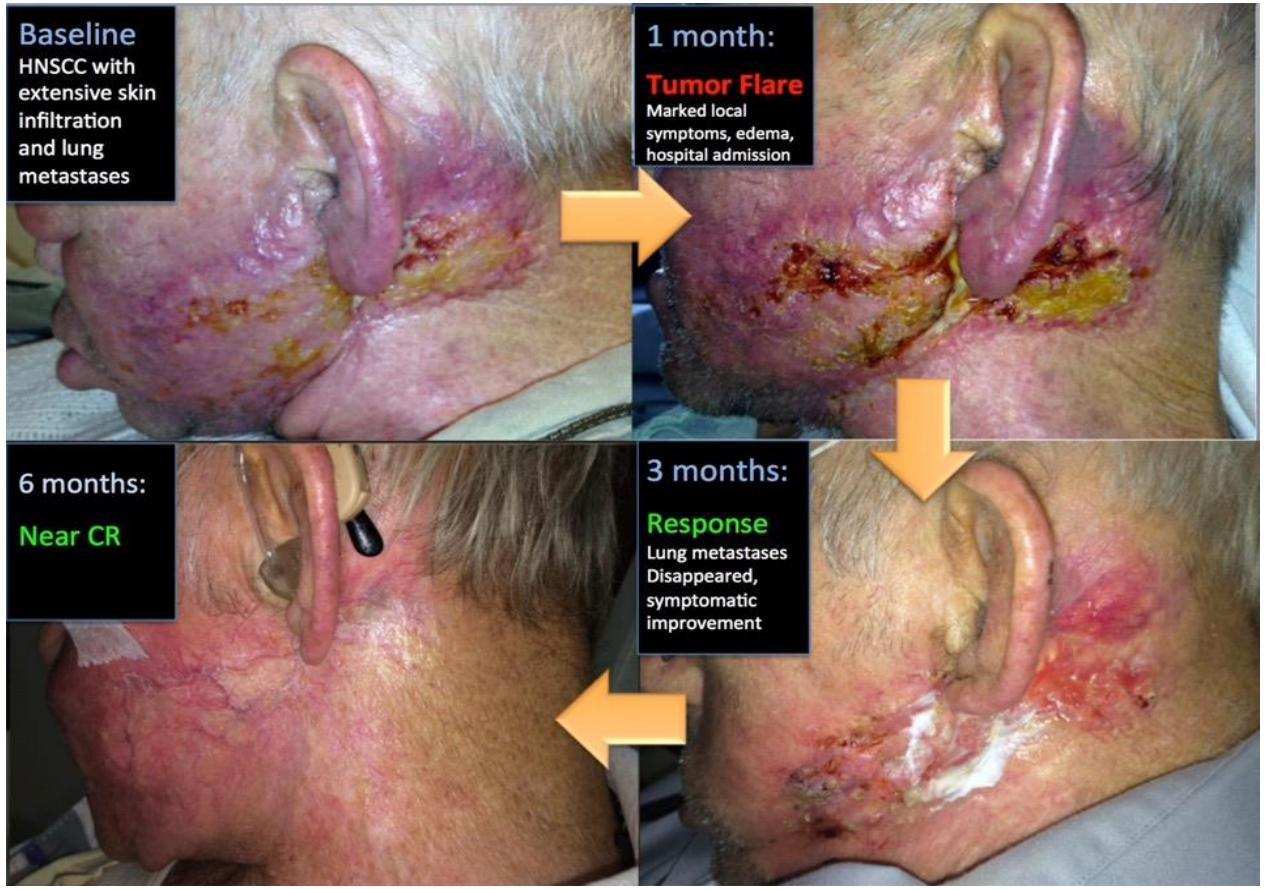
- Early appearance of an increase in tumor burden, subsequently followed by tumor regression
- Initially recognized in the melanoma trials, with incidence up to 10%



Ferris RL, et al. N Engl J Med. 2016
Seiwert TY, et al. Lancet Oncol. 2016

Response to Immune Checkpoint Inhibitor Treatment with Brief Increase in Tumor Size

Case Report – KEYNOTE-012



- Both KEYNOTE-012 and CheckMate 141 trials showed an exceedingly rare rate of pseudoprogression with pembrolizumab and nivolumab, respectively.

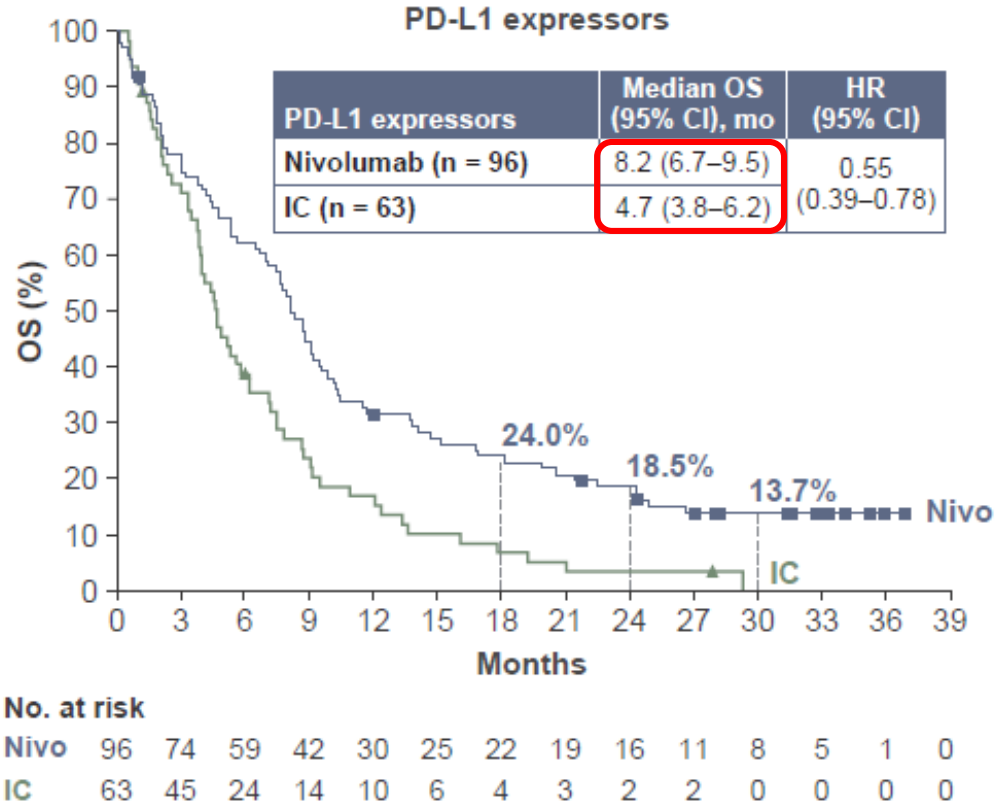
Ferris RL, et al. N Engl J Med. 2016
Seiwert TY, et al. Lancet Oncol. 2016

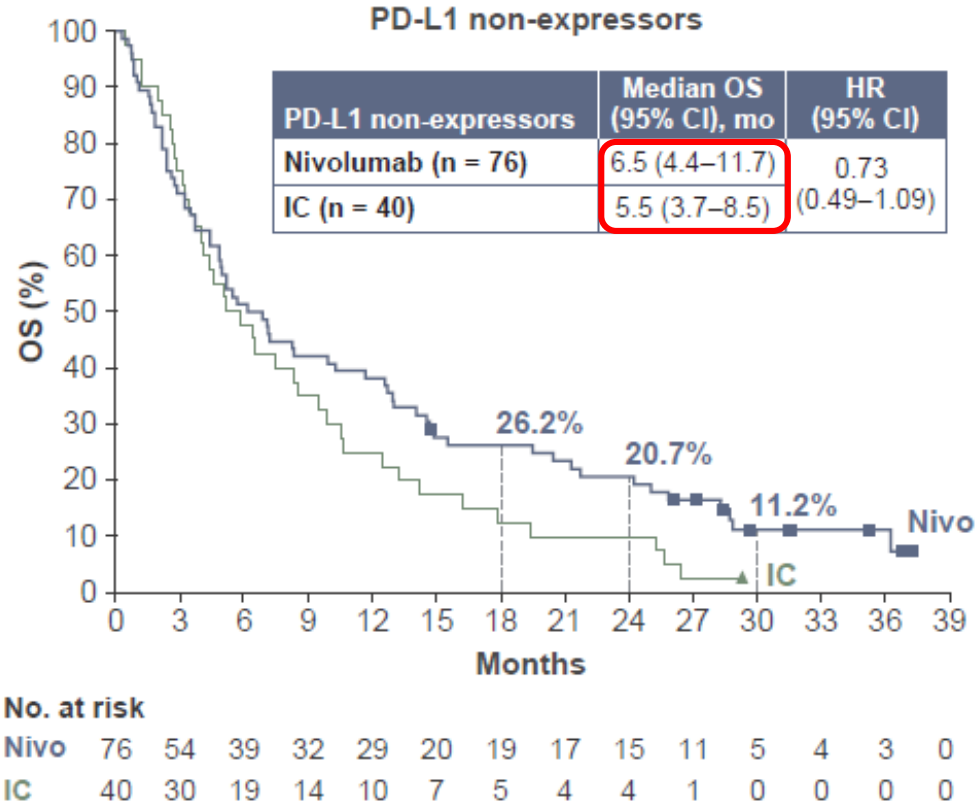
Evaluating Biomarkers in HNSCC

- Current FDA approvals of pembrolizumab and nivolumab are NOT contingent upon tumor PD-L1 status
  - KEYNOTE - 012/055: Response rates not significantly different on the basis of tumor PD-L1 staining
  - KEYNOTE - 040: Phase III pembrolizumab vs. investigator's choice chemotherapy
    - Did not meet survival endpoints in total population but improved outcomes in patients with PD-L1 expressing tumor
  - CheckMate 141: Most benefit was seen in PD-L1-positive tumors

Evaluating Biomarkers in HNSCC

CheckMate 414: 2 year update





Immune-related Adverse Events

KEYNOTE 012

Table 2. Treatment-Related Adverse Events by Grade Severity (all-patients-as-treated population; N = 132)

Treatment-Related Adverse Event	Grade 1 or 2 (≥ 10% of patients), No. (%)	Grade 3 (any occurrence), No. (%)	Grade 4 (any occurrence), No. (%)
Patients with ≥ 1 event	70 (53)	8 (6)	4 (3)
Hypothyroidism	14 (11)	0	0
Immune thrombocytopenic purpura	0	0	1 (1)
Abdominal pain	1 (1)	1 (1)	0
Colitis	0	1 (1)	0
Dysphagia	1 (1)	1 (1)	0
Nausea	6 (5)	1 (1)	0
Stomatitis	1 (1)	1 (1)	0
Facial edema	0	1 (1)	0
Fatigue	28 (21)	0	0
Localized edema	0	1 (1)	0
Infection	0	1 (1)	0
Decreased appetite	9 (7)	2 (2)	0
Dehydration	0	1 (1)	0
Diabetic ketoacidosis	0	0	1 (1)
Hyperglycemia	1 (1)	0	1 (1)
Type I diabetes mellitus	0	1 (1)	0
Laryngeal edema	0	0	1 (1)
Pneumonitis	2 (2)	2 (2)	0
Respiratory distress	0	1 (1)	0
Facial swelling	3 (2)	1 (1)	1 (1)

CheckMate 141

Event	Nivolumab (N=236)	
	Any Grade	Grade 3 or 4
Any event	139 (58.9)*	31 (13.1)
Fatigue	33 (14.0)	5 (2.1)
Nausea	20 (8.5)	0
Rash	18 (7.6)	0
Decreased appetite	17 (7.2)	0
Pruritus	17 (7.2)	0
Diarrhea	16 (6.8)	0
Anemia	12 (5.1)	3 (1.3)
Asthenia	10 (4.2)	1 (0.4)
Vomiting	8 (3.4)	0
Dry skin	7 (3.0)	0
Stomatitis	5 (2.1)	1 (0.4)
Weight loss	4 (1.7)	0
Mucosal inflammation	3 (1.3)	0
Peripheral neuropathy	1 (0.4)	0
Alopecia	0	0
Neutropenia	0	0

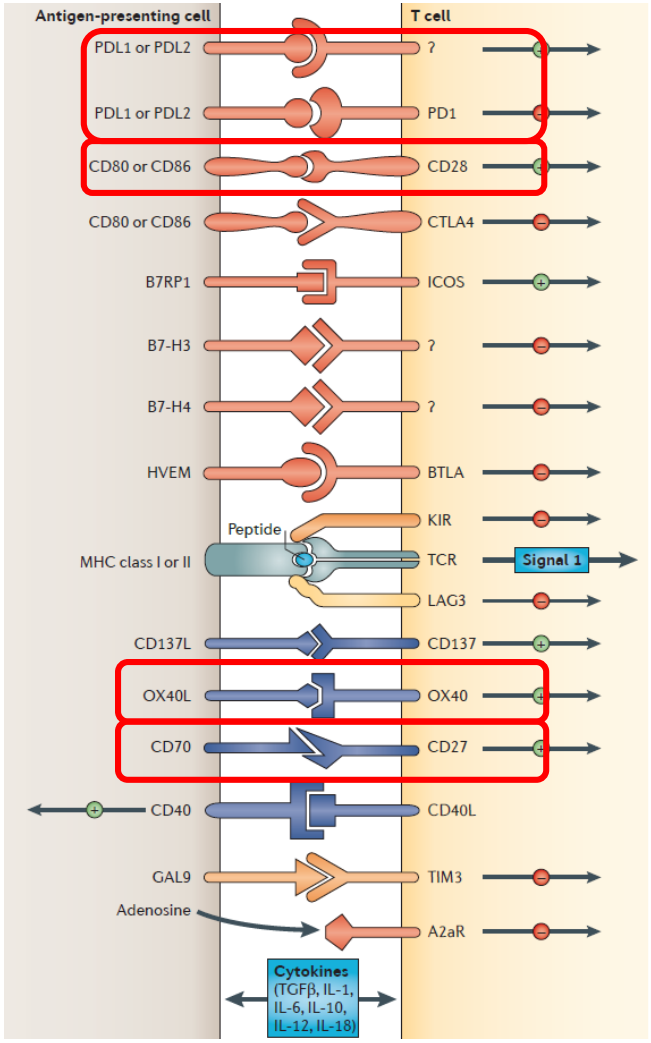
Immune-related Adverse Events

Table 2 General guidance for corticosteroid management of immune-related adverse events

Grade of immune-related AE (CTCAE/equivalent)	Corticosteroid management	Additional notes
1	• Corticosteroids not usually indicated	• Continue immunotherapy
2	• If indicated, start oral prednisone 0.5-1 mg/kg/day if patient can take oral medication. • If IV required, start methylprednisolone 0.5-1 mg/kg/day IV • If no improvement in 2–3 days, increase corticosteroid dose to 2 mg/kg/day • Once improved to ≤grade 1 AE, start 4–6 week steroid taper	• Hold immunotherapy during corticosteroid use • Continue immunotherapy once resolved to ≤grade 1 and off corticosteroids • Start proton pump inhibitor for GI prophylaxis
3	• Start prednisone 1-2 mg/kg/day (or equivalent dose of methylprednisolone) • If no improvement in 2–3 days, add additional/alternative immune suppressant • Once improved to ≤ grade 1, start 4–6-week steroid taper • Provide supportive treatment as needed	• Hold immunotherapy; if symptoms do not improve in 4–6 weeks, discontinue immunotherapy • Consider intravenous corticosteroids • Start proton pump inhibitor for GI prophylaxis • Add PCP prophylaxis if more than 3 weeks of immunosuppression expected (>30 mg prednisone or equivalent/day)
4	• Start prednisone 1-2 mg/kg/day (or equivalent dose of methylprednisolone) • If no improvement in 2–3 days, add additional/alternative immune suppressant, e.g., infliximab • Provide supportive care as needed	• Discontinue immunotherapy • Continue intravenous corticosteroids • Start proton pump inhibitor for GI prophylaxis • Add PCP prophylaxis if more than 3 weeks of immunosuppression expected (>30 mg prednisone or equivalent/day)

Puzanov Journal for ImmunoTherapy of Cancer 2017

Developmental Immunotherapies for HNSCC



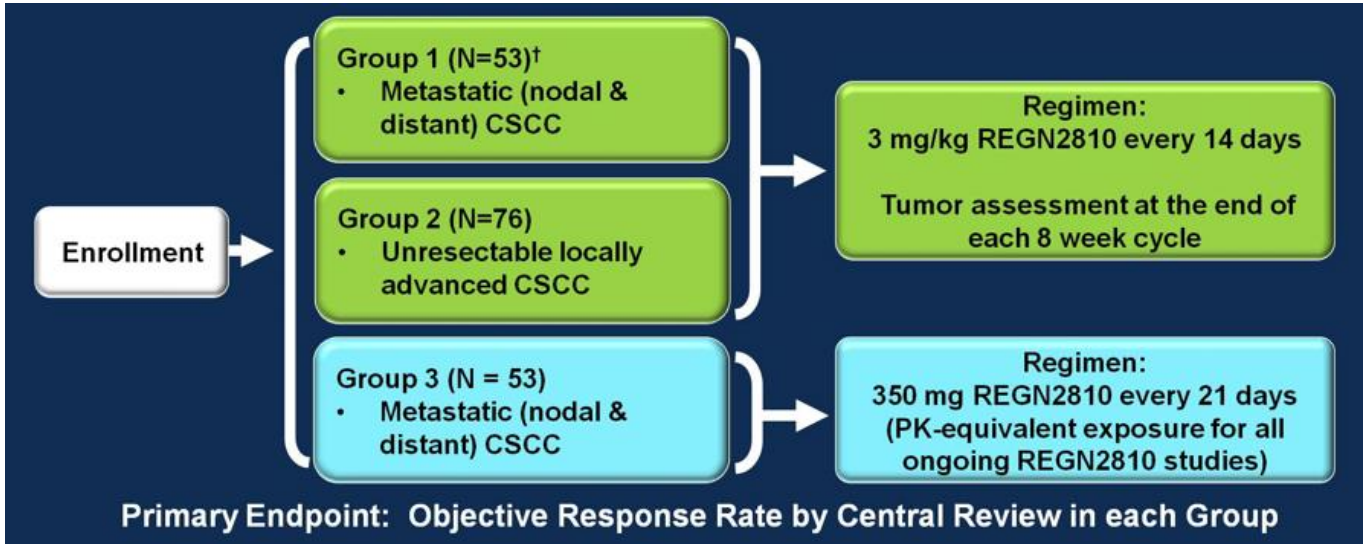
Pardoll DM Nature 2012

- Durvalumab, atezolizumab, avelumab, CK-301 (anti-PD-L1)
- Cemiplimab (anti-PD-1)
- Ipilimumab, tremelimumab (anti-CTLA-4)
- Varlilumab (anti-CD27)
- PF-04518600, tavolimab (anti-OX40)

Developmental Immunotherapies for HNSCC

Cemiplimab (REGN2810) for treatment of patients with cutaneous squamous cell carcinoma (cSCC)

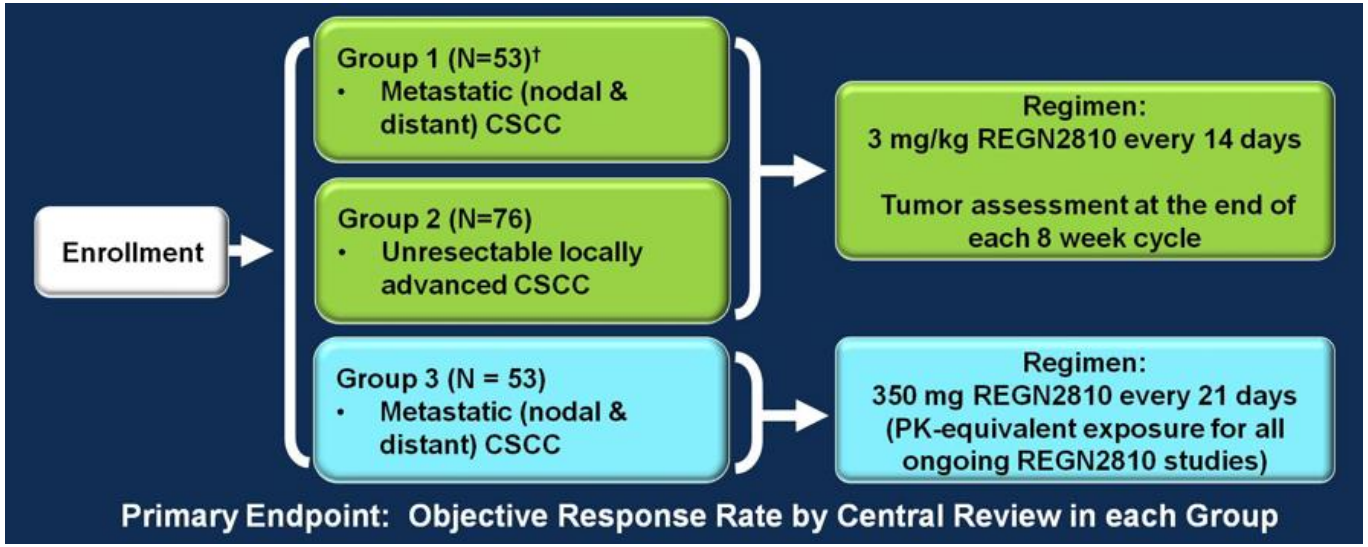
NCT02760498



- Largest prospective study in this disease
- ORR 46% in 82 patients in study
  - Much higher than RR in mucosal HNSCC as per KEYNOTE and CheckMate studies
- Responses durable, median DOR not reached
- Study ongoing

FDA approves cemiplimab for R/M cSCC

Cemiplimab (REGN2810) was FDA approved for treatment of patients with cutaneous squamous cell carcinoma (cSCC)



- FDA approval was based on clinically meaningful and durable objective response rates
- 75/108 M cSCC / 33/108 LA cSCC
- ORR 47% (4% CR / 44% PR)
- 75/108 M cSCC - RR47%
- 33/108 LA cSCC – RR -49%
- 350mg IV Q3W (30min)FDA approved dose

Recently reported Immunotherapies for HNSCC

KEYNOTE – 048 (NCT02358031)

Key Eligibility Criteria

- R/M SCCHN of the oropharynx, oral cavity, hypopharynx, or larynx considered incurable by local therapies
- No prior systemic therapy in the R/M setting
- ECOG 0-1
- Results from HPV testing (oropharyngeal)
- Tissue for PD-L1 biomarker analysis

→ R 1:1:1 →

Pembrolizumab 200 mg IV Q3W

Vs.

Pembrolizumab + Platinum + 5-FU

Vs.

Cetuximab + Platinum + 5-FU

Primary endpoint

- PFS
- OS

Other endpoints

- PFS at 6 months
- ORR
- Biomarkers
- Quality of life

Study End Points: Pembrolizumab vs EXTREME and Pembrolizumab + Chemotherapy vs EXTREME

Primary

- CPS ≥20,[a] CPS ≥1,[a] and total populations
  - OS
  - PFS[b]

Secondary

- CPS ≥20,[a] CPS ≥1,[a] and total populations
  - PFS[b] rates at 6 and 12 mo
  - ORR[b]
  - Change from baseline and time to deterioration in quality of life (EORTC QLQ-C30 and H&N-35)[c]
- Total population
  - Safety and tolerability

Key Exploratory

- CPS ≥20,[a] CPS ≥1,[a] and total populations
  - Duration of response[b]

[a]Assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay. CPS = combined positive score = number of PD-L1–positive cells (tumor cells, lymphocytes, macrophages) divided by total number of tumor cells × 100.
[b]Assessed per RECIST v1.1 by blinded, independent central review.

KEYNOTE-048 Study Design (NCT02358031)

Key Eligibility Criteria

- SCC of the oropharynx, oral cavity, hypopharynx, or larynx
- R/M disease incurable by local therapies
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment[a]
- Known p16 status in the oropharynx[b]

Stratification Factors

- PD-L1 expression[a] (TPS ≥50% vs <50%)
- p16 status in oropharynx (positive vs negative)
- ECOG performance status (0 vs 1)

R (1:1:1)

Pembrolizumab 200 mg Q3W

for up to 35 cycles

Pembrolizumab 200 mg + Carboplatin AUC 5 OR Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days

for 6 cycles (each 3 wk)

Pembrolizumab 200 mg Q3W

for up to 29 cycles

Cetuximab 250 mg/m² Q1W[c] + Carboplatin AUC 5 OR Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days

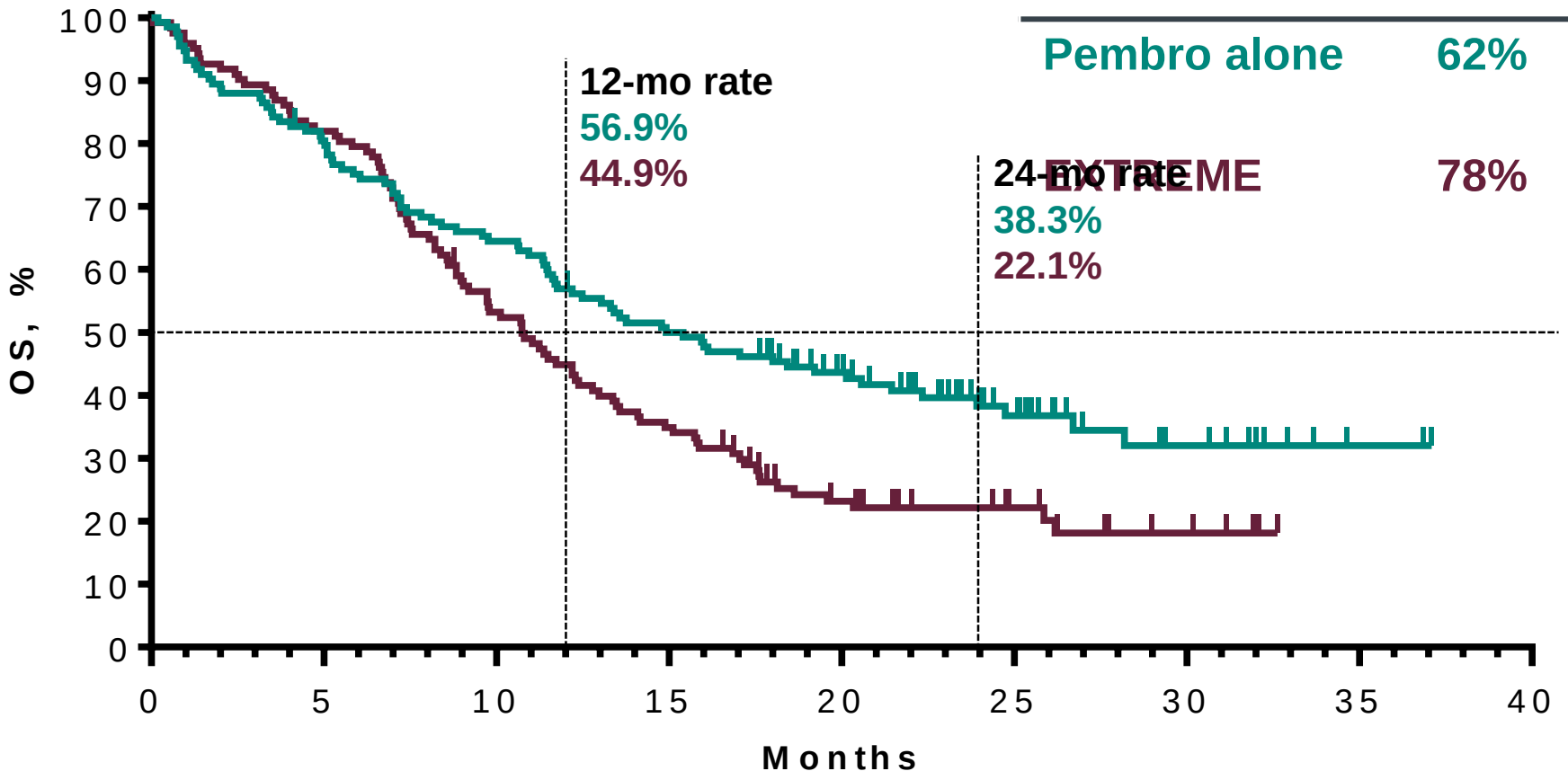
for 6 cycles (each 3 wk)

Cetuximab 250 mg/m² Q1W

[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.

Overall Survival: P vs E, CPS ≥20 Population

	Events	HR (95% CI)	*P*
Pembro alone	62%	0.61 (0.45-0.83)	0.0007
EXTREME	78%		



Median (95% CI)
14.9 mo (11.6-21.5)
10.7 mo (8.8-12.8)

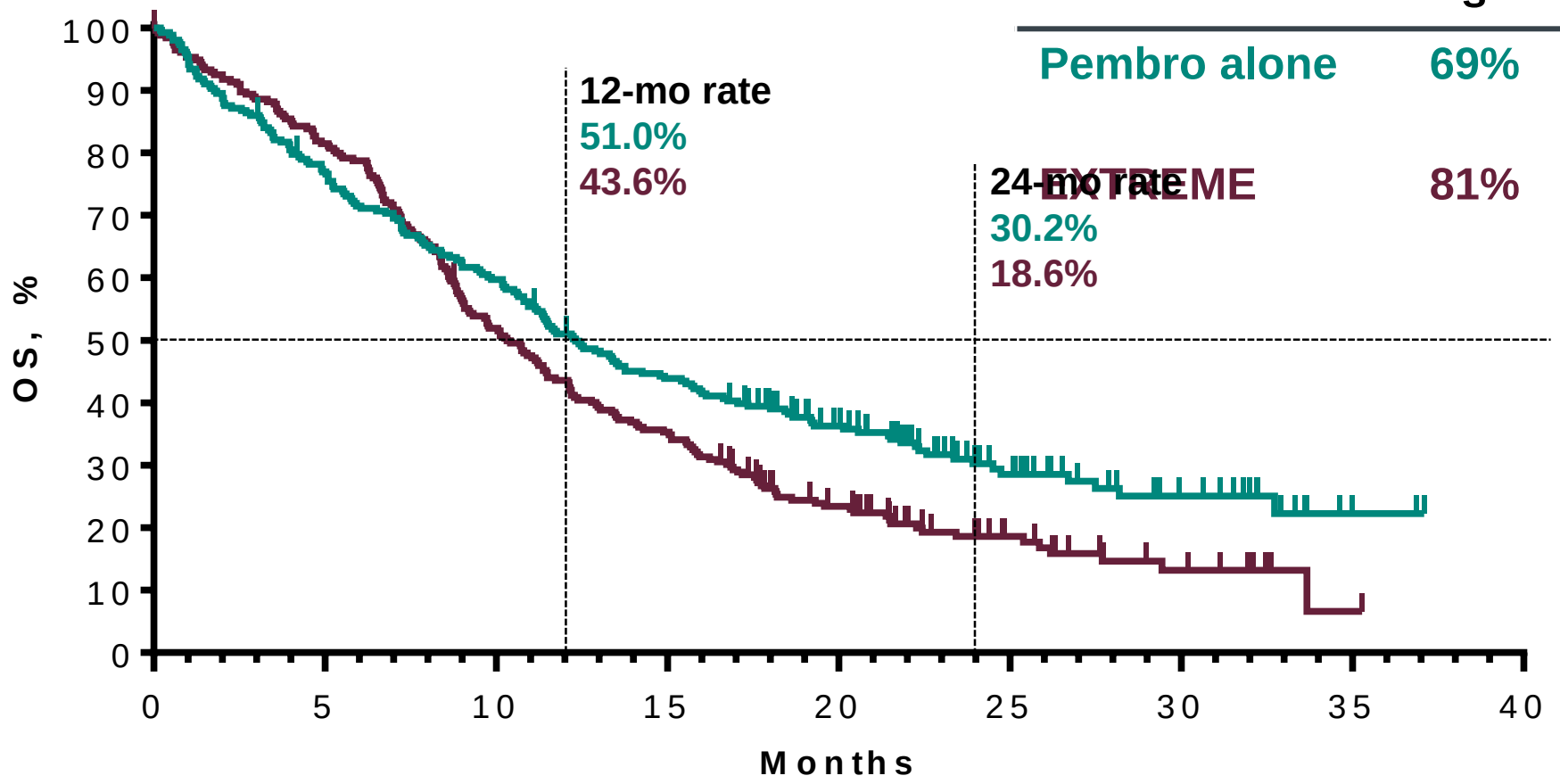
No. at Risk

133	106	85	65	47	24	11	2	0
122	100	64	42	22	12	5	0	0

Data cutoff date: Jun 13, 2018.

Overall Survival: P vs E, CPS ≥1 Population

	Events	HR (95% CI)	*P*
Pembro alone	69%	0.78 (0.64-0.96)	0.0086
EXTREME	81%		



Median (95% CI)
12.3 mo (10.8-14.9)
10.3 mo (9.0-11.5)

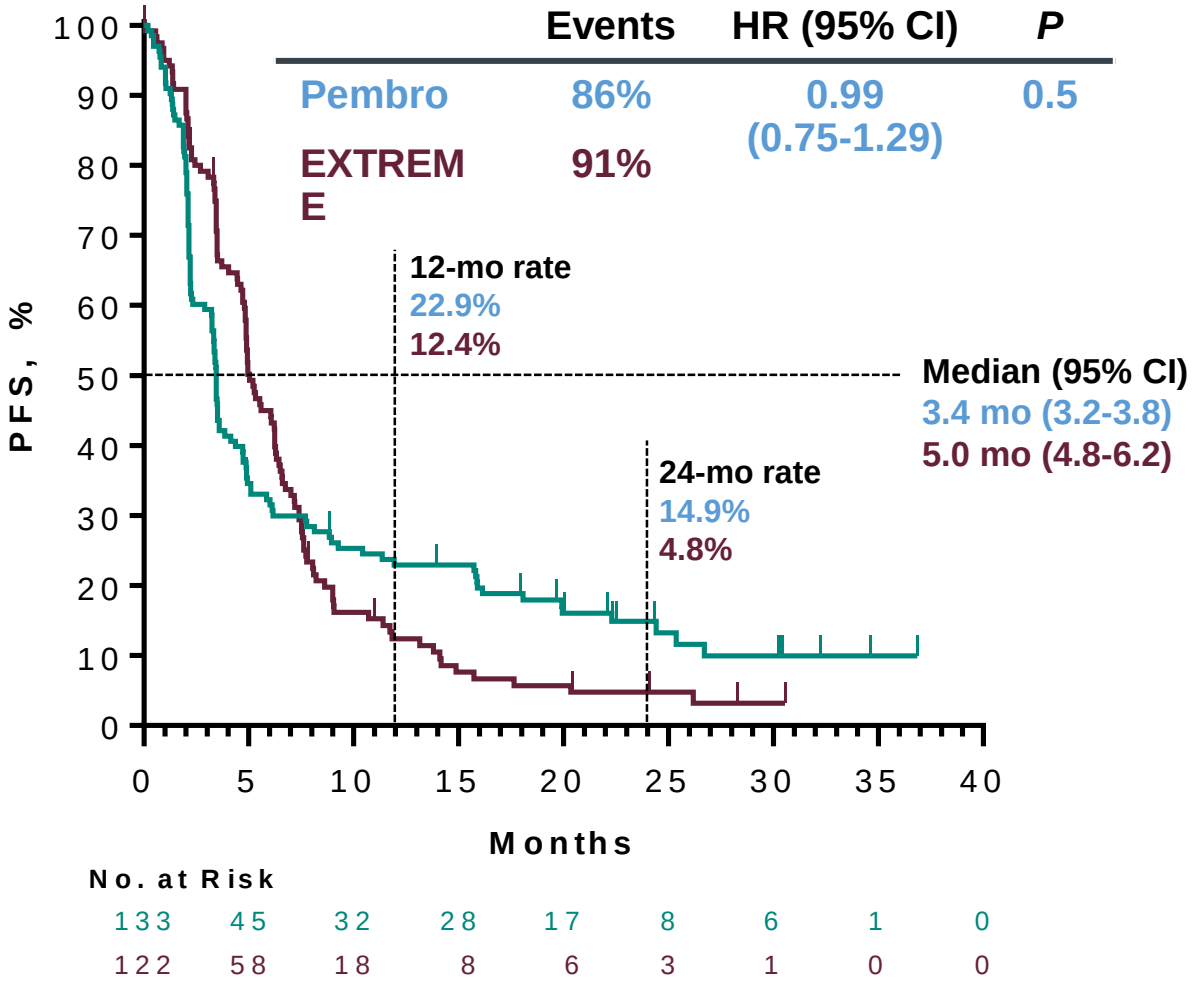
No. at Risk

257	196	152	110	74	34	17	2	0
255	207	131	89	47	21	9	1	0

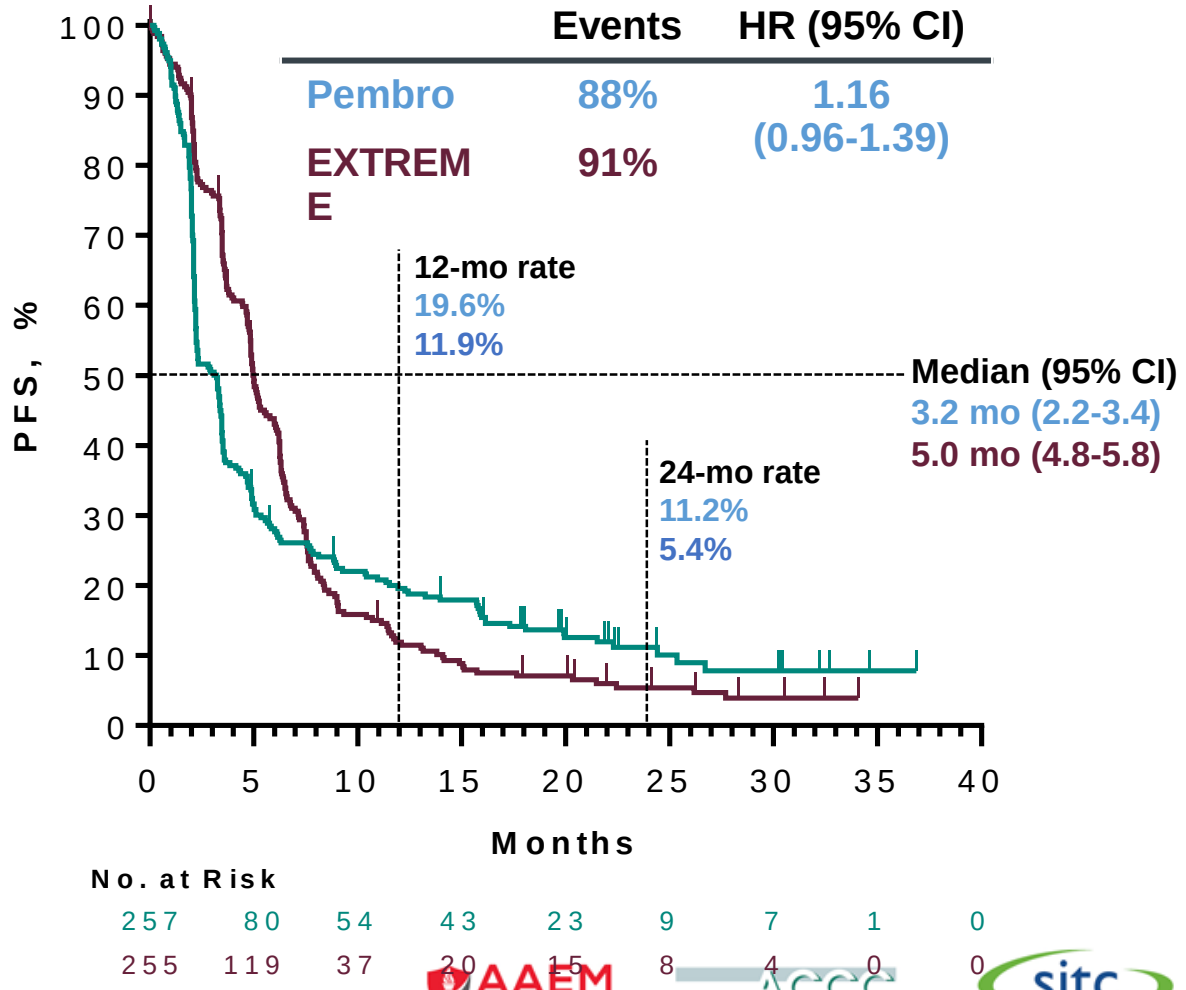
Data cutoff date: Jun 13, 2018.

Progression-Free Survival: P vs E

CPS ≥20



CPS ≥1

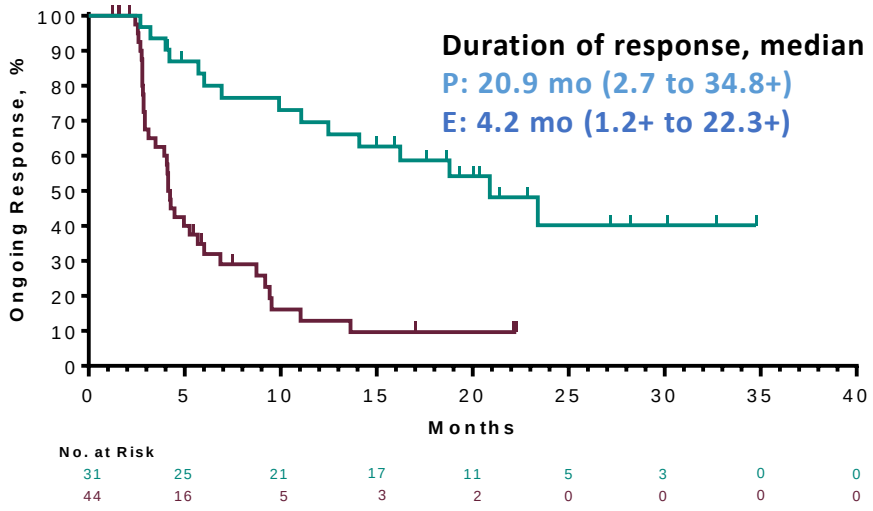


Progression-free survival assessed per RECIST v1.1 by blinded, independent central radiologic review.
Data cutoff date: Jun 13, 2018.

Response Summary, P vs E

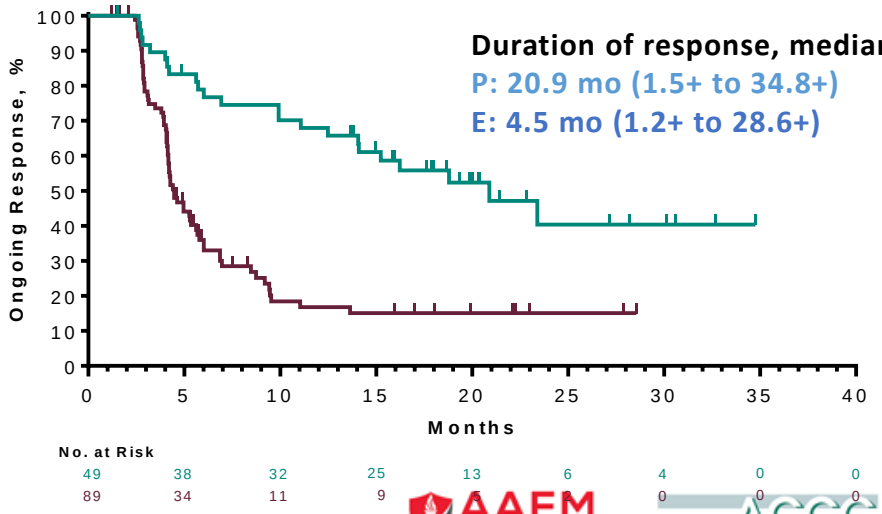
CPS ≥20

Confirmed Response, n (%)	Pembro N = 133	EXTREME N = 122
ORR	**31 (23.3)**	**44 (36.1)**
CR	10 (7.5)	4 (3.3)
PR	21 (15.8)	40 (32.8)
SD	40 (30.1)	42 (34.4)
PD	42 (31.6)	13 (10.7)
Non-CR/non-PD[a]	8 (6.0)	6 (4.9)
Not evaluable or assessed[b]	12 (9.0)	17 (13.9)



CPS ≥1

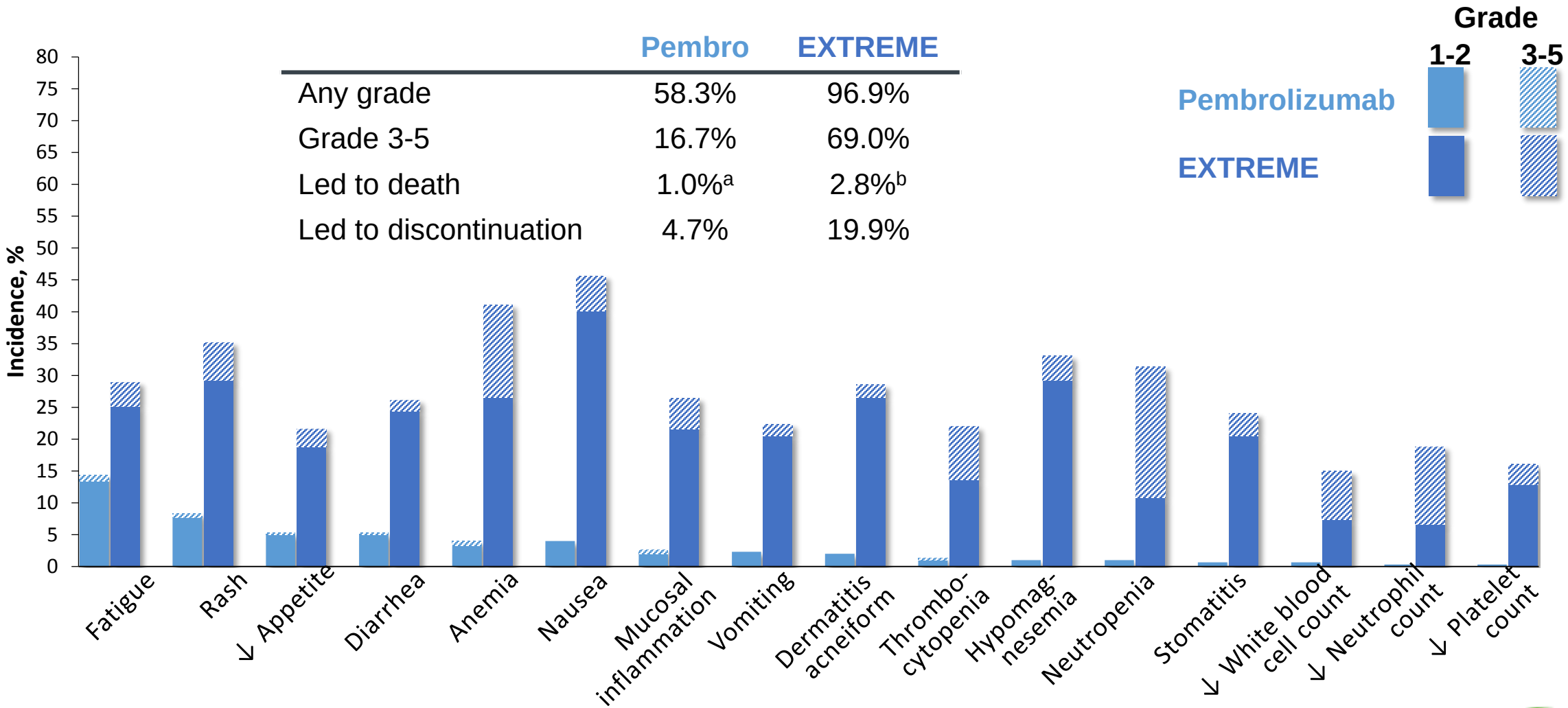
Confirmed Response, n (%)	Pembro N = 257	EXTREME N = 255
ORR	**49 (19.1)**	**89 (34.9)**
CR	14 (5.4)	7 (2.7)
PR	35 (13.6)	82 (32.2)
SD	72 (28.0)	83 (32.5)
PD	100 (38.9)	34 (13.3)
Non-CR/non-PD[a]	11 (4.3)	11 (4.3)
Not evaluable or assessed[b]	25 (9.7)	38 (14.9)



[a]Patients without measurable disease per central review at baseline who did not have CR or PD. [b]Patients who did not have a post-baseline imaging assessment evaluable for response or who did not have post-baseline imaging. Response assessed per RECIST v1.1 by blinded, independent central radiologic review. Data cutoff date: Jun 13, 2018.

Treatment-Related AEs With Incidence ≥15%, P vs E, Total Population

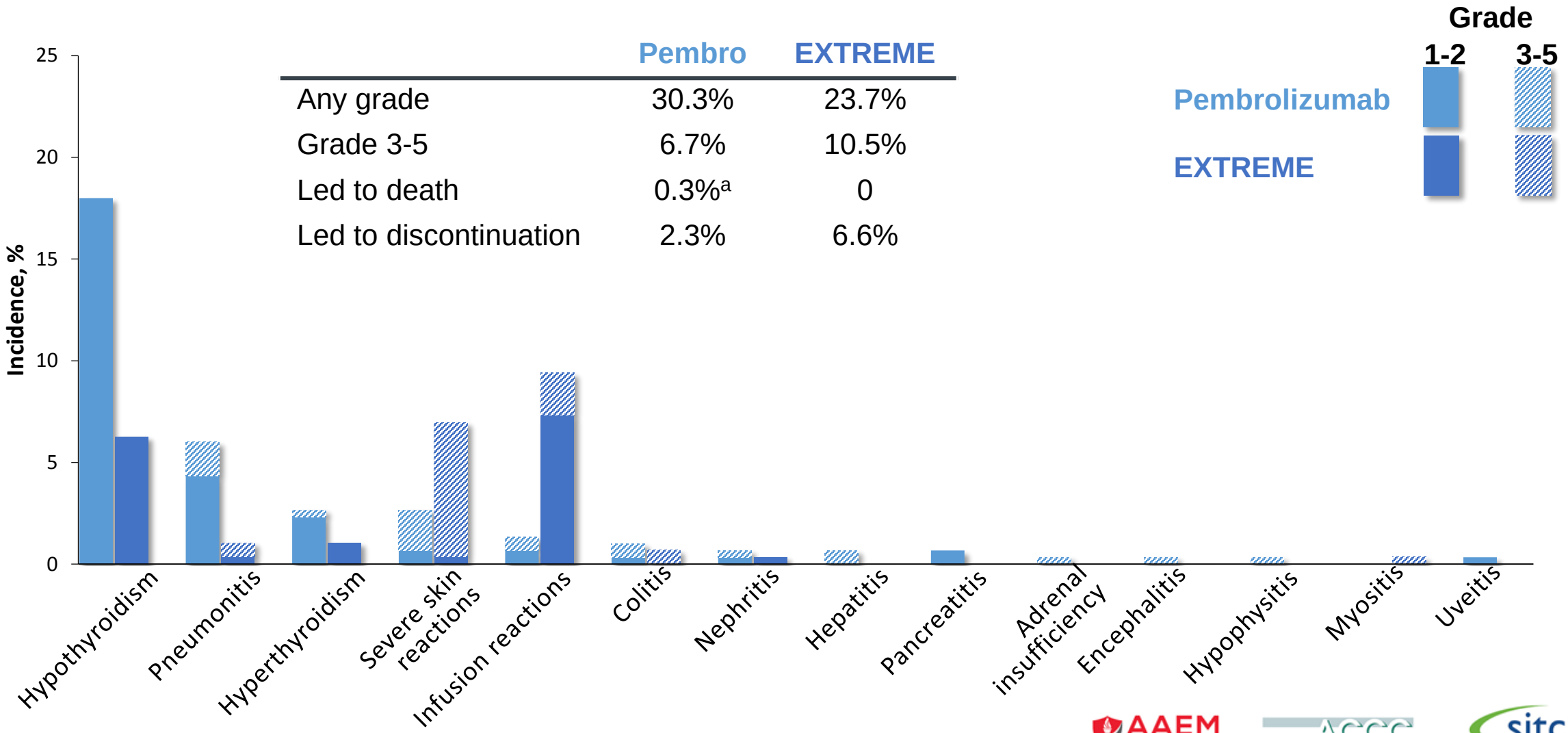
	Pembro	EXTREME
Any grade	58.3%	96.9%
Grade 3-5	16.7%	69.0%
Led to death	1.0%[a]	2.8%[b]
Led to discontinuation	4.7%	19.9%



Median (range) treatment duration was 3.5 mo (0.03-24.2) for pembrolizumab and 4.9 mo (0.03-35.3) for EXTREME.
[a]Autoinflammatory disease, disseminated intravascular coagulation, and pneumonitis (n=1 each).
[b]Pneumonia (n=3), sepsis (n=2), and hypoxia, osteomyelitis, and pulmonary artery thrombosis (n=1 each). Data cutoff date: Jun 13, 2018.

Immune-Mediated AEs and Infusion Reactions, P vs E, Total Population

	Pembro	EXTREME
Any grade	30.3%	23.7%
Grade 3-5	6.7%	10.5%
Led to death	0.3%[a]	0
Led to discontinuation	2.3%	6.6%



[a]Pneumonitis (n=1).

Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to preferred terms listed. Data cutoff date: Jun 13, 2018.

Summary and Conclusions: Pembrolizumab Monotherapy vs EXTREME

- Pembrolizumab significantly improved OS vs EXTREME in the PD-L1 CPS ≥20 (HR 0.61, *P* = 0.0007) and CPS ≥1 (HR 0.78, *P* = 0.0086) populations
  - No PFS benefit for pembrolizumab
  - Although pembrolizumab had a lower ORR, responses were substantially more durable
- Pembrolizumab had a favorable safety profile vs EXTREME
  - Lower incidence of any-grade, grade 3-4, and grade 5 treatment-related AEs
  - Lower incidence of treatment-related AEs leading to discontinuation
  - Safety profiles as expected for pembrolizumab and EXTREME
- Data support pembrolizumab monotherapy as a new first-line standard-of-care for R/M HNSCC that expresses PD-L1

KEYNOTE-048 Study Design
(NCT02358031)

Key Eligibility Criteria

- SCC of the oropharynx, oral cavity, hypopharynx, or larynx
- R/M disease incurable by local therapies
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment[a]
- Known p16 status in the oropharynx[b]

Stratification Factors

- PD-L1 expression[a] (TPS ≥50% vs <50%)
- p16 status in oropharynx (positive vs negative)
- ECOG performance status (0 vs 1)

R (1:1:1)

Pembrolizumab 200 mg Q3W

for up to 35 cycles

Pembrolizumab 200 mg + Carboplatin AUC 5 OR Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days

for 6 cycles (each 3 wk)

→ **Pembrolizumab 200 mg Q3W**

for up to 29 cycles

Cetuximab 250 mg/m² Q1W[c] + Carboplatin AUC 5 OR Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days

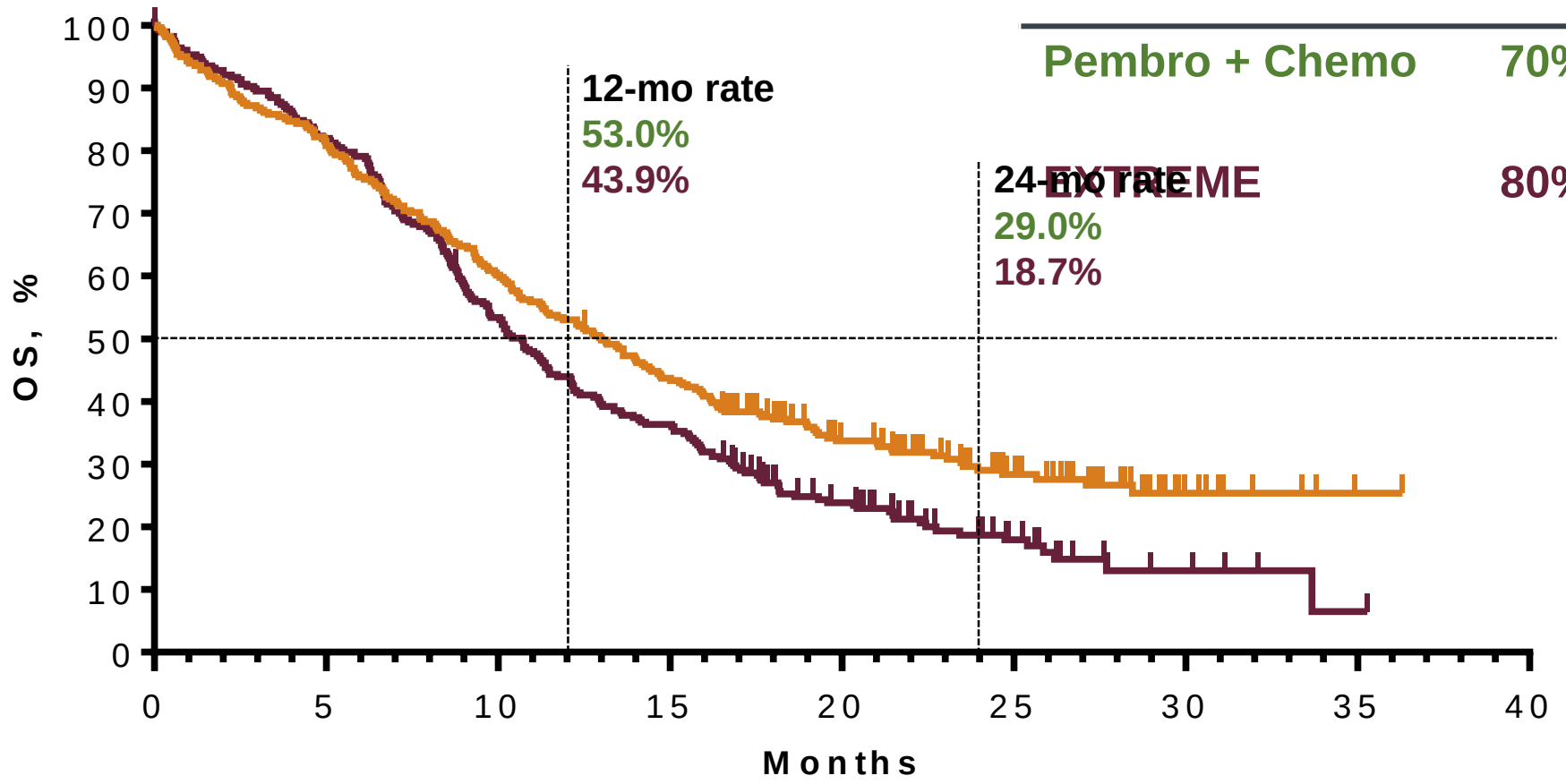
for 6 cycles (each 3 wk)

→ **Cetuximab 250 mg/m² Q1W**

[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.

Overall Survival: P+C vs E, Total Population

	Events	HR (95% CI)	*P*
Pembro + Chemo	70%	0.77 (0.63-0.93)	0.0034
EXTREME	80%		



Median (95% CI)
13.0 mo (10.9-14.7)
10.7 mo (9.3-11.7)

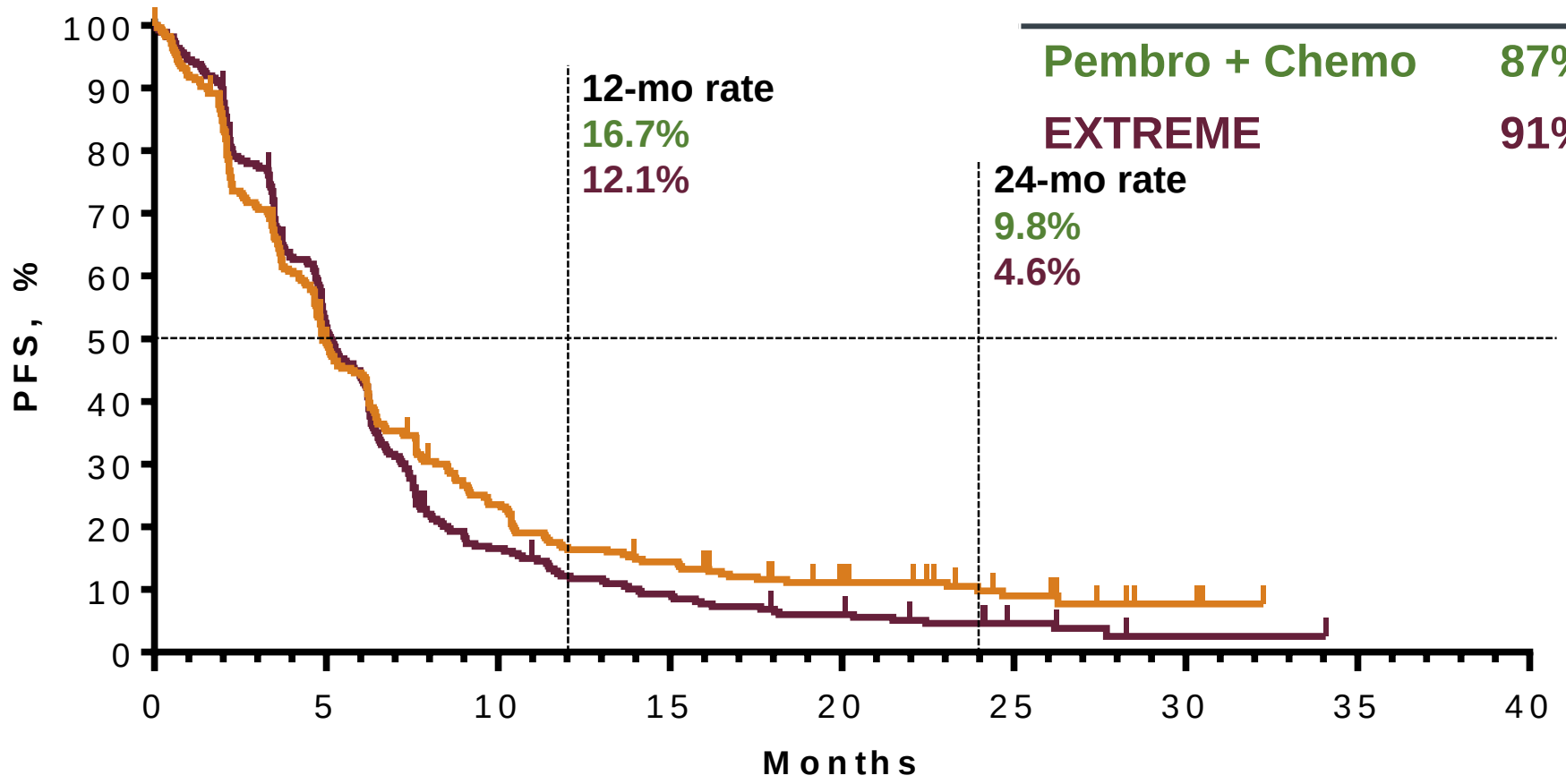
No. at Risk

281	227	169	122	75	40	10	1	0
278	227	147	100	51	20	5	1	0

Data cutoff date: Jun 13, 2018.

Progression-Free Survival: P+C vs E, Total Population

	Events	HR (95% CI)	*P*
Pembro + Chemo	87%	0.92 (0.77-1.10)	0.2
EXTREME	91%		



Median (95% CI)
4.9 mo (4.7-6.0)
5.1 mo (4.9-6.0)

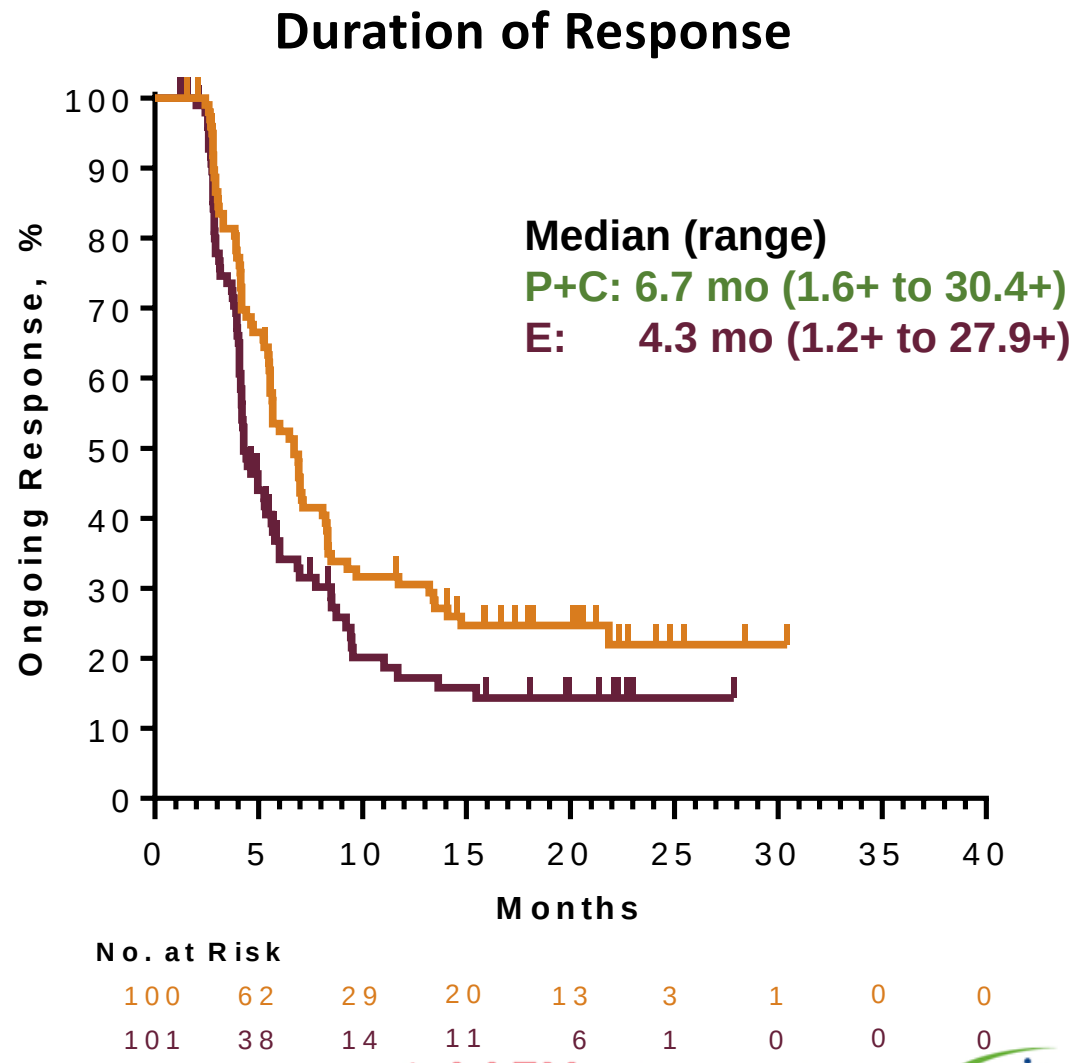
No. at Risk

281	134	62	37	22	11	3	0	0
278	136	42	23	14	6	1	0	0

Progression-free survival assessed per RECIST v1.1 by blinded, independent central radiologic review.
Data cutoff date: Jun 13, 2018.

Response Summary, P+C vs E, Total Population

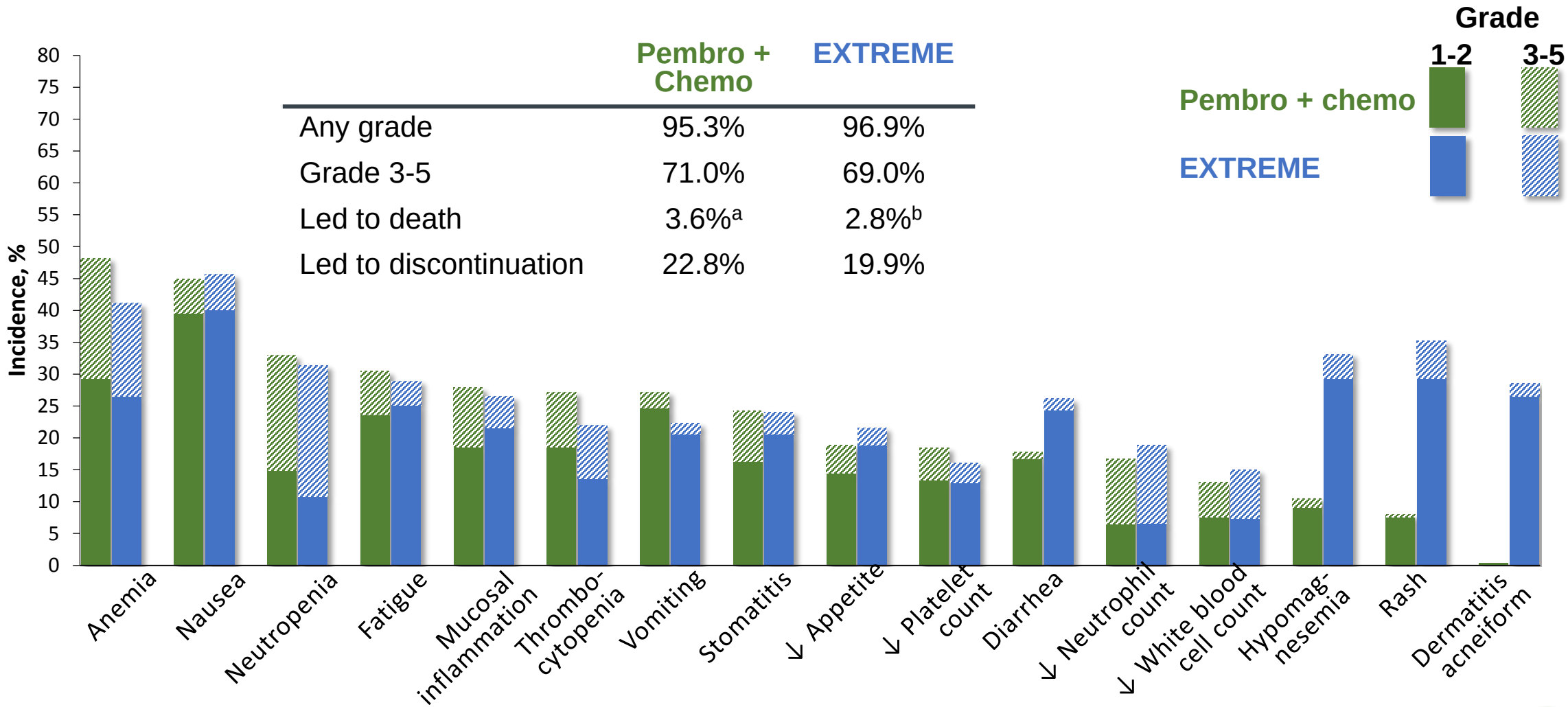
Confirmed Response, n (%)	Pembro + Chemo N = 281	EXTREME N = 278
ORR	**100 (35.6)**	**101 (36.3)**
CR	17 (6.0)	8 (2.9)
PR	83 (29.5)	93 (33.5)
SD	78 (27.8)	94 (33.8)
PD	48 (17.1)	34 (12.2)
Non-CR/non-PD[a]	13 (4.6)	9 (3.2)
Not evaluable or assessed[b]	42 (14.9)	40 (14.4)



[a]Patients without measurable disease per central review at baseline who did not have CR or PD. [b]Patients who did not have a post-baseline imaging assessment evaluable for response or who did not have post-baseline imaging. Response assessed per RECIST v1.1 by blinded, independent central radiologic review. Data cutoff date: Jun 13, 2018.

Treatment-Related AEs With Incidence ≥15%, P+C vs E, Total Population

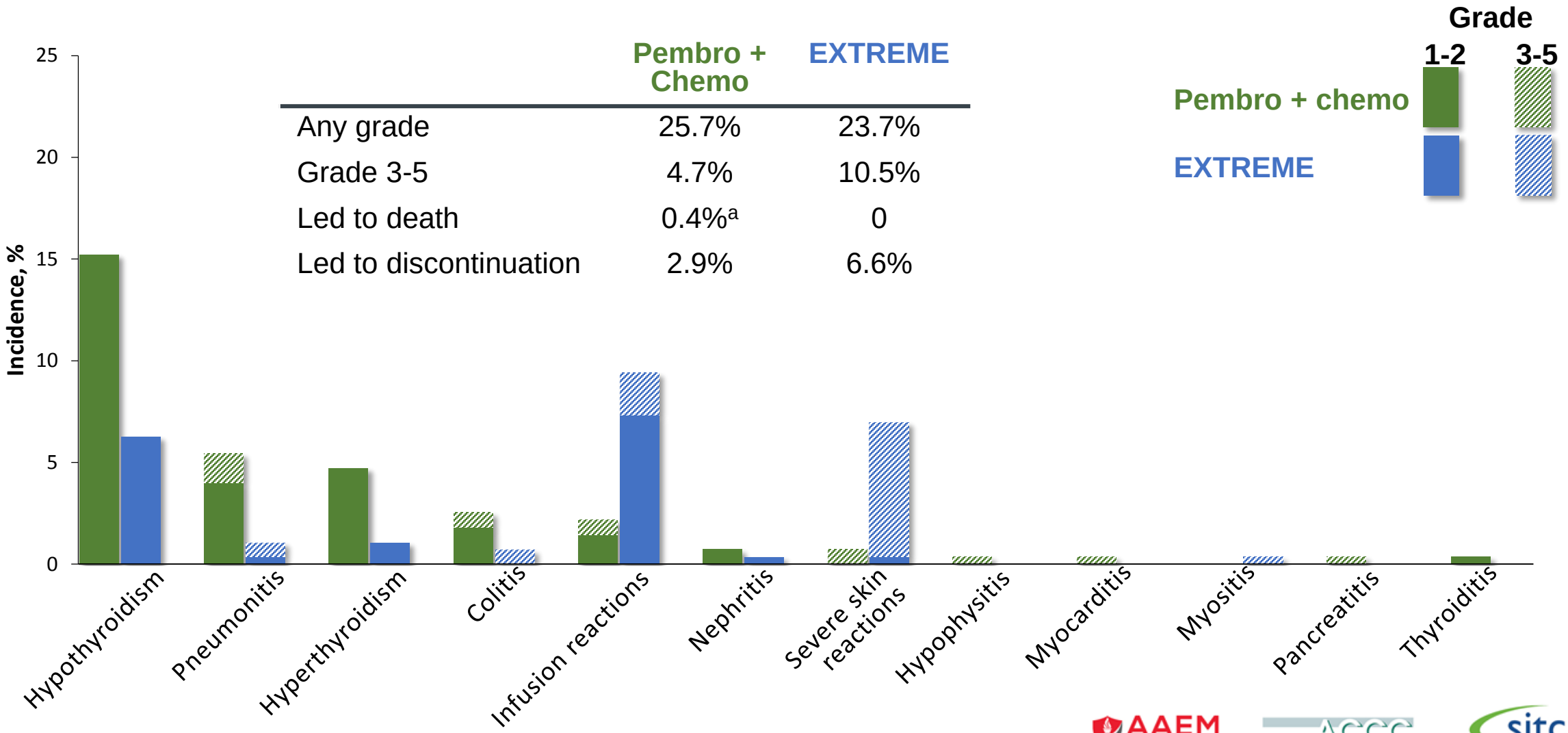
	Pembro + Chemo	EXTREME
Any grade	95.3%	96.9%
Grade 3-5	71.0%	69.0%
Led to death	3.6%[a]	2.8%[b]
Led to discontinuation	22.8%	19.9%



Median (range) treatment duration was 5.8 mo (0.1-24.2) for pembrolizumab + chemotherapy and 4.9 mo (0.03-35.3) for EXTREME.
[a]Septic shock (n=5) and cerebral ischemia, hemorrhage, interstitial lung disease, sepsis, and tumor hemorrhage (n=1 each).
[b]Pneumonia (n=3), sepsis (n=2), and hypoxia, osteomyelitis, and pulmonary artery thrombosis (n=1 each). Data cutoff date: Jun 13, 2018.

Immune-Mediated AEs and Infusion Reactions, P+C vs E, Total Population

	Pembro + Chemo	EXTREME
Any grade	25.7%	23.7%
Grade 3-5	4.7%	10.5%
Led to death	0.4%[a]	0
Led to discontinuation	2.9%	6.6%



[a]Pneumonitis (n=1).

Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to preferred terms listed. Data cutoff date: Jun 13, 2018.

Developmental Immunotherapies for HNSCC

MASTERKEY 232/KEYNOTE-137

- Talimogene laherparepvec (T-Vec)
  - Genetically engineered herpes virus
- T-Vec 10^6 PFU/mL intratumoral injection followed by 10^8 PFU/mL Q3W
- Pembrolizumab 200 mg IV Q3W
- Eligibility:
  - R/M HNSCC not suitable for curative therapy
  - Progressed after platinum treatment
  - At least 1 injectable cutaneous, subcutaneous, or nodal tumor ≥ 10 mm in longest diameter

Conclusions

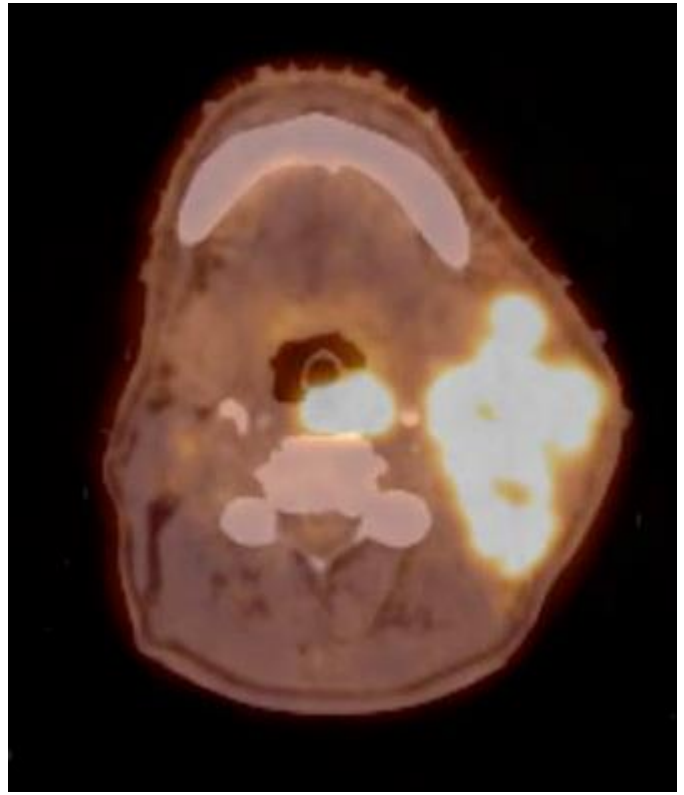
1. Chemotherapy offers short survival with many side effects
2. PD-1 antibodies nivolumab and pembrolizumab are approved in *platinum-refractory* recurrent / metastatic HNSCC.
3. Most patients have fewer side effects on PD-1 Abs than on chemotherapy
4. Clinical trials are underway to improve immunotherapy response rates and testing immunotherapy in other settings

Patient Case Study 1

- Patient Background Information:
  - 78 yo M with a history of CAD, HTN, HLD
  - Presents with painful L sided neck mass
  - Lost 30 lbs due to anorexia

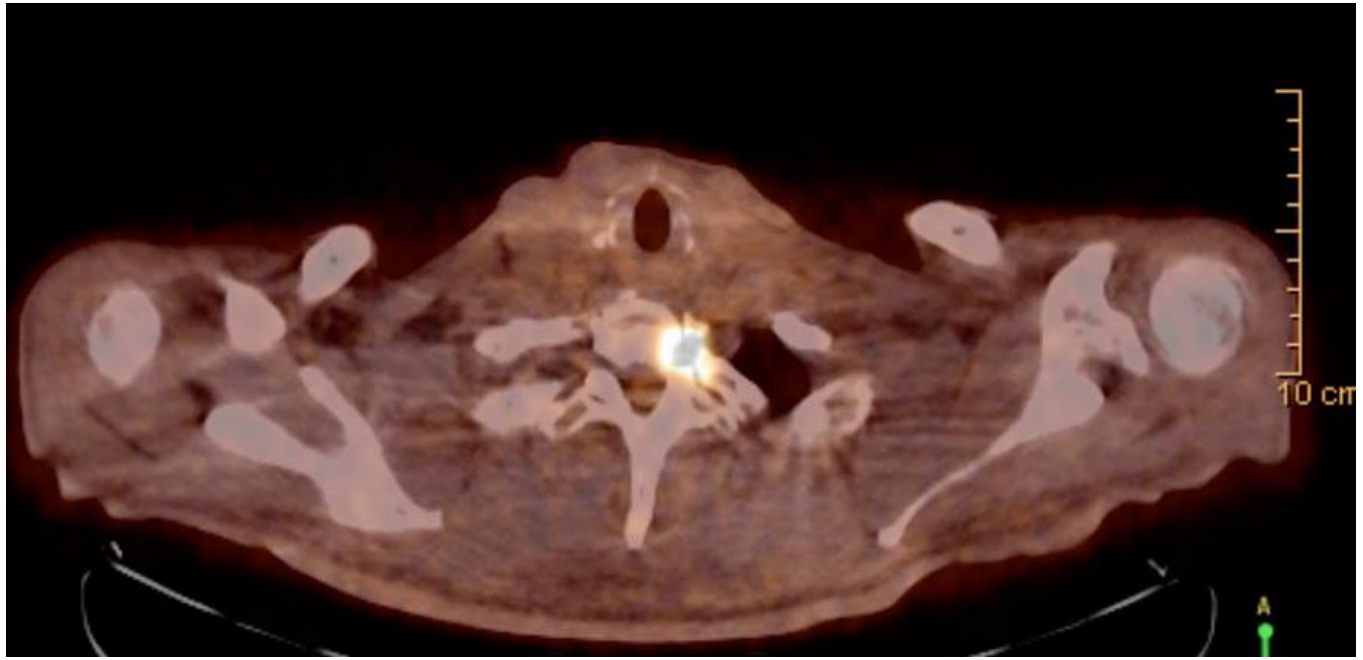
Patient Case Study 1
November 2014

- PET CT
  - Large L sided cervical mass
  - Periepiglottic tumor with no airway compromise
  - Multiple cervical osseous metastases
- Palliative hypofractionated XRT initiated



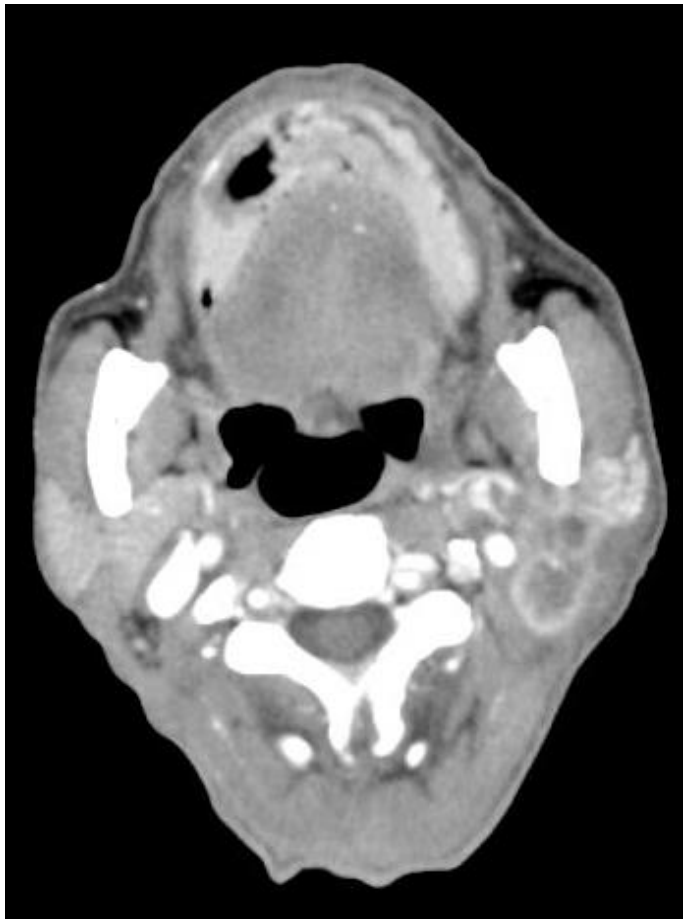
Patient Case Study 1
January 2015

- Cervical disease decreased – pain improved
  - Carboplatin/paclitaxel 1st line
- PET CT revealed new osseous and axillary mets
  - Started on cetuximab 2nd line



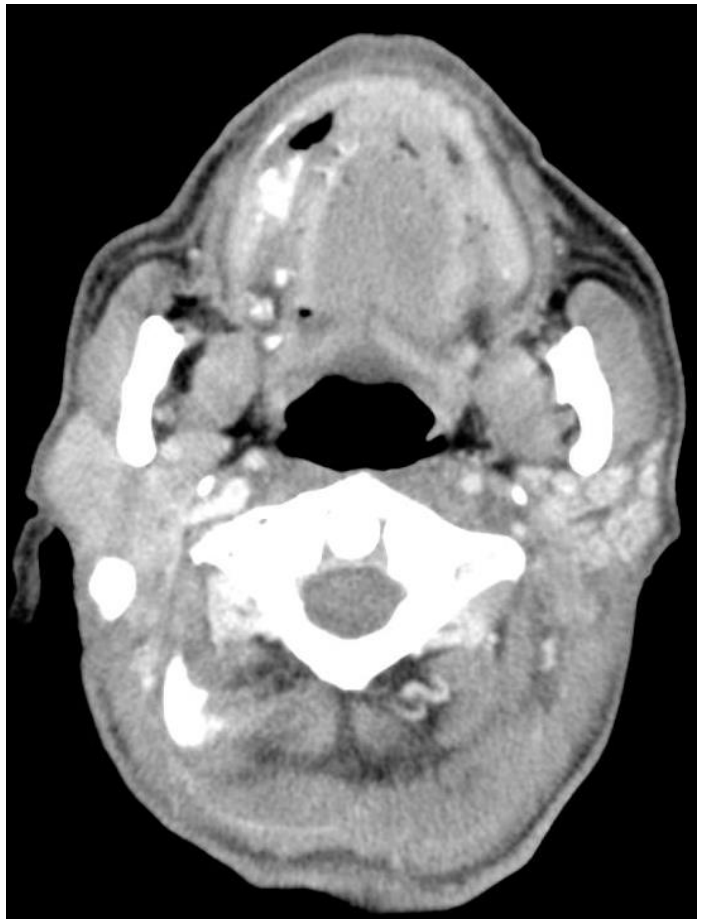
Patient Case Study 1
June 2015

- Progression in cervical nodes
  - Re-irradiation not an option
- Enrolled in KEYNOTE-055
  - Started on pembrolizumab



Patient Case Study 1
October 2015

- Patient experienced near CR
  - Response lasted 1 year
  - No side effects of note

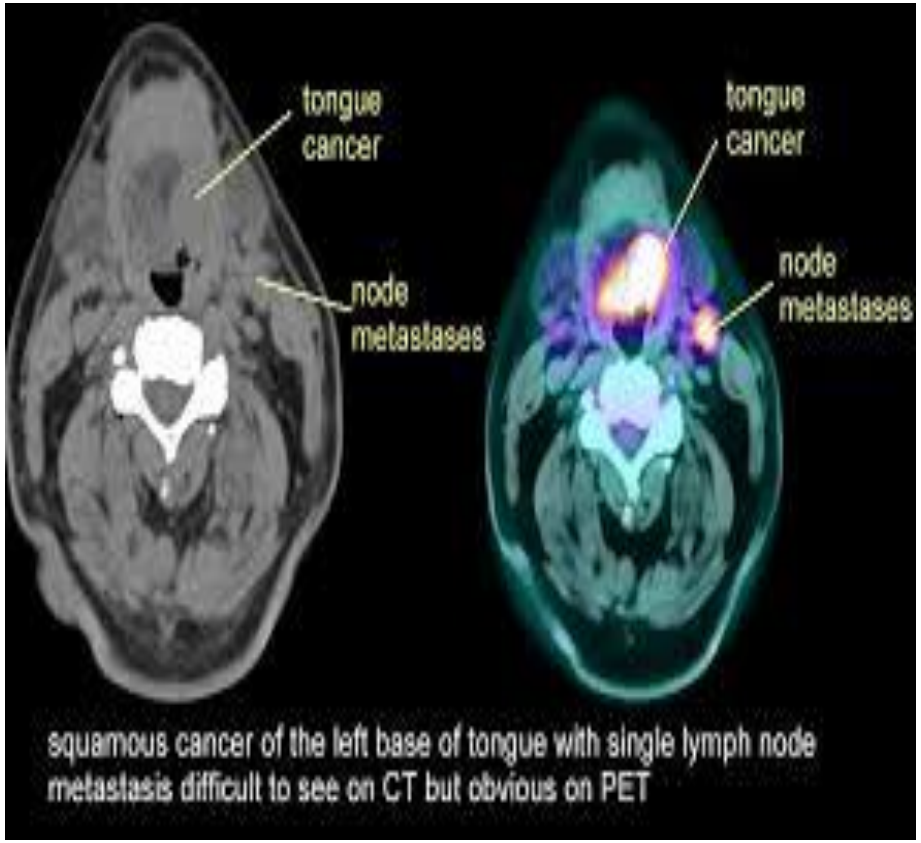


Patient Case Study 2

- Patient Background Information:
  - 56 yo M with a history of smoking
  - Presents with painful L oral tongue mass and L sided neck mass
  - Lost 30 lbs due to anorexia

Patient Case Study 2
November 2014

- PET CT
  - L sided oral tongue mass
  - L neck metastases
  - No DM
- S/p surgical resection followed by adjuvant CRT with Cisplatin (+margins/ +ECE)
- Early recurrence 2 months after CRT completion



Patient Case Study 2

- Treatment options discussed :
  - CF + Erbitux followed by Erbitux (EXTREME) : RR 35% , OS 10.7m
  - Single agent chemotherapy or Erbitux alone
  - Doublet with Cis/Carb + Taxane
  - Immunotherapy ?

Patient Case Study 2

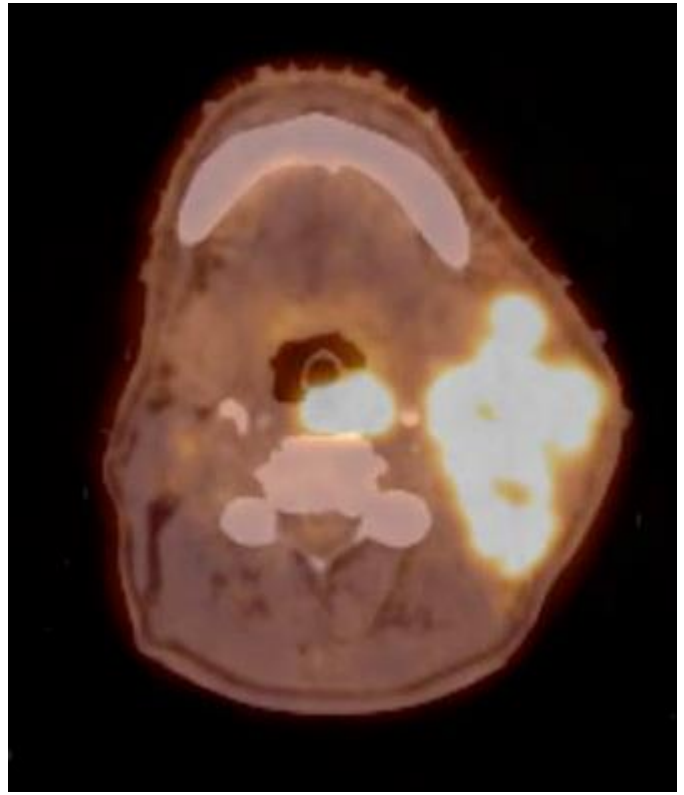
- Treatment received :
- Nivolumab (FDA approval for persistent disease)

Patient Case Study 3

- Patient Background Information:
  - 60 yo M with a history of LA SCCHN tx in 2016 with definitive CRT
  - Presents now with painful L sided neck mass and DM on PET scan
  - Lost 30 lbs due to anorexia

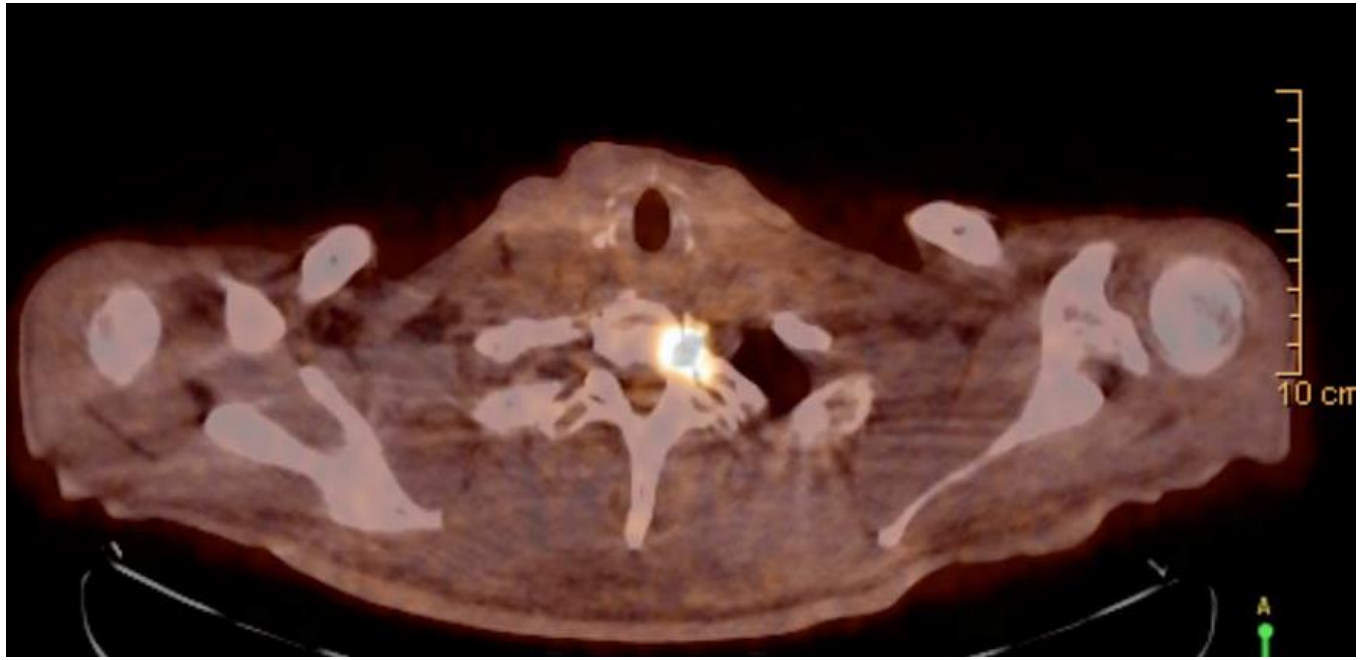
Patient Case Study 3

- PET CT
  - Large L sided cervical mass
  - Periepiglottic tumor with no airway compromise
  - Multiple cervical osseous metastases
- Palliative hypofractionated XRT initiated



Patient Case Study 3
November 2018

- Cervical disease decreased – pain improved
  - 1st line treatment as of 11/2018 ?
- PET CT revealed new osseous and axillary mets



Patient Case Study 3

- Treatment options discussed
- CFE + E (EXTREME)
- Pembro alone
- CF Pembro + Pembro
- Clinical trial