

12th Annual  
**WCS**<sup>TM</sup>

WINTERCANCER  
**SYMPOSIUM**

**MARCH 3-5, 2023**

WYNDHAM GRAND RIO MAR  
PUERTO RICO

# Head and Neck Cancers: *Where are we in 2023?*

**Cesar A. Perez, M.D.**

*Director of Drug Development,*

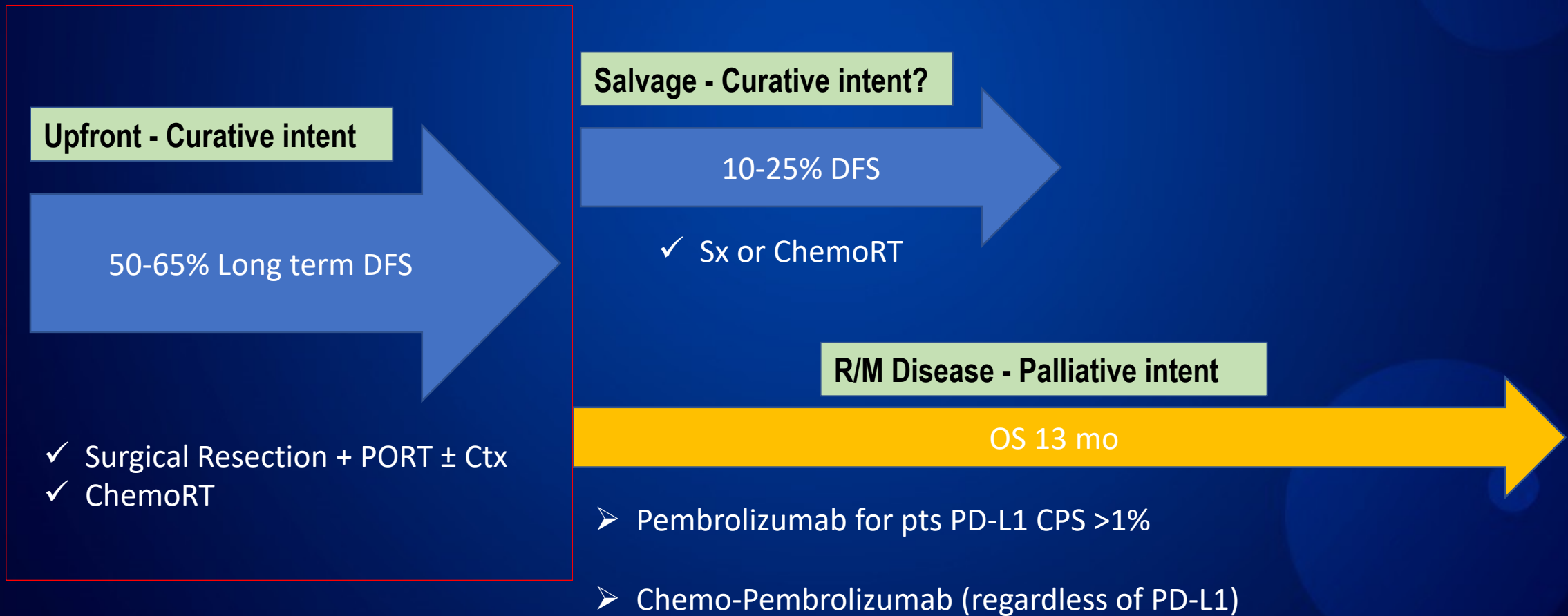
*Sarah Cannon Research Institute at Florida Cancer Specialists - Lake Nona Orlando, FL*

*Head and Neck Cancer Track Leader, ASCO Education Committee*

*Associate Professor of Medicine, University of Central Florida*

# Head and Neck Cancer Treatment approach

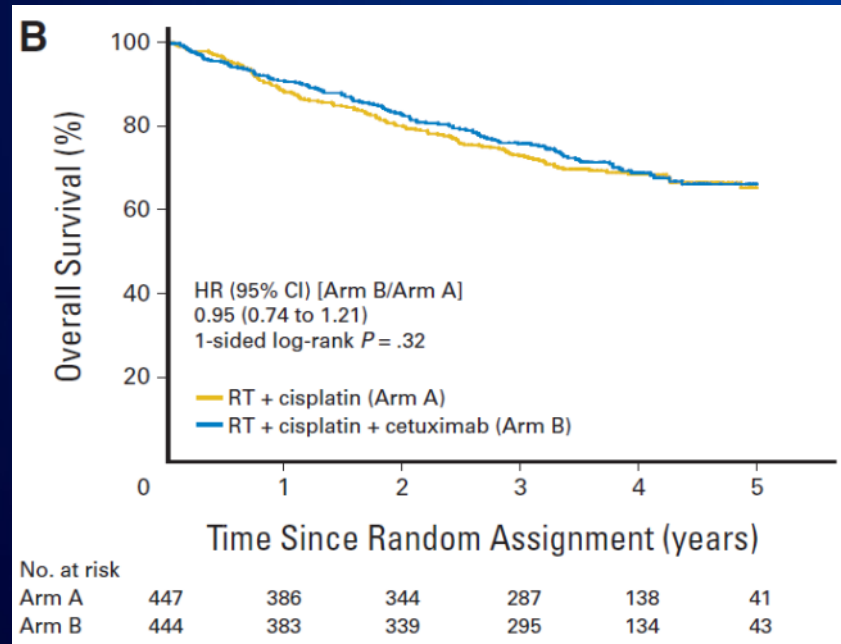
*Current Landscape...*



# Locally Advanced SCCHN

*Cisplatin-based chemoRT CONTINUES to be our standard*

RTOG 0522 → adding Cetuximab to Cisplatin-RT failed to improve OS



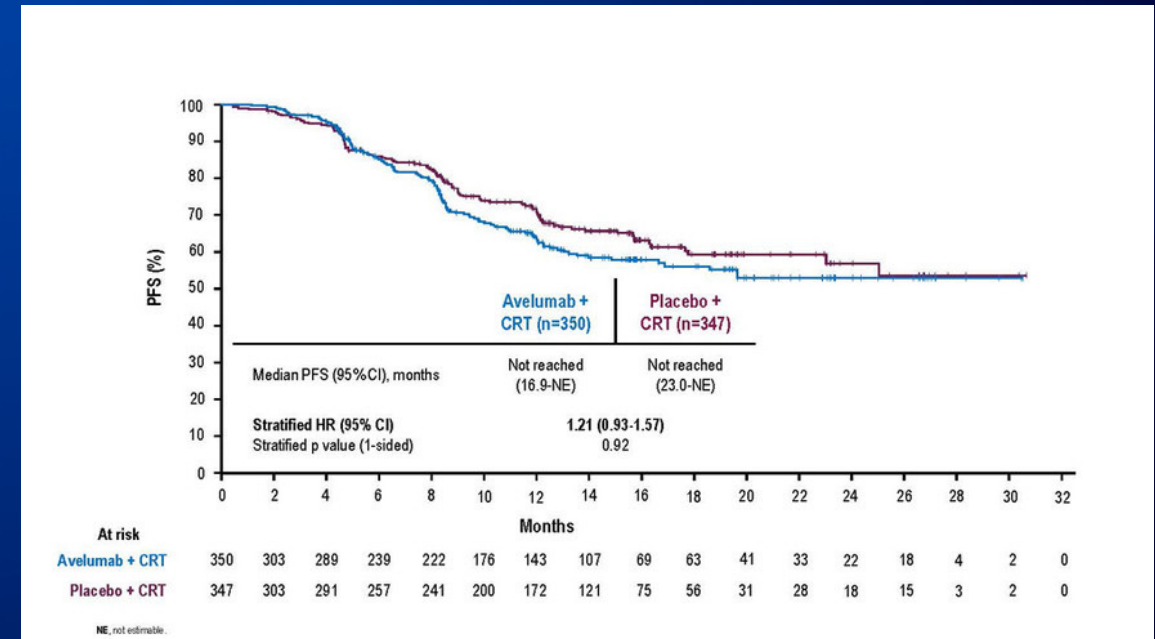
Can we do better by adding a  
Checkpoint inhibitor??

# Can we do better by adding a checkpoint inhibitor?

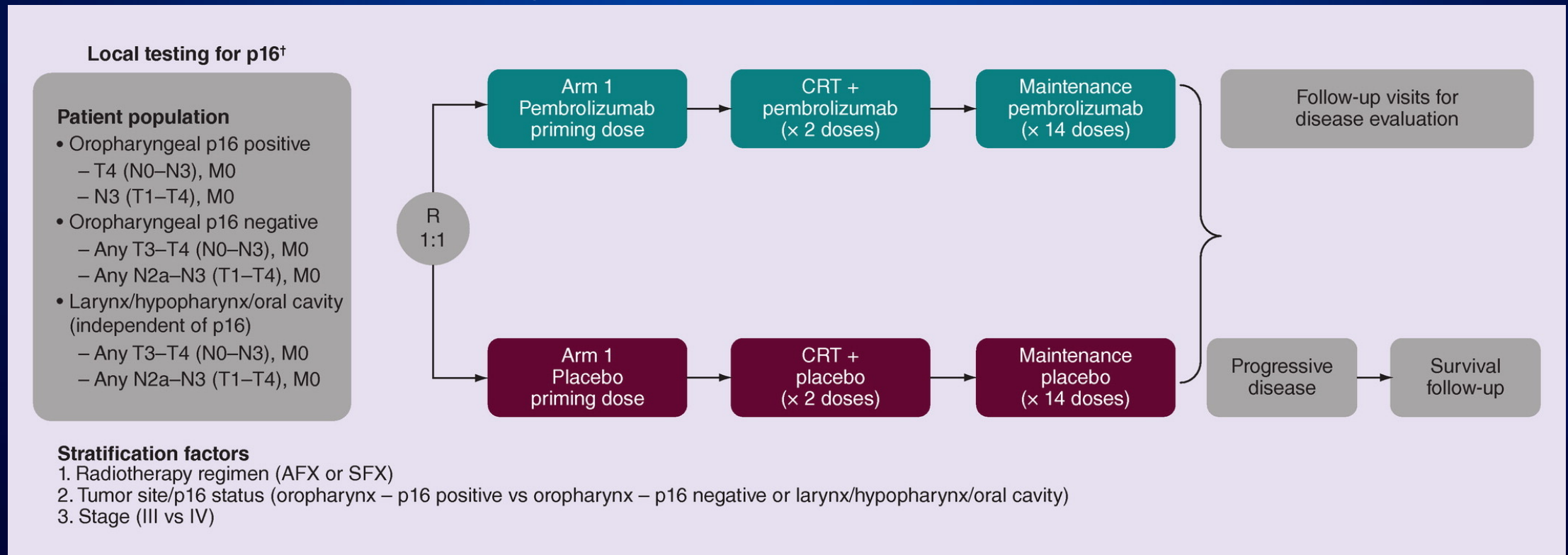
## *Javelin 100 HN*

- Cisplatin-based definitive ChemoRT with or without Avelumab
- Median PFS was NOT improved by the addition of Avelumab when compared to placebo  
*(trend in favor of the placebo group)*

Avelumab plus standard-of-care chemoradiotherapy versus chemoradiotherapy alone in patients with locally advanced squamous cell carcinoma of the head and neck: a randomised, double-blind, placebo-controlled, multicentre, phase 3 trial

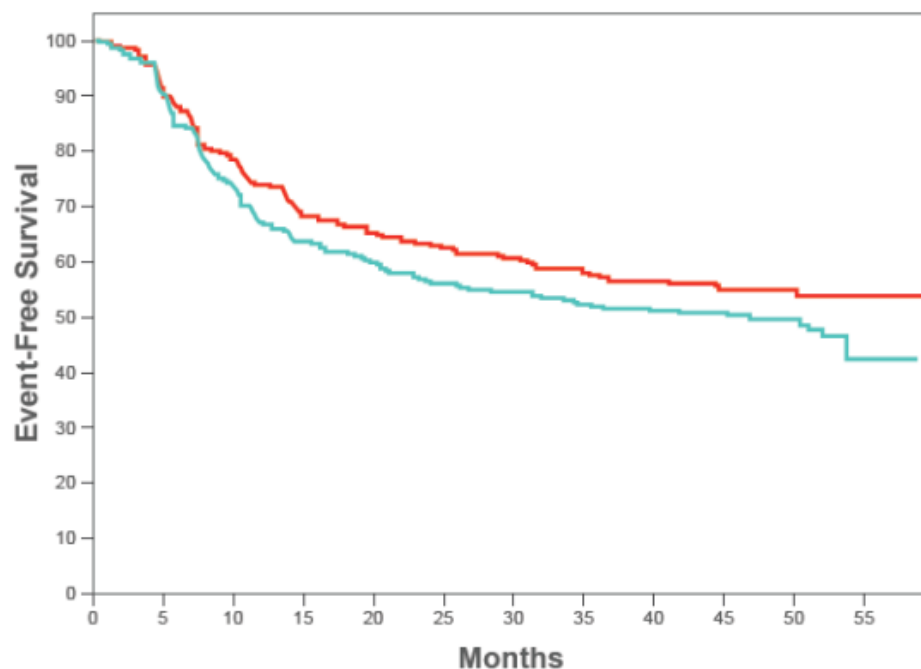


# Primary results of the phase III KEYNOTE-412 study: Pembrolizumab (pembro) with chemoradiation therapy (CRT) vs placebo plus CRT for locally advanced (LA) head and neck squamous cell carcinoma (HNSCC) *JP Machiels et al. ESMO 2022 Presidential Symposium II*



# Phase III KEYNOTE-412 study

Event-free survival: ITT population



	HR (95% CI)	P-value
Pembrolizumab + Chemoradiation therapy vs Placebo + Chemoradiation therapy	0.83 (0.68 - 1.03)	0.0429

Pembro + CRT → Favorable trend toward improved EFS vs placebo + CRT  
... but not statistically significance

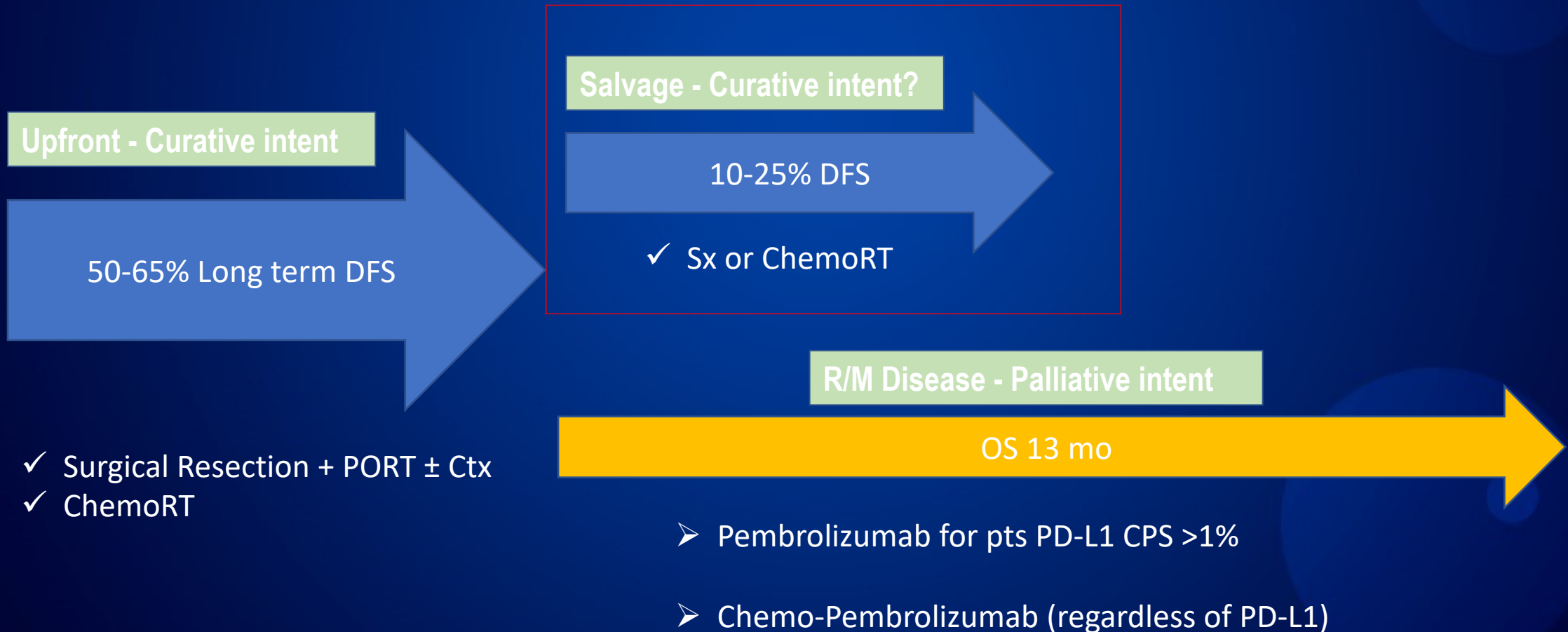


# Checkpoint inhibitors in the curative setting

- In pts with NSCLC → PACIFIC trial demonstrated that adding Durvalumab consolidation after CRT has an OS benefit (not concurrently)
- Negative results for **Javelin100** and **Keynote-412**
  - Trend towards better outcome in PD-L1 positive pts  
→ *T cell dysfunction/suppression during concurrent therapy?*
- “*Throwing the kitchen sink*” to our High-Risk pts doesn’t work!
- How about consolidation tx in PD-L1 positive pts??

# Head and Neck Cancer Treatment approach

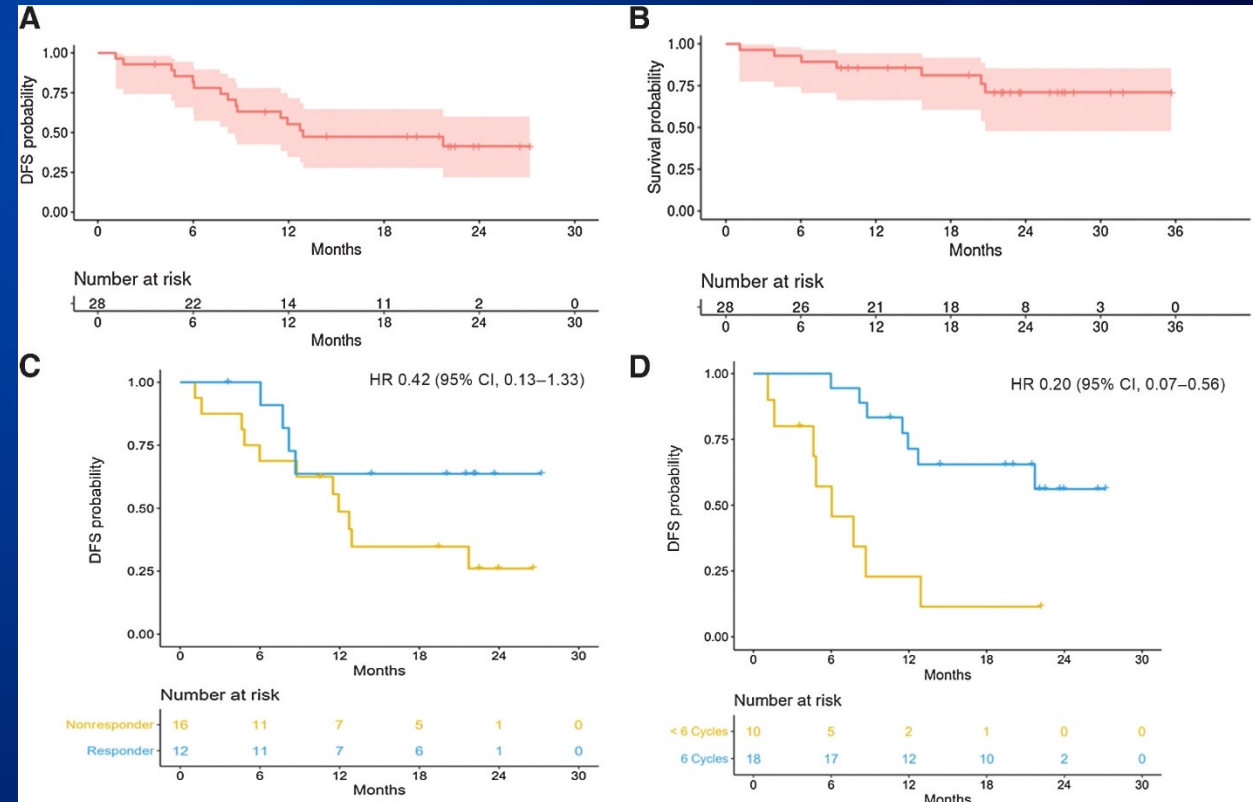
*Current Landscape...*





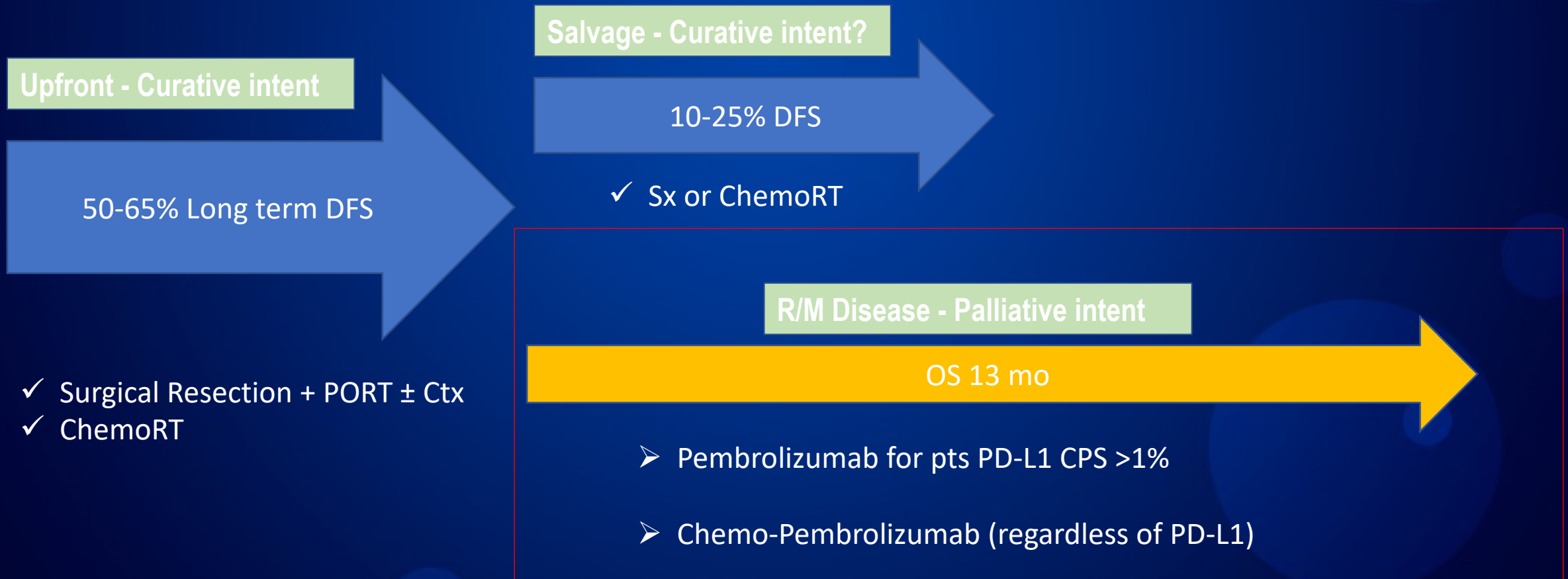
# Neoadjuvant and Adjuvant Nivolumab and Lirilumab in Patients with Recurrent, Resectable Squamous Cell Carcinoma of the Head and Neck *Hanna et al Clin Cancer Res (2022) 28 (3): 468–478*

- Lirilumab is a mAb against KIR2DL
- 28 patients, 96% previously radiated
- Nivo + Liri one cycle before, and 6 cycles after Sx
- 43% pathologic response rate
- Two-year DFS and OS of 64% and 80% among pathologic responders

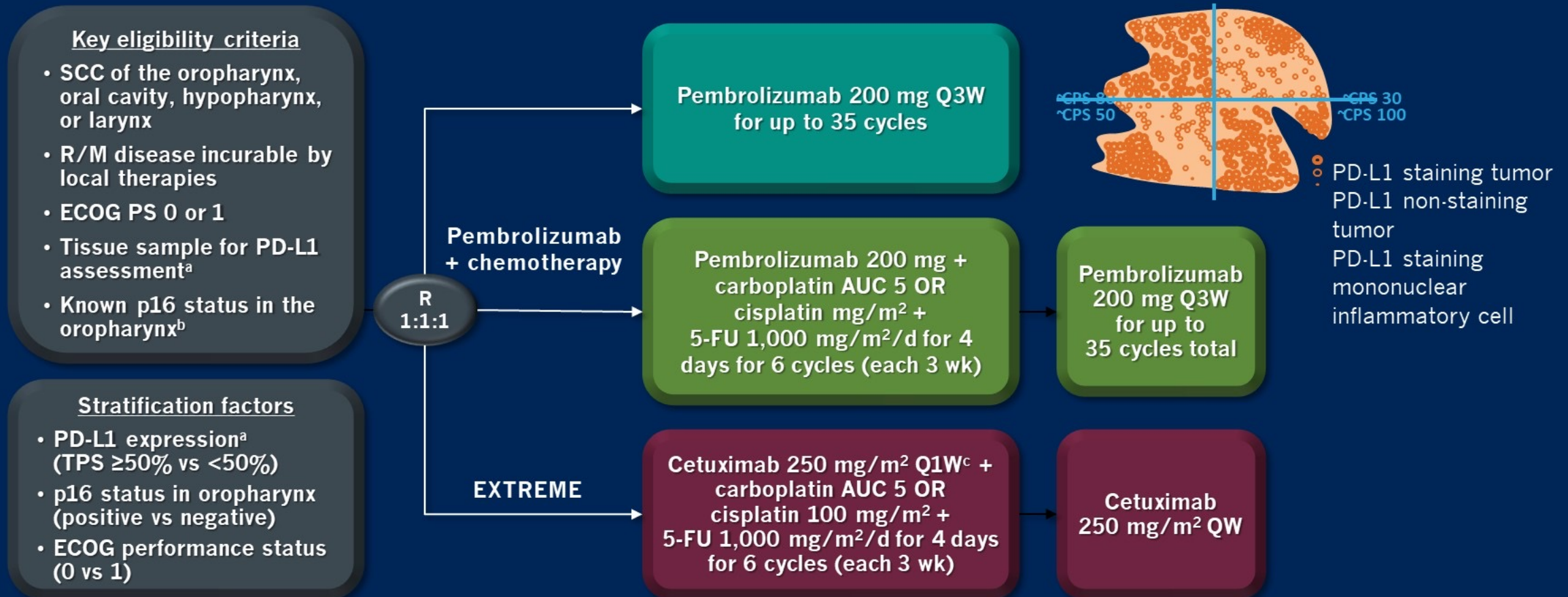


# Head and Neck Cancer Treatment approach

*Current Landscape...*



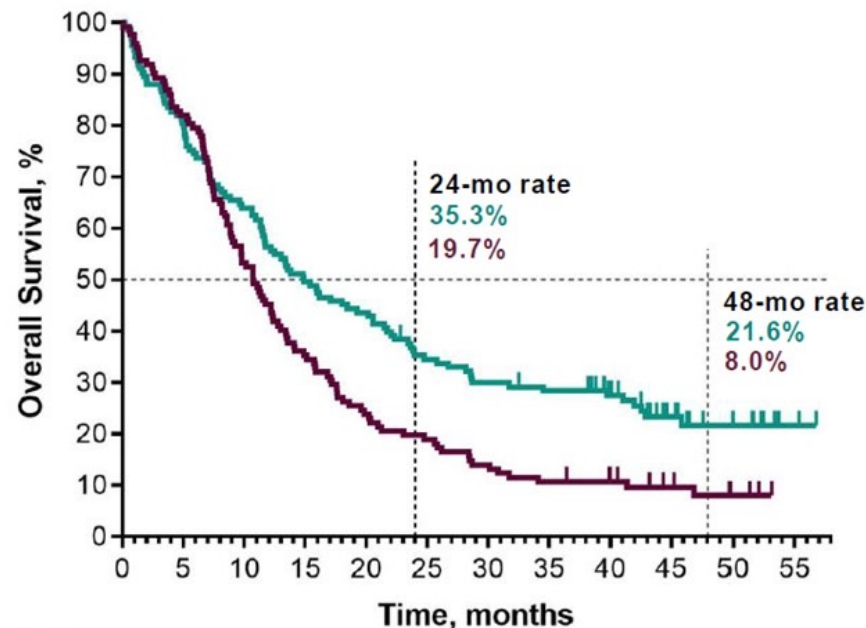
# KEYNOTE-048: Pembrolizumab ± Chemotherapy



Burtness et al, *Lancet* 2019

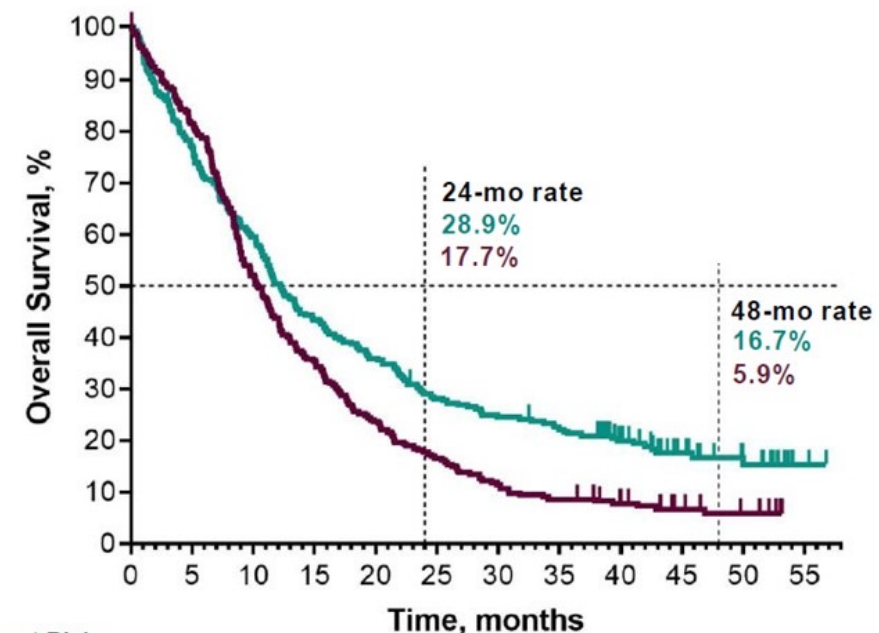
# Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for R/M SCCHN: KEYNOTE-048

PD-L1 CPS $\geq 20$				
	Events	Median OS, mo (95% CI)	HR (95% CI)	P value <sup>a</sup>
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	0	5	10	15	20	25	30	35	40	45	50	55
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 $\geq 1$				
	Events	Median OS, mo (95% CI)	HR (95% CI)	P value <sup>a</sup>
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	0	5	10	15	20	25	30	35	40	45	50	55
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

CI, confidence interval; HR, hazard ratio.

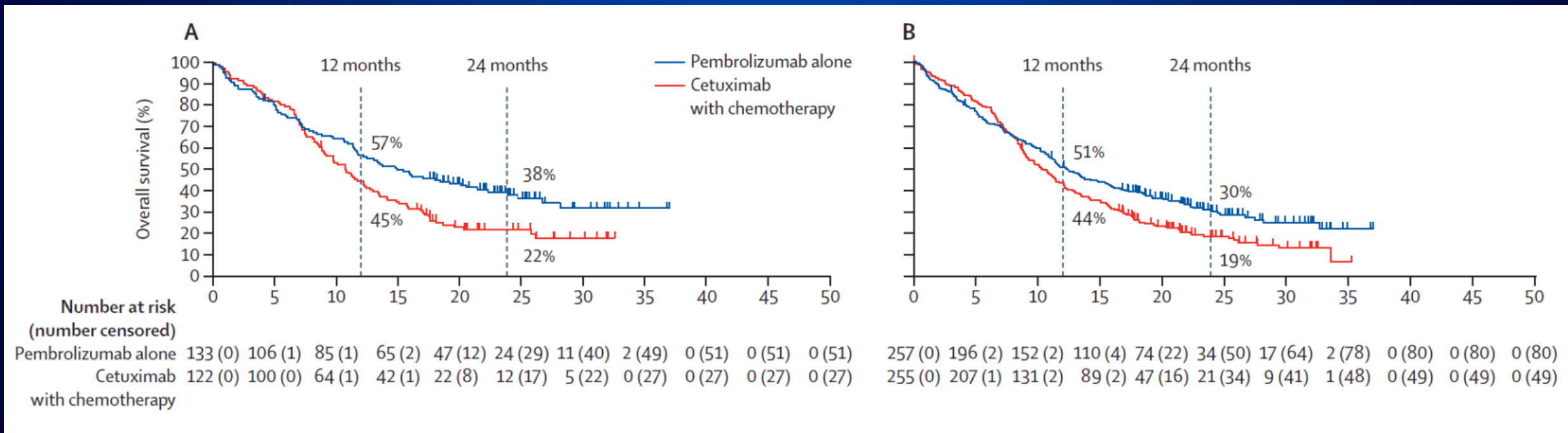
<sup>a</sup>Nominal, unadjusted one-sided P value based on log-rank test. Data cutoff: February 18, 2020.



# Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for R/M SCCHN: KEYNOTE-048

PD-L1 CPS  $\geq 20$

PD-L1 CPS  $\geq 1$



# **Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for R/M SCCHN: KEYNOTE-048**

- Median duration of response (DOR) in pts with PD-L1 CPS > 1
  - Pembrolizumab 23.4 months vs 4.5 mo EXTREME
- Median (DOR) in pts with PD-L1 CPS > 1
  - Pembro+Chemo 6.7 months vs 4.3 months in EXTREME

**Check PD-L1 on your pts... if CPS > 1 and low disease burden/Symptoms  
Use single agent Pembrolizumab**



# *But most are not fans of Carbo-5FU*

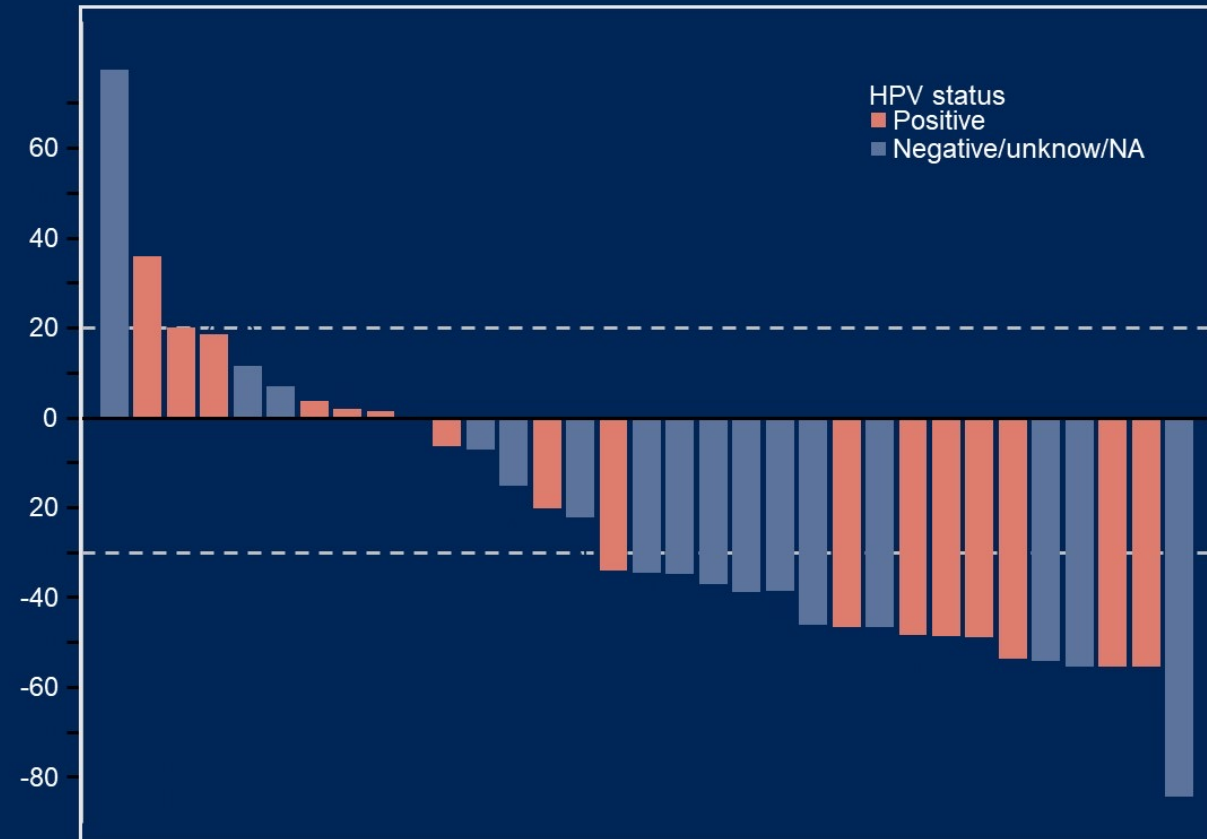
## KEYNOTE-B10 study

**Pembrolizumab (pembro) + carboplatin (carbo) + paclitaxel (pacli) as first-line (1L) therapy in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). *M.R. Dzienis et al. ESMO 2022***

- *100 pts enrolled, 41 still on Tx at data cutoff*
- *Confirmed ORR was 43% (95% CI, 32-54).*
- *Combination similar efficacy than Keynote048, known safety*

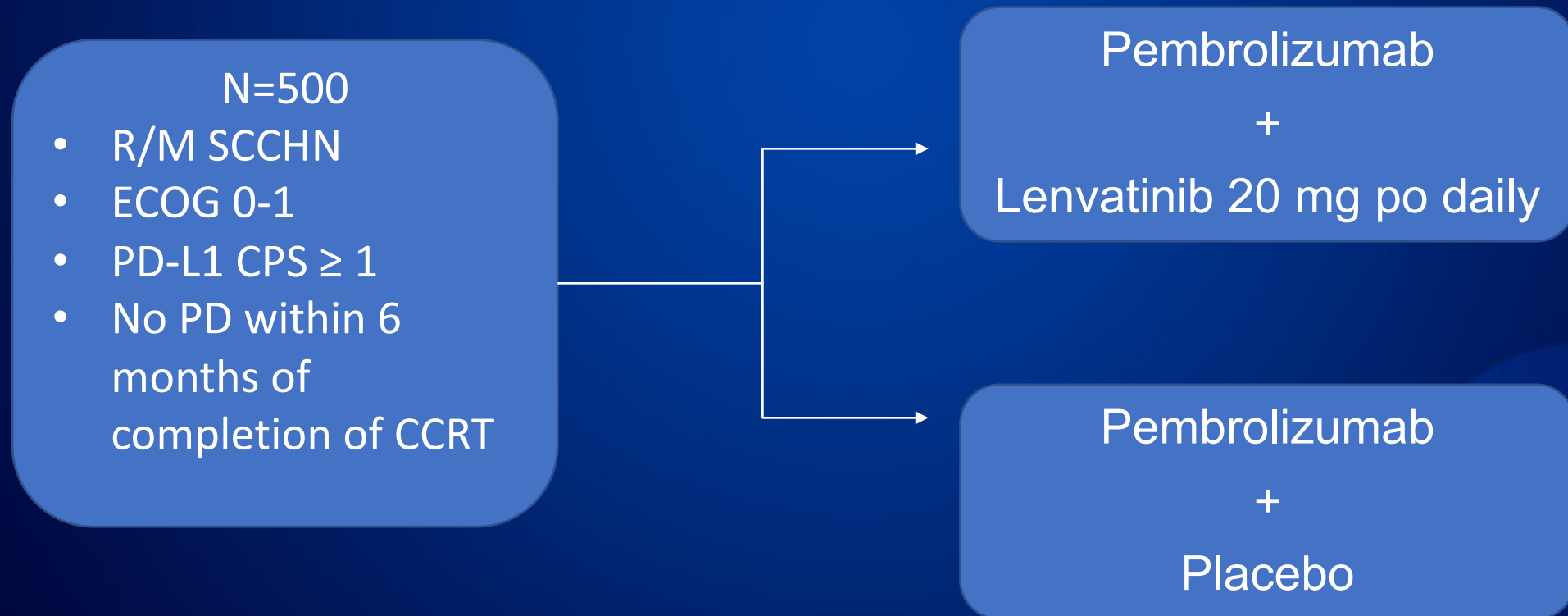
# A phase II trial of pembrolizumab and cabozantinib in patients (pts) with recurrent metastatic head and neck squamous cell carcinoma (RMHNSCC) *Saba et al ASCO 2022*

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



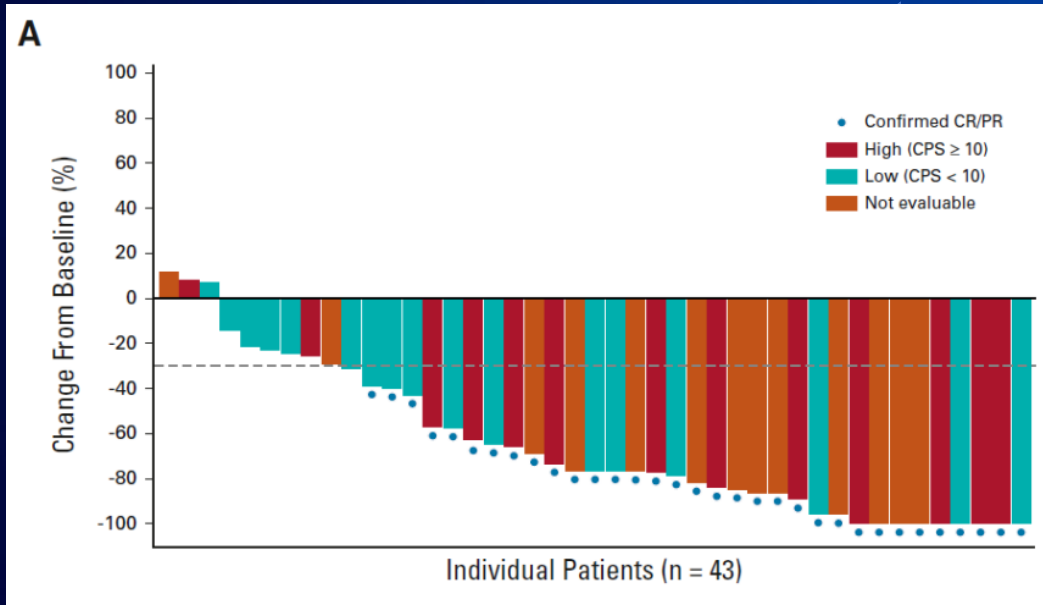
CR = complete response; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease

# Phase III LEAP-010 study: first-line pembrolizumab with or without lenvatinib in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).



# What about ADCs?

## *Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer*

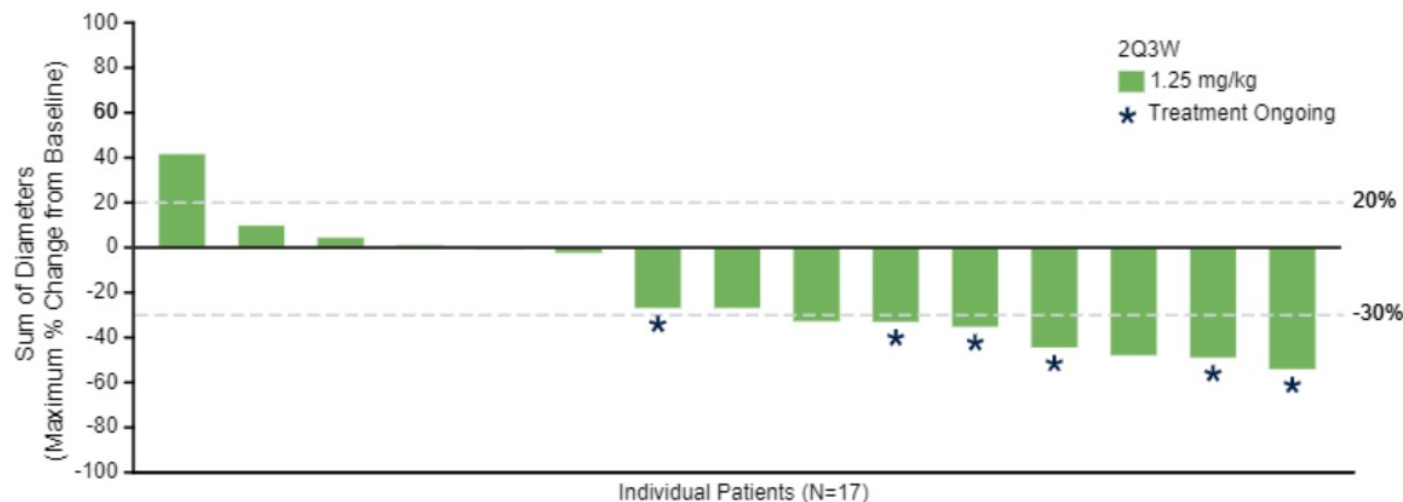


- Impressive responses of Enfortumab plus pembro in BladderCa
- Can we develop a similar approach for R/M SCCHN?

# SITC 2022: A first-in-human trial of an integrin beta-6 targeted antibody-drug conjugate (ADC), SGN-B6A, in patients with advanced solid tumors: Interim results

## HNSCC, 2Q3W (Dose Expansion)<sup>a</sup> Median 3 (range: 1–6) lines of prior therapy

Best Percentage Change in Target Lesion SoD from Baseline per RECIST v1.1



	2Q3W, HNSCC 1.25 mg/kg (N=17)
cORR, n (%)	5 (29.4)
95% CI	(10.3, 56.0)
Best Overall Response (Overall, n [%])	
cCR	0
cPR	5 (29.4)
SD	5 (29.4)
PD	5 (29.4)
NE	1 (5.9)
NA	1 (5.9)

- To date, the HNSCC safety profile is consistent with the 2Q3W escalation cohort
- 17 of 18 (94%) treated patients experienced TEAEs and 9 of 18 (50%) treated patients experienced Grade  $\geq 3$  TEAEs

## Educational program

Session Type	Session Title
Case-Based Panel	Multidisciplinary Management of Salivary Gland Cancers
Education Session	Current Treatment Strategies and Risk Stratification for Oral Carcinoma
Education Session	How to Approach Advanced Thyroid Cancer in 2023
Education Session	Personalizing Surveillance in Head and Neck Cancer



# Head and Neck Cancer in 2023

- Cisplatin based Chemo-RT continues to be standard in curative setting  
Adding CPI's has not proven to be beneficial...YET
- Novel CPI combinations in salvage setting might improve outcome
- Pembro-Chemo is standard first line therapy for R/M SCCHN, or Pembrolizumab for pts with PD-L1 CPS > 1
- Watch for TKI+CPI combos in first line (LEAP trial)
- ADCs are coming for pts with SCCHN...