

# First-Line treatment and beyond in Advanced Head and Neck Cancer

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Cliniques universitaires  
**SAINT-LUC**  
UCL BRUXELLES

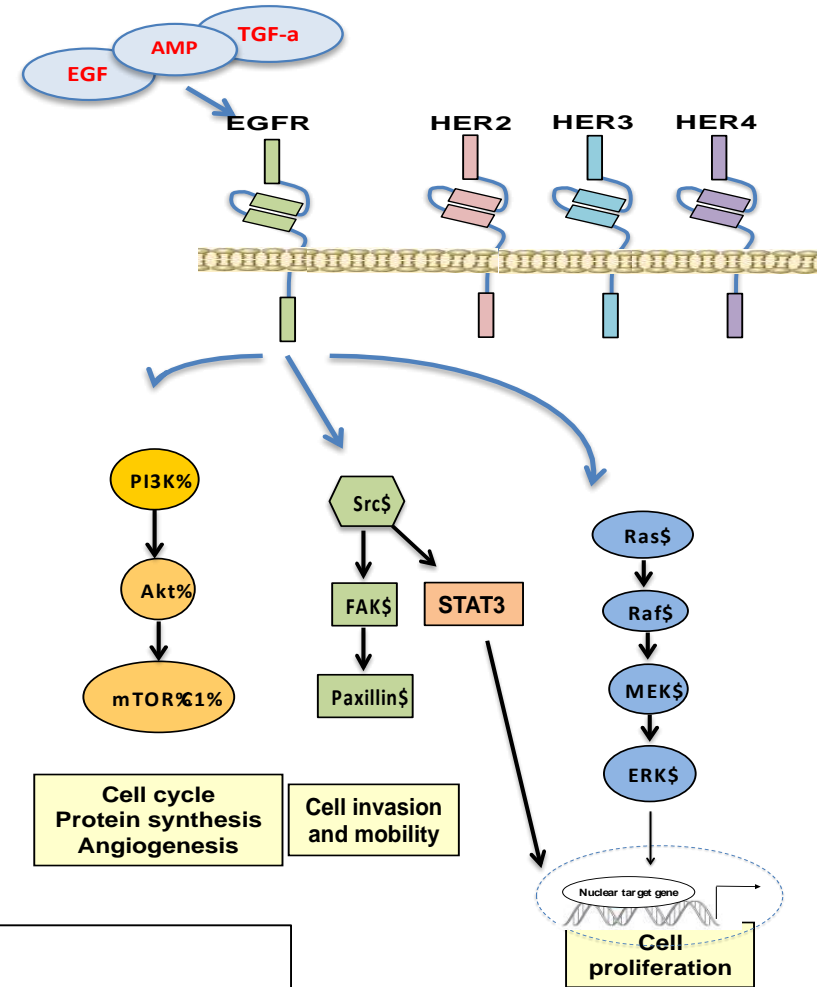


Disclosure for this presentation

Consultancy, advisory, travel :  
MSD, BMS, Merck,

# Recurrent/metastatic Head and Neck Squamous Cell Carcinoma

Tumor Type	Percentage of Tumors Expressing EGFR (range)
Colorectal	25-82%
Head and Neck	80-100%
Pancreatic	30-95%
NSCLC	40-81%
Renal Carcinoma	50-90%
Breast	14-91%
Ovarian	35-70%
Glioma	40-63%
Bladder	31-48%



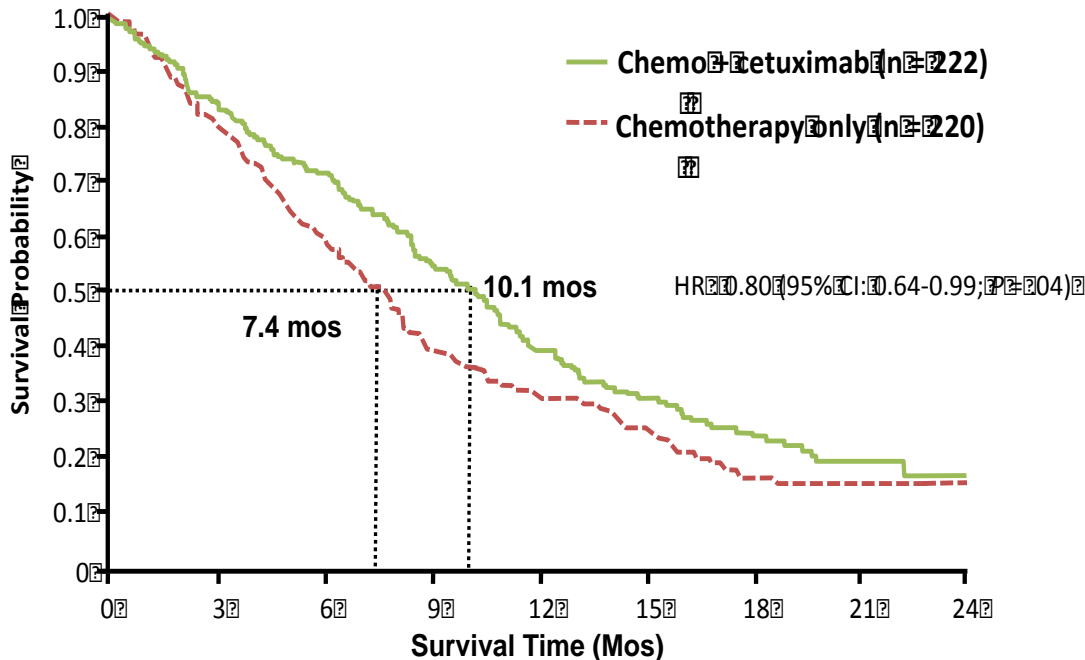
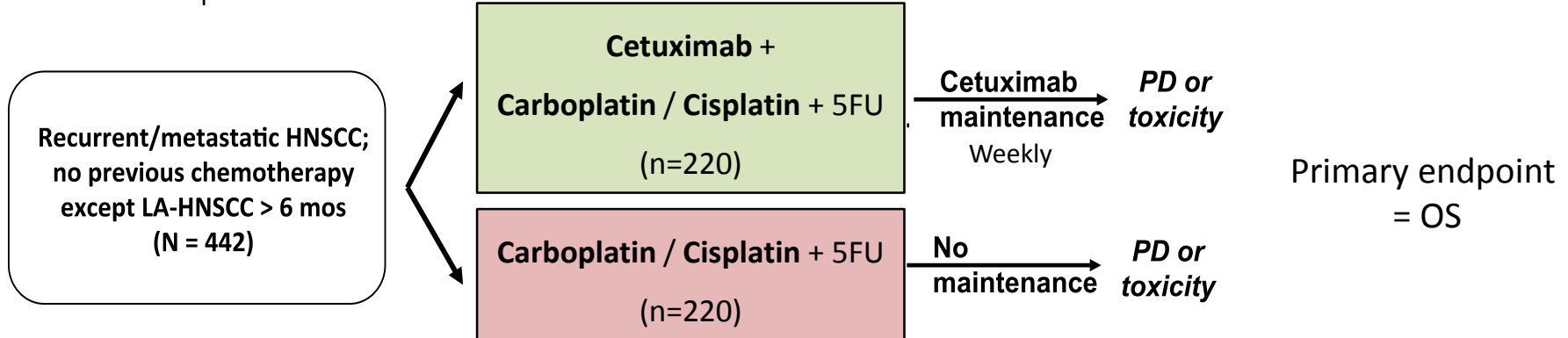
EGFR expression  
 Advanced stage  
 Decreased survival  
 Decreased sensitivity to treatment

# Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer

**EXTREME regimen**

Jan B. Vermorcken, M.D., Ph.D., Ricard Mesia, M.D., Fernando Rivera, M.D., Ph.D.,

Randomized phase III trial



OS benefit = 10mths vs 7 mths

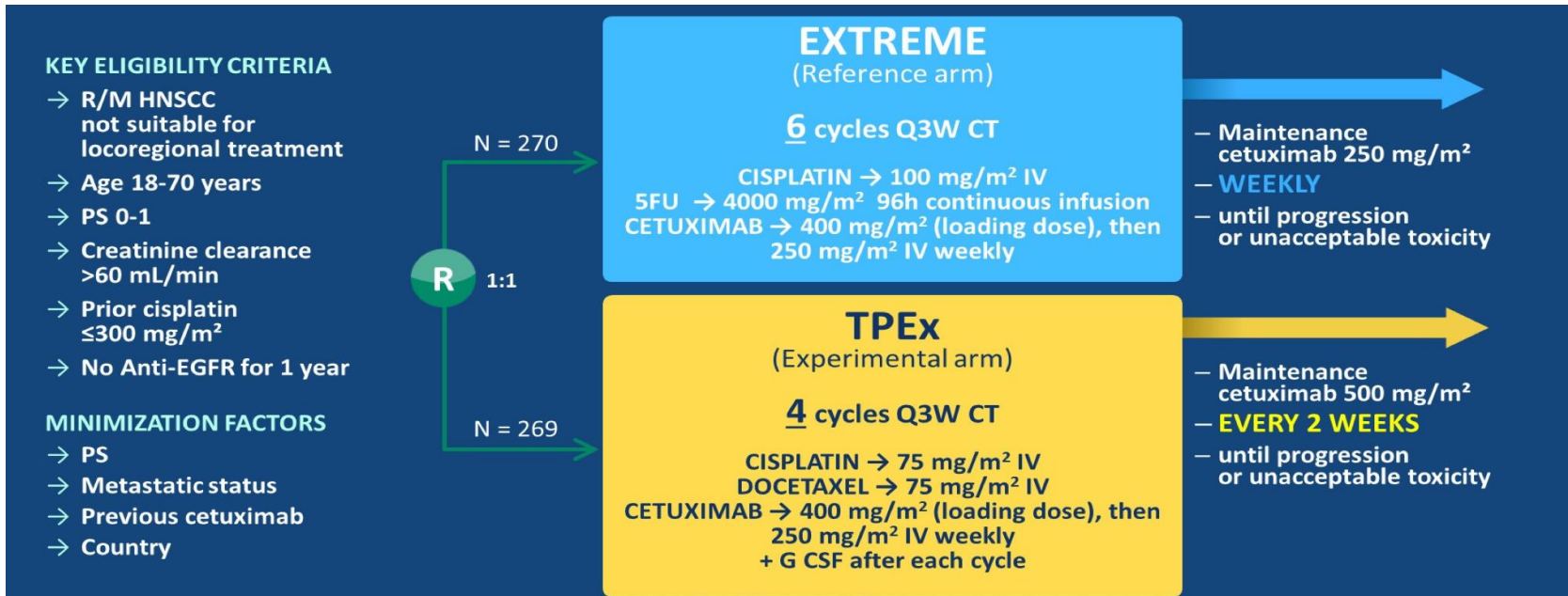
ORR = 36% vs 20%

82% of Gr 3-4 !!

**SoC in First-line setting**

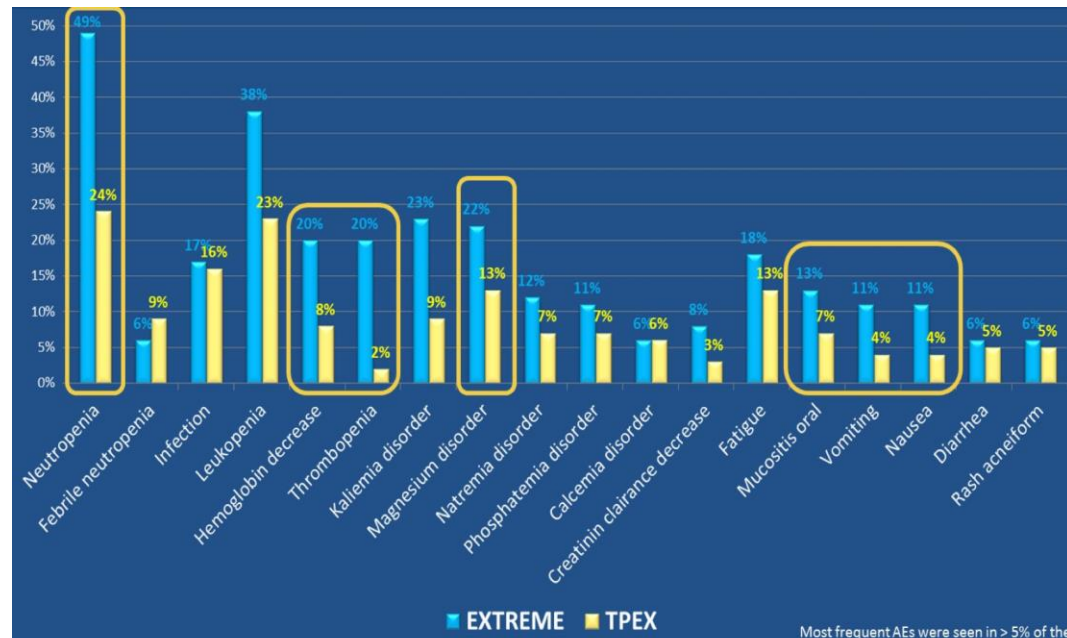
**Efficacy of Cetux in HPV + and -**

# TPEX versus EXTREME: study design



SIMILAR PFS  
 SIMILAR OS  
 SIMILAR ORR

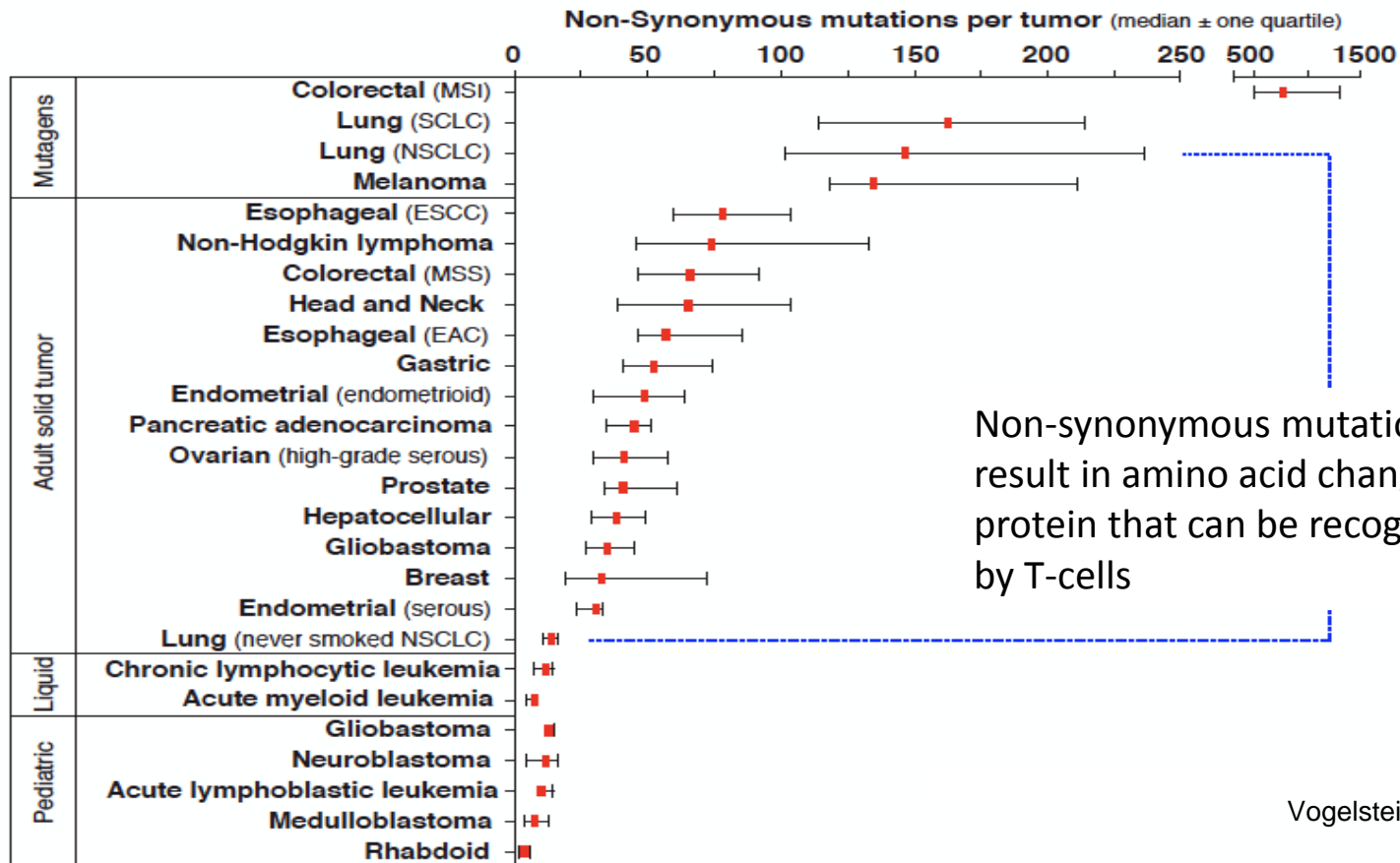
BETTER toxicity profile



# Efficacy of Immune Checkpoints Inhibitors in HNC

Antigens resulting from HPV infection

Antigens resulting from mutation (single nucleotide variations)



# Immune Checkpoint Inhibitors are active in 2<sup>nd</sup> line setting !

ORIGINAL ARTICLE

## Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck

R.L. Ferris, G. Blumenschein, Jr., J. Fayette, J. Guigay, A.D. Colevas, L. Licitra,

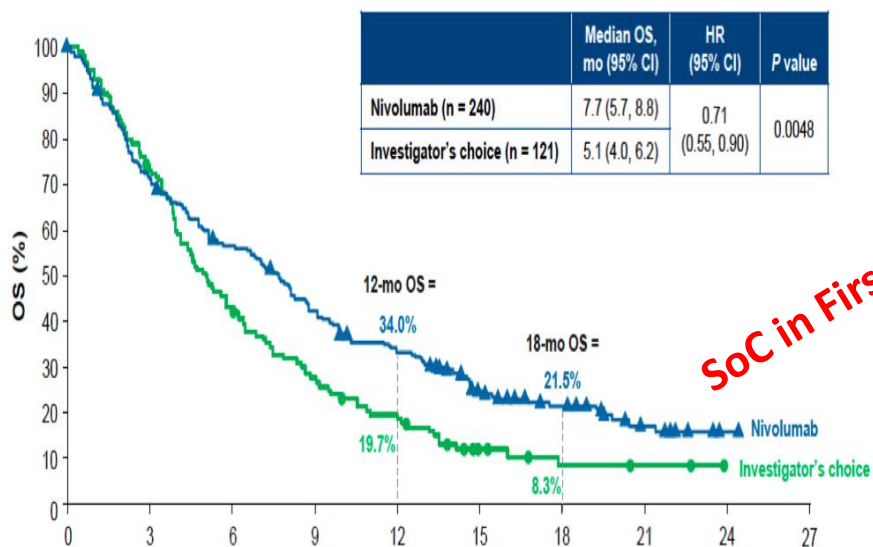
Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study



Ezra E.W. Cohen, Denis Soulières, Christophe Le Tourneau, José Dinis, Lisa Licitra, Myung-Ju Ahn, Aina Soria, Jean-Pascal Machiels, Nicolas Mach,

## Overall Survival, Minimum Follow-up: 11.4 Months

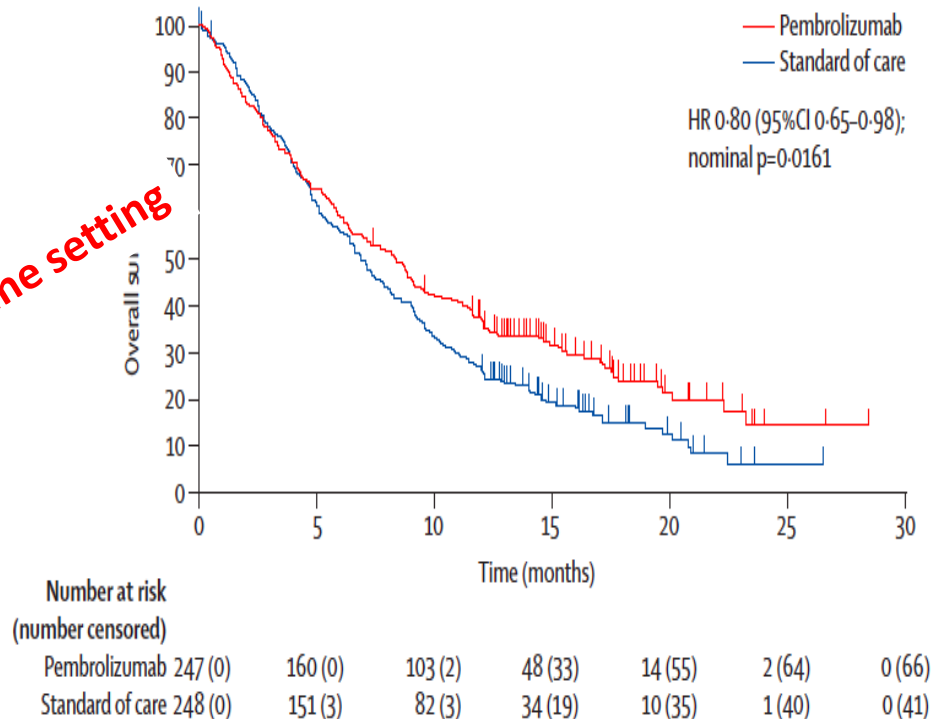
CheckMate 141: Nivolumab in R/M SCCHN After Platinum Therapy



SoC in First-line setting

No. of patients at risk	Months									
	0	3	6	9	12	15	18	21	24	27
Nivo	240	169	132	98	76	45	27	12	3	0
IC	121	88	51	32	22	9	4	3	0	0

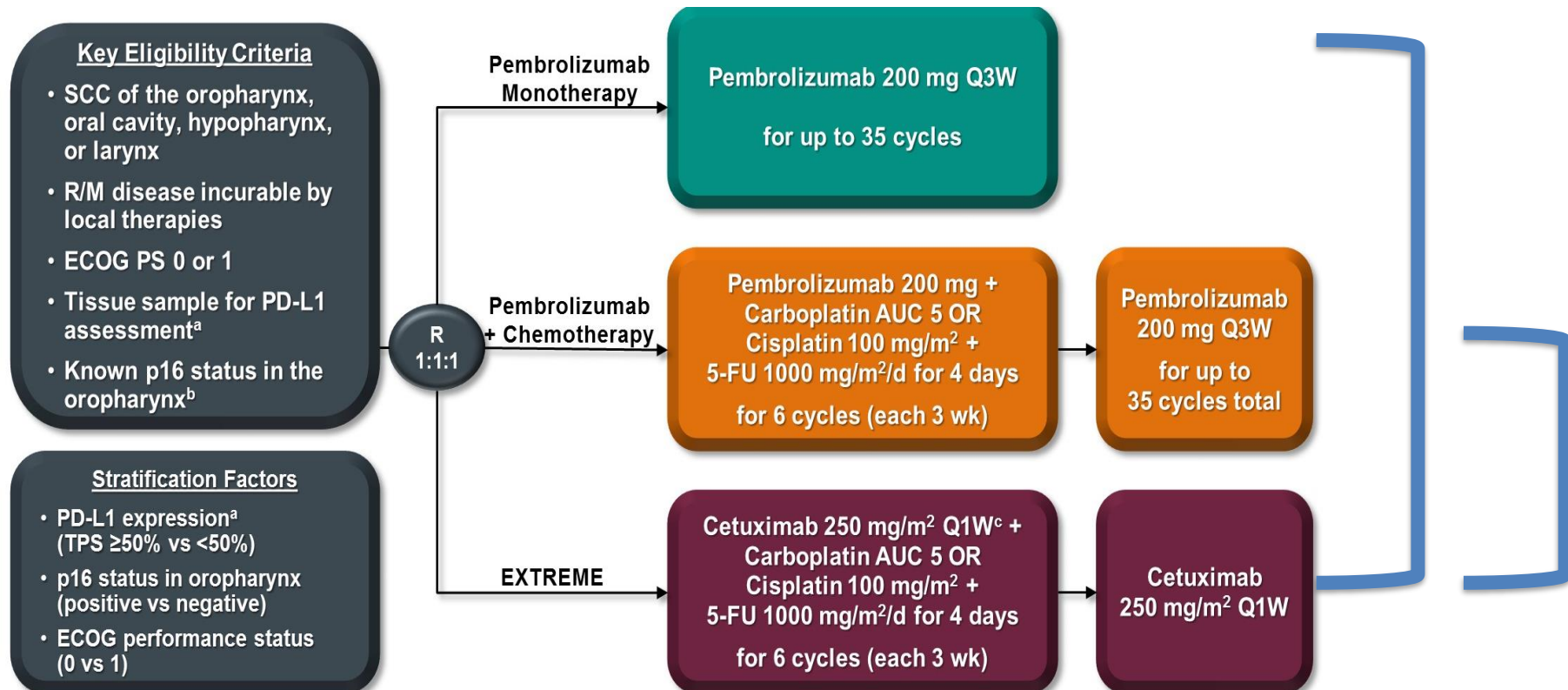
A



# Immune Checkpoint Inhibitor is active in **1st line setting** !

## Protocol-Specified Final Results of the KEYNOTE-048 Trial of Pembrolizumab as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma (R/M HNSCC)

Danny Rischin<sup>1</sup>, Kevin Harrington,<sup>2</sup> Richard Greil,<sup>3</sup> Denis Soulières,<sup>4</sup> Makoto Tahara,<sup>5</sup>



<sup>a</sup>Assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent). TPS = tumor proportion score = % of tumor cells with membranous PD-L1 expression.

<sup>b</sup>Assessed using the CINtec p16 Histology assay (Ventana); cutpoint for positivity = 70%. <sup>c</sup>Following a loading dose of 400 mg/m<sup>2</sup>.

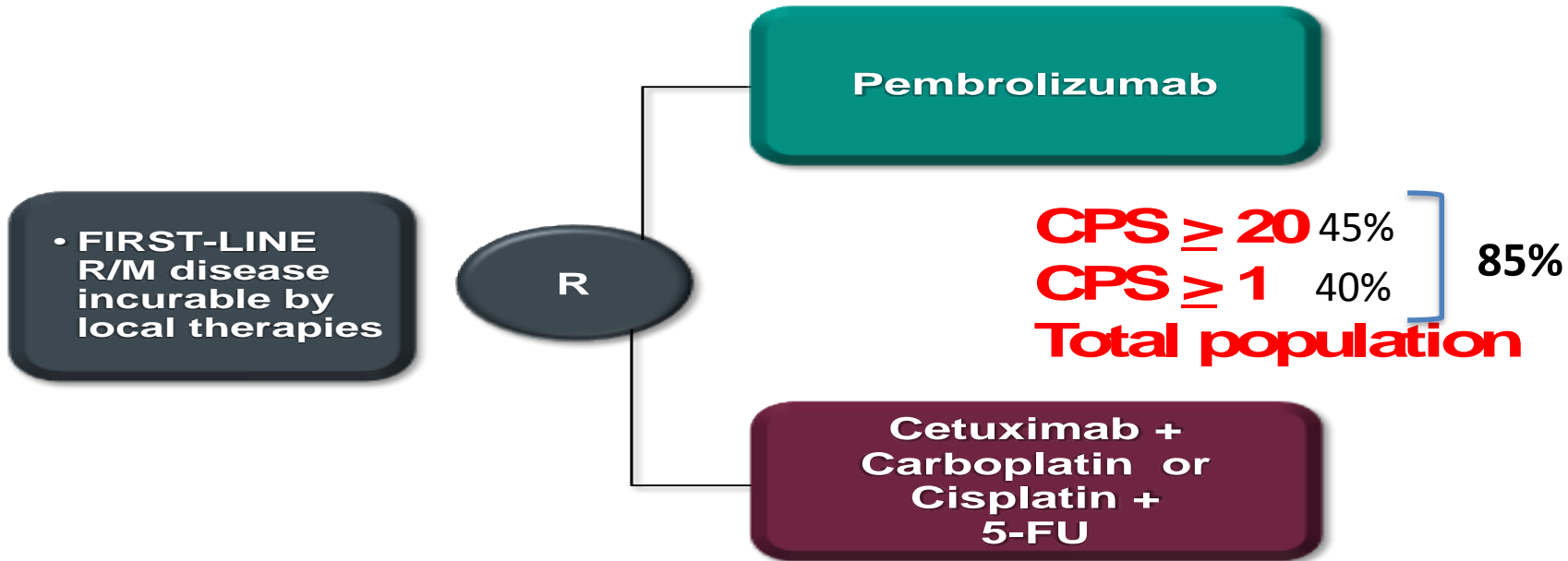


**Dual primary endpoint****S**: OS and PFS for **CPS ≥ 20, CPS ≥ 1** and **total population**

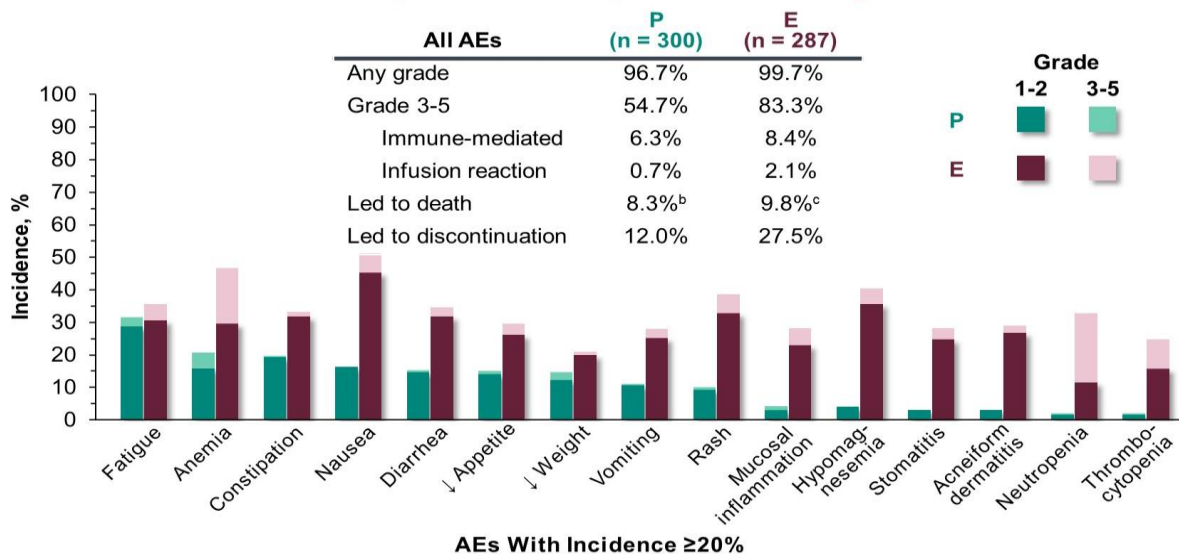
**CPS** (Combined Positive Score)

$$\text{CPS} = \frac{\text{Number of PD-L1 stained cells} \\ \text{(tumor cells, lymphocytes, macrophages)}}{\text{Total number of viable tumor cells}} \times 100$$

*Reported as a number  
(capped at 100)*

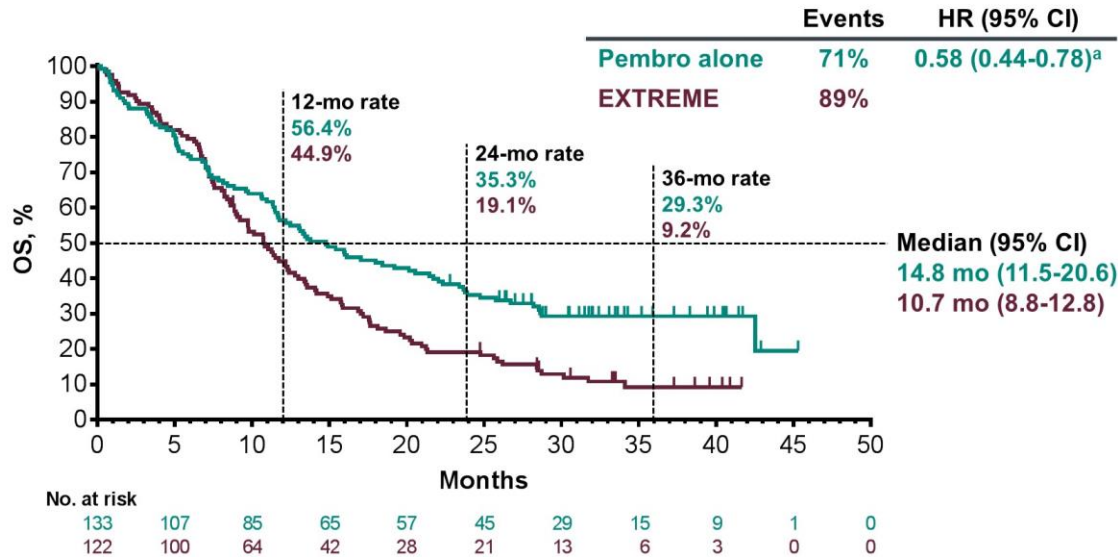


## All-Cause AEs,<sup>a</sup> P vs E, Total Population



<sup>a</sup>Data for treatment-related AEs were presented at ESMO 2018. <sup>b</sup>Events were considered treatment related in 1.0%. <sup>c</sup>Events were considered treatment related in 2.8%. FA (data cutoff date: Feb 25, 2019).

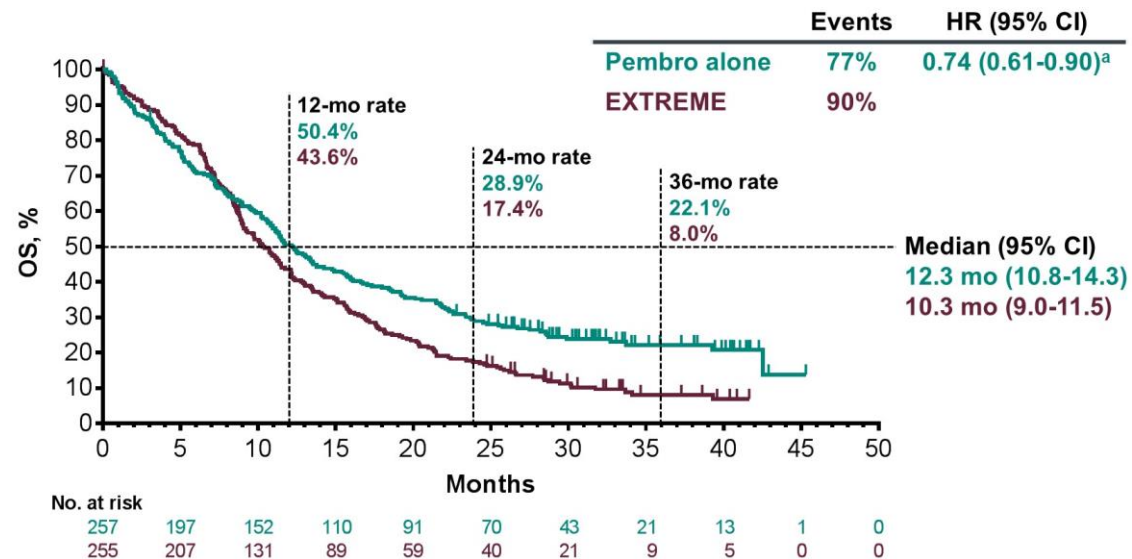
# OS, P vs E, CPS ≥20 Population



Pembro superior to Extreme  
in **CPS>20**

<sup>a</sup>At IA2 (data cutoff date: Jun 13, 2018): HR 0.61 (95% CI 0.45-0.83).  
FA (data cutoff date: Feb 25, 2019).

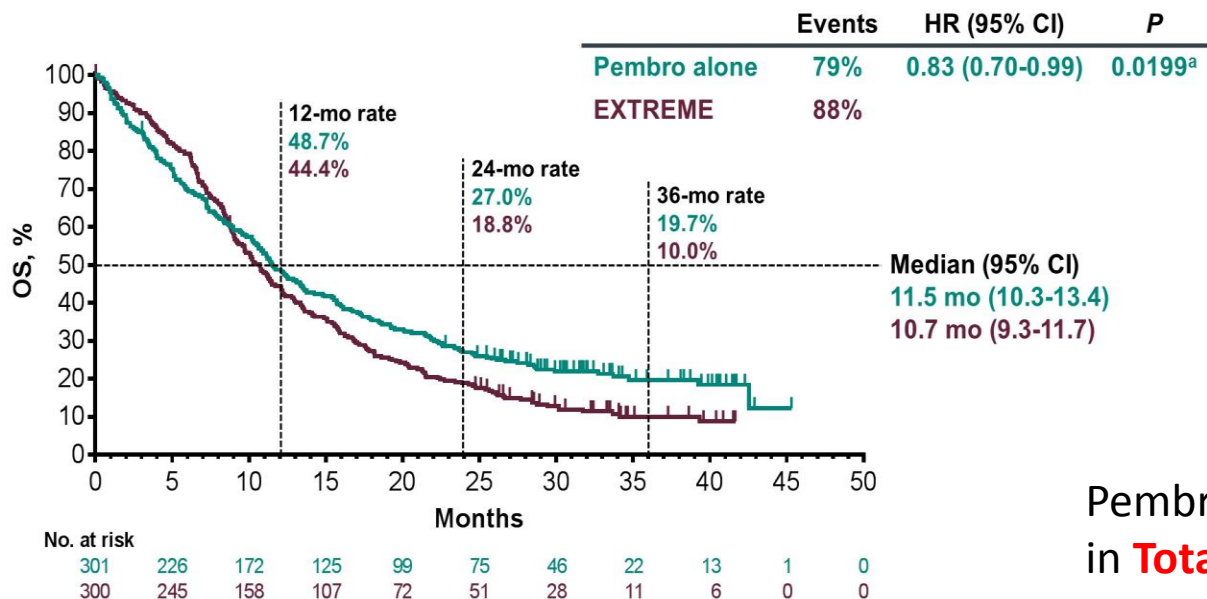
# OS, P vs E, CPS ≥1 Population



Pembro superior to Extreme  
in **CPS>1**

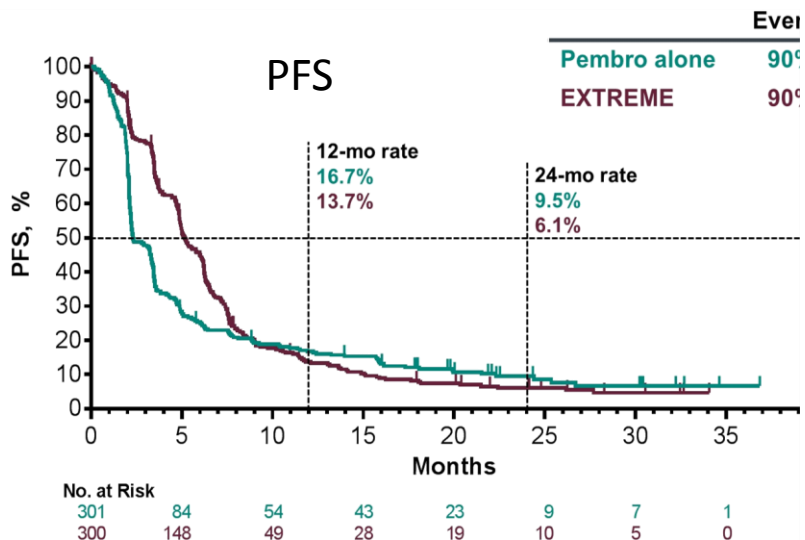
<sup>a</sup>At IA2 (data cutoff date: Jun 13, 2018): HR 0.78 (95% CI 0.64-0.96).  
FA (data cutoff date: Feb 25, 2019).

# OS, P vs E, Total Population



Pembro NOT SUPERIOR to Extreme in **Total Population!**

<sup>a</sup>Not statistically significant at the superiority threshold of  $P = 0.0059$ .  
FA (data cutoff date: Feb 25, 2019).



	Pembro	EXTREME
ORR Total population	17%	36%
ORR CPS $\geq 1$	19%	35%
ORR CPS $\geq 20$	23%	36%

• **FIRST-LINE**  
R/M disease  
incurable by  
local therapies

**R**

**Pembrolizumab +  
Carboplatin or  
Cisplatin + 5-FU**

**CPS ≥ 20** 45%

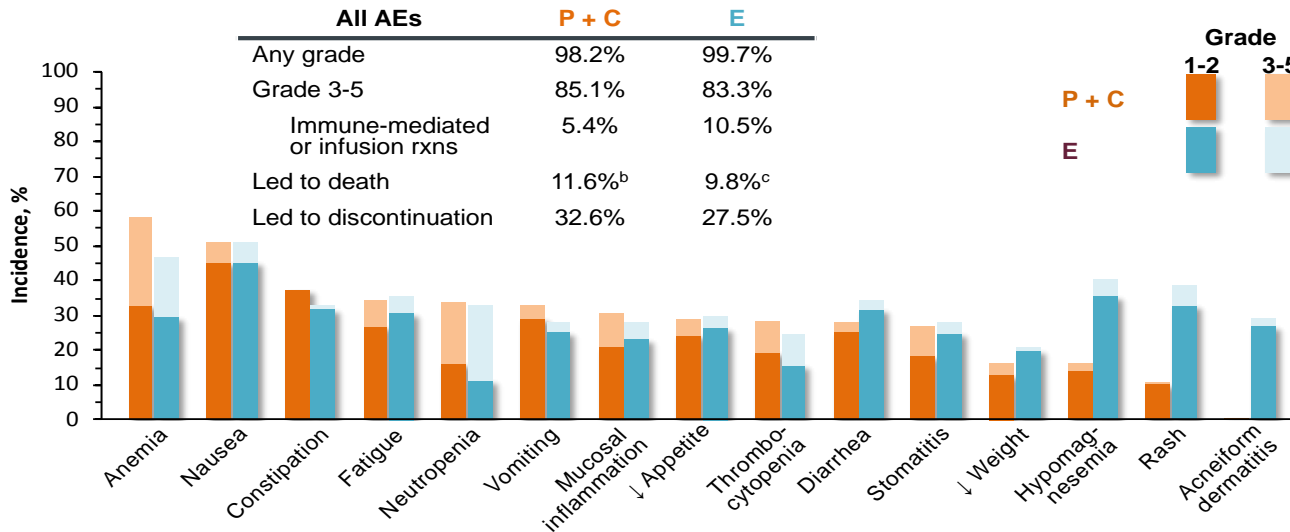
**CPS ≥ 1** 40%

**85%**

**Total population**

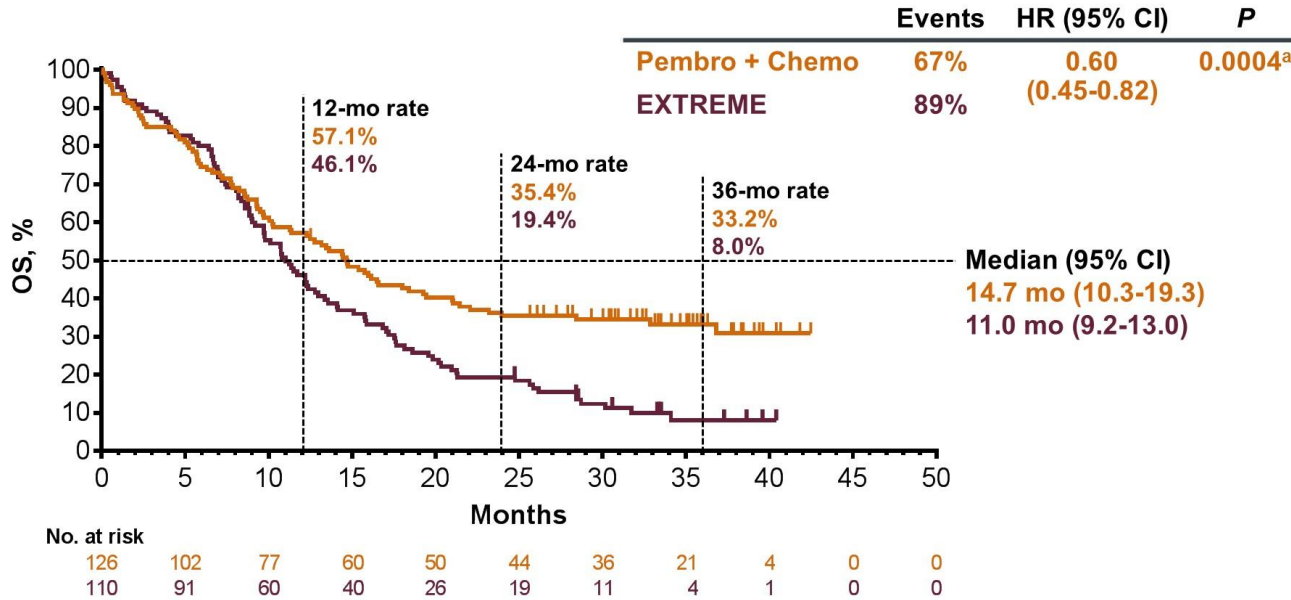
**Cetuximab +  
Carboplatin or  
Cisplatin +  
5-FU**

### All-Cause AEs,<sup>a</sup> P + C vs E, Total Population



**AEs With Incidence ≥20%**

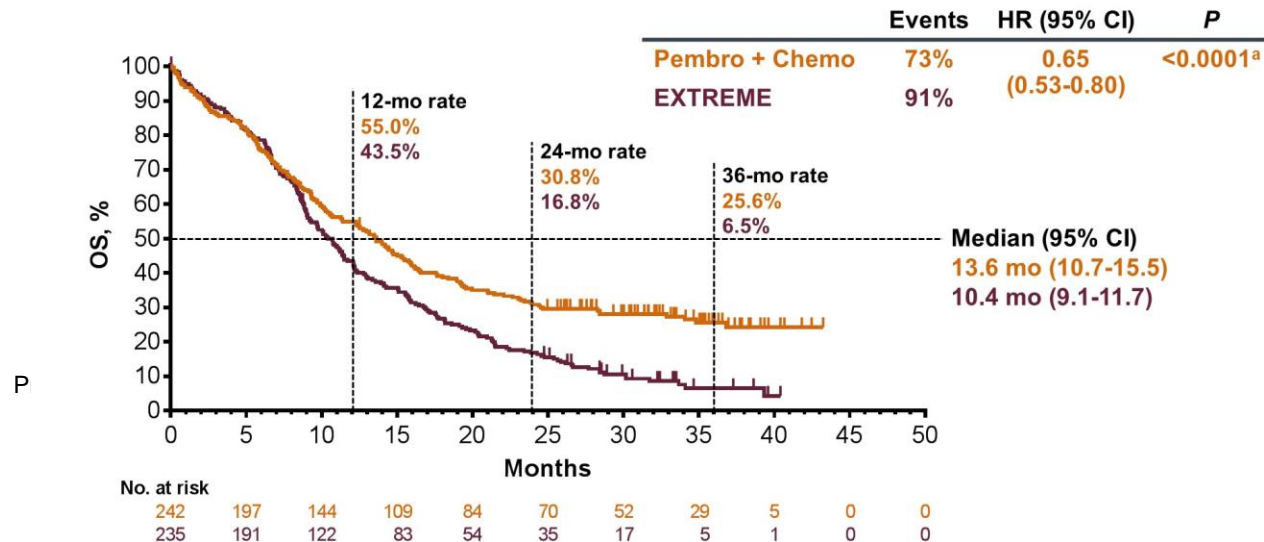
# OS, P+C vs E, CPS ≥20 Population



CT+ Pembro superior to Extreme  
in CPS >20

<sup>a</sup>Statistically significant at the superiority threshold of  $P = 0.0023$ .  
FA (data cutoff date: Feb 25, 2019).

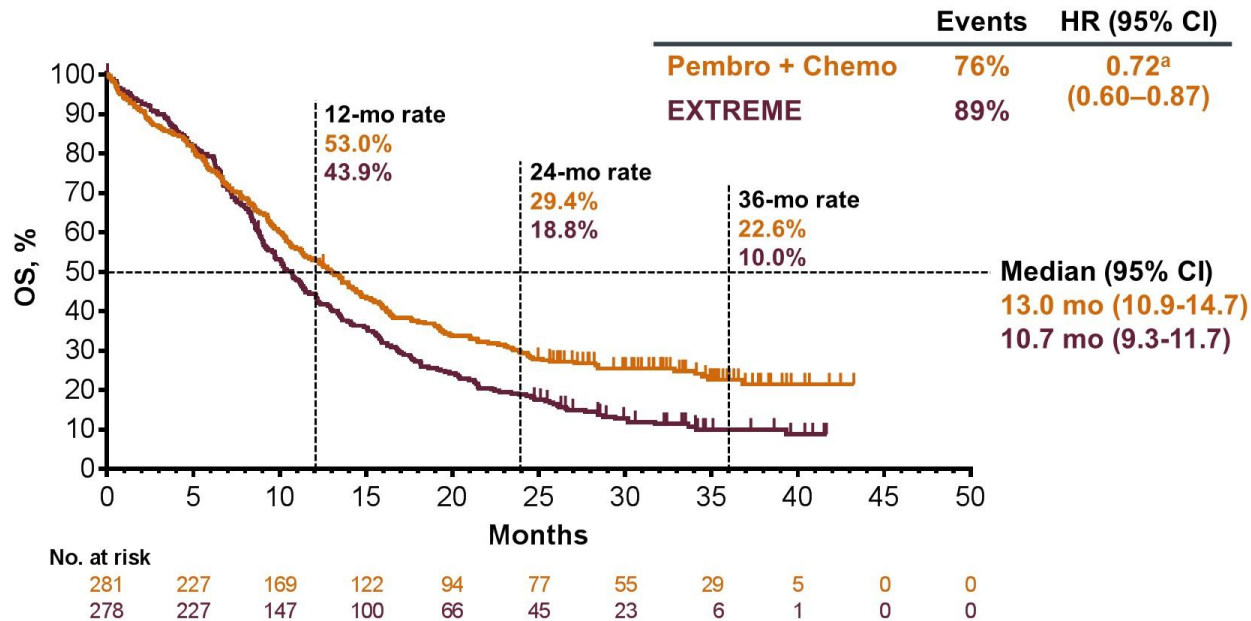
# OS, P+C vs E, CPS ≥1 Population



CT+ Pembro superior to Extreme  
in CPS >1

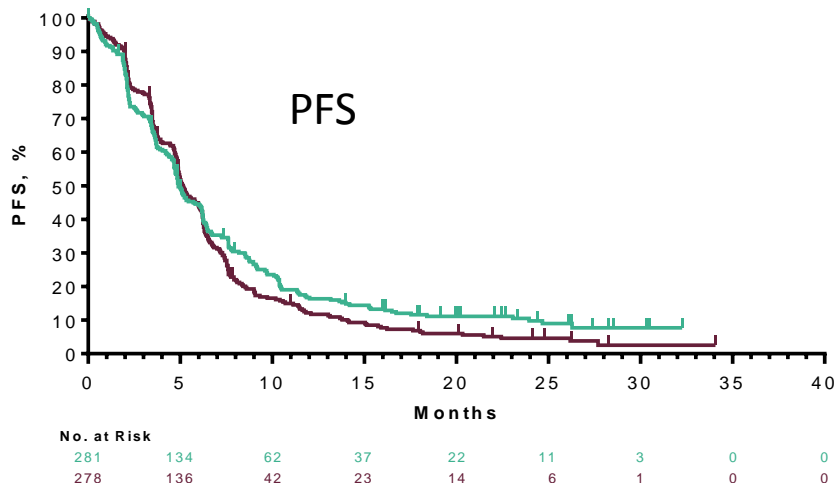
<sup>a</sup>Statistically significant at the superiority threshold of  $P = 0.0026$ .  
FA (data cutoff date: Feb 25, 2019).

# OS, P+C vs E, Total Population

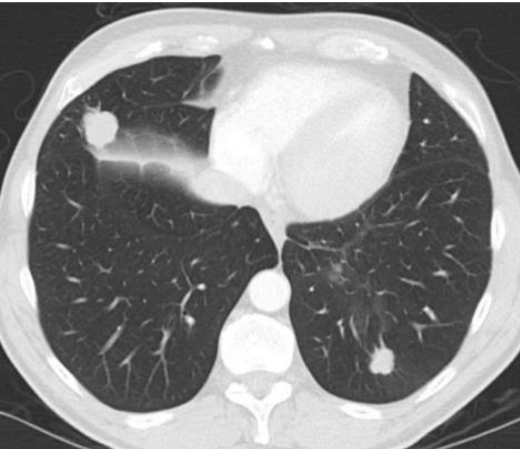


<sup>a</sup>At IA2 (data cutoff date: Jun 13, 2018): HR 0.77 (95% CI 0.53–0.93).  
<sup>b</sup>FA (data cutoff date: Feb 25, 2019).

CT + Pembro superior to Extreme **in total population**

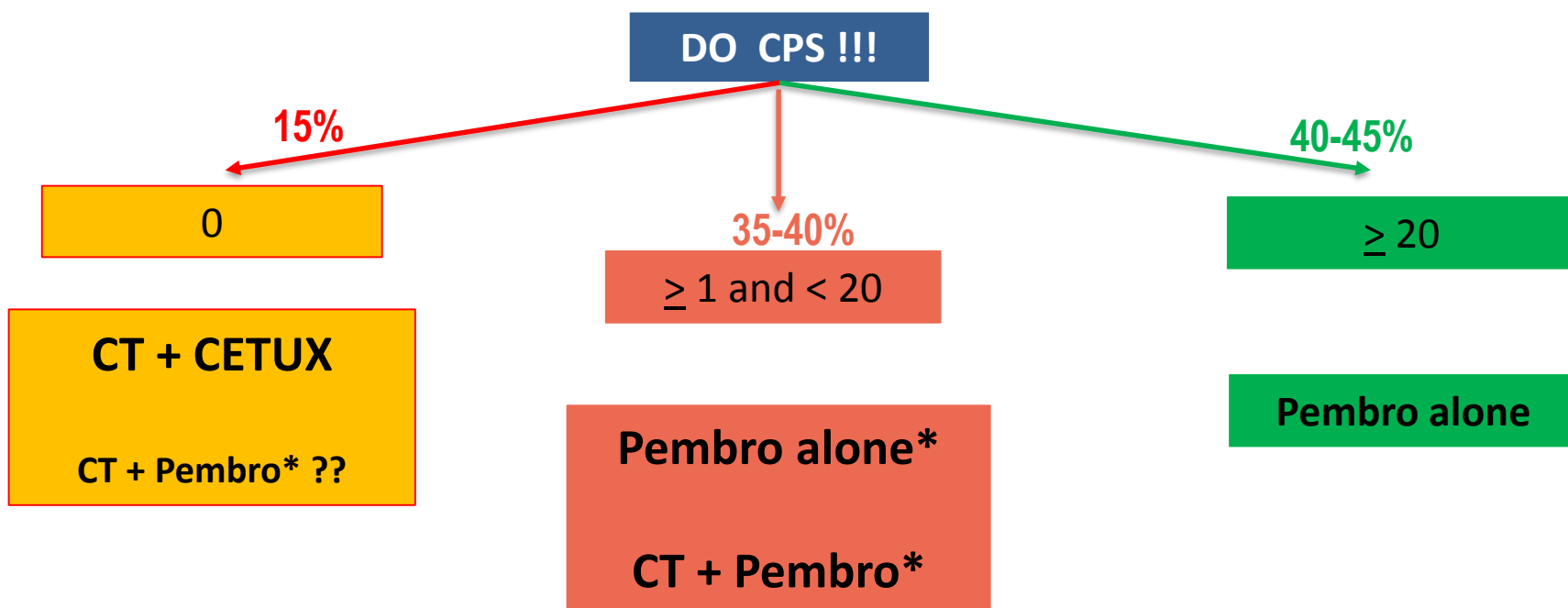


Confirmed Response, n (%)	Pembro + Chemo N = 281	EXTREME N = 278
<b>ORR</b>	<b>100 (35.6)</b>	<b>101 (36.3)</b>
CR	17 (6.0)	8 (2.9)
PR	83 (29.5)	93 (33.5)
SD	78 (27.8)	94 (33.8)
PD	48 (17.1)	34 (12.2)
Non-CR/non-PD <sup>a</sup>	13 (4.6)	9 (3.2)
Not evaluable or assessed <sup>b</sup>	42 (14.9)	40 (14.4)



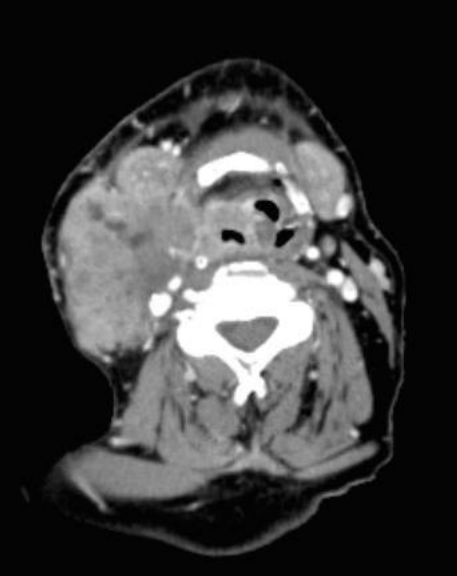
Patients in stable condition and asymptomatic

You do not need a tumor shrinkage



\*Exploratory analysis in CPS 1-19 subgroup (monotherapy vs. EXTREME): HR=0.90 (95% CI: 0.68, 1.18) (US prescribing information)  
Data for CPS <1 (monotherapy and combination) and CPS 1-19 (combination therapy) subgroups are not available





Rapid tumor shrinkage needed

CPS available

15%

0

85%

$\geq 1$

NO CPS Done

Extreme= CT + CETUX

CT + Pembro ??

CT + Pembro

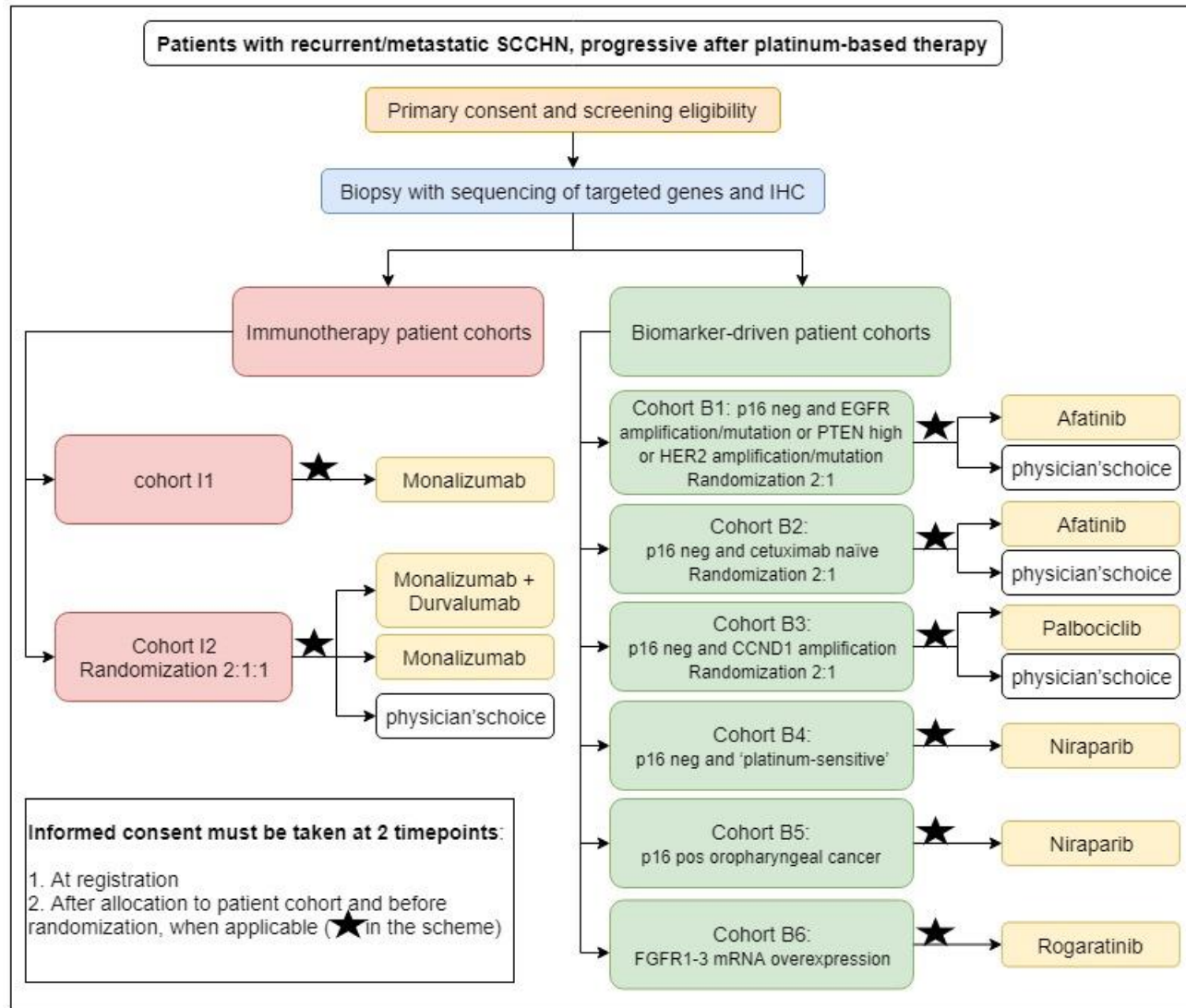
CT + Pembro

No place for Pembrolizumab alone !!!!

# EORTC – HNCG

## Study 1559 (UPSTREAM):

A pilot study of personalized biomarker-based treatment strategy or immunotherapy in patients with recurrent/metastatic squamous cell carcinoma of the head and neck



Thank you

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