Updates in Head and Neck Cancer

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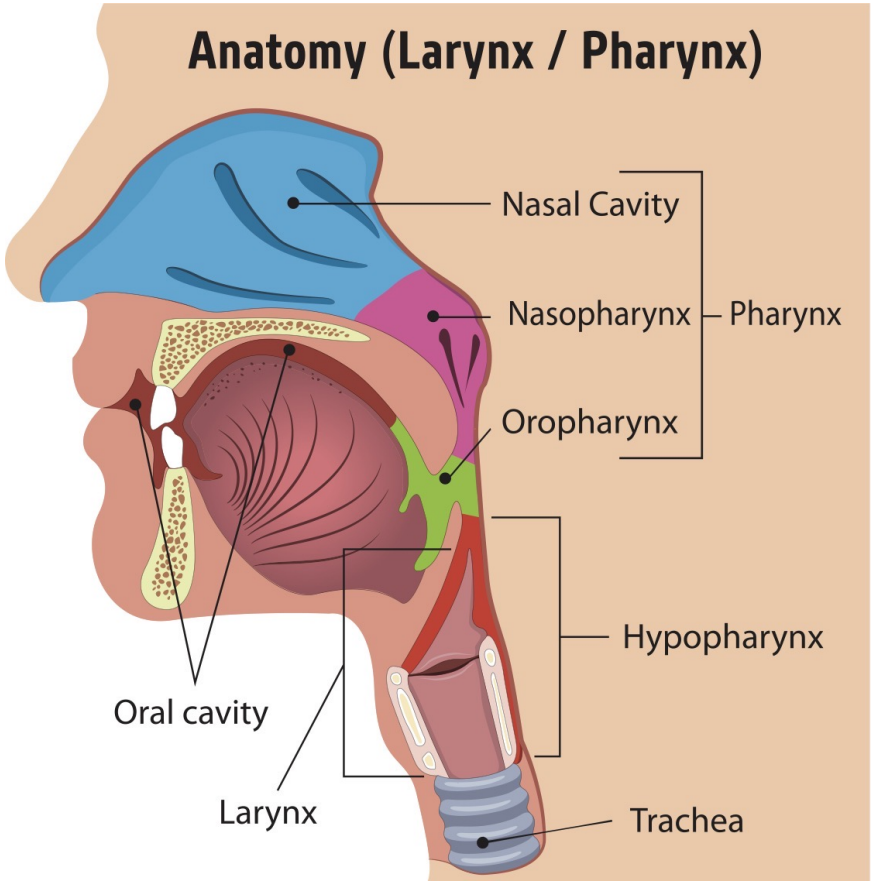
H&N Cancer is a Broad Headline for a plethora of diagnosis



Curative Intent Setting

Primary Results of the Phase 3 KEYNOTE-412 Study: Pembrolizumab Plus Chemoradiation Therapy (CRT) vs Placebo Plus CRT for Locally Advanced Head and Neck Squamous Cell Carcinoma

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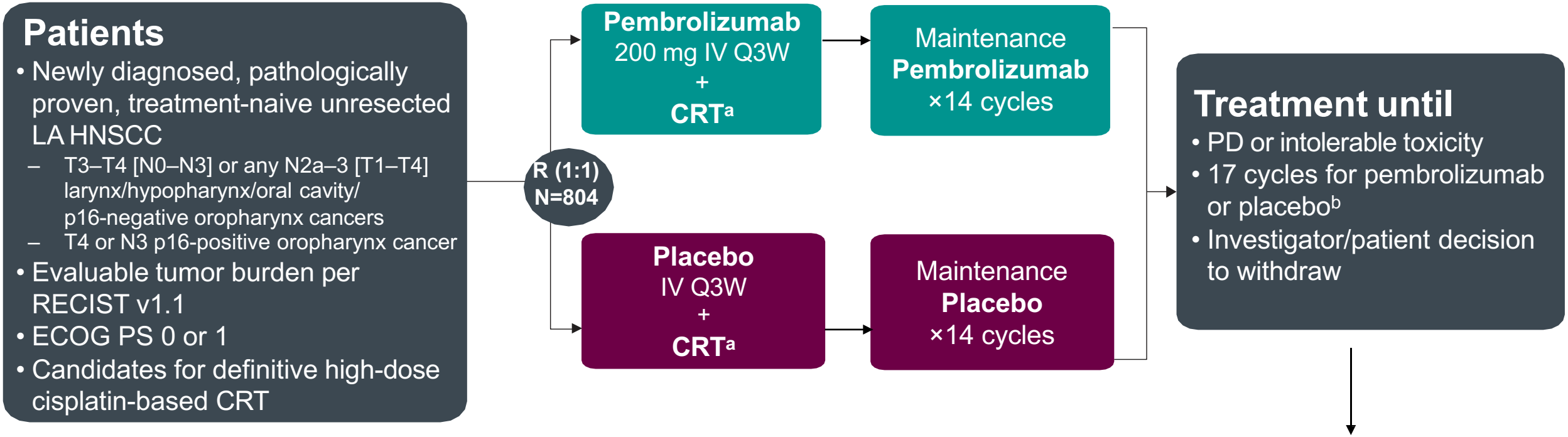
KEYNOTE-412 Study Design (NCT03040999)



Stratification Factors
- Radiotherapy regimen (AFX vs SFX)
- Tumor site/p16 status (oropharynx [p16+ vs p16-] or larynx/hypopharynx/oral cavity)
- Disease stage (III vs IV)

Primary endpoint
- Event-free survival (EFS)

Secondary endpoints included:
- OS
- Safety/tolerability

Post-treatment follow-up to assess
- Safety
- Disease status
- Survival

[a]CRT included cisplatin (100 mg/m^2, Q3W) and accelerated fractionation (AFX) (70 Gy, 6 fractions/week for 5 weeks and then 5 fractions for the 6th week, 35 fractions in total) or standard fractionation (SFX) (70 Gy, 5 fractions/week for 7 weeks, 35 fractions in total). [b]A pembrolizumab/placebo priming dose was given 1 week before CRT, followed by 2 doses during CRT and 14 doses of maintenance therapy after CRT, for a total of 17 doses.

Baseline Characteristics, ITT Population

n (%)	Pembro + CRT N = 402	Placebo + CRT N = 402
Age, median (range), years	59.0 (27-81)	59.0 (36-79)
≥65 years, n (%)	109 (27.1)	96 (23.9)
Male	331 (82.3)	329 (81.8)
Race, white	311 (77.4)	311 (77.4)
Region		
North America	43 (10.7)	43 (10.7)
Western Europe	198 (49.3)	182 (45.3)
Rest of the world	161 (40.0)	177 (44.0)
PD-L1 CPS ≥1	339 (84.3)	346 (86.1)
PD-L1 CPS ≥20	146 (36.3)	145 (36.1)
ECOG PS 1	137 (34.1)	151 (37.6)
Primary tumor site		
Oropharynx	200 (49.8)	204 (50.7)
Oral cavity	39 (9.7)	39 (9.7)
Larynx	92 (22.9)	86 (21.4)
Hypopharynx	71 (17.7)	73 (18.2)
HPV+	109 (27.1)	104 (25.9)

n (%)	Pembro + CRT N = 402	Placebo + CRT N = 402
RT		
Accelerated fractionation	11 (2.7)	9 (2.2)
Standard fractionation	391 (97.3)	393 (97.8)
Overall stage[a]		
II-III	140 (34.8)	137 (34.1)
IVA-IVB	262 (65.2)	265 (65.9)
Tumor stage[a,b]		
T1-T2	67 (16.7)	54 (13.4)
T3-T4-T4a-T4b	335 (83.3)	347 (86.3)
Nodal stage[a,c]		
N0-N1	122 (30.3)	134 (33.3)
N2-N2a-N2b-N2c	225 (56.0)	222 (55.2)
N3-N3a-N3b	54 (13.4)	46 (11.4)
Baseline tumor burden (mm)		
Patients with data	383	389
Median (range)	50.0 (10.0-173.0)	50.0 (12.0-264.0)
Former/current smoker	346 (86.1)	346 (86.1)
Alcohol use	308 (76.6)	305 (75.9)

[a]Tumors were staged according to the American Joint Committee on Cancer (AJCC) staging manual (the 7th edition for patients enrolled before January 1, 2018, and the 8th edition for those enrolled starting on that date). [b]TX=1 with placebo + CRT. [c]NX=1 with pembrolizumab + CRT. Data cutoff date: May 31, 2022.

Summary of Patient Disposition and Analysis Populations

804 patients randomized 1:1 from April 19, 2017 to May 2, 2019

Patient disposition, n (%)	Pembro + CRT (N = 402)	Placebo + CRT (N = 402)
Concurrent CRT phase, treated	**398**	**398**
Completed, continued with MT	343 (86.2)	351 (88.2)
Completed, did not continue with MT	27 (6.8)	19 (4.8)
Discontinued, continued with MT	5 (1.3)	2 (0.5)
Discontinued, did not continue with MT	23 (5.8)	26 (6.5)
MT phase, treated	**348**	**353**
Completed	210 (60.3)	223 (63.2)
Analysis populations, n (%)	**Pembro + CRT**	**Placebo + CRT**
Efficacy (ITT)	402	402
Safety (as treated)	398	398

Median (range) follow-up[a]: 47.7 (range, 37.0-61.4) mo

[a]Defined as median time from randomization to data cutoff. MT, maintenance therapy. Data cutoff date: May 31, 2022.

Summary of Treatment Exposure

Summary of Exposure to RT

	Pembro + CRT N = 398	Placebo + CRT N = 398
Patients exposed to RT, n	**396**	**397**
RT dosage delivered (Gy)		
<70	28 (7.1)	28 (7.1)
≥70	368 (92.9)	369 (92.9)
Median (range)	70.0 (6.0-70.0)	70.0 (2.0-74.0)

Summary of Exposure to Pembrolizumab/Placebo

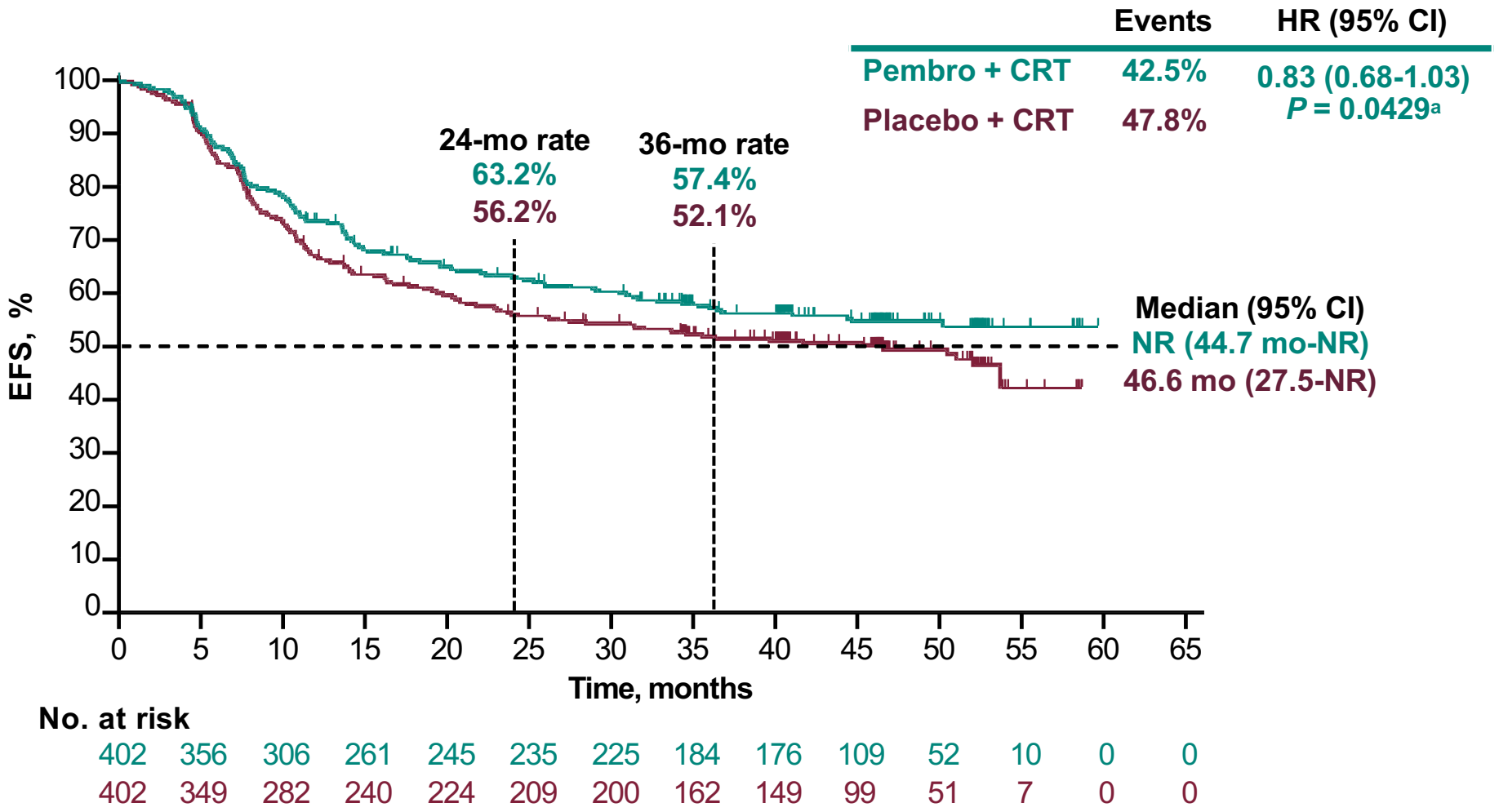
	Pembro + CRT N = 398	Placebo + CRT N = 398
Overall duration on therapy, median (range), mo	11.1 (0.03-14.6)	11.1 (0.03-15.2)
Overall number of cycles, n (%)		
<3	36 (9.0)	30 (7.5)
3	15 (3.8)	17 (4.3)
>3 to <17	137 (34.4)	128 (32.2)
≥17	210 (52.8)	223 (56.0)
Median (range)	17.0 (1.0-17.0)	17.0 (1.0-18.0)

Summary of Exposure to Cisplatin

	Pembro + CRT N = 398	Placebo + CRT N = 398
Patients exposed to cisplatin, n	**395**	**396**
Total dose (mg/m^2), n (%)		
>0 to <200	49 (12.4)	46 (11.6)
≥200 to <300	164 (41.5)	142 (35.9)
≥300	182 (46.1)	208 (52.5)
Median (range)	280.0 (60.0-300.0)	300.0 (80.0-300.0)
Number of administrations, median (range)	3.0 (1.0-3.0)	3.0 (1.0-3.0)
Dose reduction, n (%)	89 (22.5)	78 (19.7)
Dose discontinuation, n (%)	149 (37.7)	128 (32.3)

Data cutoff date: May 31, 2022.

Event-Free Survival, ITT Population



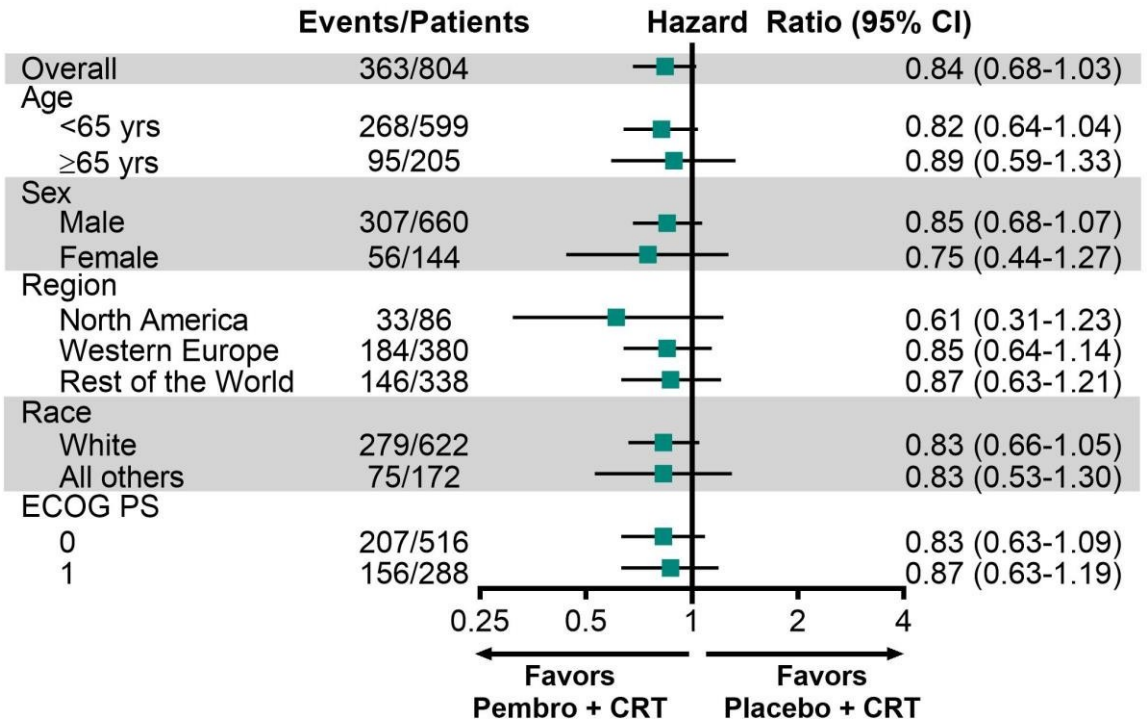
[a]*P* value did not meet the superiority threshold of one-sided α of 0.0242. Data cutoff date: May 31, 2022.

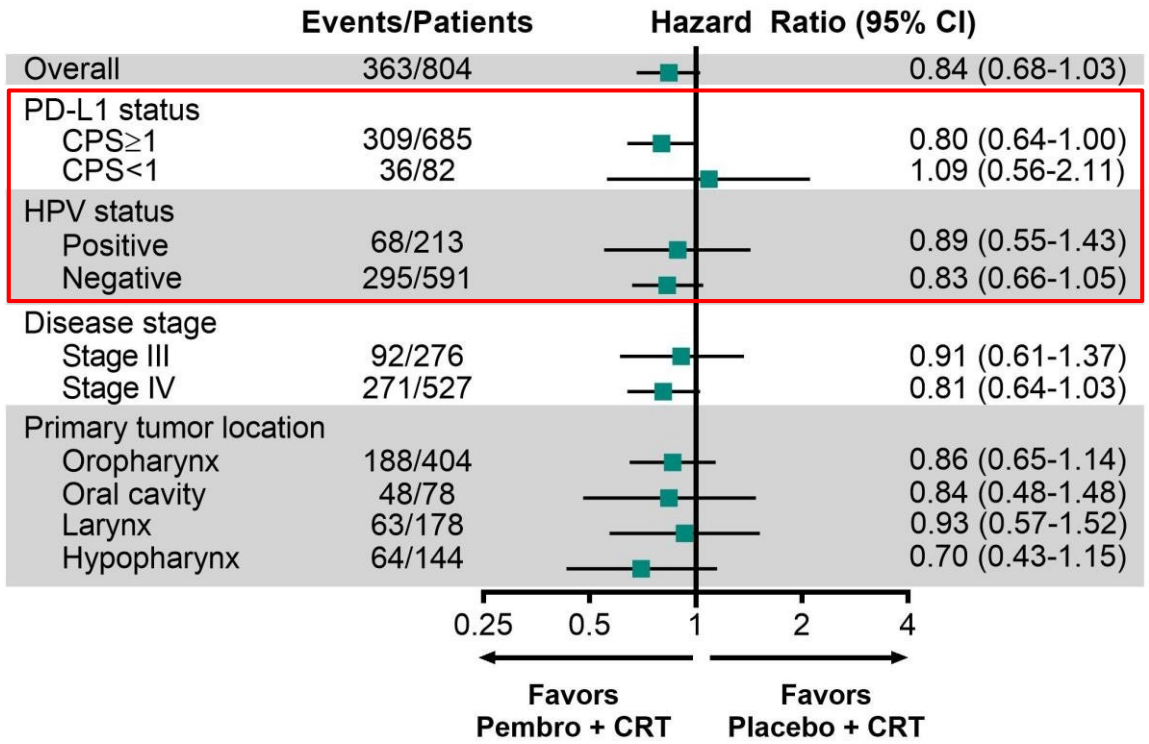
Event-Free Survival, ITT Population

	Pembro + CRT N = 402	Placebo + CRT N = 402
Events, n (%)	171 (42.5)	192 (47.8)
Death	54 (13.4)	48 (11.9)
Locoregional PD[a]	53 (13.2)	57 (14.2)
Distant PD[a]	52 (12.9)	67 (16.7)
Incomplete neck dissection w/ residual invasive cancer	0	1 (0.2)
Locoregional and distant PD	3 (0.7)	4 (1.0)
Residual disease[b] of neck LN alone	1 (0.2)	3 (0.7)
Residual disease[b] of primary tumor site alone	8 (2.0)	11 (2.7)
Residual disease[b] of primary tumor site & neck LN	0	1 (0.2)

[a]Pathologically or radiographically (per RECIST 1.1 by BICR) confirmed PD. [b]Residual disease required pathological confirmation. Data cutoff date: May 31, 2022.

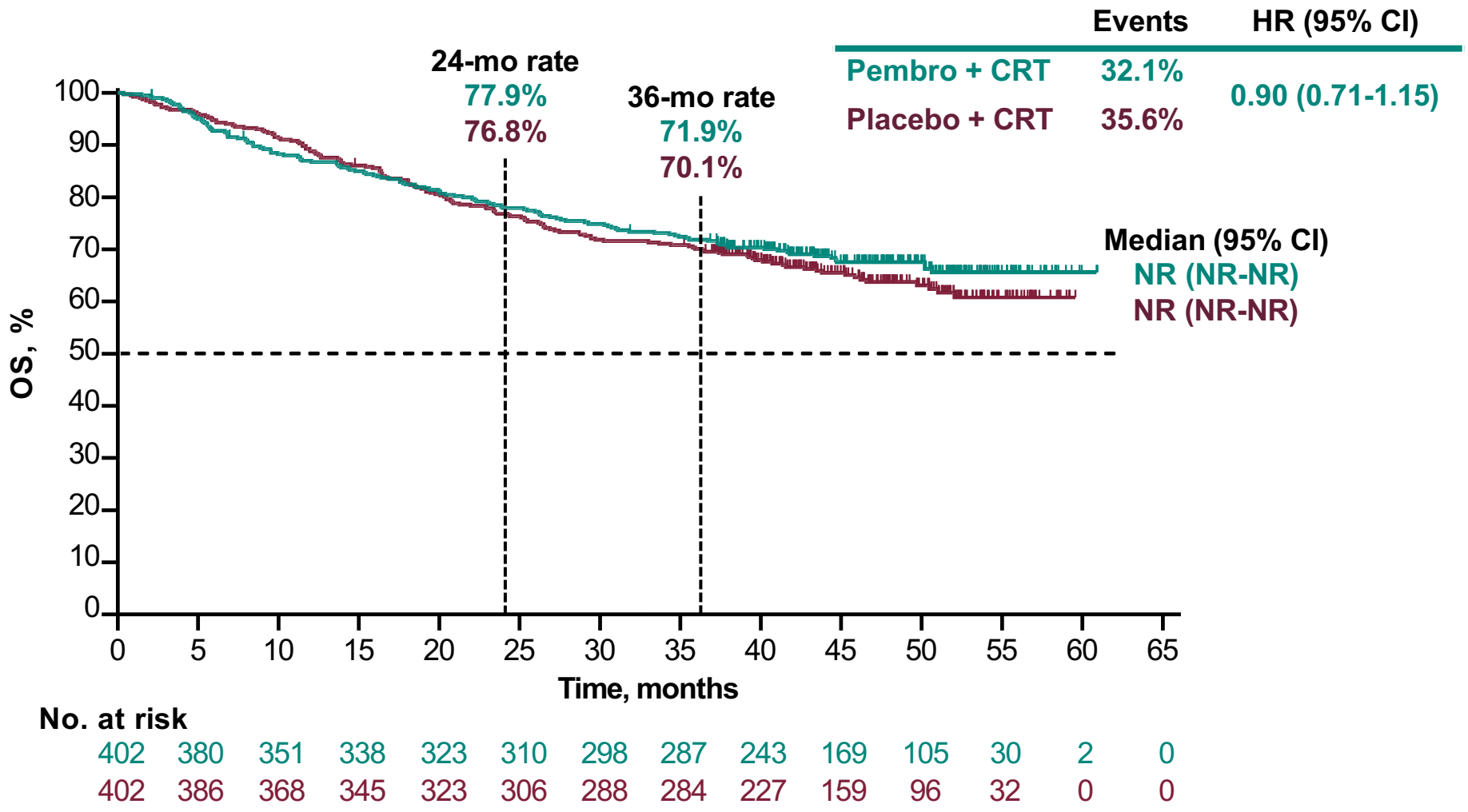
EFS in Prespecified Subgroups, ITT Population





All prespecified subgroup analyses. Subgroup analysis per RT regimen (AFX vs SFX) not displayed due to small patient population.
Data cutoff date: May 31, 2022

Overall Survival, ITT Population

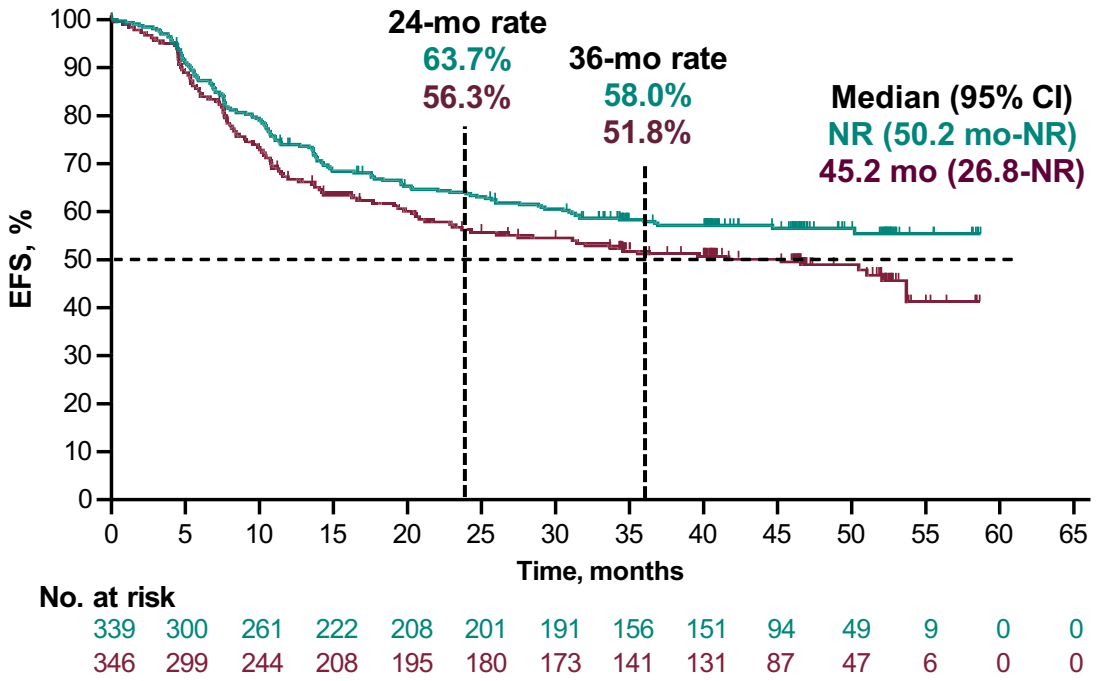


Data cutoff date: May 31, 2022

EFS and OS in Patients With PD-L1 CPS ≥1 (Prespecified Subgroup Analysis)

EFS

	Events	HR (95% CI)
Pembro + CRT	41.6%	0.80 (0.64-1.00)
Placebo + CRT	48.6%	

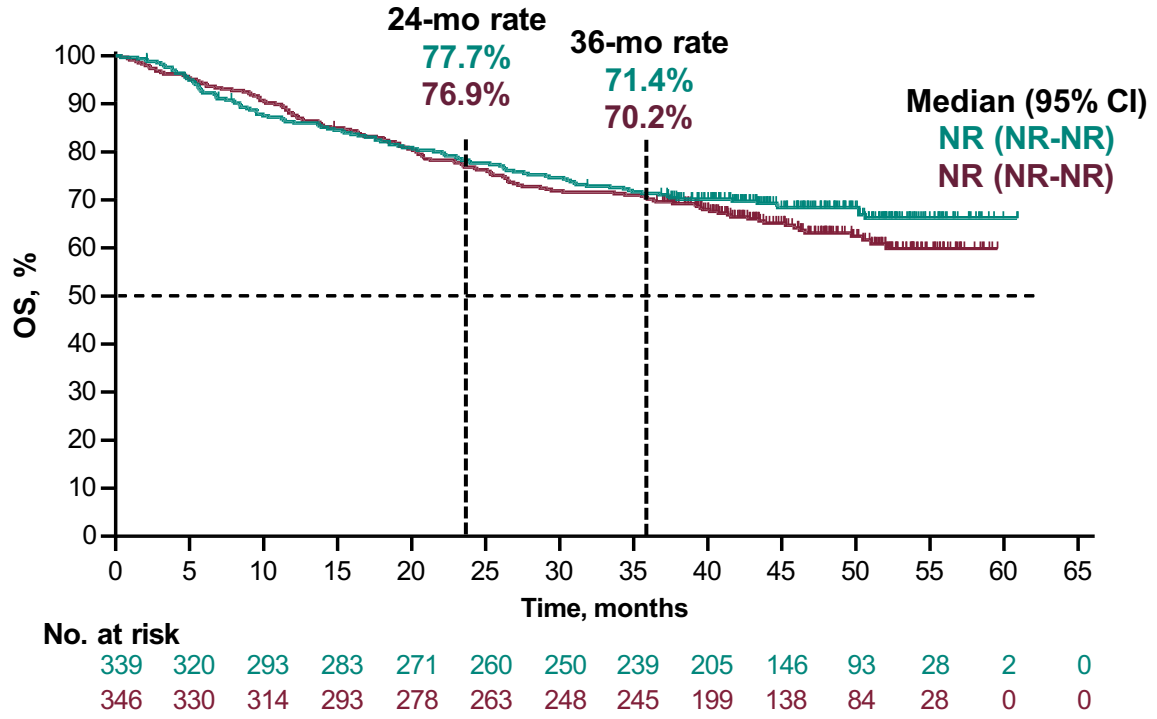


No. at risk

339	300	261	222	208	201	191	156	151	94	49	9	0	0
346	299	244	208	195	180	173	141	131	87	47	6	0	0

OS

	Events	HR (95% CI)
Pembro + CRT	31.6%	0.88 (0.68-1.14)
Placebo + CRT	36.1%	



No. at risk

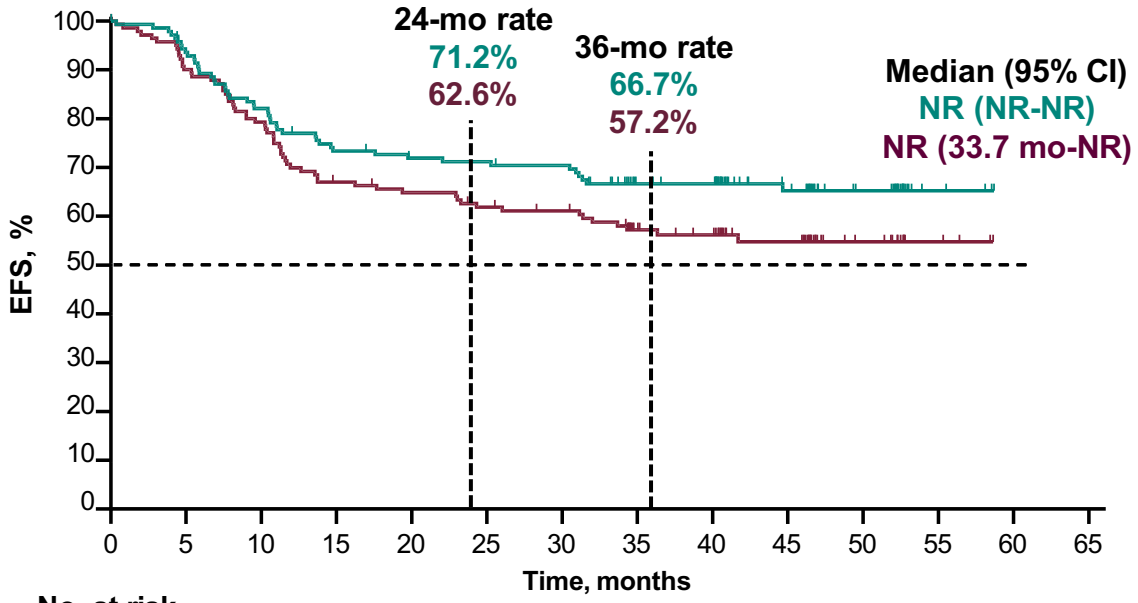
339	320	293	283	271	260	250	239	205	146	93	28	2	0
346	330	314	293	278	263	248	245	199	138	84	28	0	0

Data cutoff date: May 31, 2022

EFS and OS in Patients With PD-L1 CPS ≥20 (Post Hoc Analysis)

EFS

	Events	HR (95% CI)
Pembro + CRT	32.2%	0.73 (0.49-1.06)
Placebo + CRT	42.1%	

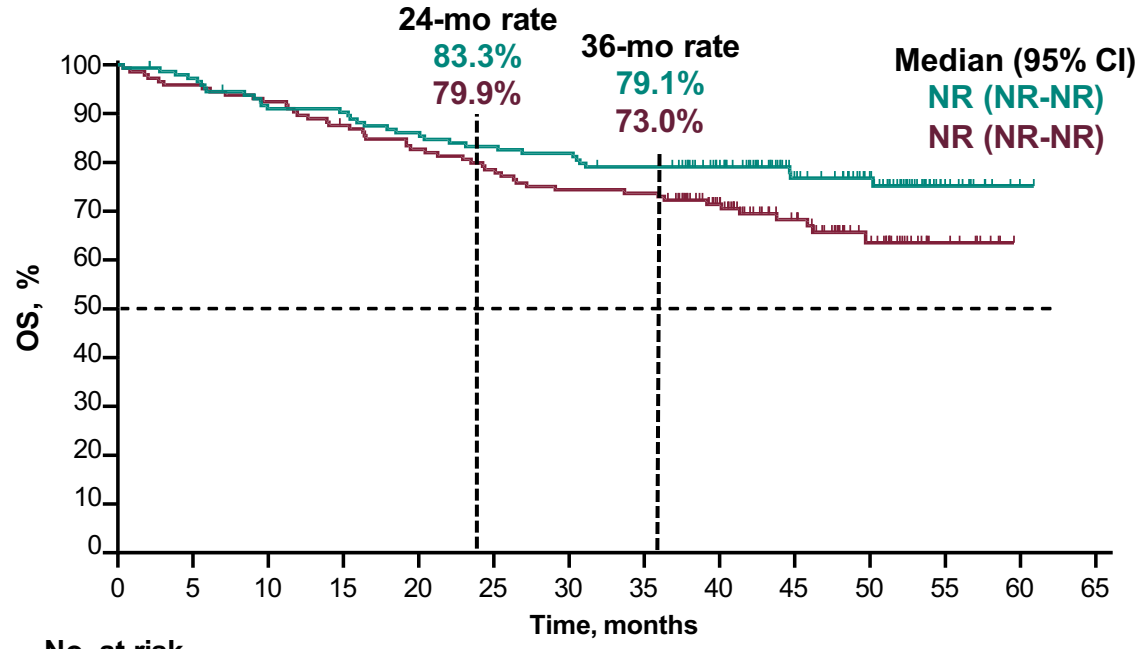


No. at risk

146	130	114	101	97	96	94	75	73	44	27	4	0	0
145	126	110	92	88	83	80	57	52	37	14	4	0	0

OS

	Events	HR (95% CI)
Pembro + CRT	22.6%	0.67 (0.43-1.04)
Placebo + CRT	32.4%	



No. at risk

146	140	130	129	123	119	117	112	94	65	49	13	1	0
145	139	134	126	119	113	107	106	80	56	29	9	0	0

Data cutoff date: May 31, 2022

Summary and Conclusions

- Pembrolizumab plus CRT was associated with a favorable trend toward improved EFS vs placebo plus CRT in patients with LA HNSCC (HR, 0.83; *P* = 0.0429)
  - The difference did not reach statistical significance (superiority threshold, one-sided *P* = 0.0242)
  - 24-mo EFS rate: 63.2% vs 56.2%
- PD-L1 expression[a] may be an informative predictive biomarker
  - CPS ≥1: 24-mo EFS rate, 63.7% vs 56.3%; 36-mo OS rate, 71.4% vs 70.2%
  - CPS ≥20: 24-mo EFS rate, 71.2% vs 62.6%; 36-mo OS rate, 79.1% vs 73.0% (post hoc analysis)
- No new safety signals with the combination of pembrolizumab plus CRT
- LA HNSCC remains a challenging disease to treat

[a]Measured by CPS using PD-L1 IHC 22C3 pharmDx

Pembrolizumab + Carboplatin + Paclitaxel as First-Line Therapy in Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma: Phase 4 KEYNOTE-B10 Study

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[1]Gold Coast University Hospital, Southport, QLD, Australia; [2]IDIM Instituto de Diagnostico e Investigaciones Metabolicas, Buenos Aires, Argentina; [3]Fundacion Respirar, Buenos Aires, Argentina; [4]Princess Margaret Cancer Centre, Toronto, ON, Canada; [5]Thomas Jefferson University Hospital, Philadelphia, PA, USA; [6]Hospital Provincial del Centenario, Rosario/Santa Fe, Argentina; [7]Washington University School of Medicine, St. Louis, MO, USA; [8]Baptist MD Anderson Cancer Center, Jacksonville, FL, USA; [9]Cancer Centre of Southeastern Ontario at Kingston General Hospital, Kingston, ON, Canada; [10]Centro Regional Integrado de Oncologia, Fortaleza, Brazil; [11]Oncosite Centro de Pesquisa Clínica em Oncologia, Ijuí, Brazil; [12]CETUS Oncologia, Belo Horizonte, Brazil; [13]Orlando Health Cancer Institute, Orlando, FL, USA; [14]Erie County Medical Center, Buffalo, NY, USA; [15]The Townsville University Hospital, Douglas, QLD, Australia; [16]Dr. H. Bliss Murphy Cancer Centre, St. John's, NL, Canada; [17]MSD (UK) Limited, London, United Kingdom; [18]Merck & Co., Inc., Rahway, NJ, USA; [19]Instituto do Cancer do Estado de Sao Paulo – ICESP, São Paulo, Brazil

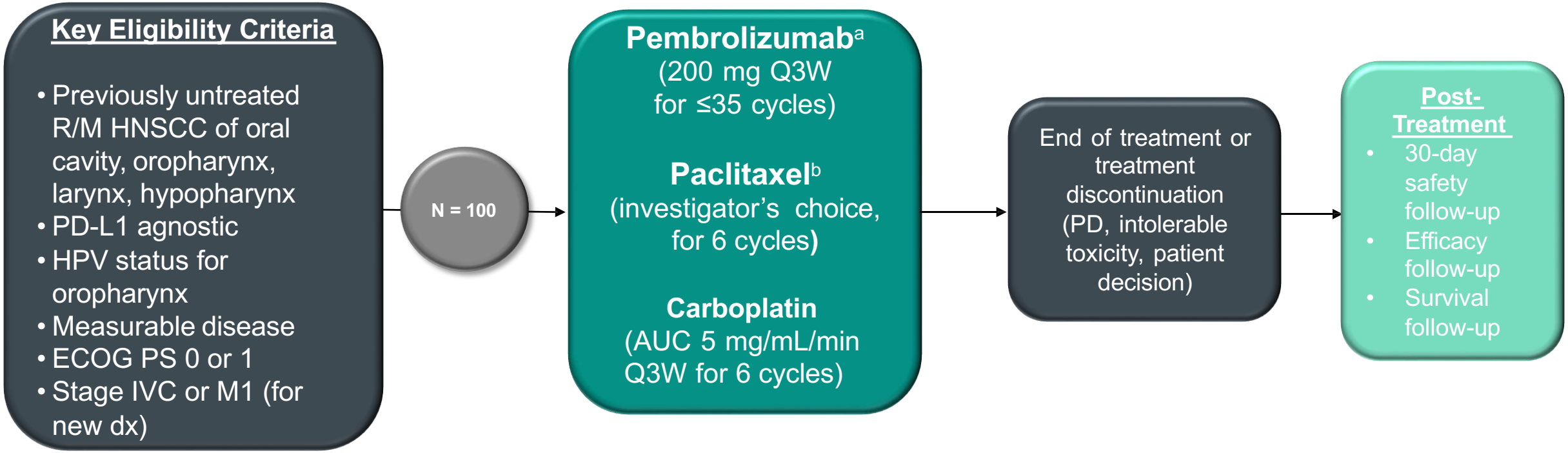
Background

- Pembrolizumab combined with platinum + 5-FU is approved for first-line treatment for R/M HNSCC, based on improvement in OS, from the pivotal KEYNOTE-048 study[1-3]
  - Alternatives to 5-FU are needed because of toxicities (esp. CVS and DPD deficiency related), patient inconvenience, costs, and complications associated with continuous 4-day infusion[4,5]
  - Cisplatin + paclitaxel was shown to be no less efficacious than cisplatin + 5-FU in a phase 3 clinical study in R/M HNSCC[6]
  - In a phase 1/2 study, pembrolizumab + docetaxel showed encouraging activity in platinum-resistant R/M HNSCC[7]
  - A retrospective analysis of 9 patients who received first-line pembrolizumab + carboplatin + paclitaxel suggested this regimen may be considered in place of pembrolizumab, platinum and 5-FU and warrants further investigation[8]
- We present initial results from the ongoing, global, open-label, phase 4 KEYNOTE-B10 study (NCT04489888) of pembrolizumab in combination with carboplatin + paclitaxel as first-line treatment for patients with R/M HNSCC

5-FU, 5-fluorouracil; CVS, cardiovascular system; DPD, dihydropyrimidine dehydrogenase deficiency; OS, overall survival.

1. KEYTRUDA® (pembrolizumab) injection, for intravenous use. 6/2022. Merck Sharp & Dohme, LLC: Rahway, NJ, USA. 2. European Commission approves two new regimens of Merck's KEYTRUDA® (pembrolizumab) as first-line treatment for metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC). 2019 11/20/2019. https://www.merck.com/news/european-commission-approves-two-new-regimens-of-mercks-keytruda-pembrolizumab-as-first-line-treatment-for-metastatic-or-unresectable-recurrent-head-and-neck-squamous-cell-carcinoma/. 3. Burtness B et al. *Lancet.* 2019;394:1915-1928. 4. Guigay J et al. *Front Oncol.* 2019;9(668):1-10. 5. Guigay J et al. *Critical Issues in Head and Neck Oncology* In: Vermorken et al. (eds) Critical Issues in Head and Neck Oncology. Springer, Cham. 2018:267-276. 6. Gibson MK et. *J Clin Oncol*. 2005;23(15):3562-3567. 7. Fuereder T et al. *Ann Oncol.* 2020;31(suppl4)921P. 8. Valdez A et al. *J Immunother Cancer.* 2020;8(suppl 3).

KEYNOTE-B10 Study Design (NCT04489888)



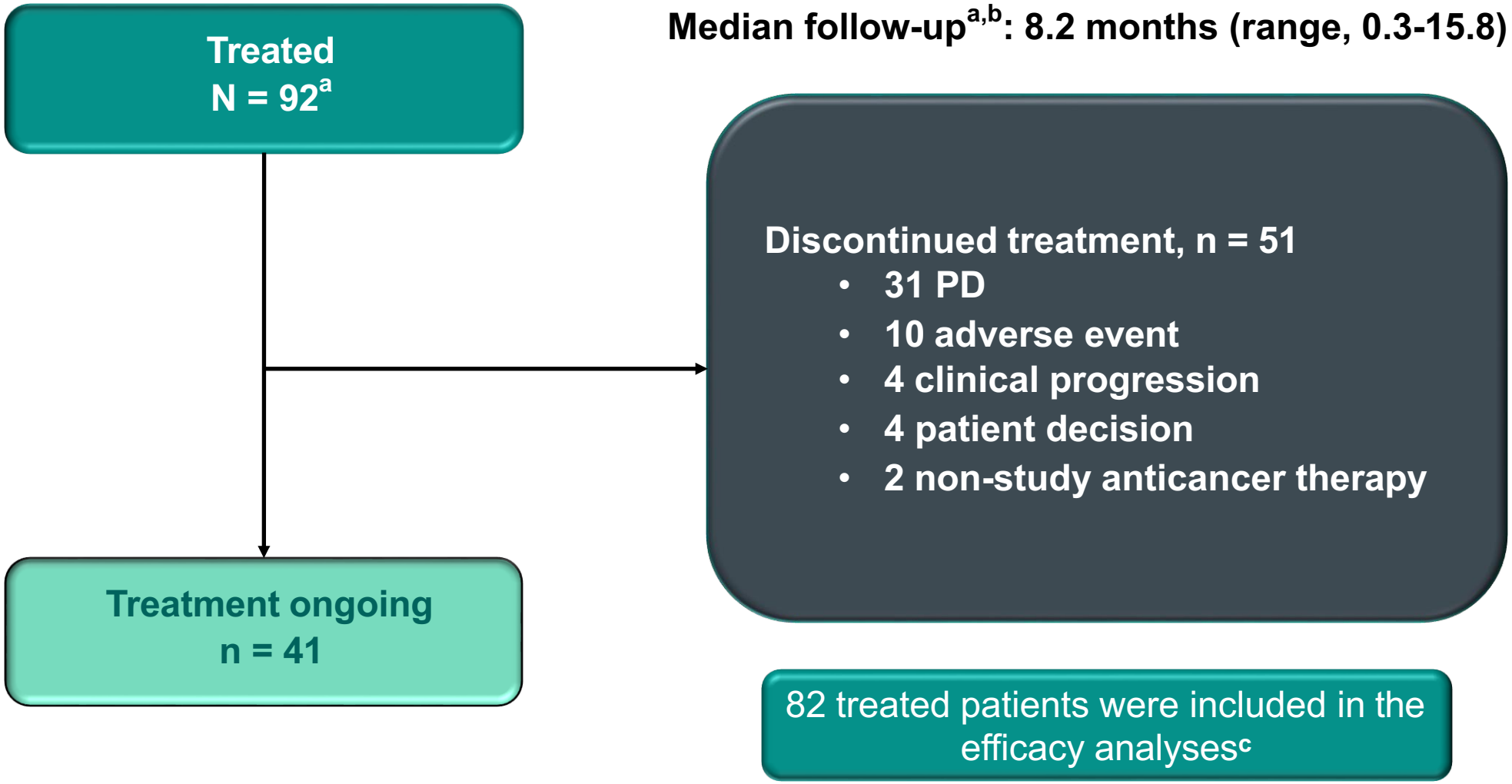
Primary End point
- ORR per RECIST v1.1 by BICR, confirmed

Secondary End points
- DOR per RECIST v1.1 by BICR
- PFS per RECIST v1.1 by BICR
- OS
- Safety/tolerability

Tumor Assessments
- Q6W for 1 year then Q9W thereafter

DOR, duration of response; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival. [a]Patients who complete 35 cycles of pembro study treatment after achieving SD/PR/CR may be eligible to receive an additional

Patient Disposition



[a]All patients who received ≥1 dose of study treatment (all patients as treated [APaT] population). [b]Defined as time from first dose to data cutoff. [c]Full analysis set (FAS) population includes the first 82 patients who had the opportunity for ≥3 months of

Baseline Characteristics and Demographics

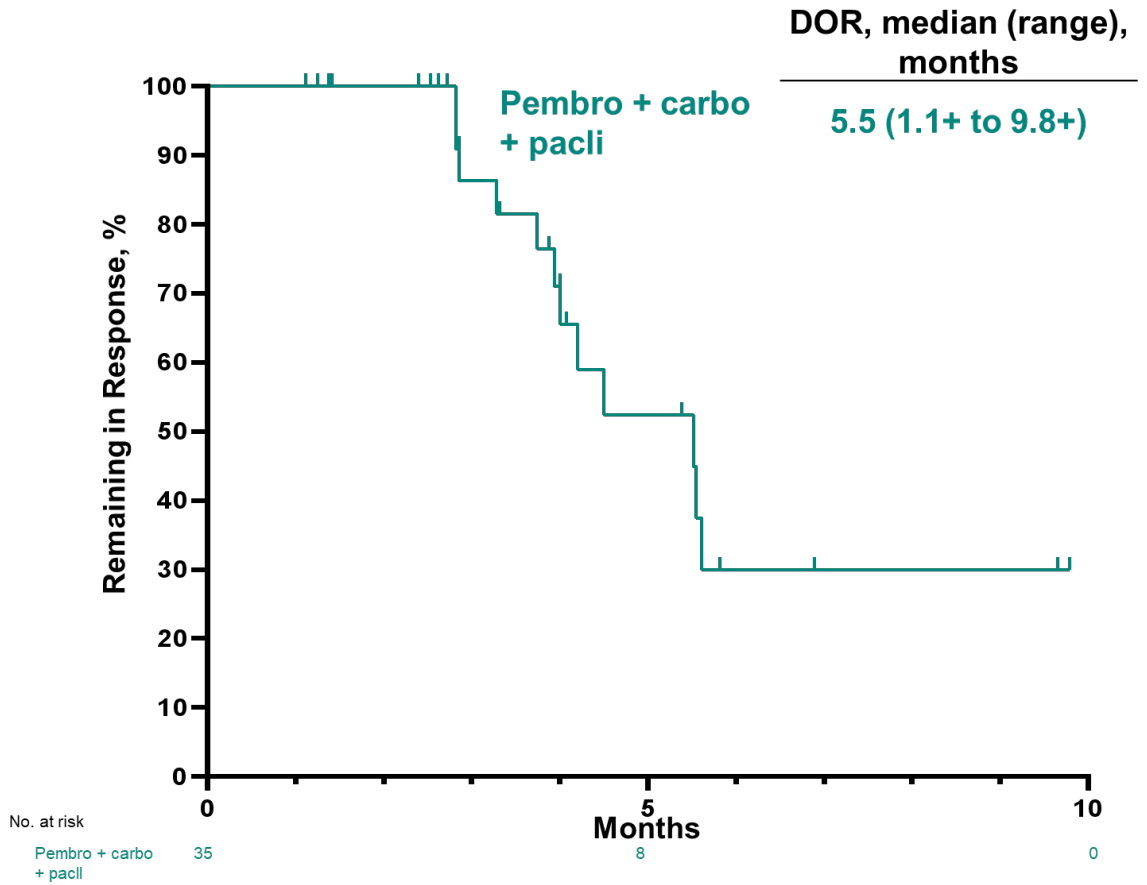
	Pembro + Carbo + Pacli N = 92
Age, median (range), yr	64.0 (29-89)
≥65 yr, n (%)	42 (45.7)
Sex, n (%)	
Male	76 (82.6)
Female	16 (17.4)
Race, n (%)	
Black or African American	5 (5.4)
Black or African American White	7 (7.6)
White	80 (87.0)
Geographic region, n (%)	
North America (Canada and USA)	43 (46.7)
Rest of the world (Argentina, Australia, Brazil)	49 (53.3)
Choice of paclitaxel dosage, n (%)	
100 mg/m^2 Q1W	21 (22.8)
175 mg/m^2 Q3W	71 (77.2)
PD-L1 expression, n (%)	
CPS <1	17 (18.5)
CPS ≥1	75 (81.5)
CPS ≥1 to 19	38 (41.3)
CPS ≥20	37 (40.2)
ECOG PS, n (%)	
0	38 (41.3)
1	54 (58.7)

	Pembro + Carbo + Pacli N = 92
Distant metastasis, n (%)	
M0	31 (33.7)
M1	61 (66.3)
Primary tumor location, n (%)	
Hypopharynx	4 (4.3)
Larynx	20 (21.7)
Oral cavity	25 (27.2)
Oropharynx	42 (45.7)
Cervical lymph node[a]	1 (1.1)
HPV status[b], n (%)	
Positive (oropharynx)	20 (21.7)
Negative (oropharynx)	22 (23.9)
Negative (non-oropharynx)	50 (54.3)
Disease presentation, n (%)	
Recurrent[c]	32 (34.8)
Metastatic[d]	29 (31.5)
Recurrent and metastatic[e]	31 (33.7)
Overall cancer stage, n (%)	
Stage I	1 (1.1)
Stage II	2 (2.2)
Stage III	5 (5.4)
Stage IV[f]	15 (16.3)
Stage IVA	13 (14.1)
Stage IVB	11 (12.0)
Stage IVC	45 (48.9)

[a]Entered as cervical lymph node in error; corrected primary tumor location is oropharynx. [b]HPV status is defaulted to negative for non-oropharynx primary tumor location. [c]Patients with locally recurrent disease in primary tumor location and/or disease that spreads to regional lymph nodes. [d]Patients with newly diagnosed local/regional disease and distant metastatic disease (OR) patients with recurrent distant metastatic disease only. [e]Patients with recurrent disease in primary tumor location and/or regional lymph node disease AND distant metastatic disease. [f]Per AJCC[1], 8th edition, Stage IV applies to participants with HPV p16+ oropharynx cancer and distant metastases. Data cutoff date: March 16, 2022. [1]AJCC. AJCC cancer staging form supplement: AJCC cancer staging manual, 8th edition: American College of Surgeons;

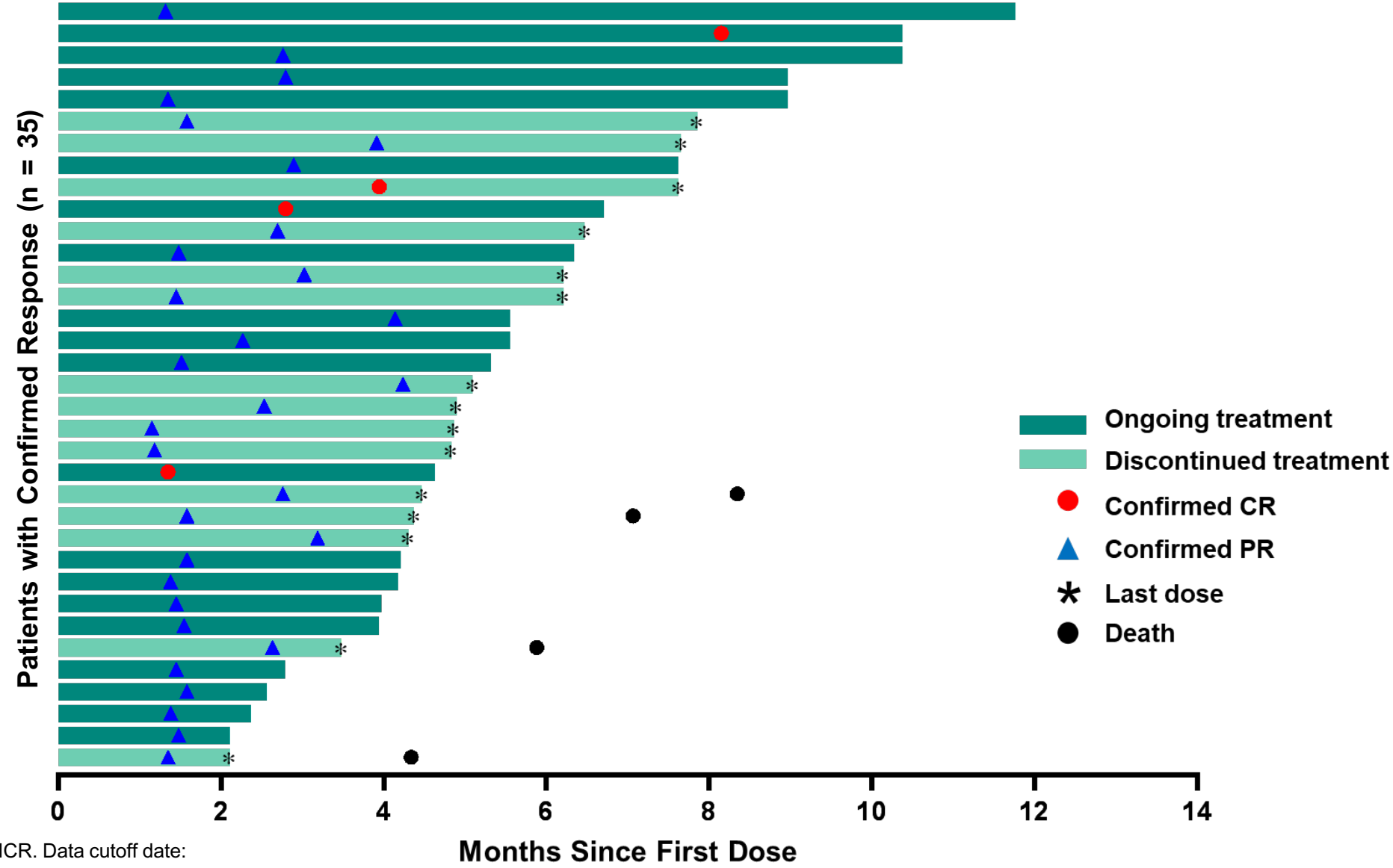
Confirmed Objective Response Rate and Duration of Response per RECIST v1.1 by BICR[a]

	Pembro + Carbo + Pacli n = 82[b]
ORR, % (95% CI)	42.7 (31.8-54.1)
Best objective response, n (%)	
CR	4 (4.9)
PR	31 (37.8)
SD	24 (29.3)
PD	15 (18.3)
No assessment	8 (9.8)
TTR, median (range), months	1.5 (1.1-4.2)
DCR, % (95% CI)[c]	58.5 (47.1-69.3)



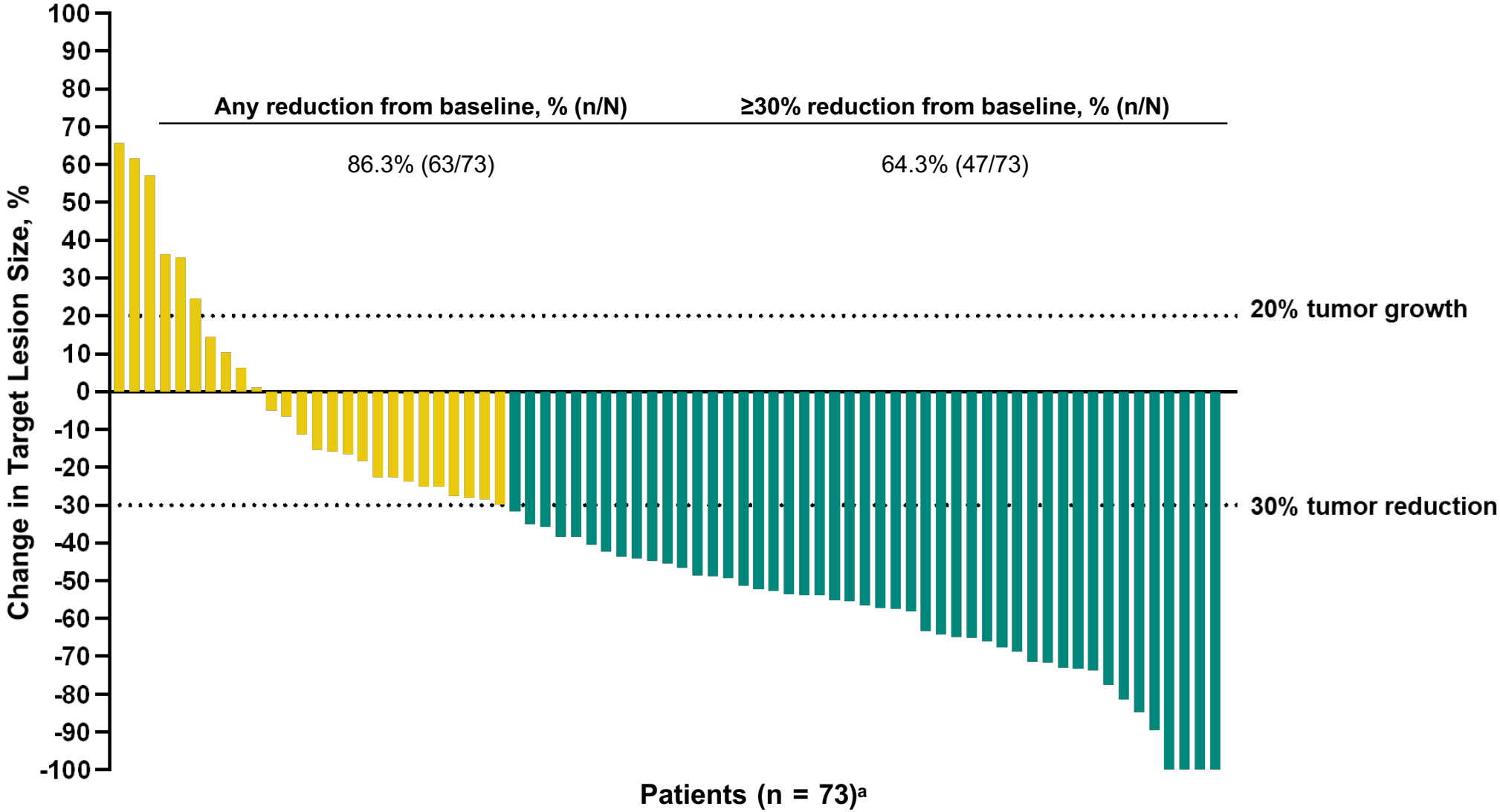
CR, complete response; DCR, disease control rate; PR, partial response; SD, stable disease; TTR, time to response. "+" indicates response is ongoing. [a]FAS population includes the first 82 patients who had the opportunity for ≥3 months of follow-up. [b]No assessment n=8: 7 patients discontinued study treatment prior to the week 6 imaging; 1 patient censored at C1D1 after new anticancer therapy (surgery + radiation therapy for

Time on Study Treatment and Response Evaluation for Responders



Response per RECIST v1.1 by BICR. Data cutoff date:

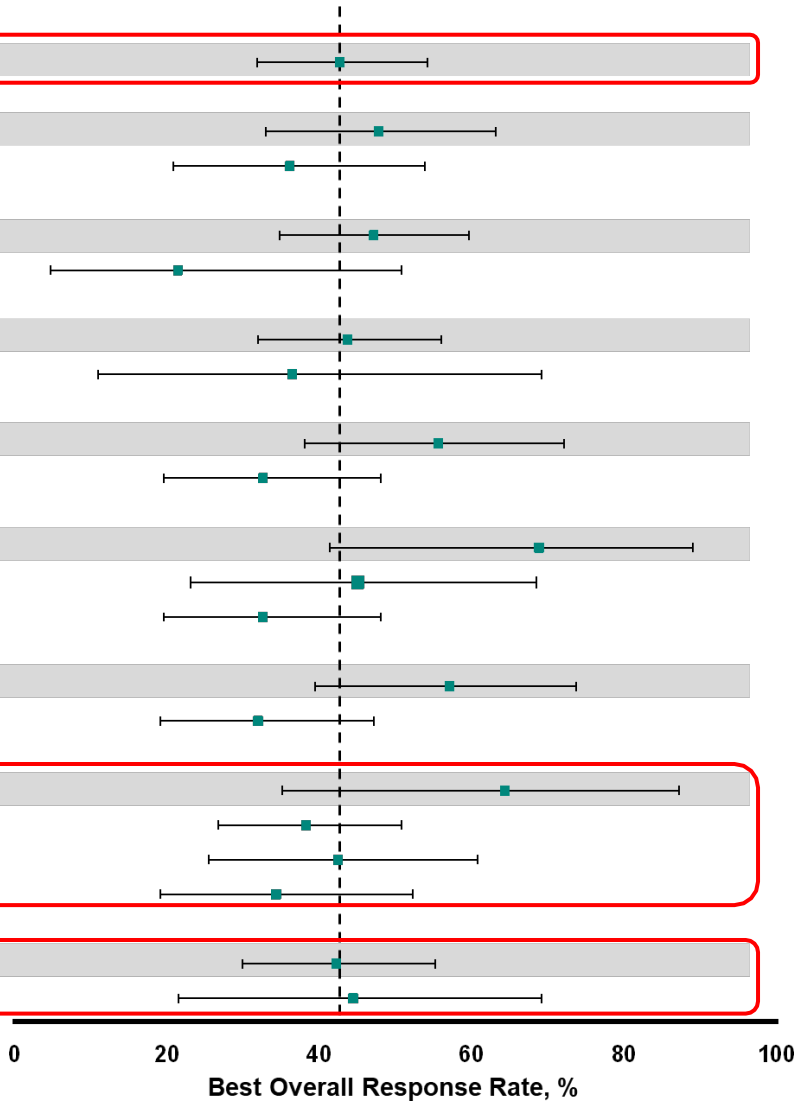
Best Percentage Change From Baseline for Target Lesions



Response per RECIST v1.1 by BICR. [a]n = 73 treated patients of FAS population with measurable baseline disease and with measurable post-baseline assessment.
Data cutoff date: March 16, 2022

Subgroup Analysis of Confirmed Objective Response Rate per RECIST v1.1 by BICR[a]

	N	ORR	95% CI
Overall	82	42.7	(31.8-54.1)
Age			
<65 years	46	47.8	(32.9-63.1)
≥65 years	36	36.1	(20.8-53.8)
Sex			
Male	68	47.1	(34.8-59.6)
Female	14	21.4	(4.7-50.8)
Race			
White	71	43.7	(31.9-56.0)
All others	11	36.4	(10.9-69.2)
Region[b]			
North America	36	55.6	(38.1-72.1)
Rest of World	46	32.6	(19.5-48.0)
HPV[c]			
Positive (oropharynx)	16	68.8	(41.3-89.0)
Negative (oropharynx)	20	45.0	(23.1-68.5)
Negative (non-oropharynx)	46	32.6	(19.5-48.0)
ECOG PS			
0	35	57.1	(39.4-73.7)
1	47	31.9	(19.1-47.1)
PD-L1			
CPS <1	14	64.3	(35.1-87.2)
CPS ≥1	68	38.2	(26.7-50.8)
CPS ≥1 to 19	33	42.4	(25.5-60.8)
CPS ≥20	35	34.3	(19.1-52.2)
Investigator's choice of paclitaxel			
175 mg/m^2 Q3W	64	42.2	(29.9-55.2)
100 mg/m^2 Q1W	18	44.4	(21.5-69.2)



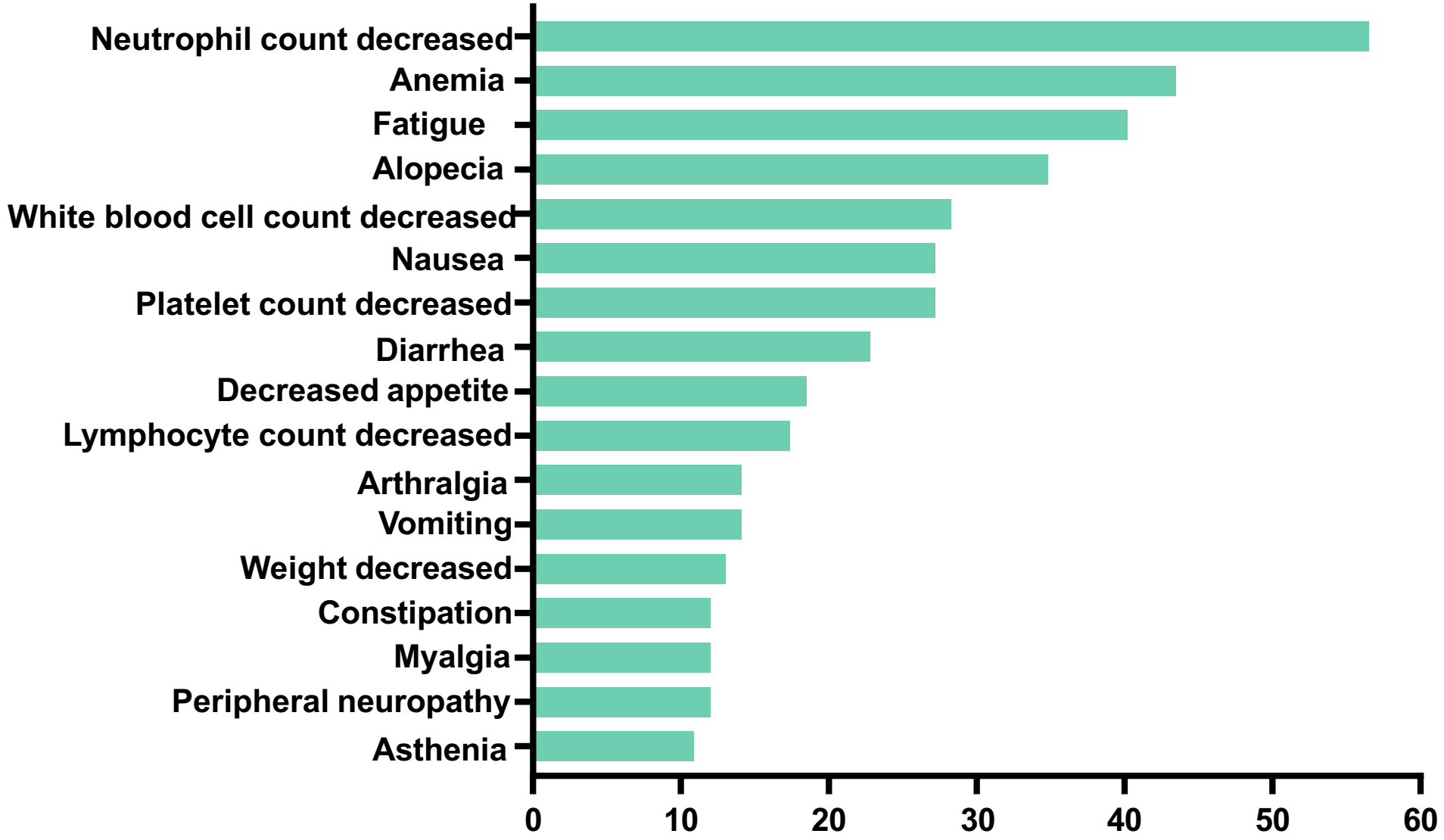
Subgroups were prespecified by the sponsor. [a]FAS population includes the first 82 patients who had the opportunity for for ≥3 months of follow-up. [b]North America comprises of sites in Canada and USA. Rest of World comprises of sites in Argentina, Australia, and Brazil. [c]HPV status is defaulted to negative for non-oropharynx primary tumor location. Data cutoff date: March 16, 2022.

Treatment-Related Adverse Event Summary[a]

	Pembro + Carbo + Pacli N = 92
Any treatment-related AE	88 (95.7)
Grade 3-5 treatment-related AE	65 (70.7)
Serious treatment-related AE	16 (17.4)
Discontinued ≥1 drug because of treatment-related AE	12 (13.0)
Discontinued pembrolizumab	4 (4.3)
Discontinued any chemotherapy	9 (9.8)
Discontinued all components	2 (2.2)
Death due to treatment-related AE[b]	2 (2.2)

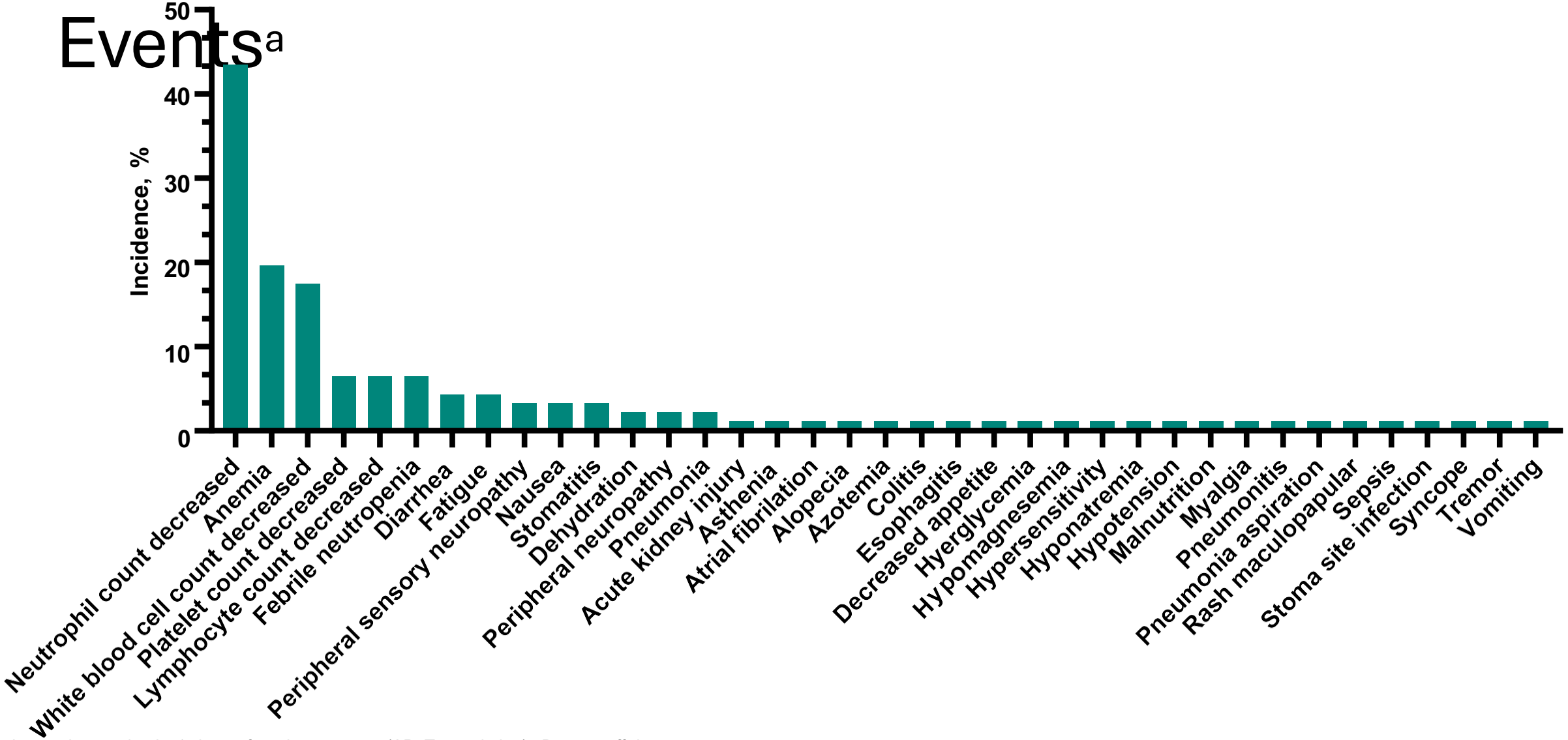
Values are n (%). [a]All patients who received ≥1 dose of study treatment (APaT population). [b]Grade 5 chemotherapy-related AEs: sepsis, hypersensitivity.
Data cutoff date: March 16, 2022

Treatment-Related Adverse Events with Incidence ≥10%[a]



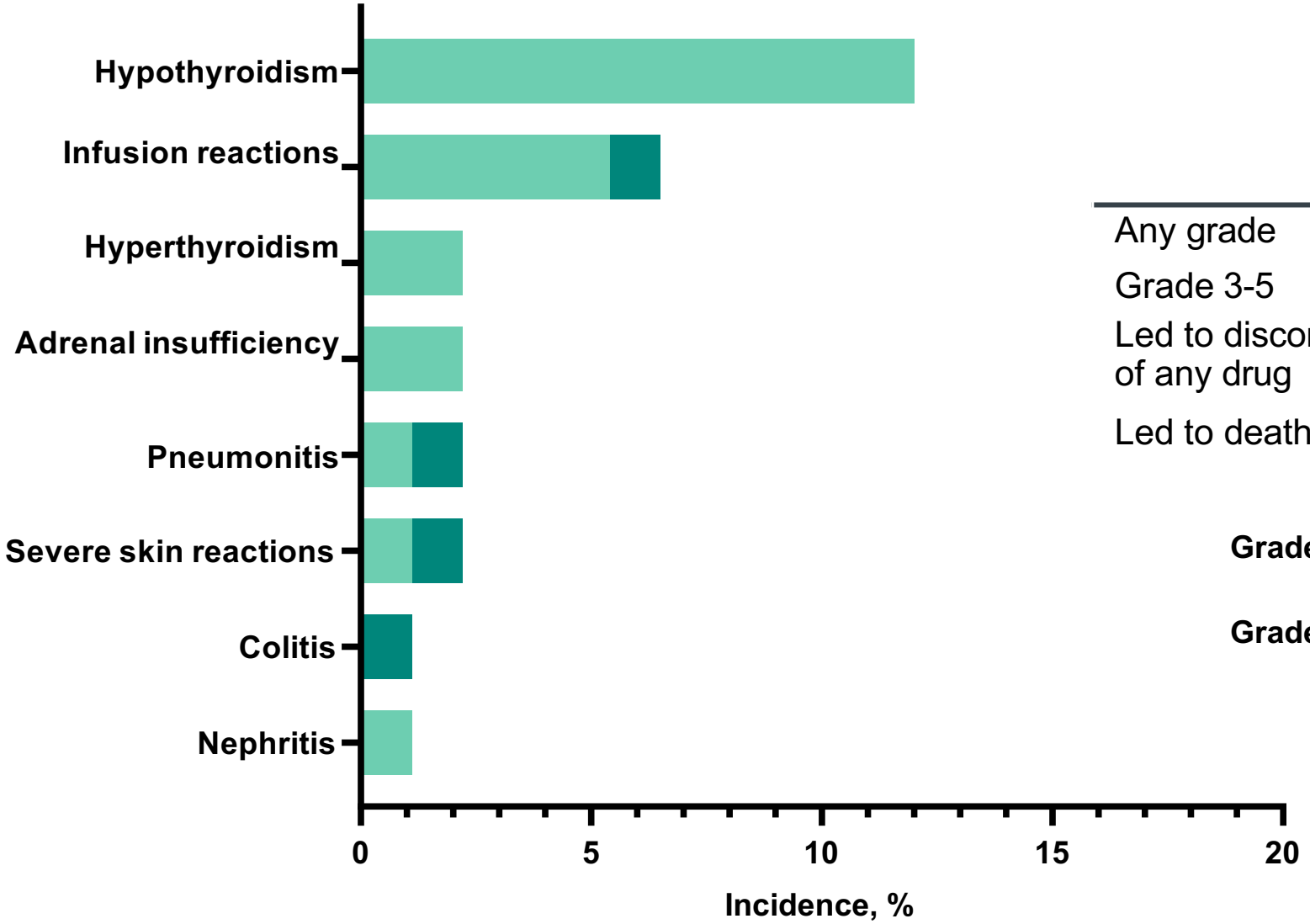
[a]All patients who received ≥1 dose of study treatment (APaT population). Data cutoff date: March 16, 2022

All Grade 3-5 Treatment-Related Adverse Events[a]



[a]All patients who received ≥1 dose of study treatment (APaT population). Data cutoff date: March 16, 2022

Immune-Mediated AEs and Infusion Reactions[a]



	Pembro + Carbo + Pacli
Any grade	26.1%
Grade 3-5	4.3%
Led to discontinuation of any drug	6.5%
Led to death	1.1%[b]

Grade 1/2

Grade 3-5

Considered regardless of attribution to treatment or immune relatedness by the investigator. [a]All patients who received ≥1 dose of study treatment (APaT population). [b]Chemotherapy-related infusion reaction (hypersensitivity).

Conclusions

- This first global, prospective trial of combination pembrolizumab + carboplatin + paclitaxel demonstrated antitumor activity in first-line R/M HNSCC
  - ORR: 42.7% (95% CI, 31.8-54.1) regardless of PD-L1 status

- The safety profile of pembrolizumab + carboplatin + paclitaxel was consistent with the known safety profiles of each therapy and manageable with supportive care
  - Any-grade treatment-related AEs occurred in 95.7% of patients
  - Most common grade ≥3 treatment-related AEs were decreased neutrophil count (43.5%), anemia (19.6%), and WBC count decrease (17.4%)
  - Serious treatment-related AEs occurred in 17.4% of patients
  - Two grade 5 chemotherapy-related serious AEs occurred: sepsis, hypersensitivity reaction

- Efficacy and safety results of KEYNOTE-B10 may suggest this 5-FU-free chemotherapy combination with pembrolizumab may be an alternative to current SOC and may expand treatment options for first-line R/M HNSCC irrespective of PD-L1 status

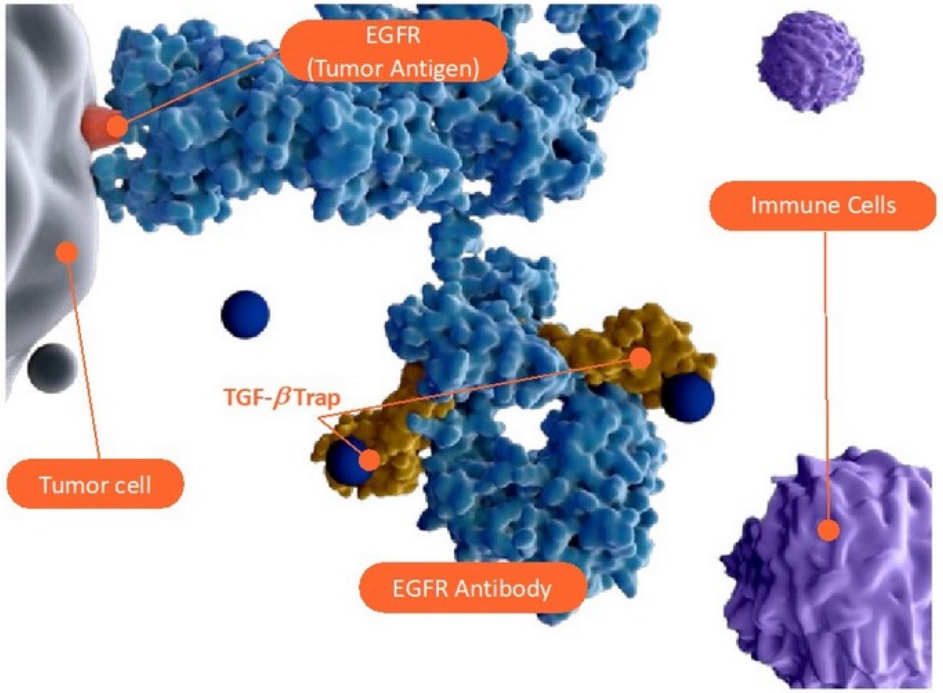
2023 ASCO ANNUAL MEETING

Dose expansion results of the bifunctional EGFR/TGF-β inhibitor BCA101 with pembrolizumab in patients with R/M HNSCC

Glenn J. Hanna, John M. Kaczmar, Dan P. Zandberg, Deborah J. Wong, Emrullah Yilmaz, Eric Sherman, Alberto Hernando-Calvo, Assuntina G. Sacco, Christine H. Chung, David Bohr, Ralf Reiners, Rachel Salazar, Elham Gharakhani, Sanela Bilic and Jameel Muzaffar

Abstract #6005

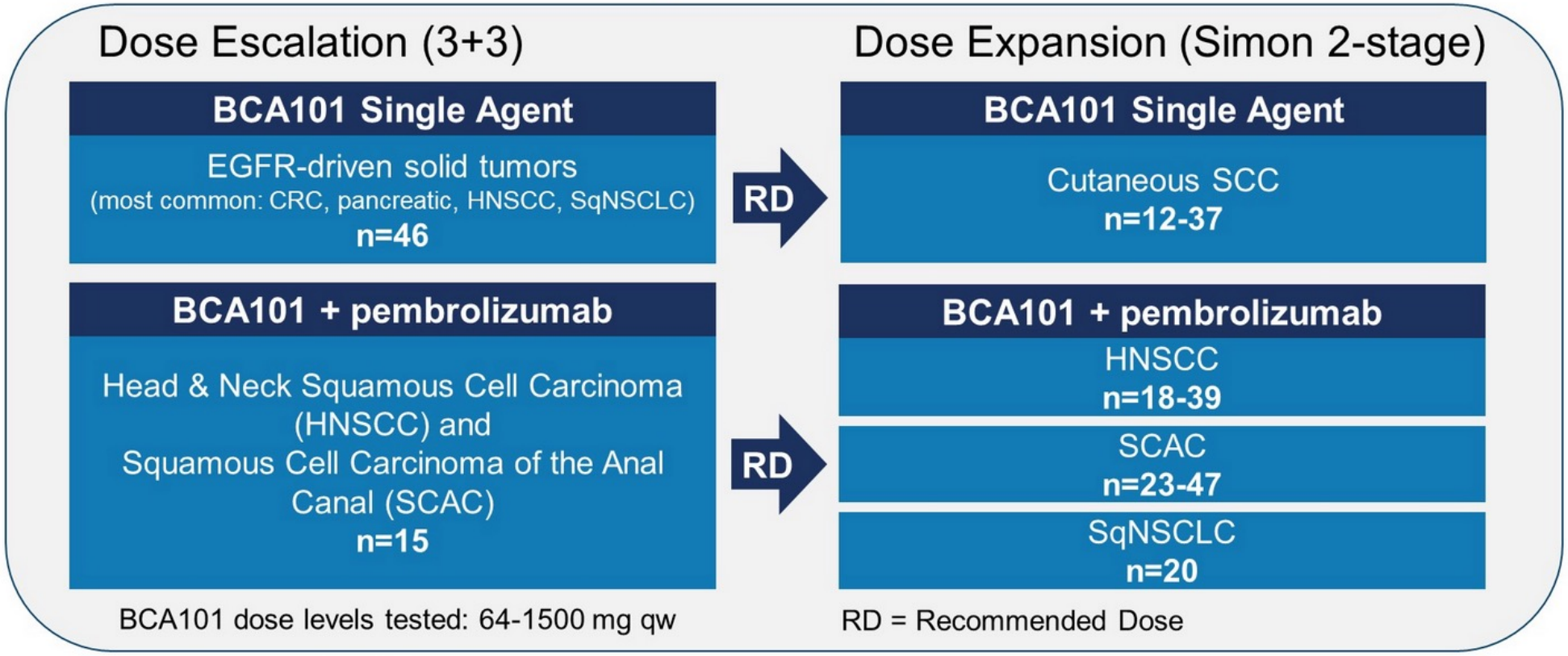
BCA101: Targeting a TGF-β trap to EGFR expressing tumors



Proposed mechanisms of action

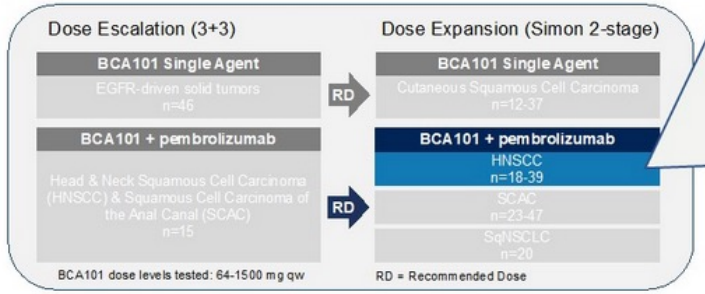
1. Localizes TGF-β inhibition to the TME through an EGFR-directed approach
2. Aims to increase anti-tumor activity via enhanced ADCC and increased NK cell activation
3. Dual inhibition of EGFR and TGF-β prevents epithelial-mesenchymal transition (EMT) and metastasis

BCA101 Ph1/1b study design



Primary Objective: Safety/Tolerability
Secondary Objectives: Preliminary efficacy, pharmacokinetics, immunogenicity

BCA101 (anti-EGFR/TGF-β trap) + pembrolizumab R/M HNSCC expansion cohort



At the data cutoff, **31 of 39 evaluable patients** were enrolled and had at least two restaging scans.

Population

- R/M HNSCC
- Oral cavity, oropharynx, hypopharynx & larynx
- HPV (p16) testing required for oropharyngeal cancer
- CPS≥1
- No prior systemic therapy in R/M setting

Simon 2-stage (H0 vs. HA, 19% vs. 38%)

- Stage 1: 18 evaluable pts, ≥4 responses required to proceed to stage 2
- Stage 2: Additional 21 patients (total n=39), 11 responses required to warrant further assessment in larger cohort

PRESENTED BY: Glenn J. Hanna, MD

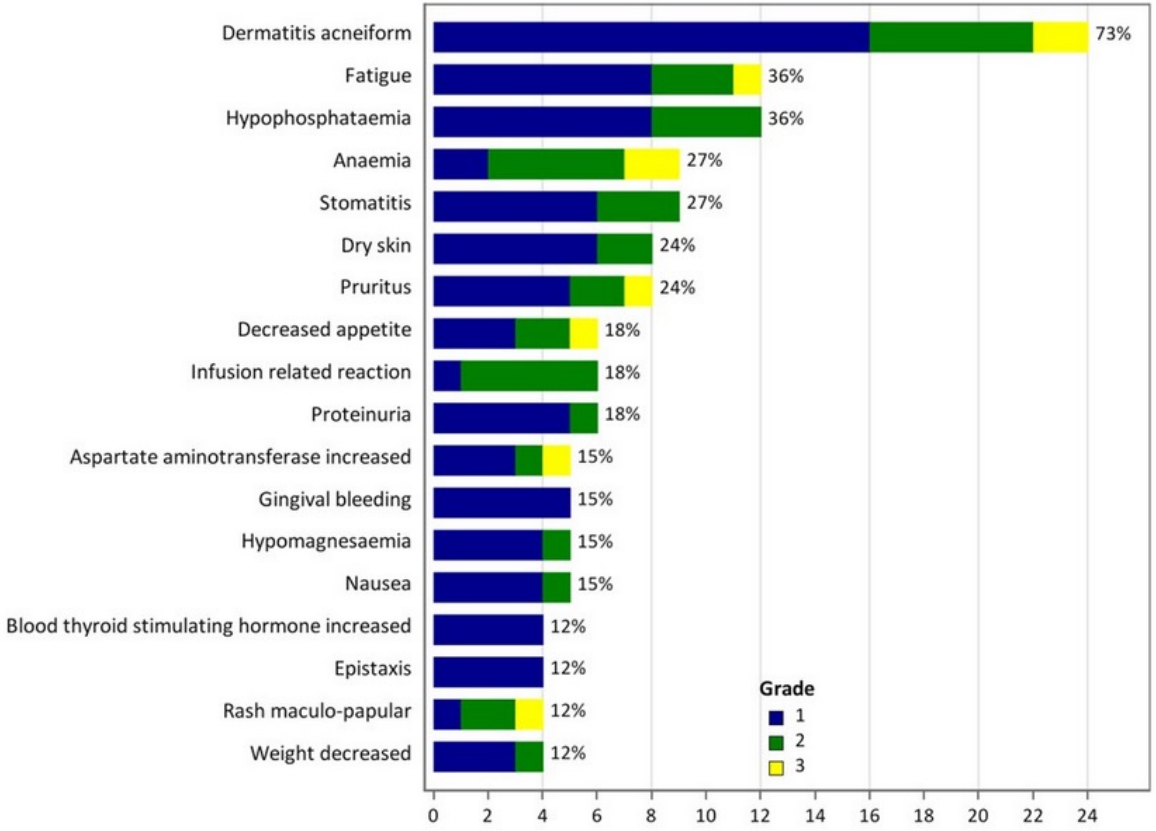
HNSCC Dose Expansion Baseline Characteristics

		N = 33 (100%)
Age	Median (range)	65 (31-80)
Sex – n (%)	Male/Female	23/10 (70% vs. 30%)
HNSCC Primary site of disease	Oropharynx	18 (55%)
	HPV-pos	12 (67% of Oropharynx)
	HPV-neg	6 (33% of Oropharynx)
	Oral Cavity	10 (30%)
	Hypopharynx	3 (9%)
	Larynx	2 (6%)
CPS - n (%)	≥20	15 (45%)
	1-19	18 (55%)
Distant metastasis – n (%)		25 (76%)
ECOG Performance Status – 0 vs.1 (%)		16 vs. 17 (48% vs. 52%)

Source: Open clinical database, as of 22-May-2023

BCA101 + pembrolizumab yields manageable safety profile

AEs, treatment-related, in ≥10% of subjects, preferred term & grade



Adverse Events of Interest:

- Skin toxicity
  - Acneiform rash in 73% of subjects (two G3 events)
- Mucosal bleeding
  - Generally low-grade and manageable without the need for dose interruptions
  - One G3 drug-related tracheal hemorrhage

Treatment-related AEs leading to:

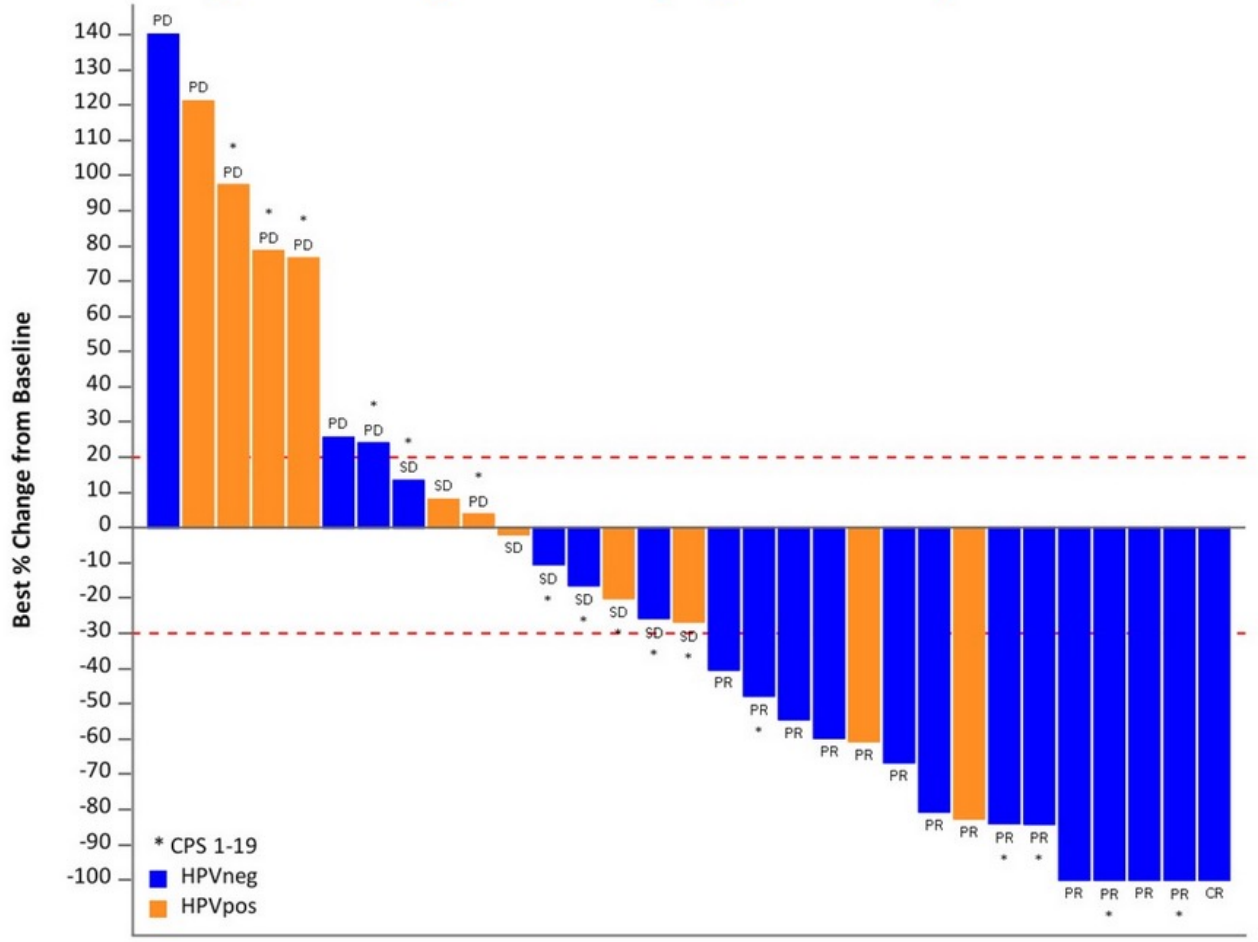
- Dose interruption: 12/33 (36%)
  - Incl. four G2 infusion related reaction
- Dose reduction: 3/33 (9%)
  - G3 acneiform rash
  - G2 blood alkaline phosphatase increased
  - G3 maculo-papular rash
- Permanent discontinuation: 3/33 (9%)
  - G3 tracheal hemorrhage
  - G4 pericarditis
  - G3 blood alkaline phosphatase increased

Total n=33

Source: Open clinical database, as of 22-May-2023

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L)

Preliminary Efficacy – Total population (N=31 evaluable)

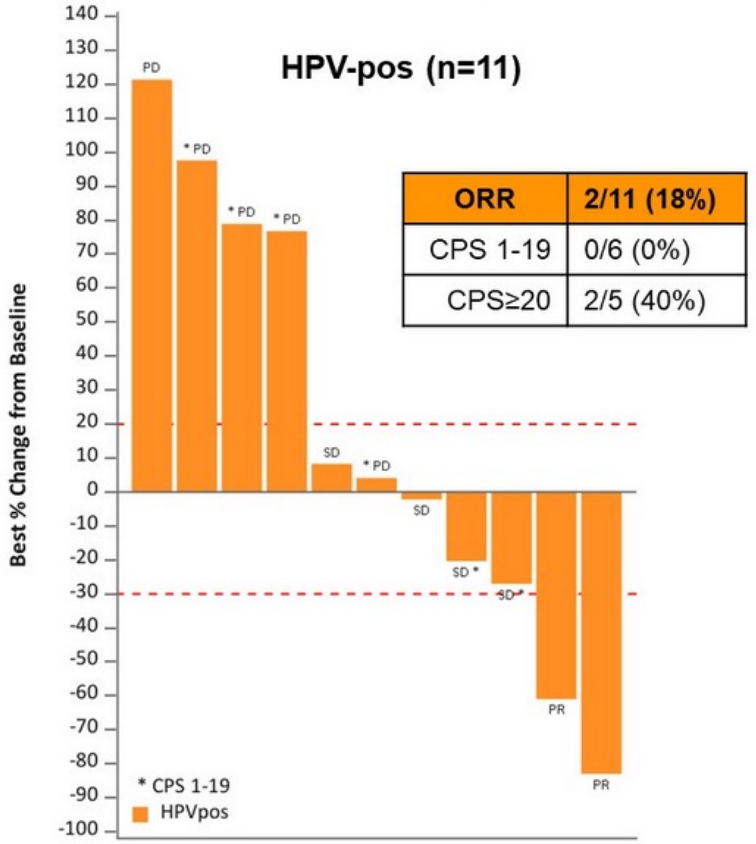


ORR	15/31 (48%)
CR	1 (3%)
PR	14 (45%)
SD	8 (26%)
PD	8 (26%)

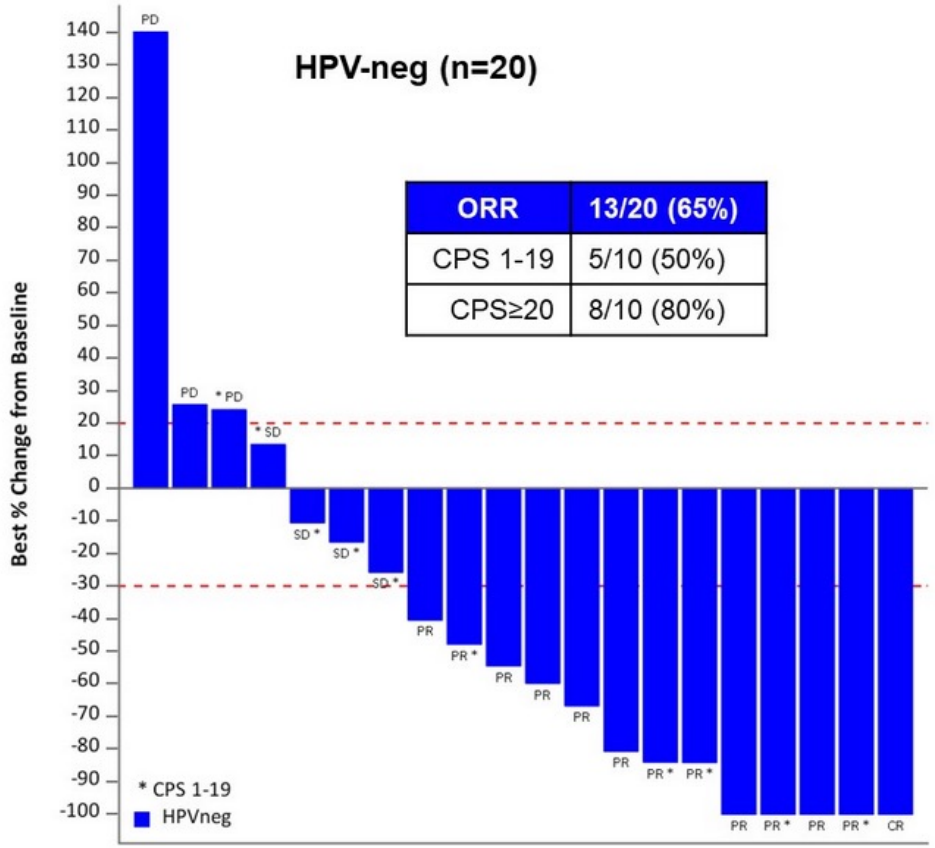
Source: Open clinical database, as of 22-May-2023

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L)

Preliminary Efficacy – by HPV status



ORR	2/11 (18%)
CPS 1-19	0/6 (0%)
CPS≥20	2/5 (40%)



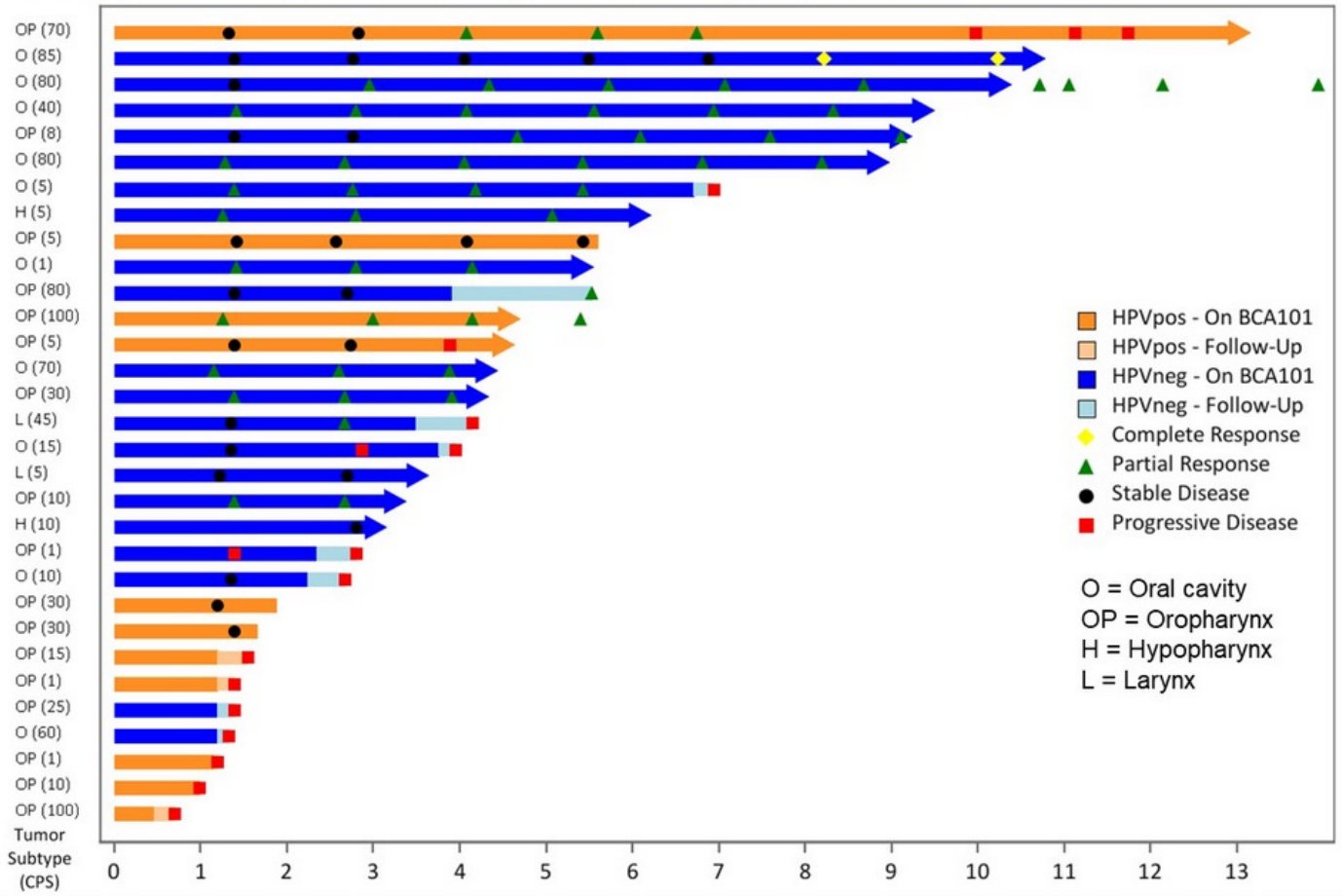
ORR	13/20 (65%)
CPS 1-19	5/10 (50%)
CPS≥20	8/10 (80%)

- ORR 65% in HPV-neg subjects with responses observed in both CPS subgroups

Source: Open clinical database, as of 22-May-2023

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L)

Preliminary Efficacy – Total population



- Median time to response 1.4 months (range 1.2-8.2 months)
- Responses in HPV-neg subjects observed across all subsites:
  - Oral cavity (7/10, 70%)
  - Oropharynx (4/6, 67%)
  - Hypopharynx (1/2)
  - Larynx (1/2)

PRESENTED BY: Glenn J. Hanna, MD

Source: Open clinical database, as of 22-May-2023

Summary and future directions

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L):

- ORR total population = 48% (15/31)
- **HPV-neg ORR = 65% (13/20)**, including responses in:
  - Oral cavity (7/10, 70%), oropharynx (4/6, 67%), hypopharynx (1/2), larynx (1/2)
  - CPS 1-19 (5/10, 50%) and CPS ≥20 (8/10, 80%)
  - Distant metastatic (9/14, 64%) and locoregional disease (4/6, 67%)
- Preliminary mPFS in (stage 1) HPV-neg subjects not reached (range 1.3-14.6+ months, at least 6.6 months) with 7 responses ongoing
- Manageable safety profile

Data warrants further evaluation of the combination in HPV-negative patients in a randomized study.

PRESENTED BY: Glenn J. Hanna, MD

Source: Open clinical database, as of 22-May-2023

Nasopharyngeal Carcinoma

- rare type of cancer that develops in the upper part of the throat, behind the nose and above the soft palate.
- Causative agent is Epstein Barr Virus (EBV infection)
- Symptoms are distinct from other H&N cancers including nasal congestion, hearing difficulties, epistaxis and tinnitus.
- Histology resembles SCC, requiring EBV confirmation on pathology (EBER DNA ISH).
- EBV DNA is highly sensitive to predict recurrence and able to non invasively monitor disease.

Updates in Metastatic NPC Treatment

Recurrent, Unresectable, Oligometastatic, or Metastatic Disease (with no surgery or RT option)

Preferred Regimens

First-Line[d]

- Cisplatin/gemcitabine (category 1)[16,17]
- Cisplatin/gemcitabine + toripalimab-tpzi (category 1)[18]
- Cisplatin/gemcitabine + other PD-1 inhibitor (eg, pembrolizumab or nivolumab)[19,20]

Subsequent-Line

- Toripalimab-tpzi (if disease progression on or after platinum-containing therapy)[21]

Other Recommended Regimens

First-Line[d]

- Combination Therapy
  - Cisplatin/5-FU[22,23]
  - Cisplatin or carboplatin/docetaxel[24] or paclitaxel[22]
  - Carboplatin/cetuximab[25]
  - Gemcitabine/carboplatin[1]
- Single Agents
  - Cisplatin[26,27]
  - Carboplatin[28]
  - Paclitaxel[29]
  - Docetaxel[30,31]
  - 5-FU[27]
  - Methotrexate[23,32]
  - Gemcitabine[33]
  - Capecitabine[34]

Subsequent-Line

- Immunotherapy
  - Nivolumab if previously treated, recurrent or metastatic non-keratinizing disease (category 2B)[35,36]
  - Pembrolizumab if previously treated, PD-L1–positive, recurrent or metastatic disease (category 2B)[37]

Useful in Certain Circumstances

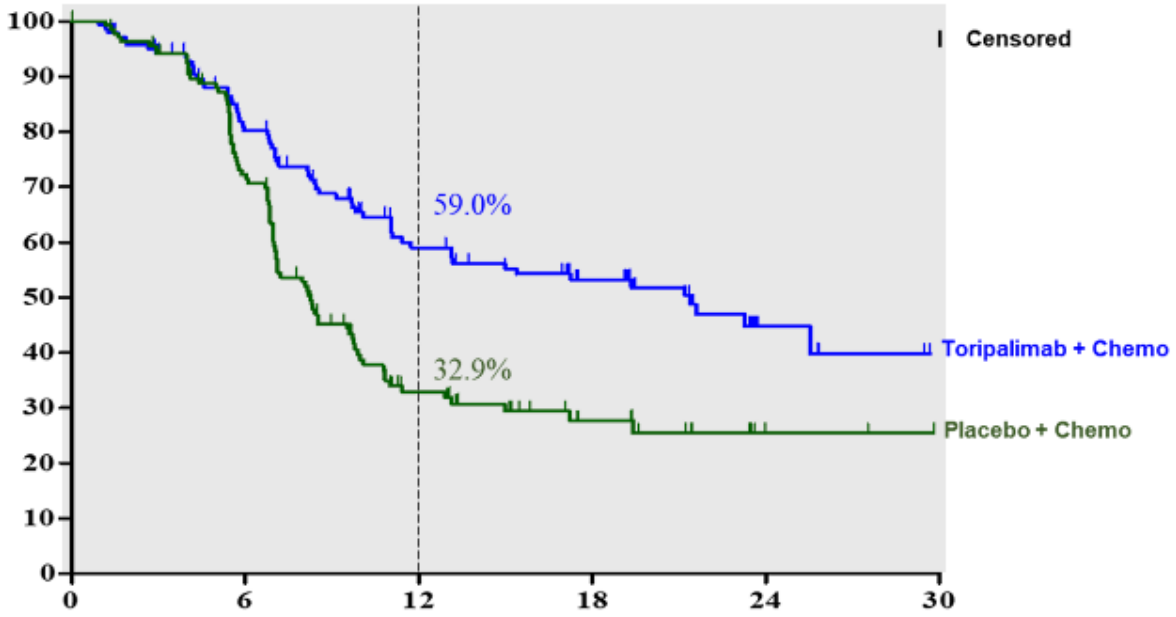
Subsequent-Line

- Pembrolizumab (for tumor mutational burden-high [TMB-H] tumors [≥10 mut/Mb])[36]

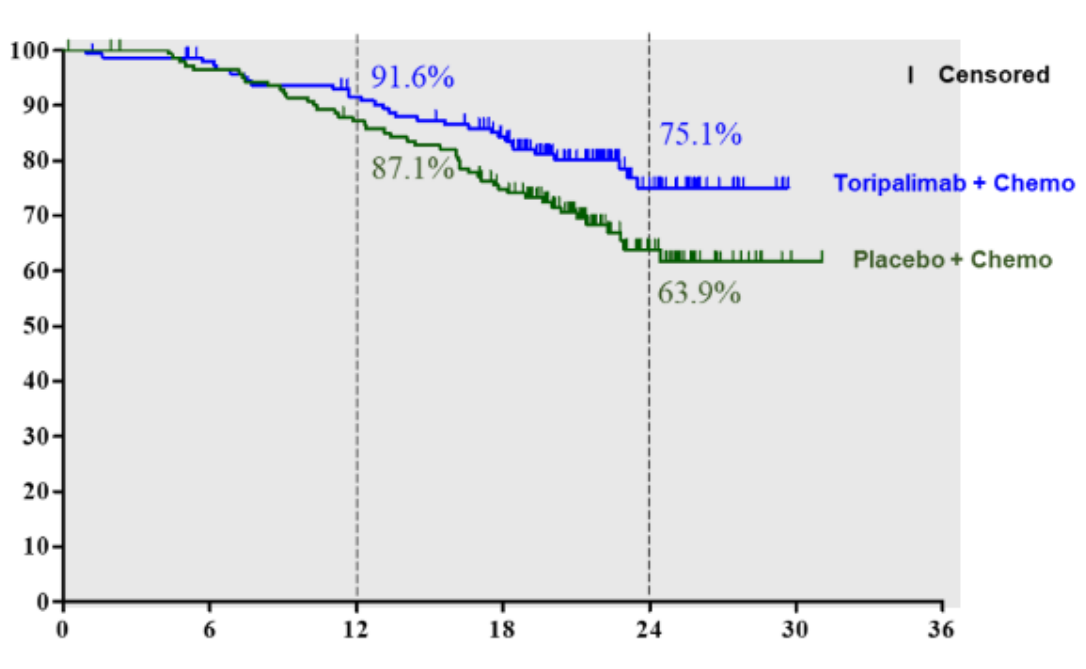
Adapted from NCCN Guidelines Version 2.2024.

Efficacy Evaluation with Toripalimab +/- Chemotherapy

Progression-free Survival



Overall Survival



- mPFS 21.4 vs 8.2 months, HR=0.52 (95%CI: 0.37-0.73), p=0.0001
- mOS not evaluable, HR 0.59 (95% CI: 0.37, 0.94), *P*=0.0238
- No unanticipated safety signals

Summary

- No changes in treatment for curative intent therapy: reliance on surgery, radiation therapy and chemotherapy.
- Carboplatin, Paclitaxel and Pembrolizumab shows promise to reduce need for 5-FU in treatment of metastatic disease; more studies warranted.
- BCA101 (TGFb ab) shows promise in HPV(-) disease.
- Toripalimab is 1st FDA approved agent in combination with chemotherapy and as single agent in R/M NPC.

Thank you!

The US Oncology Network