

HMP Education



Oncology Learning Network

OPTIMIZING PRECISION CARE IN RECURRENT/ METASTATIC HNSCC

Translating Emerging Therapies
Into Proactive, Patient-Centered
Treatment Strategies

Supported by an educational grant from Johnson & Johnson.

Faculty

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Faculty Disclosures

- **Aarti Bhatia, MD, MPH:** Advisory Board—Genmab, MERCK, Merus, Regeneron
- **Faith Mutale, DNP, CRNP:** Speakers' Bureau—AstraZeneca, Daiichi Sankyo

Disclosures

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Learning Objectives

- Explain key molecular drivers and tumor biology in HNSCC, including differences between HPV-related and HPV-unrelated disease, and their implications for targeted therapeutics
- Assess treatment strategies in R/M HNSCC after progression on platinum and immunotherapy, including the rationale and emerging evidence for EGFR/MET-directed approaches
- Apply proactive, team-based toxicity management strategies for treatment-related AEs associated with EGFR-directed therapies to support early intervention, treatment continuity, and patient outcomes

HNSCC = head and neck squamous cell carcinoma; HPV = human papillomavirus; R/M = recurrent/metastatic; EGFR = epidermal growth factor receptor; MET = mesenchymal-epithelial transition factor; AE = adverse event.

Program Information

- This program is provided by HMP Education, an HMP Global Company
- Supported by an educational grant from Johnson & Johnson

Polling

- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response



HNSCC Overview

- Heterogeneous disease
- **4%**
- **90% squamous histology** excluding nonmelanoma skin cancers
- **Oral cavity, oropharynx, hypopharynx, and larynx**
- Nasopharyngeal carcinoma, salivary gland cancers, and sinonasal tumors—distinct biology & treatment approaches

American Cancer Society. 2026. Accessed September 2026. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2026/2026-cancer-facts-and-figures.pdf>. Lewis JS Jr, et al. *Arch Pathol Lab Med*. 2025;149(6):e115-e150. Dunn LA, et al. *JAMA*. 2026;335(6):531-541. National Cancer Institute. 2021. Accessed September 2026. <https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet>.

Epidemiology & Disease Burden of HNSCC

Burden	Worldwide	United States
New cases	~ 890,000 head & neck cancers* in 2026	60,480 oral cavity & oropharyngeal cancers projected in 2026
Deaths	~ 450,000 in 2026	13,150 projected in 2026
Major sites	Lip/oral cavity, larynx, oropharynx, hypopharynx	Oral cavity/oropharynx dominate
Key epidemiologic pattern	Burden varies substantially by region, sex, tobacco/alcohol exposure, betel quid, and HPV	Oropharyngeal cancer increasing , while laryngeal cancer incidence is declining
Who is most affected?	~ 72% male for lip/oral cavity/pharyngeal cancers	Incidence of oral/oropharyngeal cancer is ~ 3× higher in men than women

Bhatia A, Burtneess B. *Drugs*. 2023;83(3):217-248. Sung H, et al. *CA Cancer J Clin*. 2026;76(4):e70090. American Cancer Society. 2026. Accessed September 2026. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2026/2026-cancer-facts-and-figures.pdf>. American Cancer Society. 2026. Updated March 23, 2026. Accessed September 2026. <https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-cancer/key-statistics.html>.

Epidemiology & Disease Burden: US

HPV + HPV-

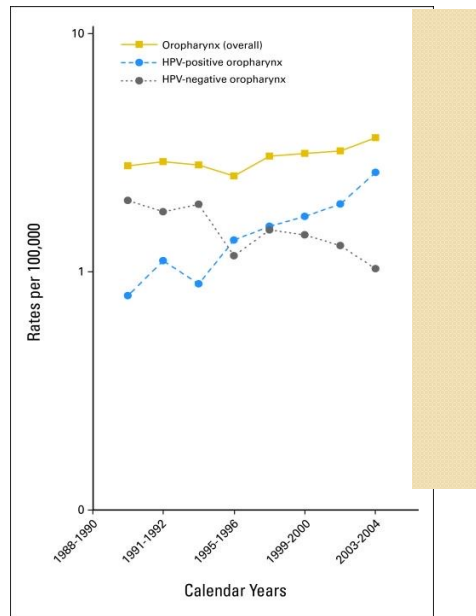
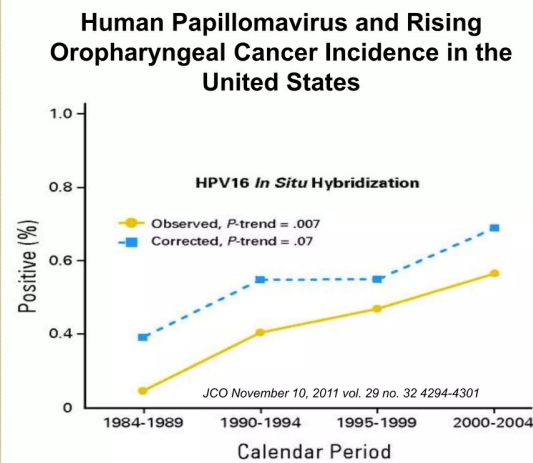
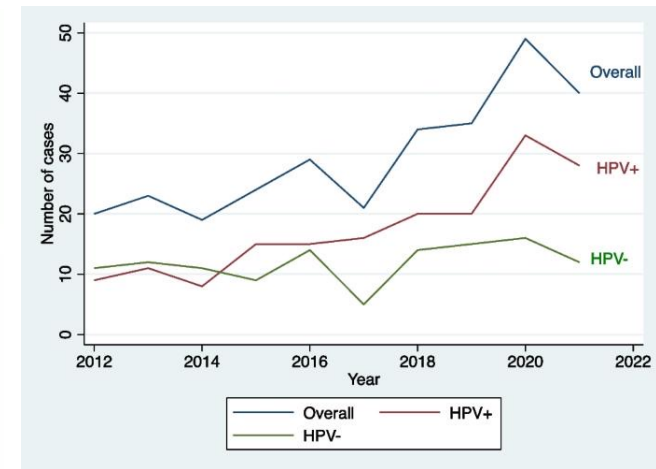
Disease Group	2000	2019	Trend, 2000–2019
HPV-related HNC <i>(oropharyngeal anatomic proxy)</i>	3.3/100,000	4.4/100,000	↑ 1.5%/yr
Non-HPV-related HNC	9.3/100,000	7.7/100,000	↓ 1.1%/yr
All HNC	11.5/100,000	10.5/100,000	↓ 0.6%/yr

HNC = head and neck cancer.

Mel A, et al. *J Clin Oncol*. 2026;44(suppl 16):e22584.

HPV Is Reshaping the Epidemiology of Oropharyngeal Cancer

HPV-positive incidence is rising while HPV-negative disease is declining



Chaturvedi AK, et al. *J Clin Oncol.* 2011;29(32):4294-4301. Mel A, et al. *J Clin Oncol.* 2026;44(suppl 16):e22584.

The Epidemiologic Shift: Tobacco ↓, HPV-Associated OPSCC ↑

Disease Biology and HPV Distinction

- HPV- Negative
 - Older
 - Tobacco
 - Alcohol
 - Oral cavity, larynx, hypopharynx
 - Multiple comorbidities
 - TP53/CDKN2A alterations common
- HPV-Positive
 - Primarily oropharyngeal
 - Middle-aged adults
 - Tonsil & base of tongue
 - Fewer traditional comorbidities
 - Viral E6/E7-driven biology

OPSCC = oropharyngeal squamous cell carcinoma.

Lewis JS Jr, et al. *Arch Pathol Lab Med*. 2025;149(6):e115-e150. National Cancer Institute. Oropharyngeal Cancer Treatment (PDQ®). Updated May 14, 2025. Accessed September 2026. <https://www.cancer.gov/types/head-and-neck/hp/adult/oropharyngeal-treatment-pdq>.

Molecular Drivers in HNSCC (EGFR, MET, Etc.)

Pathway / Driver	Common Alterations	Clinical Relevance
EGFR / HER family	EGFR overexpression/amplification	Proliferation, survival, invasion; validated therapeutic target
PI3K–AKT–mTOR	PIK3CA mutation/amplification; PTEN loss	Growth, survival, treatment resistance
TP53 / Cell Cycle	TP53 mutation; CDKN2A loss; CCND1 amplification	Major driver of HPV– HNSCC ; genomic instability
NOTCH	NOTCH1/2 loss-of-function	Abnormal squamous differentiation
MET / HER3 / FGFR	Amplification, overexpression, activating alterations	Emerging therapeutic targets
HPV E6/E7	p53 and RB pathway disruption	Defines biologically distinct HPV+ OPSCC

HER = human epidermal growth factor receptor; FGFR = fibroblast growth factor receptor.

Li Q, et al. *Signal Transduct Target Ther.* 2023;8:31. Liu Y, et al. *MedComm* (2020). 2024;5(9):e702. Nadal A, et al. *Virchows Arch.* 2024;485(6):965-976.

Current Standard of Care and Unmet Needs in R/M HNSCC

Treatment selection driven by

- **PD-L1/CPS**
- Prior platinum exposure and timing of recurrence
- Disease burden, symptoms, and need for rapid response
- Performance status and comorbidities
- Prior immunotherapy exposure
- Resectability/local control options

CPS = combined positive score.

Bhatia A, Burtneess B. *Drugs*. 2023;83(3):217-248.

Current Standard of Care and Unmet Needs in R/M HNSCC

Patient population

PD-L1 CPS ≥ 1

PD-L1 CPS < 1

Need for rapid tumor response/high disease burden

Lower disease burden/indolent disease

Preferred approach

**Pembrolizumab monotherapy OR
pembrolizumab + platinum + 5-FU**

Pembrolizumab + platinum + 5-FU remains an option

Pembrolizumab + platinum + 5-FU generally favored

Pembrolizumab monotherapy may be appropriate

Current Standard of Care and Unmet Needs in R/M HNSCC

Other Systemic Options

- Platinum-based chemotherapy
- Cetuximab-containing regimens
- Taxanes
- Methotrexate or other single-agent chemotherapy (in selected later-line patients)
- **Clinical trials** → after progression

Treatment After Progression

Platinum-Refractory R/M HNSCCA

- **Nivolumab or pembrolizumab** regardless of PD-L1 CPS
- CheckMate 141 demonstrated improved OS with nivolumab versus investigator's-choice therapy
- KEYNOTE-040 demonstrated improved OS with pembrolizumab versus standard single-agent therapy
- **Clinical challenge:**
landscape substantially less defined after progression on **both platinum chemotherapy and immune checkpoint inhibition**

OS = overall survival.

Ferris RL, et al. *N Engl J Med*. 2016;375:1856-1867. Tahara M, et al. *Cancer Treat Rev*. 2025;136:102938. Yilmaz E, et al. *J Clin Oncol*. 2023;41(5):1132-1146. National Cancer Institute. Hypopharyngeal Cancer Treatment (PDQ®). Updated May 14, 2025. Accessed September 2026. <https://www.cancer.gov/types/head-and-neck/hp/adult/hypopharyngeal-treatment-pdq>.

Current Standard of Care and Unmet Needs in R/M HNSCC

Progression after Platinum and Immune Checkpoint Inhibition

- Prior therapies and response duration
- Site and rate of progression
- PS and goals
- Potential for local therapy
- Clinical trial availability

Unmet Needs in HNSCC

- Despite advances with immunotherapy, major challenges remain
- Response in a minority
- Durable benefit in a smaller subset
- Primary & Acquired resistance → progression

Xie J, et al. *Front Public Health*. 2026;14:1776834. Meci A, et al. *Cancers (Basel)*. 2024;16(4):703. Okano S. *Auris Nasus Larynx*. 2024;51(4):684-695. Rosenberg AJ, et al. *ASCO Educ Book*. 2024;44(3):e433330. Tahara M, et al. *Cancer Treat Rev*. 2025;136:102938.

Unmet Needs in HNSCC

Treatment After Immunotherapy progression

- Few effective options
- Chemotherapy → **modest response rates and limited durability**
- Need for effective PD-L1 **therapies & better biomarkers.**
- PD-L1/CPS is useful but NOT **perfect**
- Patients with low CPS can still respond, while some CPS-high tumors fail to respond
- Better predictive biomarkers are needed to identify
 - Responders
 - Primary resistance
 - Acquired resistance
 - Patients likely to benefit from combination strategies

Xie J, et al. *Front Public Health*. 2026;14:1776834. Meci A, et al. *Cancers (Basel)*. 2024;16(4):703. Okano S. *Auris Nasus Larynx*. 2024;51(4):684-695. Rosenberg AJ, et al. *ASCO Educ Book*. 2024;44(3):e433330. Tahara M, et al. *Cancer Treat Rev*. 2025;136:102938.

Unmet Needs in R/M HNSCC

- **Balancing efficacy with QOL**
- HNSCC can compromise **speech, swallowing, nutrition, breathing, appearance, and social functioning**
- Treatment-related toxicities → can compound preexisting functional deficits
- Consider **patient goals and functional outcomes**, NOT survival alone

QOL = quality of life.

Goyal N, et al. *Laryngoscope Investig Otolaryngol*. 2022;7(1):70-92. Manduchi B, et al. *Head Neck*. 2024;46(4):951-972. Seth I, et al. *Head Neck*. 2024;46(1):86-117.

Unmet Needs in R/M HNSCC

Frail Patients

- **Limited treatment options**
- Substantial comorbidity, malnutrition, tobacco/alcohol exposure, or poor PS
- Intensive chemotherapy may not be feasible
- Less-toxic, effective therapies are needed

PS = performance status.

Goyal N, et al. *Laryngoscope Investig Otolaryngol*. 2022;7(1):70-92. Manduchi B, et al. *Head Neck*. 2024;46(4):951-972. Seth I, et al. *Head Neck*. 2024;46(1):86-117.

Unmet Needs in R/M HNSCC

- **Need for effective targeted therapies**
- EGFR is an important biologic driver, but resistance to EGFR-directed therapy is common
- Novel targets and therapeutic strategies—including **bispecific & ADCs**—under investigation
- **Current paradigm**
- **PD-L1 testing → Immunotherapy ± chemotherapy → Progression → Limited systemic options**

ADC = antibody-drug conjugate.

Yilmaz E, et al. *J Clin Oncol*. 2023;41(5):1132-1146. Diniz CHP, et al. *Oncol Rep*. 2024;51(6):80. Tahara M, et al. *Cancer Treat Rev*. 2025;136:102938.

Where We Need to Go

- Immunotherapy has transformed first-line treatment of R/M HNSCC, **but** durable disease control remains limited
- More precise treatment selection
- More effective therapies after PD-1 progression → overcome resistance
- Longer duration of disease control
- Less toxicity and preservation of function
- Better QOL

Clinical Guidelines and Treatment Selection

Clinical Decision-Making Framework

- **Is the recurrence potentially curable?**
- Resectable isolated recurrence → consider salvage surgery
- Local/regional disease amenable to radiation or re-irradiation → multidisciplinary evaluation
- Unresectable or disseminated disease → systemic therapy
- **Obtain PD-L1 CPS**
- Recommended for all patients with R/M HNSCC being considered for immunotherapy

Clinical Guidelines and Treatment Selection

Clinical Decision-Making Framework

- **Assess clinical urgency**
- Tumor burden
- Rate of progression
- Symptomatic disease
- Threat to airway, swallowing, or other critical structures
- Need for rapid tumor shrinkage

Clinical Guidelines and Treatment Selection

Clinical Decision-Making Framework

- **Assess patient factors**
- Performance status
- Organ function
- Prior platinum and I/O exposure
- Comorbidities
- Nutritional status
- Patient goals and wishes

I/O = immuno-oncology.

Arrazubi V, et al. *Clin Transl Oncol*. 2026;28(6):2056-2067. Kiss N, et al. *JPEN J Parenter Enteral Nutr*. 2026;50(3):274-338. Yilmaz E, et al. *J Clin Oncol*. 2023;41(5):1132-1146.

Why CPS Matters

PD-L1 CPS =

- Total viable tumor cellsPD-L1-
positive tumor cells + immune cells $\times 100$

Treatment implications

- **CPS ≥ 20** : greatest likelihood of benefit from pembrolizumab monotherapy
- **CPS 1–19**: pembrolizumab monotherapy remains an option
- **CPS < 1** : pembrolizumab + platinum/5-FU can be considered, although evidence is less robust in this subgroup

Treatment Landscape Post Platinum & PD-1 Therapy

- Few established highly effective options
- Critical need for
 - Clinical trials
 - Novel targeted therapies
 - Antibody-drug conjugates
 - Bispecific antibodies
 - Biomarker-driven treatment strategies

Key Learning Points

- **PD-L1 CPS is central to first-line treatment selection**
- **Pembrolizumab monotherapy** → option for CPS ≥ 1
- **Chemo/IO** preferred when rapid disease control is clinically important
- Treatment decisions should incorporate **prior platinum and immunotherapy exposure**
- **Post-PD-1 progression remains a major unmet need**, making clinical trial participation particularly important
- MDT essential in R/M disease, some patients may benefit from **surgery, radiation, or re-irradiation** rather than systemic therapy alone

Newer and Emerging Therapeutic Approaches

Newer Therapeutics on the Horizon

Potential Applications in HPV-Negative or Positive HNSCC, as well as in the Post-PD-1 Setting

Bispecific Antibodies

- **Amivantamab** (EGFR/MET) (FDA Breakthrough Therapy Designation)
- **Ficerafusp alfa** (FDA Breakthrough Therapy Designation)
- **Petosemtamab** (EGFR/MET) (FDA Breakthrough Therapy Designation)
- **Volrustomig** (PD-1/CTLA-4)

Antibody–Drug Conjugates (ADCs)

- **CRB-701** (Nectin-4 ADC)
- **Telisotuzumab adizutecan** (MET ADC; ABBV-400)
- **ADCE-T02** (TF-topo 1 ADC)

T-DXd (trastuzumab deruxtecan): Tumor-agnostic indication for unresectable or metastatic HER2-positive (IHC 3+) solid tumors

Cancer Vaccines

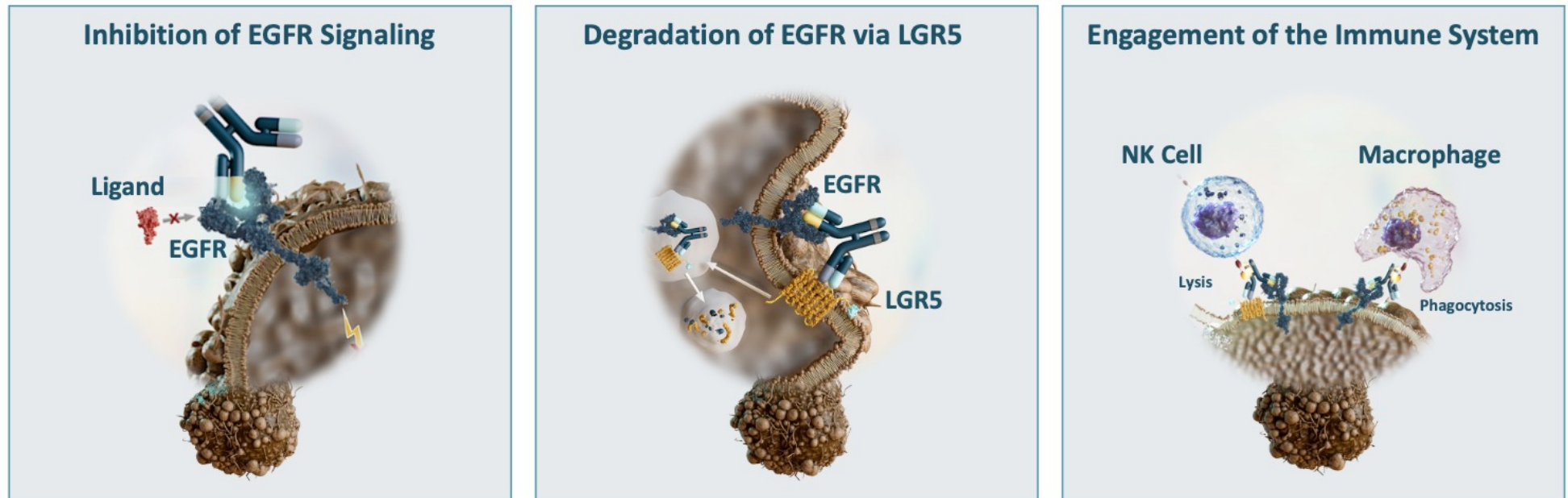
- **BNT113** (HPV16 mRNA vaccine) (FDA Fast Track Designation)

Other Emerging Strategies

- **Ficlatuzumab** (HGF/c-MET)

Petosemtamab: Bispecific Antibody Targeting EGFR/LGR5

Mechanism of action: Inhibition of EGFR-dependent signaling and EGFR degradation via LGR5/E3 ligase facilitates interaction with immune cells (ADCC- and ADCP-enhanced antibody)



ADCC = antibody-dependent cellular cytotoxicity; ADCP = antibody-dependent cellular phagocytosis.

Herpers B, et al. *Nat Cancer*. 2022;3:418-436. Xu L, et al. *Stem Cell Res Ther*. 2019;10:219. Katoh M. *Int J Oncol*. 2017;51:1357-1369. Wu Z, et al. *Int J Clin Exp Pathol*. 2017;10:11267-11275. Dally AJ, et al. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119:436-440. Cohen E, et al. Presented at: AACR 2023; April 14-19, 2023; Orlando, FL. Abstract CT012.

In a Phase 2 Study, Combining Petosemtamab With PD-1 Therapy Was Active as 1L Therapy in R/M HNSCC

Petosemtamab + Pembrolizumab in 1L PD-L1+ R/M HNSCC (N = 43 evaluable patients)

– Clinically meaningful efficacy and durability: ORR of 63%

Response Subgroup	Patients, % (n/N)
Confirmed ORR (RECIST v1.1)	63 (27/43; 95% CI 49-75)
p16-positive (oropharynx)	50 (4/8)
p16-negative	66 (23/35)
PD-L1 CPS 1-19	47 (8/17)
PD-L1 CPS ≥20	73 (19/26)

12-mo PFS and OS of 38% and 79%, respectively

ORR = objective response rate; RECIST = Response Evaluation Criteria in Solid Tumors; PFS = progression-free survival.
van Herpen CML, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract 6024.

Petosemtamab-Pembrolizumab Combination Was Well-Tolerated, With a Favorable Safety Profile

- TEAEs were reported in 45 patients; most were grade 1 or 2
- Grade ≥ 3 TEAEs occurred in 27 patients (60%), including 20 (44%) who experienced treatment-related TEAEs
- No individual grade ≥ 3 TEAE occurred in $>7\%$ of patients
- No grade 5 treatment-related TEAEs were reported
- IRRs occurred in 38% of patients, with 7% grade 3; no grade 4 or 5; mainly occurred during first infusion and were resolved
- No significant overlapping toxicities were observed

↓ Clinical note

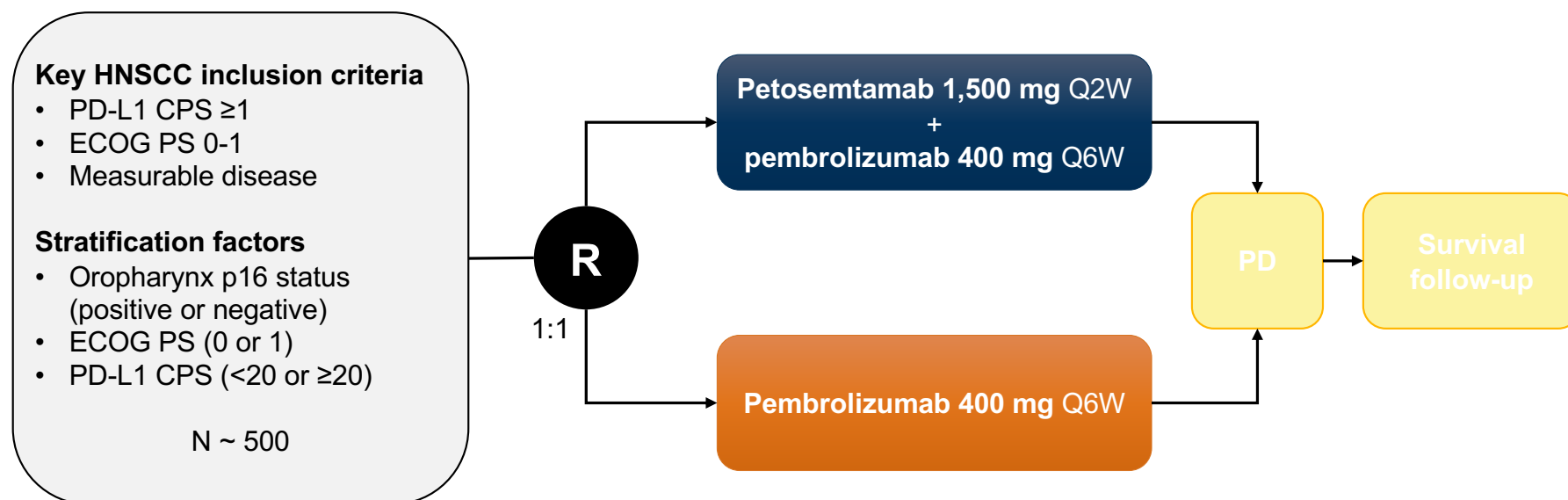
IRRs managed with premedication, prolonged infusion

TEAEs Irrespective of Causality ($\geq 20\%$ of Patients), n (%)

Preferred Term	All Grades	Grades 3-5
At least 1 TEAE	45 (100)	27 (60)
Asthenia	23 (51)	3 (7)
Acneiform dermatitis	22 (49)	3 (7)
Rash	20 (44)	0
Blood Mg decreased	18 (40)	3 (7)
Skin fissures	18 (40)	1 (2)
Constipation	16 (36)	0
Nausea	16 (36)	1 (2)
Folliculitis	15 (33)	1 (2)
Dry skin	14 (31)	1 (2)
Paronychia	14 (31)	1 (2)
Diarrhea	13 (29)	3 (7)
Pruritus	13 (29)	0
Stomatitis	13 (29)	2 (4)
Hypotension	10 (22)	2 (4)
Cough	9 (20)	0
Tumor pain	9 (20)	2 (4)

TEAE = treatment-emergent adverse event; IRR = infusion-related reaction.
van Herpen CML, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract 6024.

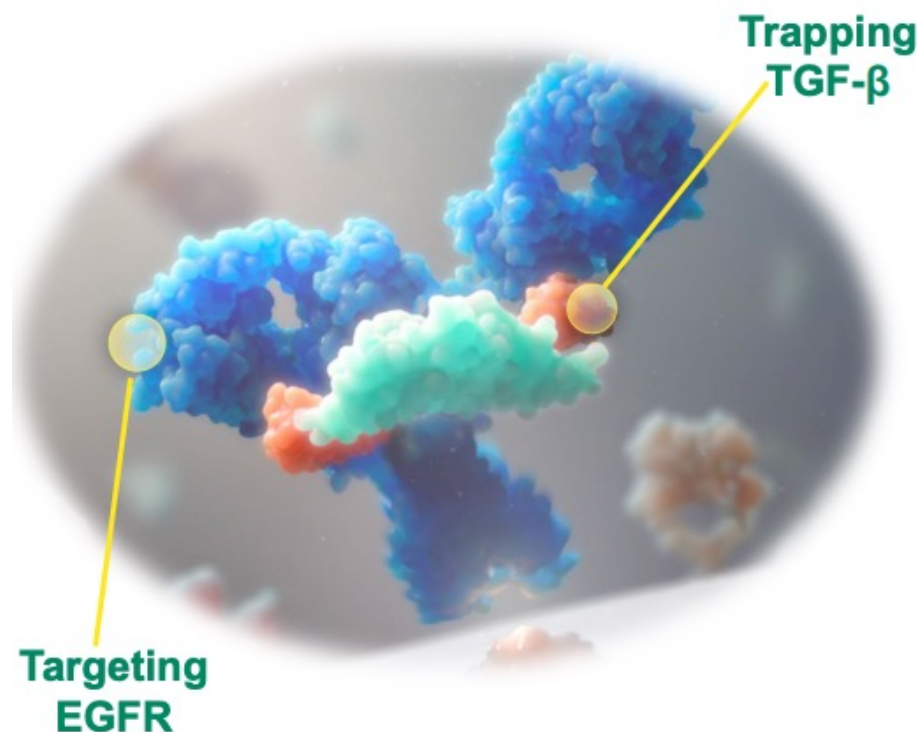
Phase 3 LiGeR-HN1 Trial Will Further Assess Petosemtamab-Pembrolizumab Combination as 1L Therapy in R/M HNSCC



ECOG = Eastern Cooperative Oncology Group; PD = progressive disease.
Machiels JP, et al. *Future Oncol.* 2025;21(16):2007-2016.

Ficerafusp Alfa Targets EGFR and TGF- β , Both Drivers of Poor Prognosis in HPV-Negative Disease

- Convergent EGFR and TGF- β signaling drives tumor progression and resistance
- Ficerafusp is designed to enable tumor penetration of immune cells by remodeling the fibrotic TME to drive deep and durable responses



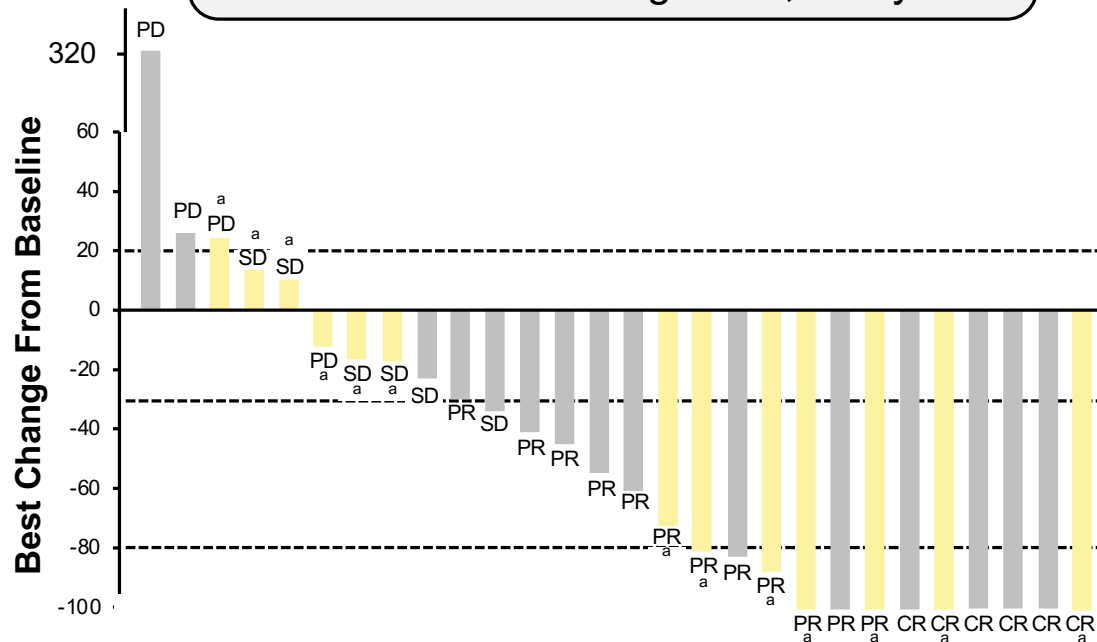
TME = tumor microenvironment.

Chung CH, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract 6017.

Ficerafusp Alfa + Pembrolizumab Shows Promising Activity in HPV-Negative, CPS ≥ 1 , 1L R/M HNSCC

Ficerafusp alfa 1500 mg IV d1, d8, d15
+
Pembrolizumab 200 mg IV d1, every 21 d

- 1L R/M HNSCC, HPV-negative
- Oral cavity, oropharynx, larynx, and hypopharynx
- CPS ≥ 1



- **Confirmed ORR = 54% (15/28)**
- **Deep responses = 80% (12/15) achieved $\geq 80\%$ tumor shrinkage**

Other efficacy outcomes

- mPFS = 9.9 mo
- mDOR = 21.7 mo
- mOS = 21.3 mo

^aCPS 1-19.

PD = progressive disease; SD = stable disease; PR = partial response; CR = complete response; DOR = duration of response. Chung CH, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract 6017.

Ficerafusp Alfa + Pembrolizumab Is a Well-Tolerated Combination in R/M HNSCC

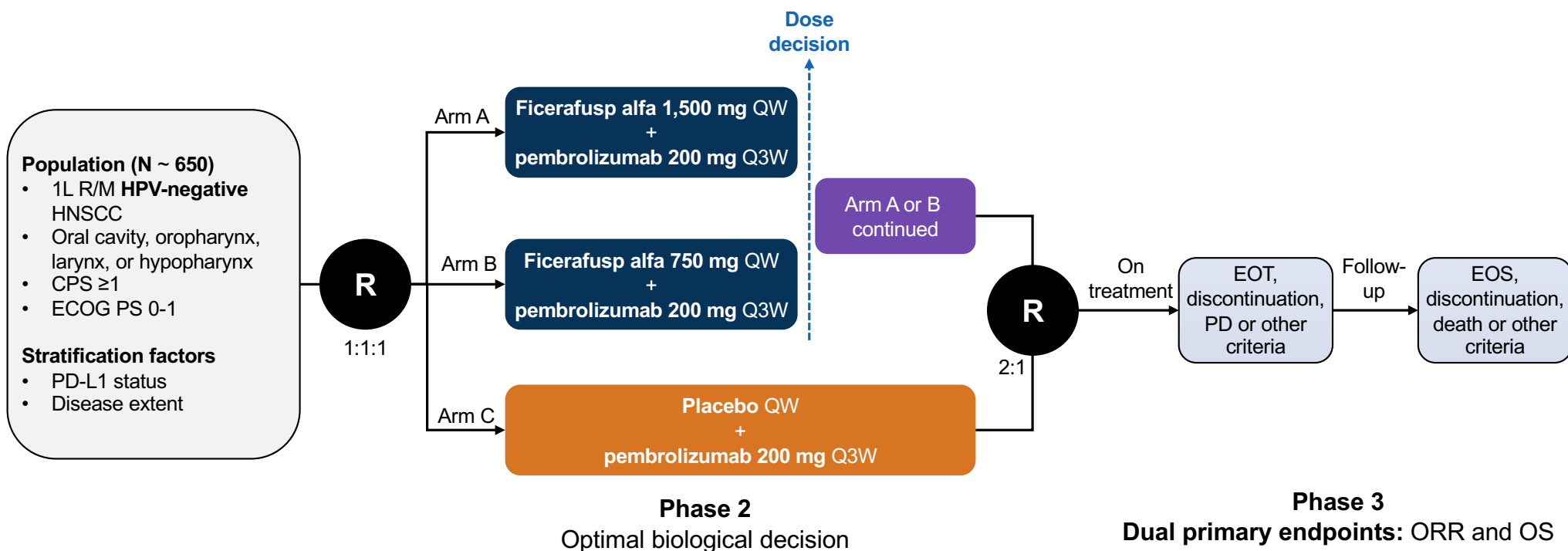
Most Frequently Reported (≥20%) TEAEs Related to Ficerafusp Alfa

Favorable safety profile
observed with no new
safety signals

Preferred Term	Safety Set (n = 30)			
	All Grades	Grade 3	Grade 4	Grade 5
Any TEAE	28 (93)	14 (47)	1 (3)	0
Dermatitis acneiform	23 (77)	4 (13)	0	0
Pruritus	16 (53)	0	0	0
Anemia	13 (43)	6 (20)	0	0
Hypomagnesemia	13 (43)	0	0	0
Fatigue	11 (37)	1 (3)	0	0
Dry skin	9 (30)	0	0	0
Hypophosphatemia	8 (27)	0	0	0
Hypokalemia	8 (27)	0	0	0
Stomatitis	7 (23)	0	0	0
Nausea	6 (20)	0	0	0

Chung CH, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract 6017.

FORTIFI-HN01 Is Assessing Ficerafusp Alfa-Based Treatment as 1L Therapy in R/M HPV-Negative Disease



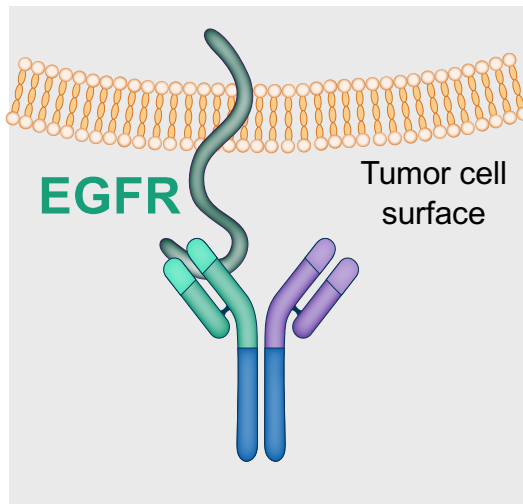
EOT = end of treatment; EOS = end of study.

Ferrarotto R, et al. Presented at: ASCO 2025; May 28, 2025; Chicago, IL. Abstract TPS6113. ClinicalTrials.gov. Accessed September 2026. <https://clinicaltrials.gov/study/NCT06788990>.

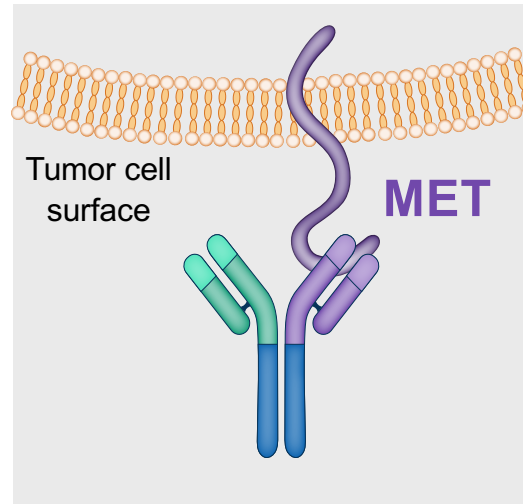
Amivantamab Achieves Anti-Tumor Effects by Inhibiting EGFR and MET, but Also Through Immune Cell Effects

Amivantamab Is an EGFR-MET Bispecific Antibody with a Triple Mechanism

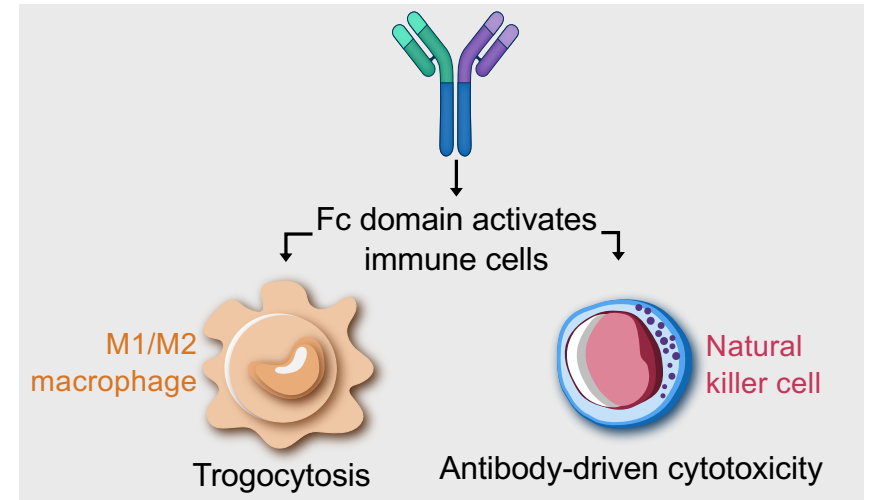
(1) EGFR inhibition



(2) MET inhibition



(3) Immune cell-directing activity



OrigAMI-4 Study Design

Eligibility Criteria for Cohort 1

- Recurrent/metastatic (R/M) head and neck squamous cell carcinoma
- No prior anti-EGFR therapy
- ECOG PS score: 0 or 1
- p16 positive oropharyngeal carcinoma was excluded

Subcutaneous amivantamab is administered at 2400 mg (or 3360 mg if ≥ 80 kg) Q3W^a

Cohort 1: Amivantamab monotherapy^b

Post-PD-(L)1 inhibitor and platinum-based chemotherapy^c

➔ **Focus of this presentation**

Cohort 2: Amivantamab plus pembrolizumab^b

Treatment naïve in the R/M setting

Cohort 3: Amivantamab plus paclitaxel^b

Post-PD-(L)1 inhibitor

Cohort 4: Amivantamab monotherapy^d

Post-PD-(L)1 inhibitor and platinum-based chemotherapy^c

Cohort 5: Amivantamab plus pembrolizumab with carboplatin^d

Treatment naïve in the R/M setting

Cohort 6: Amivantamab plus pembrolizumab^b

Treatment naïve in the locally advanced, perioperative setting

Endpoints

- Objective response rate (primary)
- Duration of response
- Clinical benefit rate^e
- Progression-free survival
- Overall survival
- Safety

Responses were assessed by the investigator per RECIST v1.1 and confirmed via BICR

Treatment beyond progression was permitted for continued clinical benefit per investigator

- A sample size of 80 response-evaluable participants would provide >99% power to reject the null hypothesis (ORR $\leq 10\%$) assuming an ORR of 30% with a 2-sided alpha of 5%^f

OrigAMI-4 (ClinicalTrials.gov Identifier: NCT06385080). Note: All cohorts of OrigAMI-4 will utilize the subcutaneous formulation of amivantamab, which is coformulated with recombinant human hyaluronidase PH20 and manually injected in the abdomen.

^aEach cycle is 21 days (3 weeks); Cycle 1: 1600 mg (or 2240 mg if ≥ 80 kg) on Day 1, 2400 mg (or 3360 mg if ≥ 80 kg) on Day 8 and Day 15; Cycle 2 (and thereafter): 2400 mg (or 3360 mg if ≥ 80 kg) on Day 1. ^bParticipants with HPV+ oropharyngeal squamous cell carcinoma were excluded. ^cEligible participants must have received an anti-PD-(L)1 and platinum-based chemotherapy in combination or as separate lines of therapy for R/M disease. A participant could have received 1 or both treatments in the locally advanced disease if progression was within 6 months. ^dParticipants with HPV+ oropharyngeal squamous cell carcinoma were included. ^eClinical benefit rate was defined as percentage of confirmed responders or durable stable disease (at the second disease assessment). ^fThe INTERLINK-1 data, which showed an ORR of 24% with cetuximab, were not available at the time of protocol/study initiation.¹

BICR = blinded independent central review.

Fayette J, et al. *Clin Cancer Res.* 2025;31(13):2617-2627. Reproduced from: Burtneess B. Presented at: 2026 ASCO Annual Meeting; May 29–June 2, 2026; Chicago, IL. Used with permission of Barbara Burtneess.

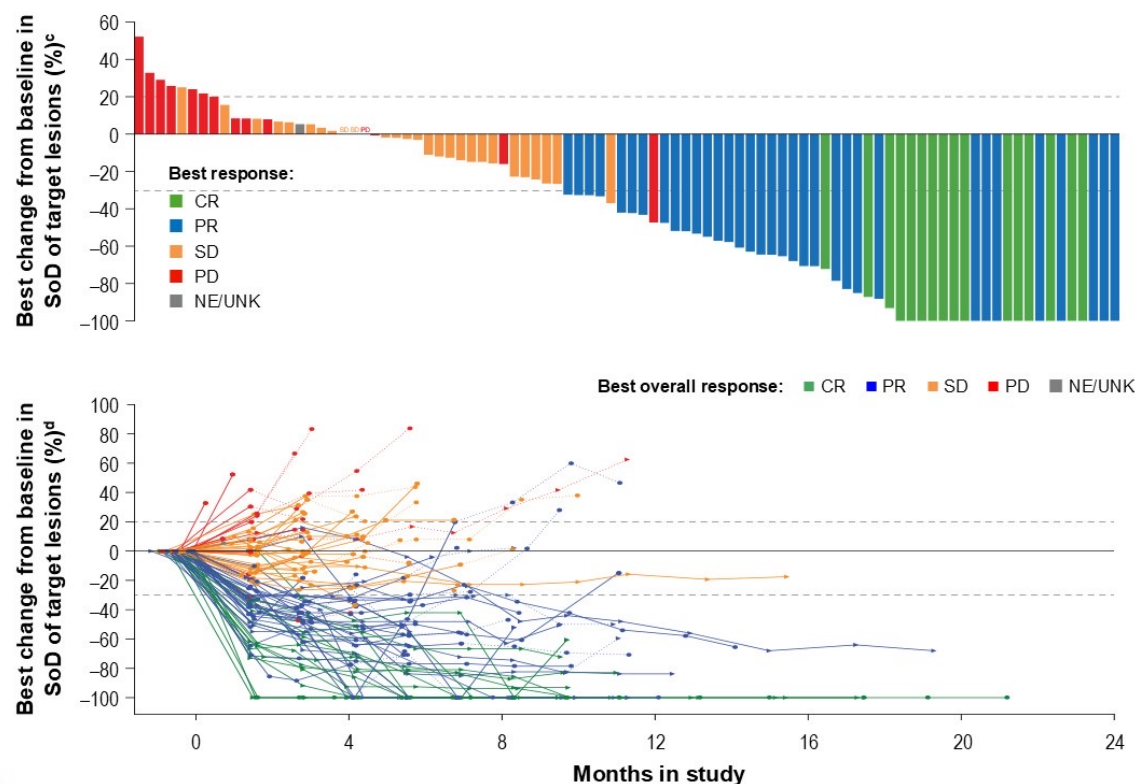
BICR-Assessed ORR and Best Response

BICR-assessed response	N=102
Confirmed ORR	42% (95% CI, 32–52)
Best response, n (%)	
CR	15 (15)
PR	28 (27)
SD ^a	36 (35)
PD	16 (16)
NE	7 (7)
Time to first response, weeks	6.6 (range, 5.6–36.9)
Clinical benefit rate ^b	63% (95% CI, 53–72)

- Investigator-assessed ORR (**47%**; 95% CI, 37–57) was consistent with the BICR results
 - Among participants with ≥1 post-baseline disease assessment, 84% experienced tumor shrinkage of target lesions

^aIncludes non-CR/non-PD with only non-target lesions at baseline and no evidence of disease with no target or non-target lesions at baseline. ^bDefined as percentage of participants achieving a response or durable SD (at second disease assessment). ^cTen participants (NE/UNK; n=6; PD; n=2; non-CR/PD; n=1; no evidence of disease: n=1) without postbaseline tumor assessments were not shown; all participants were included in the ORR analysis. ^dExcludes participants without a postbaseline tumor assessment. Triangle indicates ongoing treatment; circle indicates completed/discontinued treatment; solid line indicates before PD; dotted line indicates after PD.

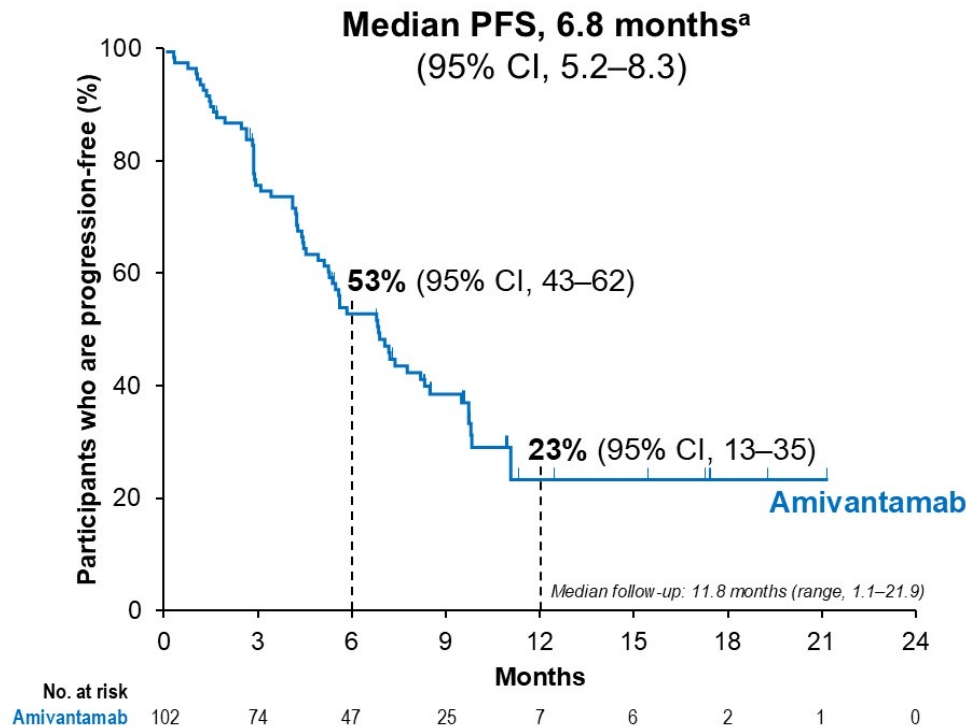
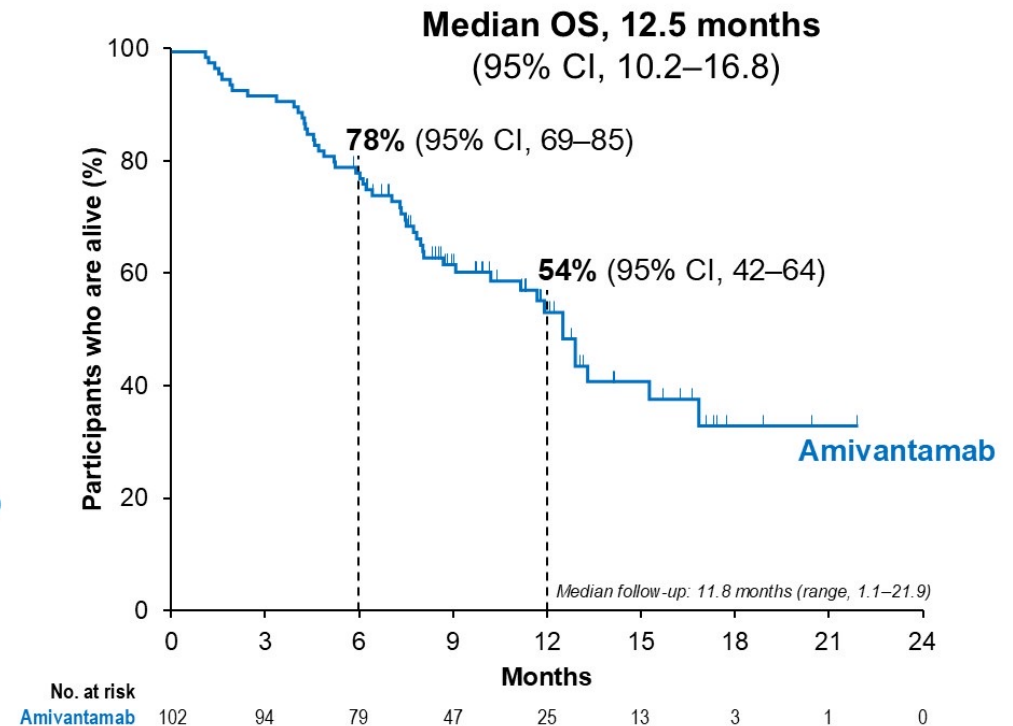
BICR-Assessed Best Response



ClinicalTrials.gov. Accessed September 2026. <https://clinicaltrials.gov/study/NCT06385080>. Reproduced from: Burtneess B. Presented at: 2026 ASCO Annual Meeting; May 29–June 2, 2026; Chicago, IL. Used with permission of Barbara Burtneess.

PFS and OS

54% of participants were alive at 1 year



^aAssessed by investigator.

ClinicalTrials.gov. Accessed September 2026. <https://clinicaltrials.gov/study/NCT06385080>. Reproduced from: Burtneess B. Presented at: 2026 ASCO Annual Meeting; May 29–June 2, 2026; Chicago, IL. Used with permission of Barbara Burtneess.

Safety

- Median treatment duration was 5.9 months^a
- AEs were largely EGFR or MET related and mostly grade 1 or 2
- Administration-related reactions were reported in 15% (grade 1: 9%; grade 2: 6%)
- Treatment-related discontinuations were 8%
- No new safety signals; profile is consistent with prior reports of subcutaneous amivantamab¹

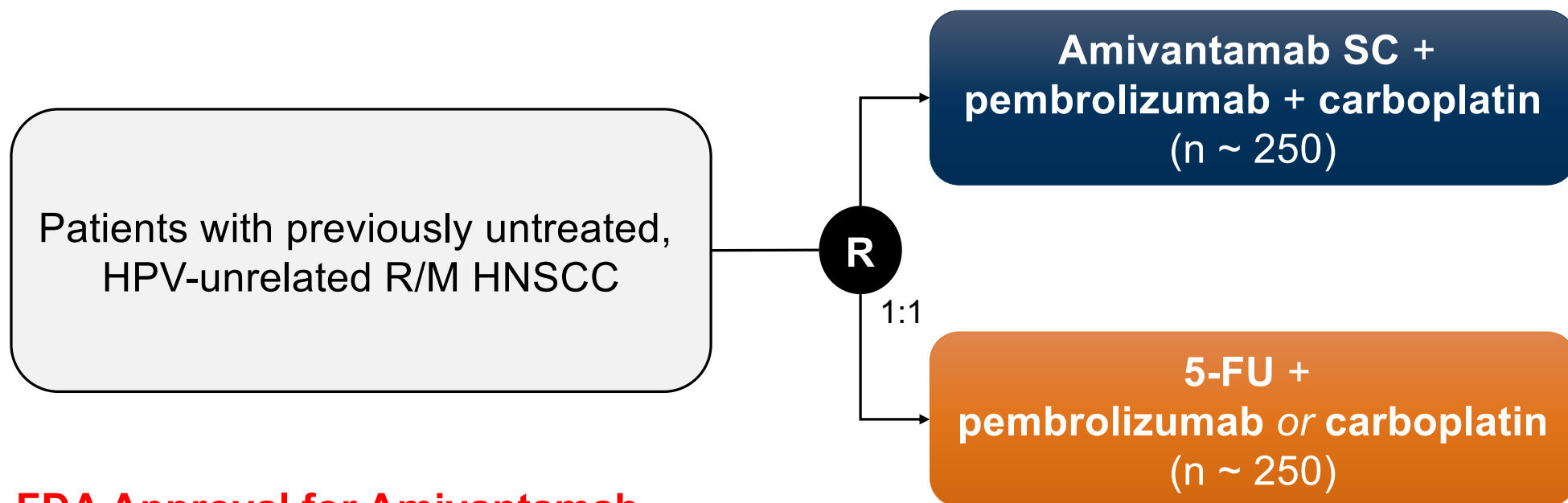
Treatment-emergent AEs (≥20%) by preferred term, n (%)	N=102	
	All grades	Grade ≥3
Related to EGFR inhibition		
Rash	38 (37)	3 (3)
Acneiform dermatitis	35 (34)	6 (6)
Paronychia	35 (34)	2 (2)
Stomatitis	29 (28)	2 (2)
Related to MET inhibition		
Hypoalbuminemia	51 (50)	5 (5)
Peripheral edema	24 (24)	1 (1)
Other		
Fatigue	29 (28)	4 (4)
Hypocalcemia	25 (25)	1 (1)
Anemia	22 (22)	5 (5)

Note: One participant had treatment-related pneumonitis resulting in death. Five additional deaths due to AEs occurred, which were deemed unrelated to amivantamab.

^aRange, 0.0–18.9 months.

Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593-3605. Reproduced from: Burtneess B. Presented at: 2026 ASCO Annual Meeting; May 29–June 2, 2026; Chicago, IL. Used with permission of Barbara Burtneess.

Next Steps: OrigAMI-5 Is Testing Amivantamab + Pembrolizumab and Carboplatin in R/M HNSCC



FDA Approval for Amivantamab monotherapy in platinum/IO refractory R/M HPV- HNSCC pending

ClinicalTrials.gov. Accessed September 2026. <https://clinicaltrials.gov/study/NCT07276399>.

Clinical Takeaway

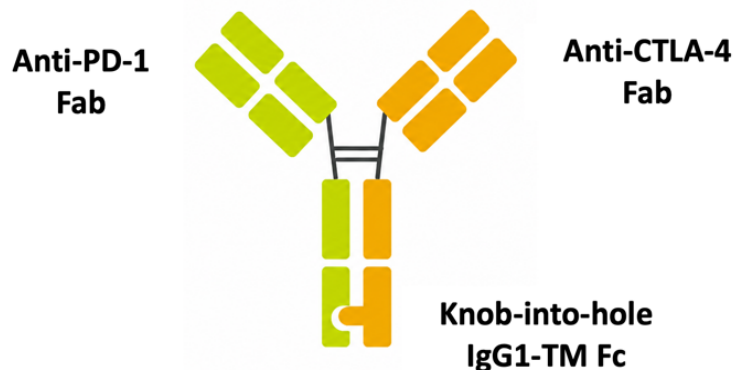
- EGFR-directed therapy is evolving beyond simple receptor inhibition
- **Amivantamab**, petosemtamab, ficerafusp alfa, and MCLA-129 represent distinct strategies to overcome resistance and/or enhance antitumor immunity
- Early efficacy signals are encouraging—but randomized trials will determine whether these approaches translate into durable improvements in PFS, OS, and patient outcomes

Volrustomig Is a Bispecific Antibody Engineered to Specifically Inhibit PD-1 and CTLA-4

Volrustomig: A monovalent, bispecific, IgG1 monoclonal antibody with increased CTLA-4 blockade on PD-1-positive activated T cells

- Preferential location and accumulation on PD-1-positive activated T cells in the TME
- Co-engagement of PD-1 and CTLA-4
- Greater levels of peripheral T-cell activation

Specifically designed to enhance CTLA-4 blockade on PD-1+ activated T-cells to widen therapeutic index



Interim Analysis from the Phase 2 eVOLVE-02 Study Shows Promising Activity of Volrustomig in R/M HNSCC

**Key Patient Characteristics
(Substudy 2 of eVOLVE-02)¹**

Patients treated	23
1L/2L treatment	12/11
PD-L1 CPS ≥ 1	82.6%

Endpoint	Result
Confirmed ORR (CPS ≥ 1), %	26.3
DCR, %	52.6
Median time to response, mo	2.6
Ongoing responses at data cutoff, %	60
Grade 3/4 TRAEs, %	8.7
Discontinuation due to AEs, %	0

Key Take-Homes

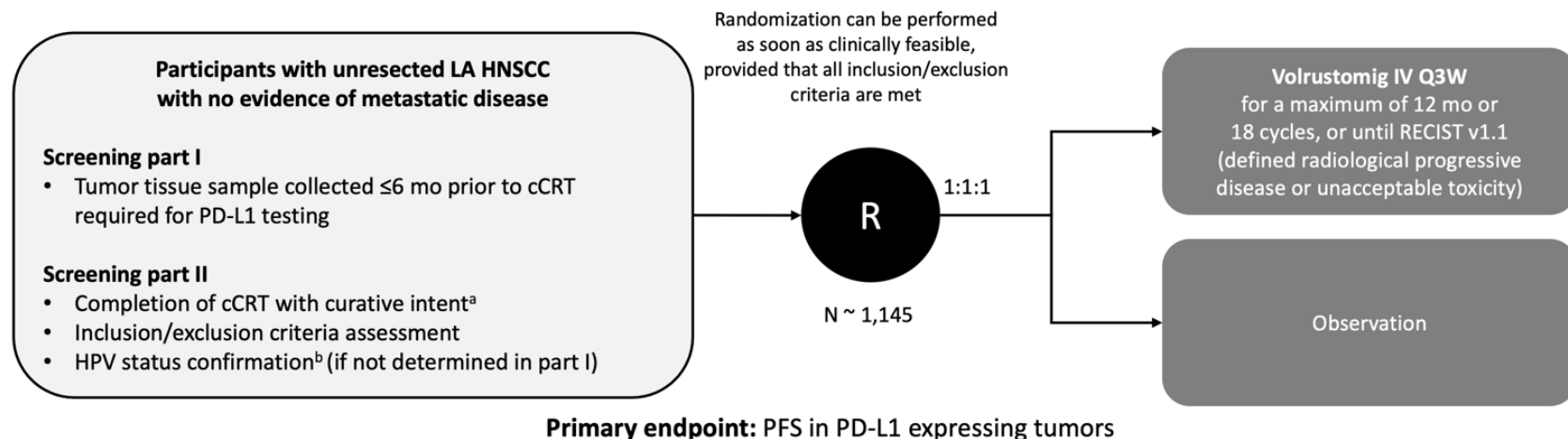
- Responses were observed across multiple primary tumor sites
- Dual PD-1/CTLA-4 targeting may enhance immune activation while limiting off-target CTLA-4 blockade
- Grade 3/4 TRAEs were relatively uncommon
- No treatment discontinuations due to AEs were reported

Guo Y, et al. Presented at: 2026 ASCO Annual Meeting; May 29–June 2, 2026; Chicago, IL. Abstract 6025.

eVOLVE-HNSCC Will Evaluate Consolidation Volrustomig for Unresected LA HNSCC That Has Not Progressed After cCRT

Rationale

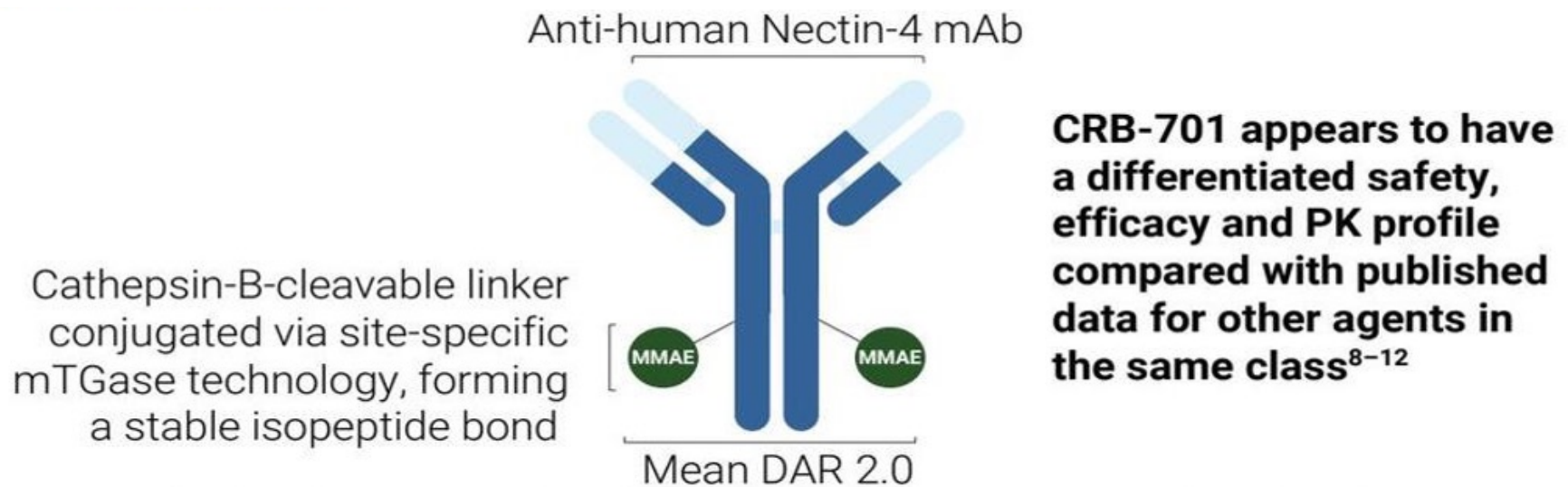
1. Lack of consolidation therapies for unresected LA HNSCC, despite high rates of recurrence
2. cCRT has been shown to have antitumor immunomodulatory effects that may increase the effectiveness of sequential immunotherapy treatment²⁻⁴
3. Phase 3 evidence across disease settings have demonstrated the clinical benefit of using immunotherapy after cCRT⁴⁻⁷



^aCisplatin or carboplatin + paclitaxel or carboplatin + 5-FU, plus concomitant RT. ^bPatients with oropharynx cancer only. FDG-PET assessment required 12 wk after completion of cCRT to evaluate potential indication for neck dissection/salvage surgery. Haddad RI, et al. *Int J Radiat Oncol Biol Phys*. 2026;125:E47-E48. Deng L, et al. *J Clin Invest*. 2014;124:687-695. Wei J, et al. *Sci Immunol*. 2021;6:eabg0117. Antonia SJ, et al. *N Engl J Med*. 2017;377:1919-1929. Kelly RJ, et al. *N Engl J Med*. 2021;384:1191-1203. Zhou Q, et al. *Lancet Oncol*. 2022;23:209-219. Cheng Y, et al. *N Engl J Med*. 2024;391:1313-1327.

HPV-Directed Therapies

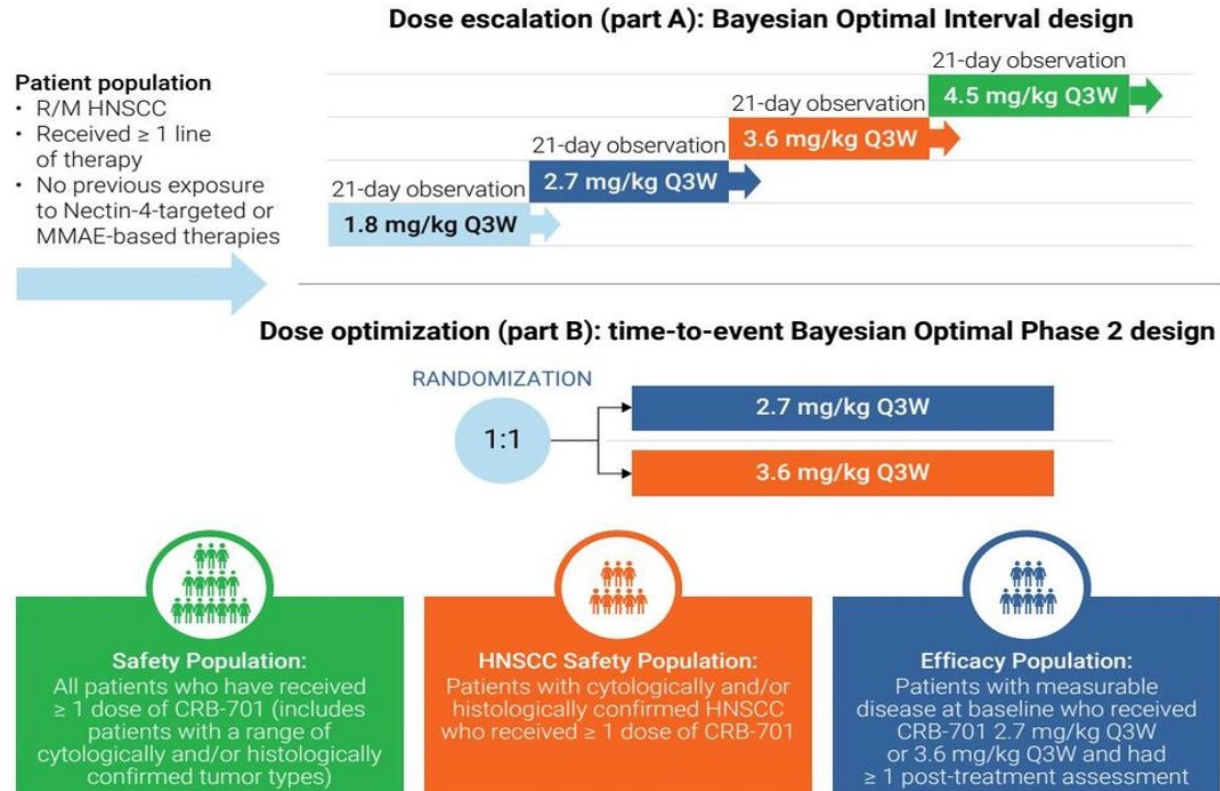
CRB-701 (anti-Nectin-4 ADC)



DAR, drug:antibody ratio; mAb, monoclonal antibody; MMAE, monomethyl auristatin E; mTGase, microbial transglutaminase; PK, pharmacokinetics.

Hanna GJ. Presented at: ASCO 2026; May 29 – June 2, 2026; Chicago, IL.

CRB-701 (anti-Nectin-4 ADC)



In part A, dose escalation/de-escalation decisions were made based on the occurrence of dose-limiting toxicities. In part B, dose levels were defined by the pharmacologically active dose range identified in part A.
HNSCC, head and neck squamous cell carcinoma; MMAE, monomethyl auristatin E; Q3W, every 3 weeks; R/M, recurrent or metastatic.

Hanna GJ. Presented at: ASCO 2026; May 29 – June 2, 2026; Chicago, IL.

Figure 4. Percentage change from baseline in sum of diameters with confirmed best overall response (A) and patient-level best overall response by dose (B) for CRB-701 Q3W

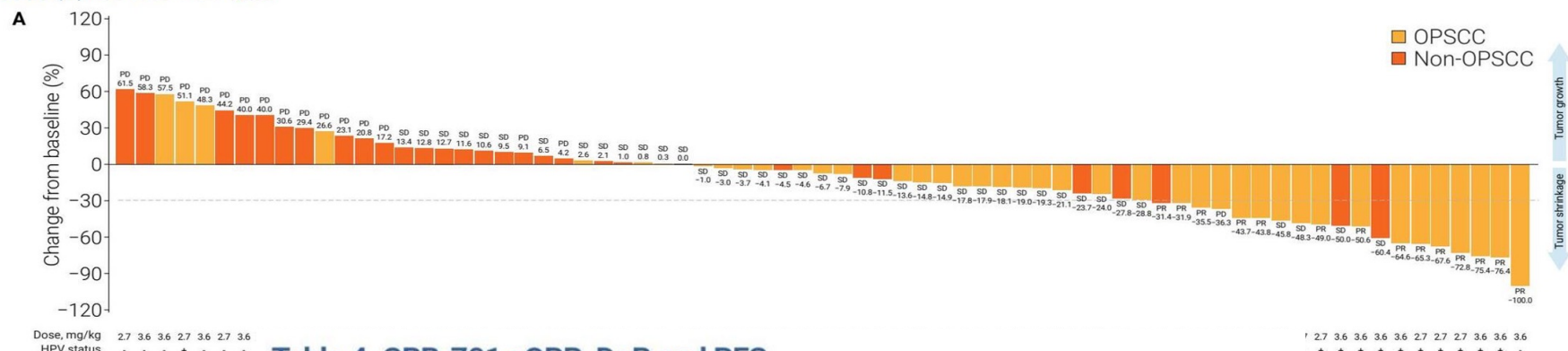
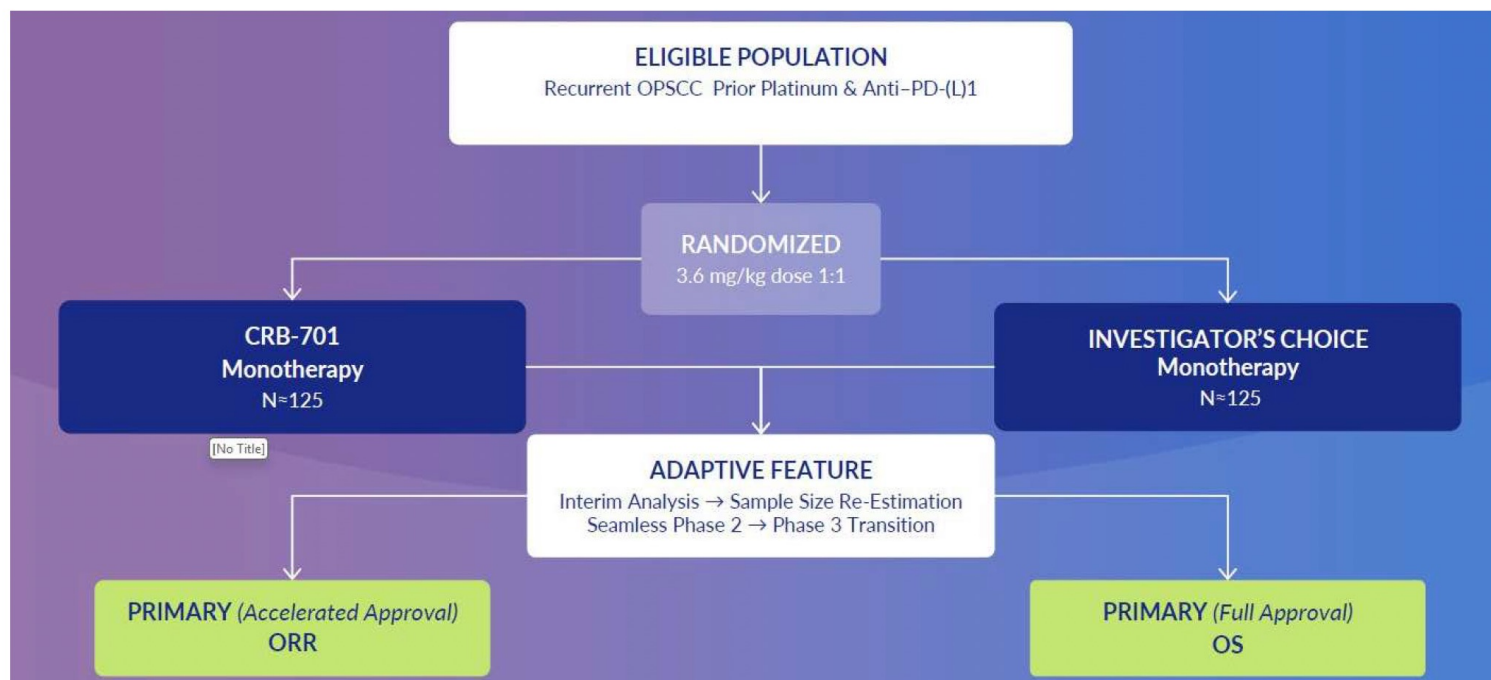


Table 4. CRB-701 cORR, DoR and PFS

Endpoint	CRB-701 2.7 mg/kg Q3W			CRB-701 3.6 mg/kg Q3W		
	OPSCC (n = 20)	Non- OPSCC (n = 14)	HNSCC (N = 34)	OPSCC (n = 21)	Non- OPSCC (n = 16)	HNSCC (N = 37)
cORR, n (%)	4 (20.0)	1 (7.1)	5 (14.7)	9 (42.9)	0	9 (24.3)
90% CI, %	7.1–40.1	0.4–29.7	6.0–28.5	24.5–62.8	0.0–17.1	13.3–38.6
DoR, ^a months, median	4.8	4.4	4.4	6.3	N/A	6.3
95% CI, %	2.7–NE	NE–NE	2.7–NE	4.4–NE	N/A	4.4–NE
PFS, months, median	4.2	2.3	3.5	5.6	2.7	4.2
95% CI, %	2.6–7.9	1.3–3.5	2.3–5.6	4.1–7.7	1.3–4.2	2.8–5.6

Hanna GJ. Presented at: ASCO 2026; May 29 – June 2, 2026; Chicago, IL.

Phase 3 trial planned



Corbus Pharmaceuticals. U.S. Securities and Exchange Commission. Accessed September 2026.
https://www.sec.gov/Archives/edgar/data/1595097/000119312526238059/crbp-ex99_2.htm.

HPV-Directed Immunotherapy in R/M HNSCC: Emerging Therapeutic Strategies

From HPV16 E6/E7 antigen targeting → antigen-specific T-cell activation → combination with checkpoint blockade

Agent	Platform / Target	Clinical Setting	Emerging Evidence	Development
BNT113	HPV16 E6/E7 mRNA vaccine	1L HPV16+ PD-L1+ R/M HNSCC + pembrolizumab	Safety run-in (n=15): ORR 40%; mPFS 3.9 mo; mOS 22.6 mo	Phase II/III AHEAD-MERIT
PDS0101	HPV16 E6/E7 peptide vaccine	1L HPV16+ R/M HNSCC + pembrolizumab	VERSATILE-002 (n=53): ORR 35.8%; mPFS 6.3 mo; mOS 30.0 mo	Phase III VERSATILE-003
ISA101b / peltopepimut-S	HPV16 E6/E7 synthetic long-peptide vaccine	HPV16+ R/M HNSCC + cemiplimab	Randomized phase II: ORR 25.3% vs 22.9% with cemiplimab; primary endpoint not met	Investigational; biomarker signal in CPS ≥20
MEDI0457	HPV16/18 E6/E7 DNA vaccine + IL-12	Previously treated HPV-associated R/M HNSCC + durvalumab	Phase Ib/IIa (n=29 evaluable): ORR 27.6%; mPFS 3.5 mo; mOS 29.2 mo; primary endpoint not reached	Early-stage / investigational

Key message: HPV-directed immunotherapy can generate antigen-specific T-cell responses, but randomized trials are essential to establish clinical benefit beyond PD-1 blockade alone.

Saba NF, et al. Exploratory analysis of antitumor activity of BNT113 in HNSCC. Presented at: ESMO 2024; September 13-17, 2024; Barcelona, Spain. Poster 877P. Weiss J, et al. *J Clin Oncol*. 2025;43(suppl 16):6037. ClinicalTrials.gov. Accessed September 2026. <https://clinicaltrials.gov/study/NCT03669718>. Aggarwal C, et al. *Clin Cancer Res*. 2023;29(3):560-570. All agents are investigational; efficacy estimates are from non-comparable early-phase studies.

BNT113 in Combination with Pembrolizumab as 1L Treatment in Patients with R/R HPV16+ HNSCC Expressing PD-L1 (AHEAD-MERIT)

Phase 2 open-label, controlled study to confirm safety and efficacy of BNT113 in combination with pembrolizumab as 1L treatment in patients with metastatic HNSCC ([NCT04534205](#))

Inclusion criteria

- Advanced, unresectable, recurrent or metastatic HNSCC
- Primary tumor locations oropharynx, oral cavity, hypopharynx, and larynx[#]
- Positive for HPV16 DNA
- Measurable disease per RECIST v1.1
- PD-L1 CPS ≥1
- ECOG PS 0 or 1

[#] Patients with primary tumor site of nasopharynx were excluded

Safety run-in

N=15

BNT113 (8xQ1W*, then Q3W) + pembrolizumab (Q3W)
up to 24 months

Randomized part

N=267

R 1:1

BNT113 (8xQ1W*, then Q3W) + pembrolizumab (Q3W)
up to 24 months

Pembrolizumab (Q3W)
up to 24 months

* The first BNT113 dose will be administered 7 days before the first treatment cycle (pre-cycle 1).



Endpoints

Primary:

Secondary:

Exploratory:

Safety run-in

TEAEs; up to 27 months

ORR, DoR, DCR

PFS, OS, biomarkers

Randomized part

OS, ORR; up to 48 months

INV-ORR, PFS, DCR, DOR, safety

1L = first line; CPS = combined positive score; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; INV = investigator assessed; iv = intravenously; HNSCC = head and neck squamous cell carcinoma; HPV16 = human papilloma virus 16; ORR = objective response rate; OS = overall survival; PD-L1 = programmed cell death protein ligand 1; PFS = progression free survival; Q3W = every three weeks; RECIST = Response Evaluation Criteria in Solid Tumors; R/M = recurrent/metastatic; R/R = relapsed/refractory; TEAE = treatment emergent adverse event.

Saba NF, et al. Exploratory analysis of antitumor activity of BNT113 in HNSCC. Presented at: ESMO 2024; September 13-17, 2024; Barcelona, Spain. Poster 877P.

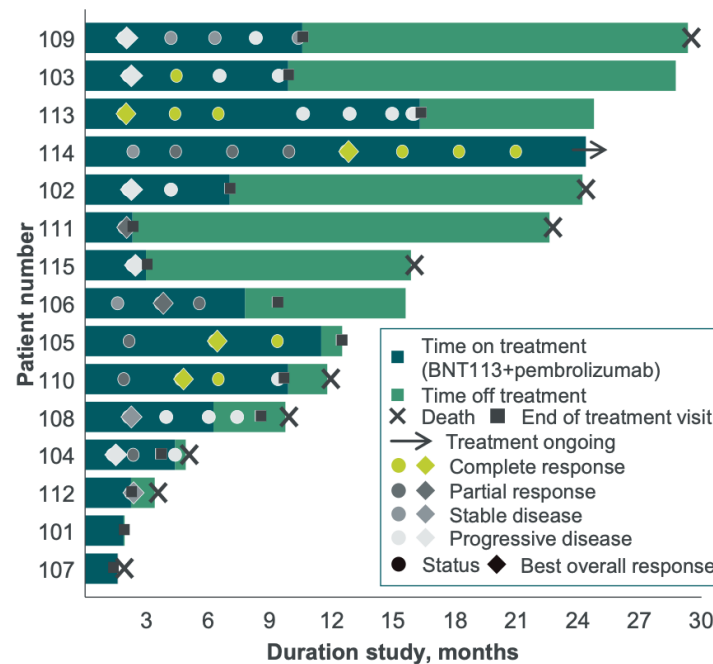
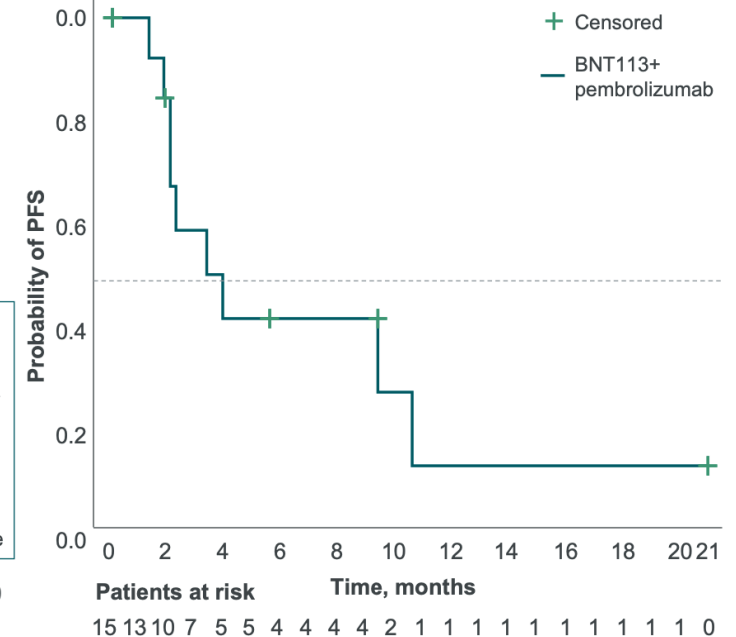
BNT113 Showed Encouraging Efficacy with Unconfirmed ORR (BICR) of 40%

The efficacy analysis set was defined as all patients who received at least one dose of BNT113 (N=15)

Patient 104, who was enrolled based on local positive CPS result, was included in this analysis.

Antitumor activity	N=15
Unconfirmed ORR (BICR), %	40.0
CR, n	4
PR, n	2
Unconfirmed DCR (BICR), %	53.3
Unconfirmed ORR (investigator), %	33.3
Unconfirmed DCR (investigator), %	60.0
PFS by BICR	
Median (95% CI), months	3.9 (2.1–10.6)
6-month rate, %	42.3
12-month rate, %	14.1
18-month rate, %	14.1
PFS by investigator	
Median (95% CI), months	6.0 (2.3–10.4)
OS, median (95% CI), months	22.6 (9.8–NE)

Tumor overall response, treatment and survival status by BICR



Data cut-off: 24 June 2024

BICR = blinded independent central review; CI = confidence interval; CR = complete response; DCR = disease control rate; NE = not estimable; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response.

Saba NF, et al. Exploratory analysis of antitumor activity of BNT113 in HNSCC. Presented at: ESMO 2024; September 13-17, 2024; Barcelona, Spain. Poster 877P.

Key Learning Points

- The goal is not simply to treat progression—it is to select and sequence therapy to maximize disease control while preserving function and quality of life

Precision Oncology & Patient-Centered Care in HNSCC

Precision Oncology

Define tumor biology

HPV/p16 status and primary site

PD-L1 CPS to inform ICI selection

Molecular profiling when clinically appropriate

Identify actionable alterations / clinical-trial opportunities

Reassess biology at progression when appropriate

Multidisciplinary/molecular tumor board input for complex cases

Patient-Centered Care

Define the patient

Performance status, comorbidities, frailty

Symptoms, disease burden & pace of progression

Swallowing, speech, nutrition & functional status

Treatment goals, preferences & tolerance for toxicity

Financial, transportation & caregiver considerations

Shared decision-making throughout the treatment journey

Adi-Wauran E, et al. *Patient Educ Couns*. 2025;136:108753. Cavalieri S, et al. *NPJ Precis Oncol*. 2026;10(1):170. Okuyama K, et al. *Mol Cancer*. 2026;25(1):120. Rieke DT, et al. *Eur J Cancer*. 2025;220:115331. Westphalen CB, et al. *Ann Oncol*. 2025;36(6):614-625.

Proactive AE Monitoring & Management: EGFR/MET-Directed Therapy

Toxicity

Rash / Acneiform Dermatitis

Paronychia / Nail Changes

Stomatitis / Mucositis

IRR

Ocular Toxicity

Edema / Fatigue

Proactive Management

Skin care + emollients • Sun protection • Early treatment

Nail protection • Early recognition • Treat infection

Baseline oral assessment • Preventive oral care • Early intervention

Premedication • Close monitoring • Rapid intervention

Ask about visual symptoms • Early ophthalmology referral

Baseline assessment • Monitor severity & function • Supportive care

Prophylactic Dermatologic Management: The COCOON Framework

Phase 2 Randomized NCT 06120140 EGFR-m NSCLC

COCOON Prophylaxis

Oral doxycycline or minocycline 100 mg BID × 12 weeks

Ceramide-based moisturizer daily

Chlorhexidine 4% nail care daily

Topical clindamycin 1% from week 13

Patient education + digital monitoring

What the Evidence Shows

Reduces inflammatory/acneiform rash

Supports skin-barrier integrity

Targets nail-bed complications/paronychia

Continued management of EGFR-related folliculitis

Improves adherence and facilitates early intervention

COCOON Trial: Primary Dermatologic Endpoint

Outcome	COCOON Enhanced Management	Standard Management
Grade ≥ 2 dermatologic AEs through Week 12	42%	75%
Patients randomized	99	102
Odds ratio	0.24	—
95% CI	0.13–0.45	—
P value	<0.0001	—

Patient-Specific Factors & Barriers to Optimal Care

- Access
- Care coordination
- Communication & support
- Social & financial

Shared Decision-Making & Team-Based Care in R/M HNSCC

- **Align Evidence Treatment Options & What Matters Most to the Patient**
- **SHARE THE OPTIONS**
 - Standard therapy **vs** clinical trial
 - Expected **response, survival & durability**
 - Toxicities, monitoring & treatment burden
 - Alternative sequencing strategies
 - Supportive and palliative-care options
- **UNDERSTAND WHAT MATTERS**
 - **“What is most important to you?”**
 - ASK → LISTEN → EXPLAIN → DELIBERATE → DECIDE → REASSESS
 - Survival **vs** **quality of life**
 - Swallowing, speech, nutrition & appearance
 - Treatment intensity, travel & time commitment
 - Independence, caregiver needs & financial concerns

Gilligan T, et al. *J Clin Oncol*. 2026;44(11):1040-1057. Heirman AN, et al. *JAMA Otolaryngol Head Neck Surg*. 2024;150(5):393-404. Punnett G, et al. *Patient Educ Couns*. 2024;123:108235. Hoesseini A, et al. *BMC Palliat Care*. 2024;23(1):54.

Proactive AE Management

Key Learning Points

- Anticipate toxicity before cycle
- Monitor early and consistently
- Intervene early
- Use a multidisciplinary approach
- Preserve treatment and quality of life
- Reassess continuously

Attili I, et al. *Crit Rev Oncol Hematol*. 2025;215:104926. Ceylan F, et al. *J Oncol Pharm Pract*. 2026;32(1):93-109. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517-1530. RYBREVANT® (amivantamab-vmjw) Prescribing Information. Drugs@FDA: FDA-Approved Drugs. Accessed September 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761210s011lbl.pdf.

Recognize & Address Barriers to Care

Key Learning Points

- Transportation & geographic access
- Financial toxicity & insurance limitations
- Nutrition / food insecurity
- Health literacy & communication barriers
- Caregiver burden & psychosocial needs
- Fragmented care & limited supportive services
- Clinical-trial access

Batool V. Designing Digital Health Tools to Address Stigma and Structural Barriers across the Mental Health Care Ecosystem. Presented at: Extended Abstracts of the 2026 CHI Conference on Human Factors in Computing Systems; April 13 – 17, 2026; Barcelona, Spain. Sanders JJ, et al. *J Pain Symptom Manage*. 2024;68(3):214-222.e6. Marrero-Gonzalez AR, Graboyes EM. *Surg Oncol Clin N Am*. 2024;33(4):669-681. Tucker-Seeley R, et al. *JCO Oncol Pract*. 2024;20(5):621-630.

Conclusion

- The future of R/M HNSCC care is not simply more therapies—it is smarter sequencing, proactive toxicity management, and patient-centered decision-making

Polling

- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response



Discussion and Live Q&A



Credit Claim Information

- Scan this QR code to claim credit after the session
- Participants who complete the evaluation online within 30 days of the event will receive documentation of credit

