2025 ASCO® ANNUAL MEETING

Ficerafusp alfa with pembrolizumab in patients with recurrent or metastatic head and neck squamous cell carcinoma: Updated results from an expansion cohort of an open-label, multicenter, phase 1/1b trial

Christine H. Chung, Glenn J. Hanna, Dan P. Zandberg, Deborah J. Wong, Eric Sherman, Assuntina G. Sacco, Tamara A. Sussman, Alberto Hernando-Calvo, Ralf Reiners, David Bohr, Rachel L. Salazar, Brenda C. O'Connell, David Raben, Jeltje Schulten, John Kaczmar

Presenter: Christine H. Chung, MD

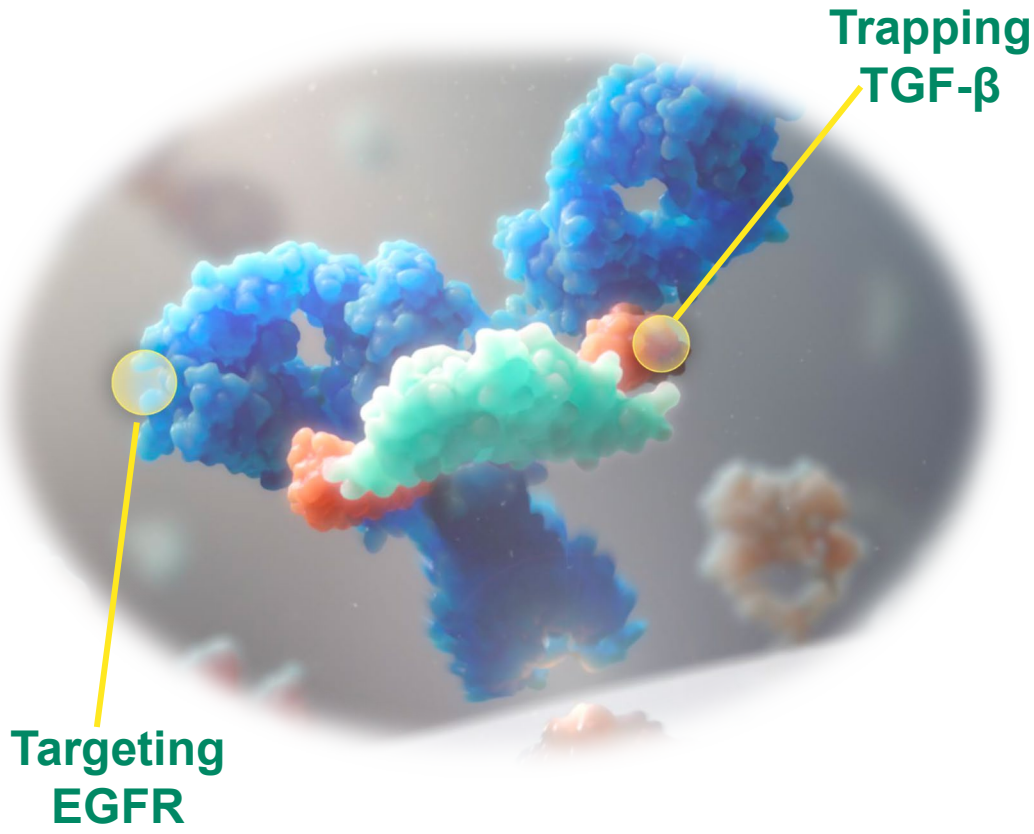
Key Takeaways

- **Ficerafusp alfa + pembrolizumab is a promising 1L regimen in HPV-negative R/M HNSCC that demonstrates:**
  - **High ORR**
  - **Deep and durable responses**
  - **Prolonged overall survival**

1L, first-line; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **ORR**, overall response rate; **R/M**, recurrent/metastatic

Background: Ficerafusp Alfa[1-9]

- **Convergent EGFR and TGF-β signaling drives tumor progression and resistance**
- **HPV-negative R/M HNSCC has a poor prognosis linked to EGFR and TGF-β expression;** in 1L HNSCC, CPS≥1
  - **10.6 months mOS** with nivolumab + cetuximab (HPV-neg)
  - **12.3 months mOS** with pembrolizumab (KN-048)
- **Ficerafusp** is designed to enable **tumor penetration** of immune cells by remodeling the fibrotic TME to drive **deep and durable responses**



1. Manuscript under review 2. He Y, et al. *J Natl Cancer Inst*. 1998;90(14):1080-1087; 3. Chung CH, et al. *J Clin Oncol*. 2006;24(25):4170-4176; 4. Schmitz S, et al. *Oncotarget*. 2015;6(33):34288-34299; 5. Boreddy SR, et al. *Cancer Res*. 2023;83(11):1883-1904; 6. Baumeister P, et al. *Cancers (Basel)*. 2021;13(21):5355; 7. Chakravarthy A, et al. *Nat Commun*. 2018;9(1):4692; 8. Kapoor SS, Zaiss DMW. *Biomedicines*. 2021;10(1):52. 9. Burtness B. et al. Lancet 2019; 394: 1915–28 **1L**, first-line; CPS, combined positive score; EGFR, epidermal growth factor receptor; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; mOS, median overall survival; TGF, transforming growth factor; **TME**, tumor microenvironment

Patient Demographics and Baseline Characteristics

Ficerafusp alfa 1500mg IV D1, D8, D15

+

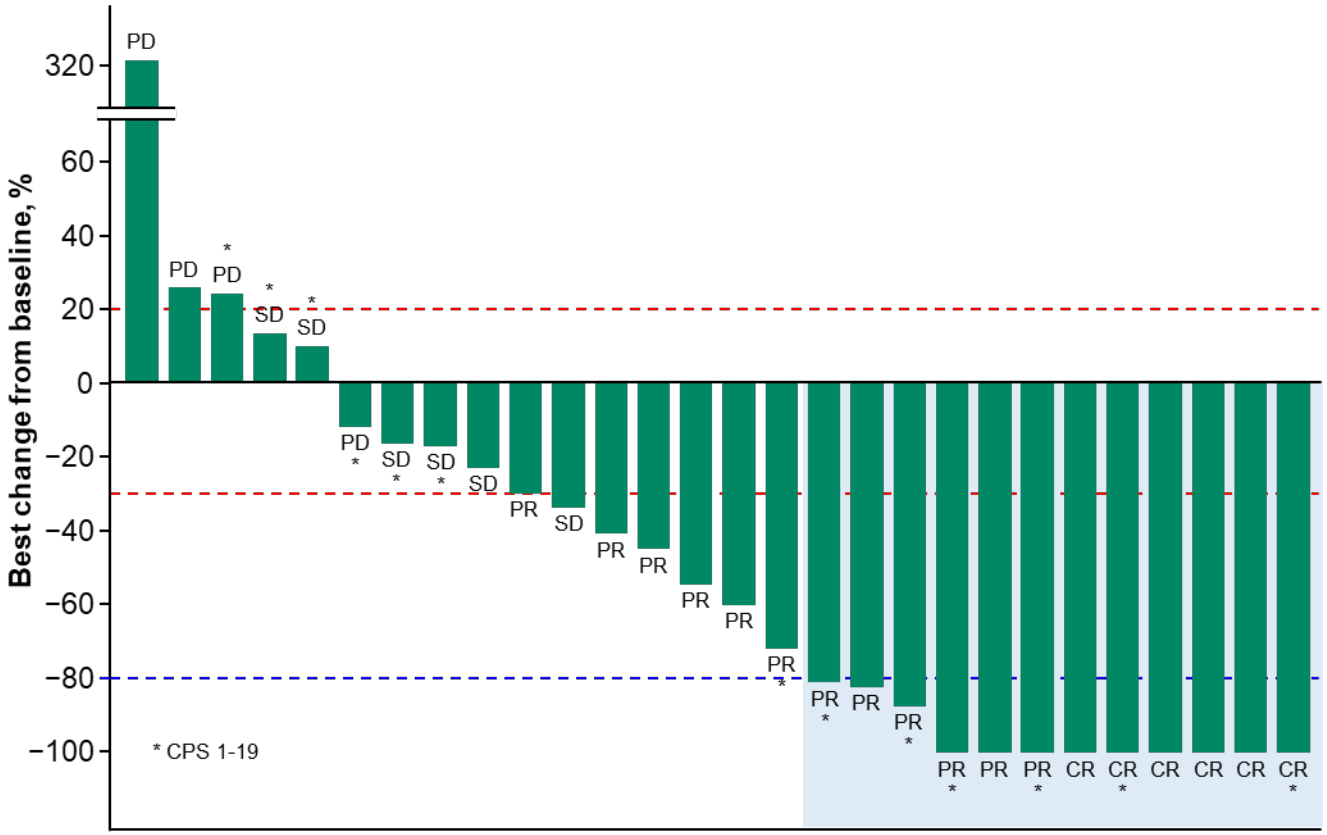
Pembrolizumab 200mg IV D1, every 21 days

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

Characteristic		Safety Set (N=30)
Age	Median (range)	63 (31-84)
Sex – n (%)	Male/Female	19/11 (63% vs. 37%)
HNSCC Primary site of disease	Oropharynx (HPV-neg)	8 (27%)
	Oral Cavity	14 (47%)
	Hypopharynx	4 (13%)
	Larynx	4 (13%)
CPS - n (%)	1-19	15 (50%)
	≥20	15 (50%)
Locoregional vs. distant metastatic disease	LR only	9 (30%)
	LR + DM	14 (47%)
	DM only	7 (23%)
Sum (mm) of Target Lesion Diameters	> 50	14 (47%)
	> 70	8 (27%)
ECOG Performance Status	0 vs.1	11 vs. 19 (37% vs. 63%)

CPS, combined positive score; **ECOG,** Eastern Cooperative Oncology Group; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **IV,** intravenous. Data snapshot: March 20, 2025.

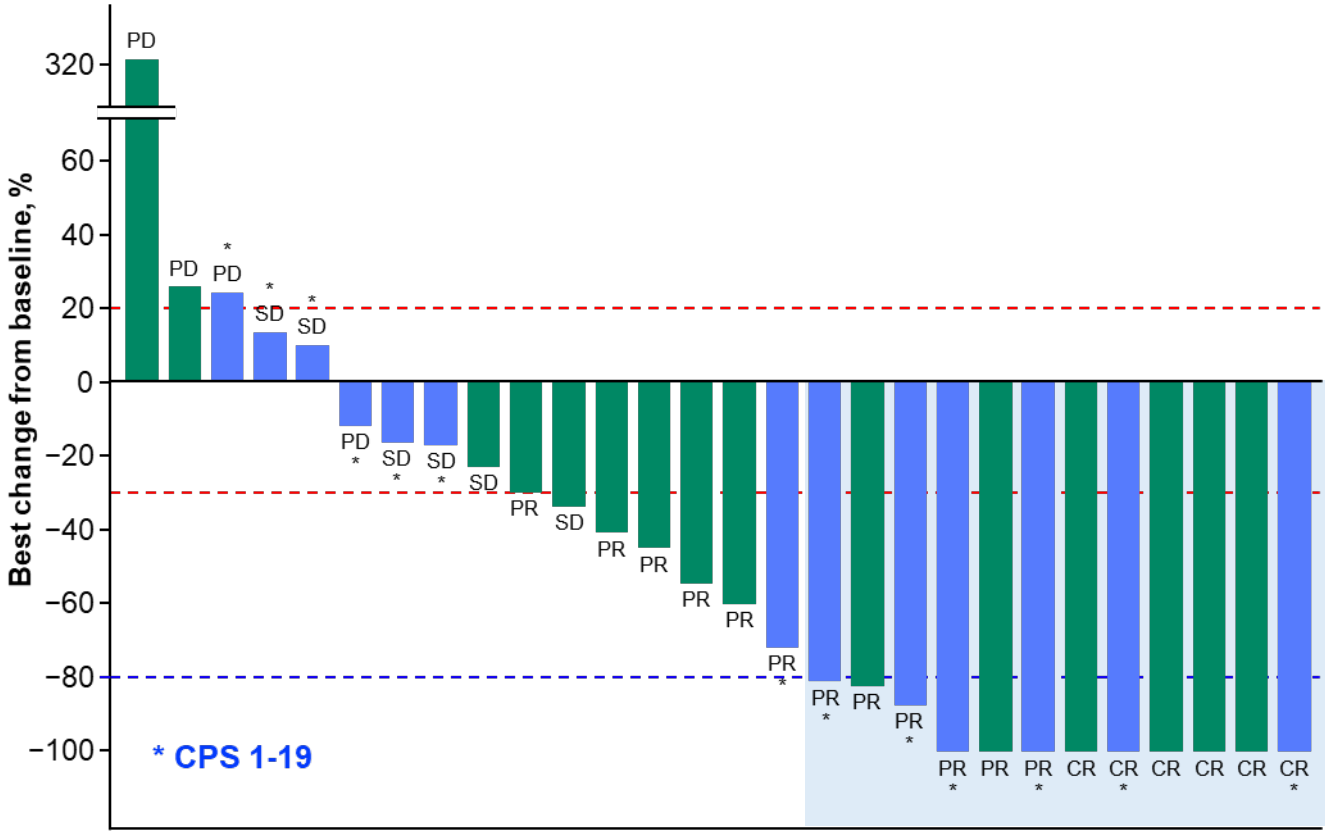
Objective Response Rate with Ficerafusp Alfa + Pembrolizumab in HPV-neg, CPS≥1 1L R/M HNSCC



- **Confirmed ORR: 54% (15/28)**
  - ORR (confirmed or unconfirmed): 64% (18/28)
- **Deep Responses: 80% (12/15) of responders achieved ≥80% tumor shrinkage**
  - CR rate: 21% (6/28)
  - Disease Control Rate: 89% (25/28)
- **Median Time to Response: 1.4 months**
- **Median PFS: 9.9 months**

Ficerafusp alfa 1500 mg QW + pembrolizumab 200 mg Q3W in patients with HPV−, CPS≥1 HNSCC; efficacy-evaluable population (n=28). Data snapshot: March 20, 2025. Investigator-assessed best overall response per RECIST 1.1.
CPS, combined positive score; **CR**, complete response; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **ORR**, objective response rate; **PFS**, progression-free survival; **PR**, partial response; **Q3W**, every 3 weeks; **QW**, weekly; **SD**, stable disease

Objective Response Rate with Ficerafusp Alfa + Pembrolizumab in HPV-neg, CPS≥1 1L R/M HNSCC



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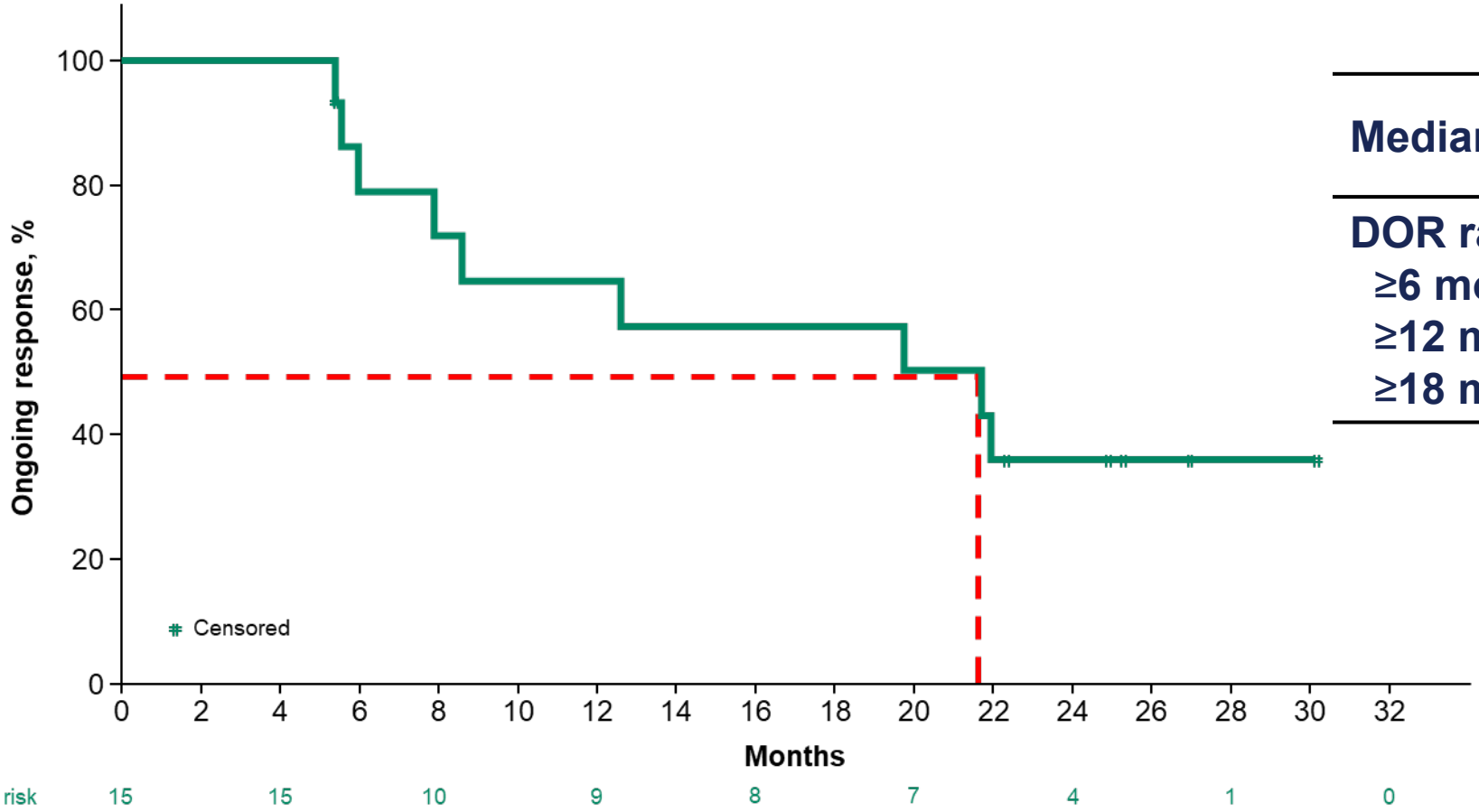
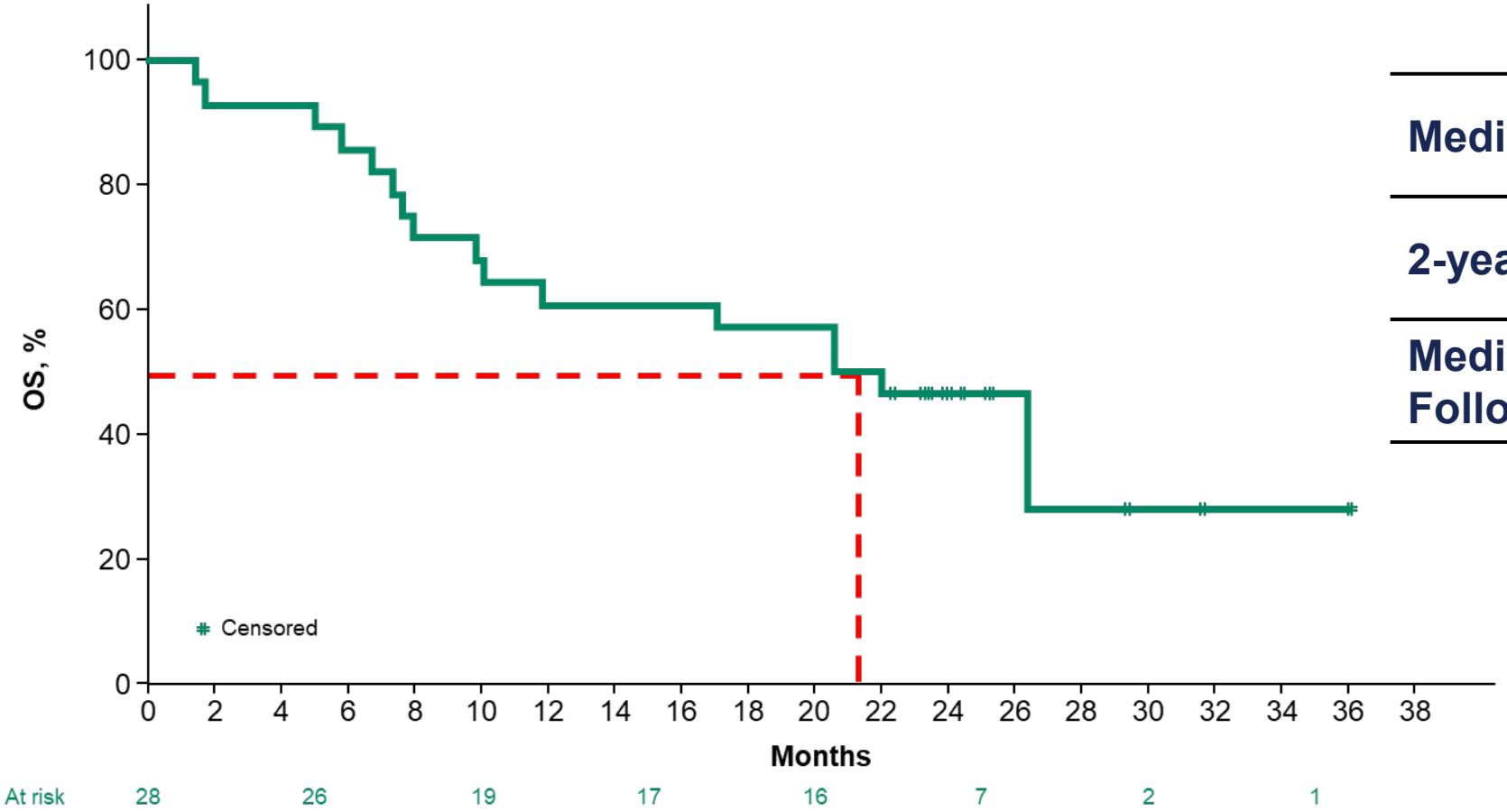
Duration of Response With Ficerafusp Alfa + Pembrolizumab in HPV-neg, CPS≥1, 1L R/M HNSCC



	n=15
Median DOR	**21.7 months***
DOR rate	
≥6 months	**79%**
≥12 months	**65%**
≥18 months	**57%**

Ficerafusp alfa 1500 mg QW + pembrolizumab 200 mg Q3W in patients with HPV−Neg, CPS≥1 HNSCC. DOR in patients with confirmed response (n=15).
* mDOR based on current information as of Apr2025, post data snapshot. At data snapshot (March 20, 2025) final mDoR not reached.
CPS, combined positive score; **DOR**, duration of response; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **NE**, not estimable; **Q3W**, every 3 weeks; **QW**, weekly

Overall Survival With Ficerafusp Alfa + Pembrolizumab in HPV-neg, CPS≥1, 1L R/M HNSCC



	n=28
Median OS	21.3 months
2-year OS rate	46%*
Median Follow-up	25.2 months

Ficerafusp alfa 1500 mg QW + pembrolizumab 200 mg Q3W in patients with HPV−Neg, CPS≥1 HNSCC; efficacy-evaluable population (n=28). Data snapshot: March 20, 2025.
In the safety population (n=30), median OS was 20.6 months and the 2-year rate OS was 43%.
* For patients with ~22-23 months of follow-up at data snapshot, subsequent follow-up confirmed that these patients remained alive at 24 months.
CPS, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **NE**, not estimable; **OS**, overall survival; **Q3W**, every 3 weeks; **QW**, weekly

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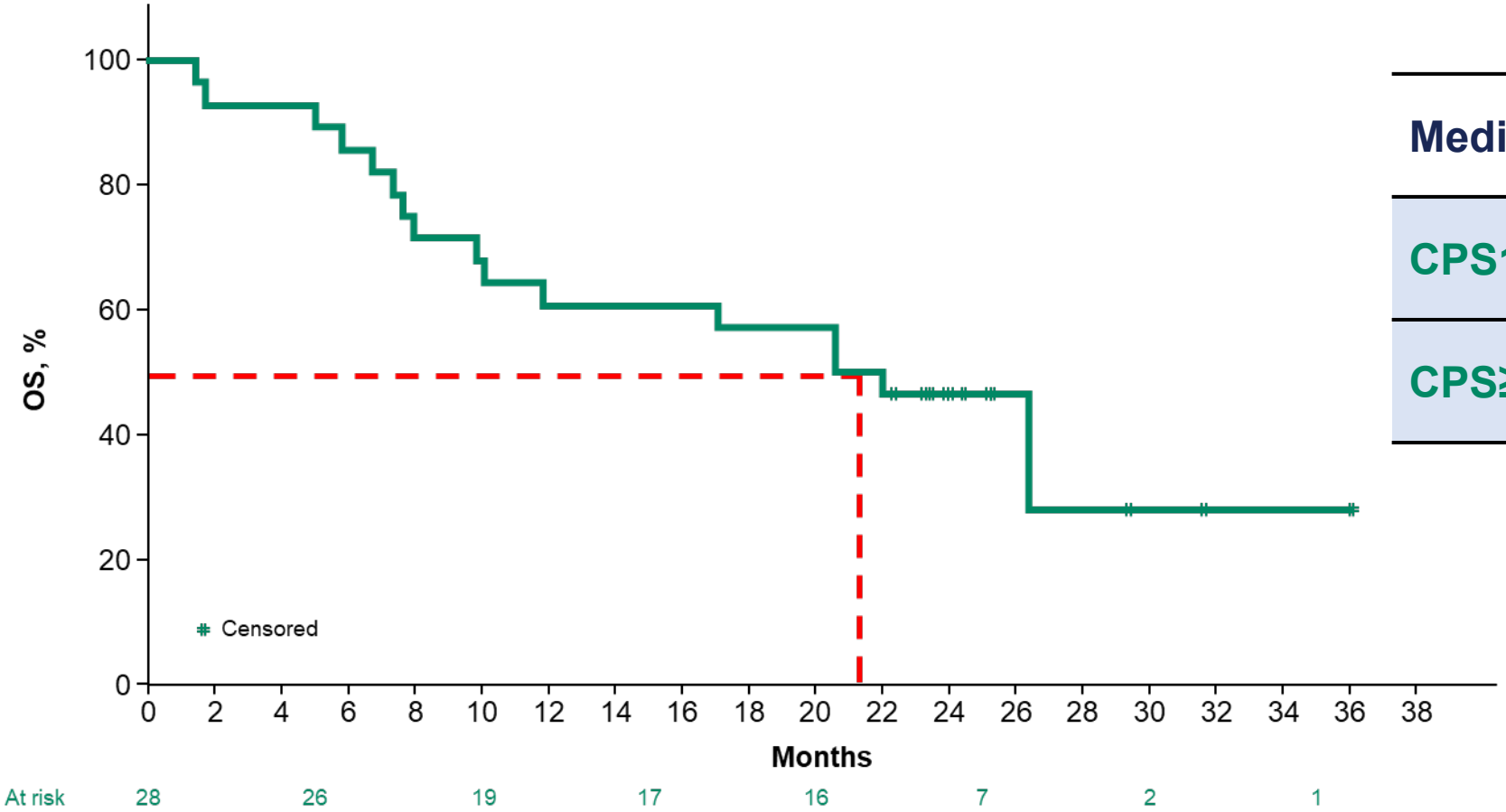

	n=28
Median OS	21.3 months
CPS1-19	22.0 months
CPS≥20	20.6 months

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Safety With Ficerafusp Alfa + Pembrolizumab in HPV-neg, CPS≥1 1L R/M HNSCC

- **Favorable safety profile observed with no new safety signals[1]**

Most frequently reported (≥20%) TEAEs related[2] to ficerafusp alfa:

	Safety set (n=30)			
Preferred term	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

Ficerafusp alfa 1500 mg QW + pembrolizumab 200 mg Q3W in patients with HPV−Neg, CPS≥1 HNSCC. At data snapshot (March 20, 2025); **CPS**, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **AE**, adverse events; **Q3W**, every 3 weeks; **QW**, weekly; 1. Hanna GJ, et al. Int J Radiat Oncol Biol Phys. 2024;118:e88. Safety findings were consistent with the known safety profile of ficerafusp alfa plus pembrolizumab. 2. Related TEAEs are those with relationship of “Possibly Related”, “Probably Related”, and “Definitely Related”. They also include TEAEs with missing drug relationships, which is treated as “Possibly Related”.

Limitations

- These results are from a multi-center, single arm dose expansion cohort with 2-year follow-up of all patients.

Key Takeaways

Ficerafusp alfa + pembrolizumab is a promising 1L R/M regimen for HPV-negative HNSCC that demonstrates:

- High ORR: **54%**
- Deep responses: **80% of responders had ≥80% tumor shrinkage**
- Durable responses: **mDOR: 21.7 months**
- Prolonged overall survival: **mOS: 21.3 months**

mDOR based on current information as of Apr2025, post data snapshot. At data snapshot (March 20, 2025) final mDoR not reached. FORTIFI-HN01: NCT06788990

1L, first-line; **CR**, complete response; **DOR**, duration of response; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **ORR**, overall response rate; **OS**, overall survival; **R/M**, recurrent/metastatic

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Trial-in-Progress Poster #519a: June 2 – 9am-12pm

FORTIFI-HN01, ***is an ongoing Phase 2/3 clinical trial evaluating this combination in 1L HPV-negative R/M HNSCC***

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Acknowledgement

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This study is conducted by Bicara Therapeutics Inc. with access to pembrolizumab in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

Ficerafusp Alfa + Pembrolizumab in HPV-Negative Head and Neck Cancer

- People with HPV-negative head and neck cancer have worse outcomes due to limited tumor penetration of immune cells from a dense tumor environment, leading to treatment resistance and disease recurrence.
- Ficerafusp alfa is specifically designed to drive tumor penetration by remodeling the tumor microenvironment in difficult to treat cancers.
- These results demonstrate combination treatment with ficerafusp alfa and pembrolizumab can lead to deep and durable tumor responses and prolonged survival, for patients with HPV negative head and neck cancer.
- A larger, Phase 2/3 international study (FORTIFI-HN01) is now enrolling patients to confirm these benefits.

HPV, human papillomavirus.