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Ficerafusp alfa 750 mg QW and pembrolizumab in HPV-negative first line recurrent/metastatic head and neck squamous cell carcinoma

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Declaration of Interests

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Consulting or Advisory Role - Coherus Biosciences; Merck; RAPT Therapeutics; Bicara Therapeutics; Merus

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Travel expenses, conference registration fee: Bicara Therapeutics, Regeneron

Key Takeaways

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

- **Manageable safety profile**
- **High ORR**
- **Rapid time to response**
- **Deep responses**

Ficerafusp alfa 750 mg + pembrolizumab demonstrated clinical efficacy and manageable safety in these preliminary data

- This is one of two doses being evaluated for optimal biologic dose in the ongoing phase 2/3 FORTIFI-HN01 study
- Data from the ficerafusp alfa 1500 mg + pembrolizumab phase 1b cohort were presented at ASCO 2025[1]

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1. Chung CH, et al. J Clin Oncol. 2025;43(16 suppl):6017.

1L, first line; **ASCO**, American Society of Clinical Oncology; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus, **ORR**, objective response rate; **R/M**, recurrent or metastatic Data snapshot: July 9, 2025. .

Background and Unmet Need in HNSCC

HPV-negative R/M HNSCC has a poor prognosis

Previously reported outcomes with 1L treatment for CPS ≥1 HNSCC[1-4]:

- ORR: 19% and mOS: **12.3 months** with pembrolizumab (allcomers)
- ORR: 36% and mOS: **13.6 months** with pembrolizumab + chemotherapy (allcomers)
- mOS: **10.6 months** with nivolumab + cetuximab (**HPV-negative**)
- mOS: **9 months** with pembrolizumab (**HPV-negative**; real-world data)

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1. Burtness B. et al. Lancet. 2019;394:1915–28. 2. Chaudhary R, et al. Clin Cancer Res. 2025; doi:10.1158/1078-0432.CCR-25-2201. Ahead of print.. 4. Vasiliadou I, et al. Int J Cancer. 2024;155(5):883-93. 4. Black CM, et al. Front Oncol. 2023;13:1160144.

1L, first line; **CPS**, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **mOS**, median overall survival; **ORR**, objective response rate.

Ficerafusp Alfa

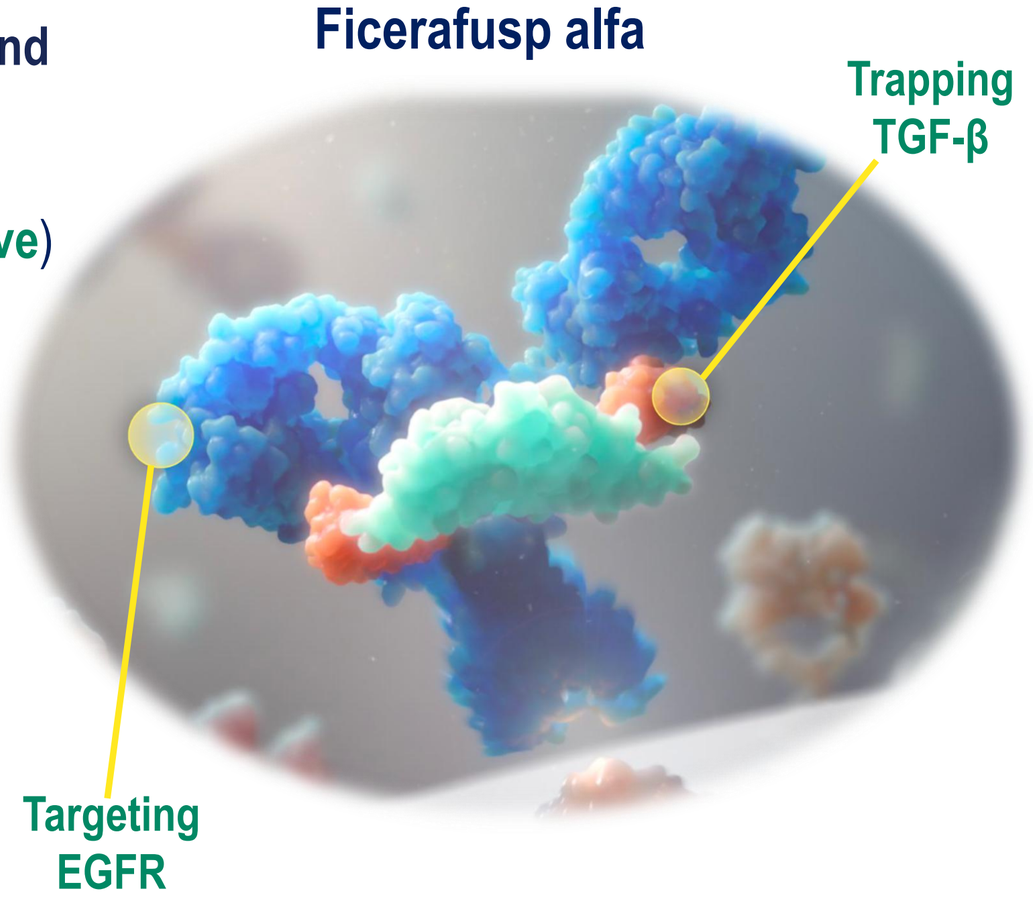
A Bifunctional EGFR-directed Antibody × TGF-β Ligand Trap[1-8]

Convergent EGFR and TGF-β signaling drives tumor progression and resistance

Results with ficerafusp alfa 1500 mg + pembrolizumab (HPV-negative)

- ORR: 54%; CR: 21%
- DCR: 89%
- Median time to response: 1.4 months
- mDOR: 21.7 months
- mOS: 21.3 months
- Manageable safety profile

Ficerafusp alfa effectively neutralized TGF-β in the TME with reduced pSMAD2 and TGF-β signaling in paired biopsies



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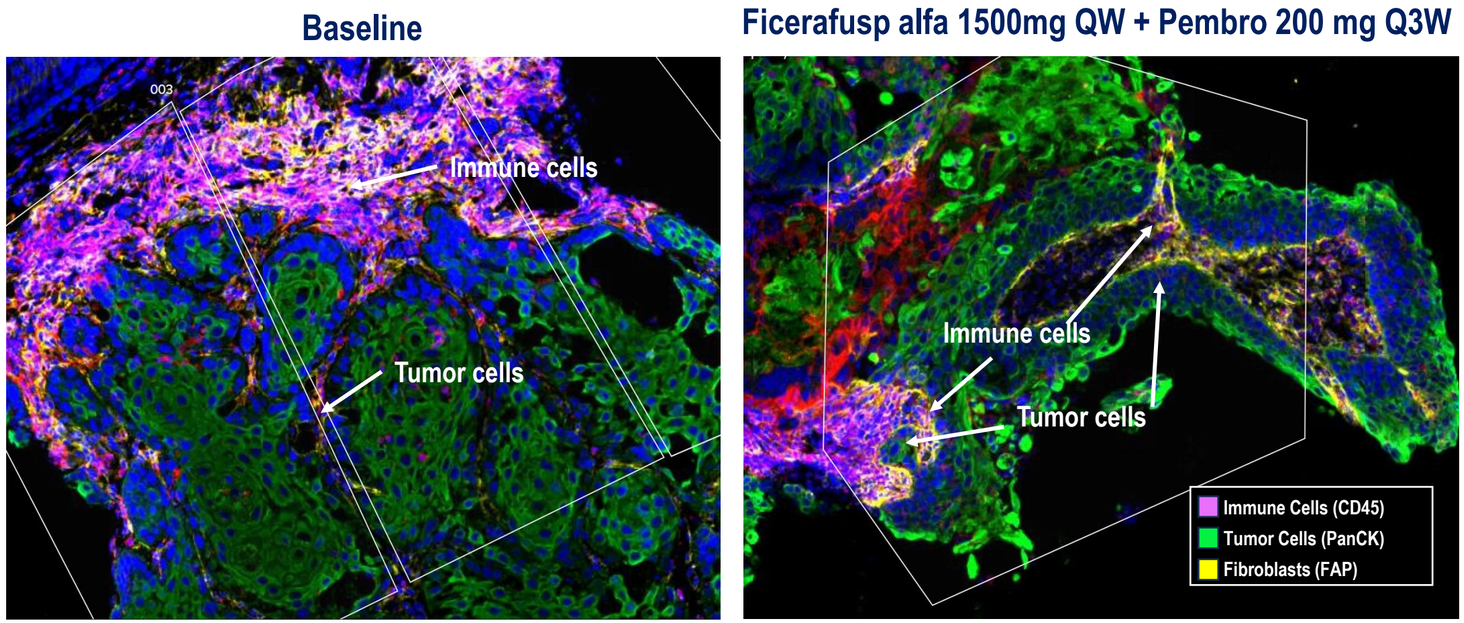
1. O'Connell BC, et al. Cancer Res. 2025;85(8_Suppl 1):3284. 2. He Y, et al. J Natl Cancer Inst. 1998;90(14):1080-7. 3. Chung CH, et al. J Clin Oncol. 2006;24(25):4170-6. 4. Schmitz S, et al. Oncotarget. 2015;6(33):34288-99; 5. Boreddy SR, et al. Cancer Res. 2023;83(11):1883-904. 6. Baumeister P, et 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. **CR,** complete response**; DCR,** disease control rate; **mDOR**, median duration of response; **EGFR**, epidermal growth factor receptor; **ORR,** objective response rate; **TGF**, transforming growth factor; **TME**, tumor microenvironment.

Ficerafusp Alfa

Designed to Enable Tumor Penetration of Immune Cells by Remodeling the Fibrotic TME to Drive Deep and Durable Responses

Enhanced immune cell tumor penetration[1]



Patient with HPV-negative HNSCC who had a partial response (−84%)

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1. O'Connell BC, et al. Cancer Res. 2025;85(8_Suppl 1):3284.

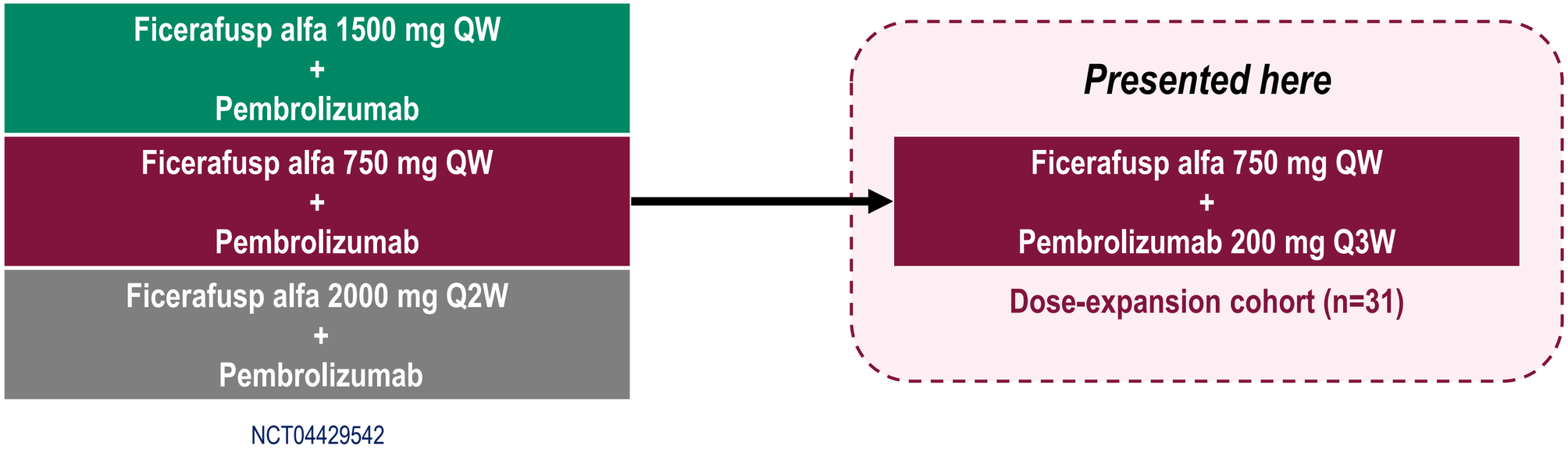
HNSCC, head and neck squamous cell carcinoma; **HPV**, human papilloma virus; **Q3W**, every 3 weeks; **QW**, weekly **TME**, tumor microenvironment.

Ficerafusp Alfa Phase 1b Dose-expansion Cohorts

1L, HPV-negative, CPS ≥1, R/M HNSCC

Dose expansion (Simon 2-stage) part B

Ficerafusp alfa + pembrolizumab



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1L, first line; **CPS**, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papilloma virus; **R/M**, recurrent or metastatic; **Q2W**, every 2 weeks; **Q3W**, every 3 weeks; **Q6W**, every 6 weeks; **QW**, weekly.

Patient Demographics and Baseline Characteristics

Population

- 1L R/M HNSCC, **HPV-negative**
- Oral cavity, oropharynx, larynx, and hypopharynx
- CPS ≥1
- ECOG performance status 0-1

Characteristic		Safety set (N=31)
Age	Median (range)	64 (28-78)
Sex, n (%)	Male/Female	20/11 (65%/35%)
Primary disease site, n (%)	Oropharynx	5 (16%)
	Oral cavity	19 (61%)
	Hypopharynx	5 (16%)
	Larynx	2 (6%)
CPS, n (%)	1-19	12 (39%)
	≥20	19 (61%)
Locoregional (LR) vs distant metastatic (DM) disease, (%)	LR only	16 (52%)
	LR + DM	9 (29%)
	DM only	6 (19%)
Sum of target lesion diameters	Median, mm	41
	>50 mm, n (%)	10 (32%)
	>70 mm, n (%)	4 (13%)
ECOG performance status	0/1, n (%)	11/20 (35%/65%)

Data snapshot: July 9, 2025.

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CPS, combined positive score; **DM**, distant metastatic; **ECOG**, Eastern Cooperative Oncology Group; **HPV**, human papillomavirus; **LR**, locoregional; **R/M**, recurrent or metastatic.

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

The combination was tolerable with a manageable safety profile

No treatment-related deaths were reported

Safety profile at 750 mg was consistent with established safety profile of ficerafusp alfa + pembrolizumab in R/M HNSCC

Most common AEs related to ficerafusp alfa (>20% of patients)*

Preferred term, n (%)	Safety set (N=31)		
	Any grade	Grade 3	Grade 4/5
Any TRAE	31 (100)	13 (42)	0
Dermatitis acneiform	26 (84)	1 (3)	0
Pruritus	12 (39)	1 (3)	0
Fatigue	12 (39)	0	0
Stomatitis	10 (32)	3 (10)	0
Epistaxis	10 (32)	1 (3)	0
Dry skin	10 (32)	0	0
Skin fissures	9 (29)	0	0
Hypophosphatemia	9 (29)	0	0
Anemia	8 (26)	3 (10)	0
Hypomagnesemia	7 (23)	0	0
Hypokalemia	7 (23)	2 (6)	0
Lipase increased	7 (23)	0	0
Amylase increased	7 (23)	0	0
TRAE leading to ficerafusp alfa discontinuation†	2 (6%)		

Data snapshot: July 9, 2025.

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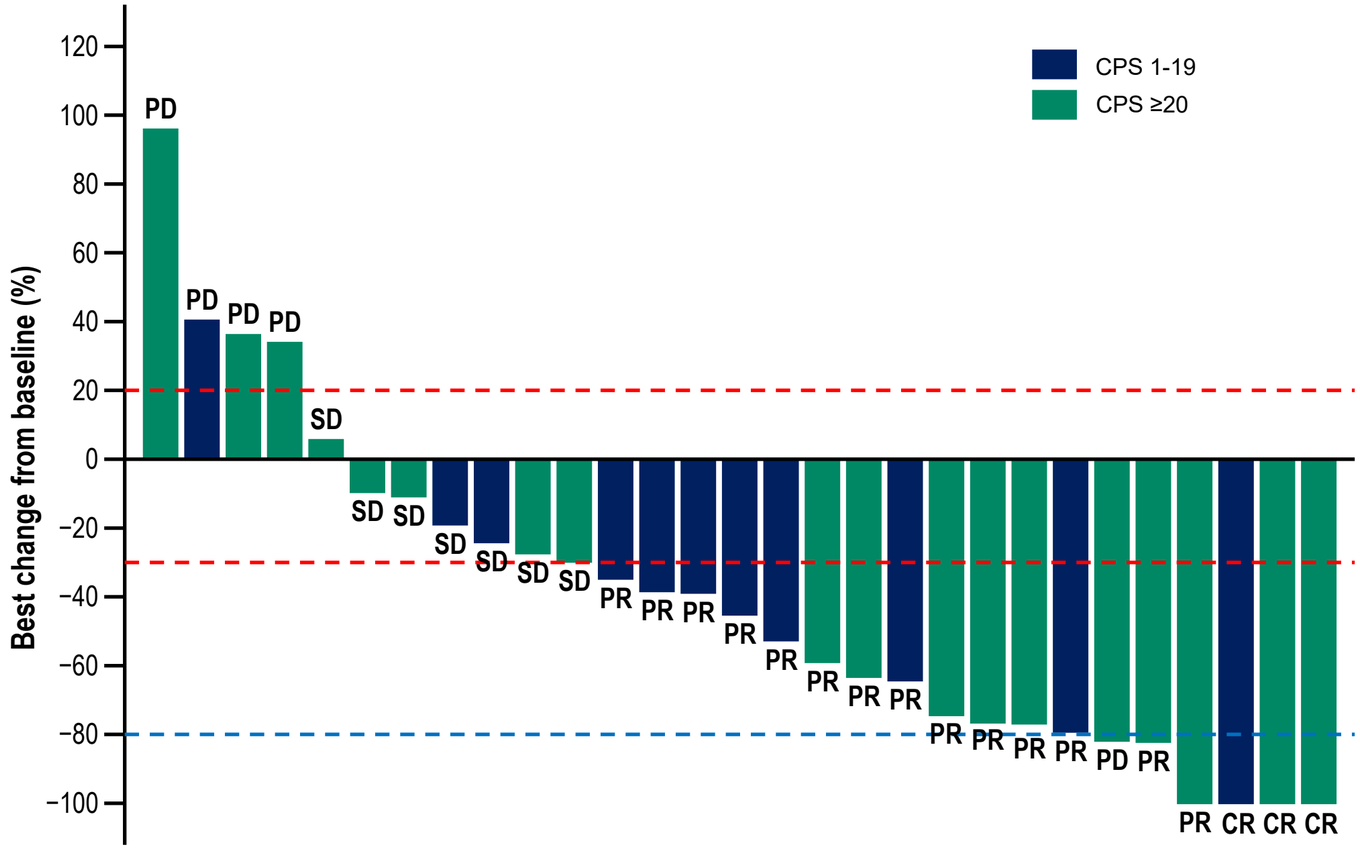
*TRAEs includes TEAEs possibly, probably, or definitely related to ficerafusp alfa; also includes TEAEs with missing drug relationships. †n=1 each for TEAEs leading to dose reduction and discontinuation.
AE, adverse event; **CPS**, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **R/M,** recurrent or metastatic; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment related adverse event.

Efficacy with 1L Ficerafusp Alfa + Pembrolizumab in HPV-negative, CPS ≥1, R/M HNSCC

Efficacy-evaluable population (n=30)*:

- **ORR: 57%** (17/30); **CR: 10%** (3/30)†
- **DCR: 83%** (25/30)
- **Median time to response: 1.6 months**
- **Deep response (≥80% tumor shrinkage): 29%** (5/17)†‡



Data snapshot: July 9, 2025.

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Data snapshot: July 9th, 2025. Investigator-assessed best overall response per RECIST 1.1 *1 patient was not evaluable for efficacy due to early death unrelated to treatment. †1 patient had 3 target lesions at baseline; 1 patient was not evaluable at the tumor assessment visit (resulting in missing data for change from baseline in sum of target lesions) is not included in waterfall plot; a new lesion was also observed. ‡A subject whose best overall response was PD showed a maximum tumor reduction of 81.5%, but a new lesion was detected at the same tumor assessment visit. Includes one unconfirmed CR at the time of data snapshot..
CPS, combined positive score; **DM**, distant metastatic; **ECOG**, Eastern Cooperative Oncology Group; **HPV**, human papillomavirus; **LR**, locoregional; **R/M**, recurrent or metastatic.

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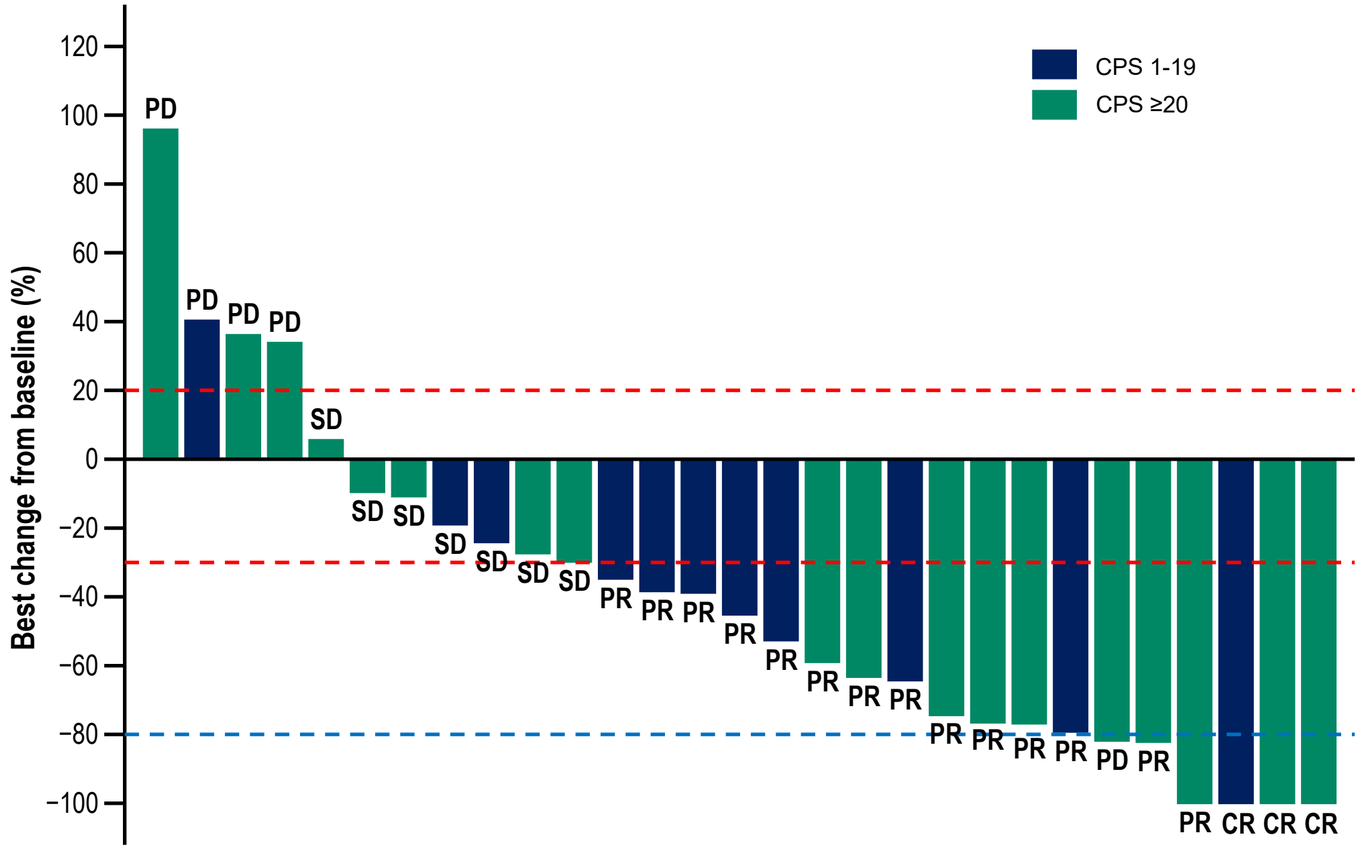
Activity Across Patient Subgroups

		ORR % (N)
CPS	CPS 1-19	73% (8/11)
	CPS ≥ 20	47% (9/19)
Tumor Burden (Sum of target lesion diameters)	≤ 50mm	55% (11/20)
	> 50mm	60% (6/10)
	> 70mm	50% (2/4)



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Conclusions

Ficerafusp alfa 750 mg + pembrolizumab is a promising 1L regimen in HPV-negative CPS ≥1 R/M HNSCC

- Manageable safety profile
- High ORR: 57%
- Rapid time to response: median 1.6 months
- Deep responses: 29% of responders had ≥80% tumor shrinkage

Ficerafusp alfa 750 mg + pembrolizumab demonstrated clinical efficacy and manageable safety, consistent with safety and early signals of efficacy observed across multiple dose levels, informing ongoing dose optimization in the phase 2/3 FORTIFI-HN01 study

Ficerafusp alfa was awarded FDA Breakthrough Therapy Designation on October 13, 2025, in combination with pembrolizumab for 1L treatment of HPV-negative CPS ≥1 R/M HNSCC

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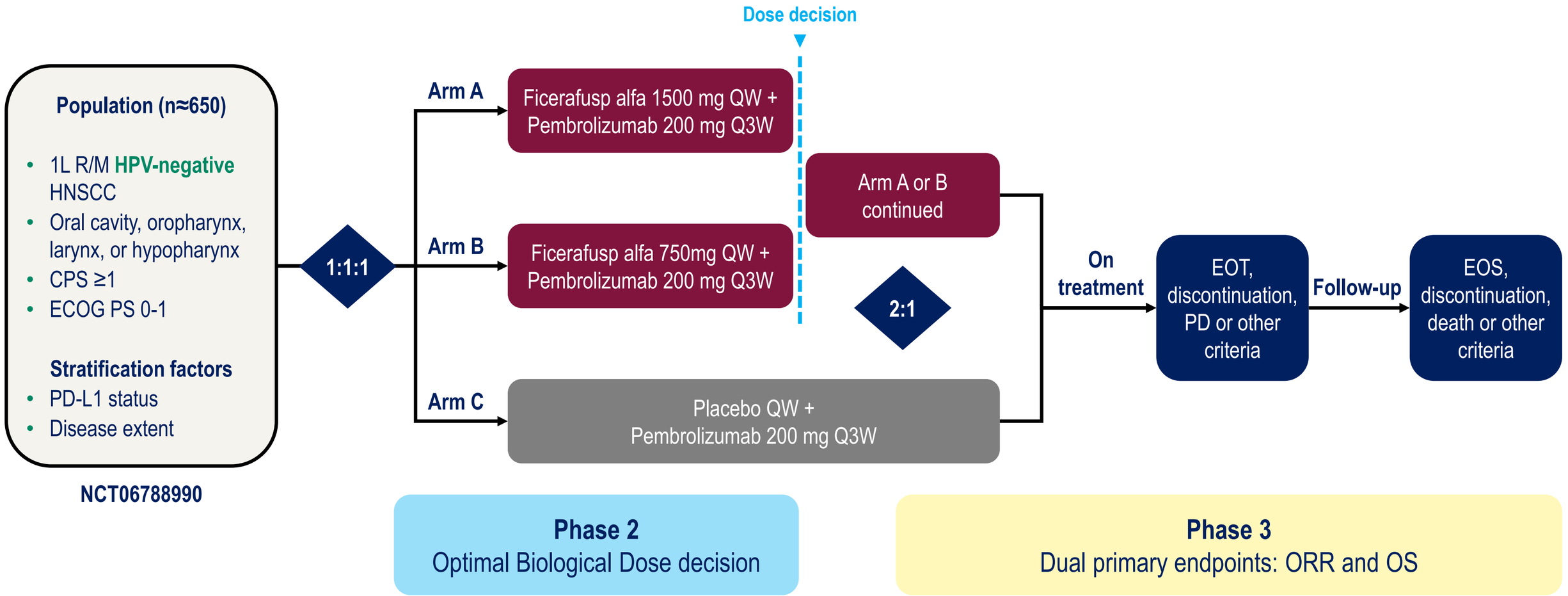
1L, first line; **CPS**, combined positive score; **HNSCC**, head and neck squamous cell carcinoma; **ORR**, objective response rate; **R/M**, recurrent or metastatic;. Data snapshot: July 9, 2025.

FORTIFI-HN01 Study:

Global, Multicenter, Randomized, Double-blind, Phase 2/3 Study of Ficerafusp Alfa or Placebo in Combination with Pembrolizumab for 1L Treatment of PD-L1-positive R/M HNSCC



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1L, first line; **CPS**, combined positive score; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **EOS**, end of study; **EOT**, end of treatment; **HNSCC**, head and neck squamous cell carcinoma; **HPV**, human papillomavirus; **ORR**, objective response rate; **OS**, overall survival; **PD-L1**, programmed death-ligand 1; **PD**, progressive disease; **Q3W**, every 3 weeks; **QW**, weekly; **R/M**, recurrent or metastatic.

Acknowledgments

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