

# Study ASP-1929-301: A phase 3, randomized, double-arm, open-label, controlled study of ASP-1929 photoimmunotherapy (PIT) versus physician's choice standard of care (SOC) for patients with locoregional, recurrent head and neck squamous cell carcinoma (HNSCC)

Anastasios Maniakas<sup>1</sup>, David Cognetti<sup>2</sup>, Makoto Tahara<sup>3</sup>, Takuma Makino<sup>4</sup>, Kai-Ping Chang<sup>5</sup>, Akihiro Homma<sup>6</sup>, Chen-Chi Wang<sup>7</sup>, Chun-Wei Huang<sup>8</sup>, Rajesh Kantharia<sup>9</sup>, Matthew John Mifsud<sup>10</sup>, Ghanishkumar Panjwani<sup>11</sup>, Nobuhiro Hana<sup>12</sup>, Hassan Danesi<sup>13</sup>, Toshiaki Suzuki<sup>13</sup>, Shiou-Yi Ethan Chen<sup>13</sup>, Haiying Dong<sup>13</sup>, Dai Imamura<sup>13</sup>, Rebecca Cheng<sup>13</sup>, Ann M. Gillenwater<sup>1</sup>, Pei-Jen Lou<sup>14</sup>

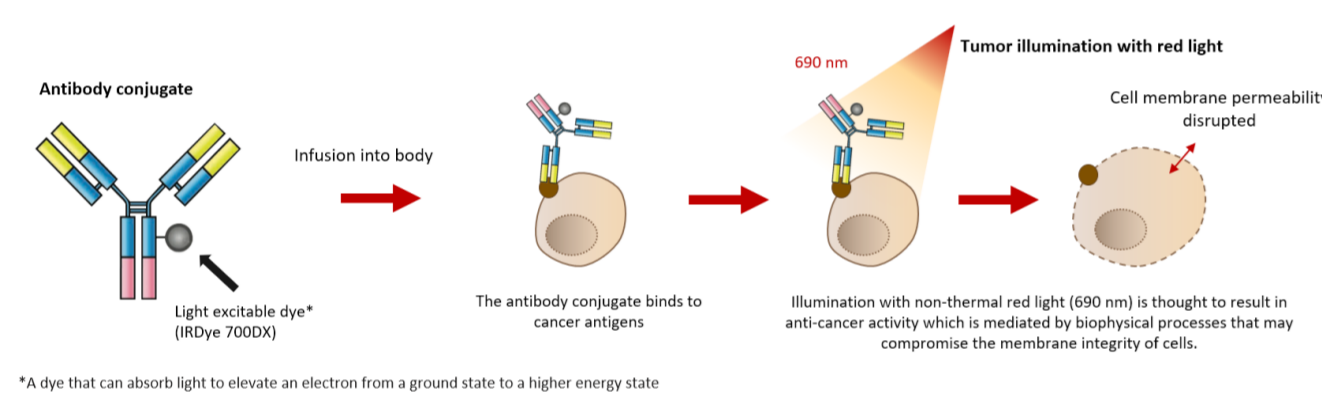
<sup>1</sup> University of Texas MD Anderson Cancer Center, Houston, TX, USA; <sup>2</sup> Thomas Jefferson University, Philadelphia, PA, USA; <sup>3</sup> National Cancer Center Hospital East, Kashiwa, Japan; <sup>4</sup> Okayama University Hospital, Okayama, Japan; <sup>5</sup> Chang Gung Memorial Hospital & Chang Gung University, Taoyuan, Taiwan; <sup>6</sup> Hokkaido University, Sapporo, Japan; <sup>7</sup> Taichung Veterans General Hospital, Taichung, Taiwan; <sup>8</sup> China Medical University Hospital, Taichung, Taiwan; <sup>9</sup> Kailash Cancer Hospital and Research Centre Bankers Heart Institute, Gujarat, India; <sup>10</sup> University of South Florida & Tampa General Hospital, Tampa, FL, USA; <sup>11</sup> Kailash Cancer Hospital and Research Centre, Vadodra, India; <sup>12</sup> Aichi Cancer Center Hospital, Nagoya, Japan; <sup>13</sup> Rakuten Medical, Inc., San Diego, CA, USA; <sup>14</sup> National Taiwan University Hospital & National Taiwan University College of Medicine, Taipei, Taiwan



## BACKGROUND

- Disease burden:** Head and neck cancers are the 7th most common cancers worldwide, with an estimated 946,456 new cases and 482,001 deaths in 2022, and >90% classified as head and neck squamous cell carcinoma (HNSCC).<sup>1-3</sup>
- Unmet clinical need:** Approximately 70% of patients present with stage III-IV disease, and despite surgery, radiation, and/or chemotherapy, 20-30% experience recurrence, with locoregional relapse accounting for ~80% of treatment failures.<sup>4-6</sup>
- Importance of locoregional control:** Locoregional progression is the primary cause of morbidity and mortality in HNSCC, and achieving locoregional control is associated with improved survival, particularly given the functional importance of the head and neck region.<sup>7,8</sup>
- Novel therapeutic approach:** Photoimmunotherapy (PIT) is a targeted anticancer strategy using monoclonal antibodies conjugated to a photoactivatable dye (IR700), which enable, based on preclinical observations, selective tumor cell destruction with minimal damage to surrounding healthy tissue.<sup>9</sup>
- ASP-1929 mechanism:** ASP-1929, a cetuximab-IR700 conjugate targeting EGFR, induce rapid, selective tumor cell death following 690-nm light illumination after infusion, offering a potential locoregional treatment option for recurrent HNSCC with limited available therapies (Figure 1).<sup>10-11</sup>

Figure 1. ASP-1929 PIT Mechanism of Action

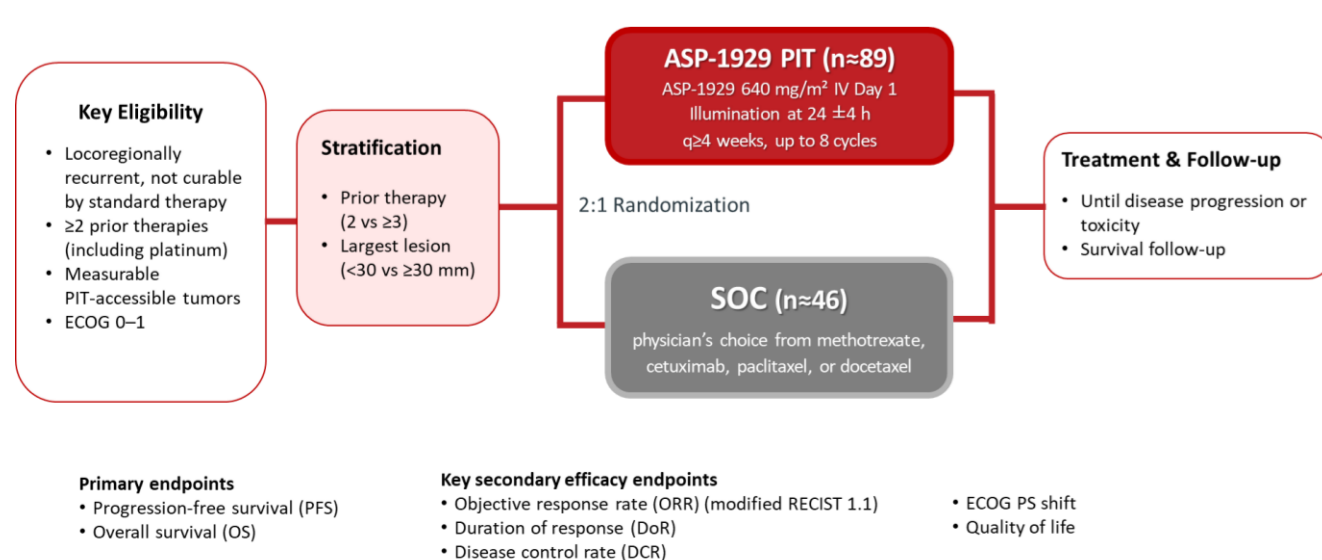


- ASP-1929 PIT clinical data:** Preliminary clinical activity and tolerability of ASP-1929 PIT were showed in a phase 1/2a study (NCT02422979), with a confirmed response rate of 26.7% and a median overall survival of 9.3 months.<sup>12</sup>

## METHODS

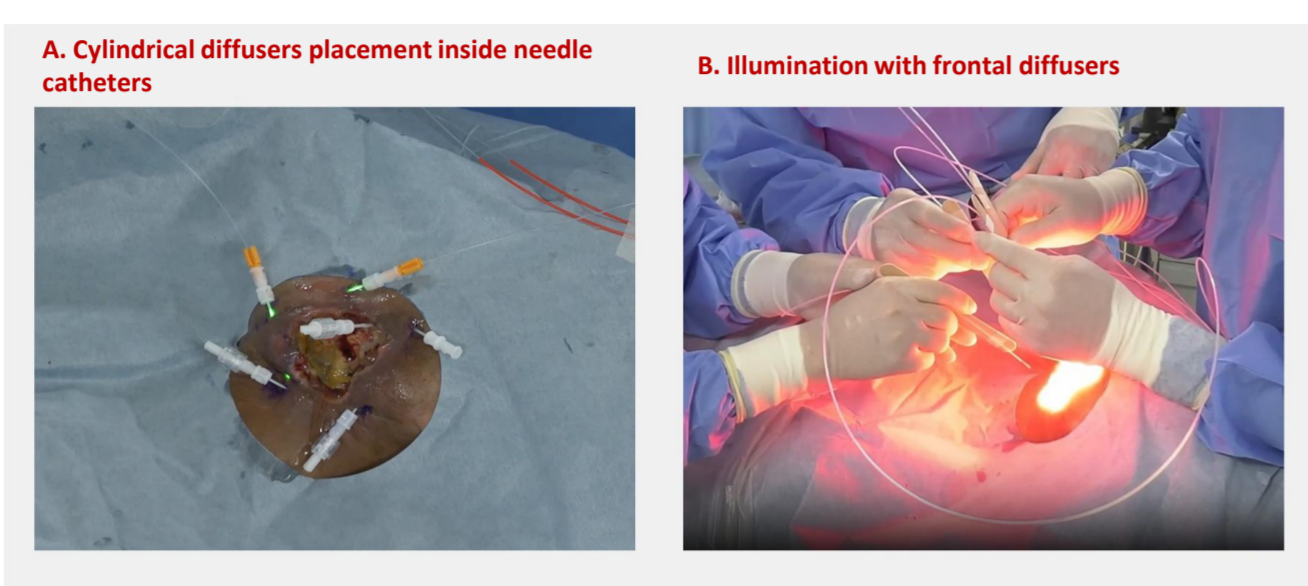
- ASP-1929-301 (NCT03769506) is a phase 3, randomized, double-arm, open-label, controlled study conducted in centers in the United States, Taiwan, Japan, India, and Ukraine.
- Patients with locoregionally recurrent, M0 HNSCC who had failed or progressed on or after at least 2 lines of therapy, including platinum-based chemotherapy, were randomized 2:1 to ASP-1929 PIT or standard of care (Figure 2).
- ASP-1929 PIT consisted of intravenous infusion of ASP-1929 followed by light illumination, with retreatment every ≥4 weeks for up to 8 cycles based on tumor response.
- Illumination is administrated using a frontal diffuser for tumors with thickness ≤1 cm from the skin or mucosal surface or a cylindrical diffuser for tumors >1 cm, with each illumination round lasting approximately 5 minutes (Figure 3).
- Data cutoff for the analysis was April 30, 2025.

Figure 2. ASP-1929-301 Study Design



Abbreviations: CR = complete response; IV = intravenous; MRI = magnetic resonance imaging; PIT = photoimmunotherapy; PR = partial response; SD = stable disease; SOC = standard of care; ECOG PS = Eastern Cooperative Oncology Group Performance Status

Figure 3. Interstitial Illumination (A) and Superficial Illumination (B)

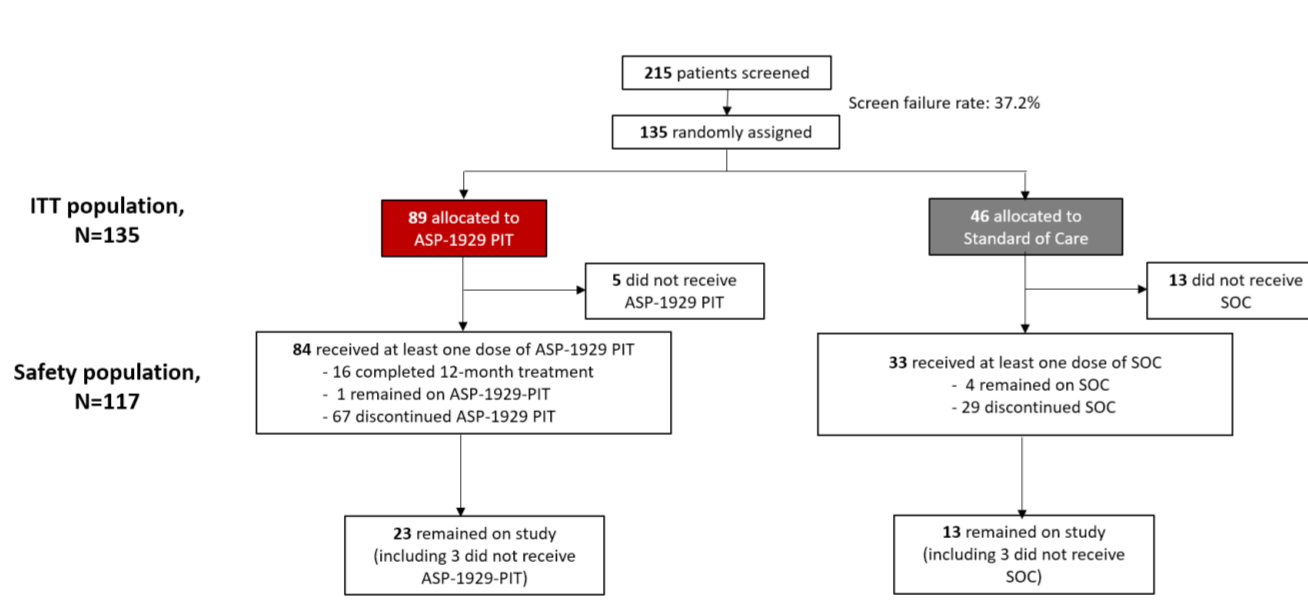


## RESULTS

### Baseline Characteristics

- Due to the evolving standard-of-care landscape, recruitment was completed in October 2024, with 135 patients randomized, compared with the originally planned 275 (Figure 4).
- In the ITT population, baseline demographic and disease characteristics were generally balanced between treatment arms (Table 1).
- Oral cavity and oropharyngeal tumors predominated, with 67.4% presenting with tumors ≥30 mm.
- The study population was heavily pretreated, with approximately two-thirds of patients having received ≥3 prior lines of therapy.

Figure 4. Patient Disposition



Abbreviations: ITT = Intent-to-Treat; PIT = photoimmunotherapy; SOC = standard of care.

Table 1. Baseline Demographics and Disease Status

	ASP-1929 PIT (N = 89)	SOC (N = 46)
<b>Age</b>	Median (Range)	Median (Range)
	60.5 (27, 88)	59.2 (39, 82)
<b>Sex</b>	Male / Female	Male / Female
	69 (77.5%) / 20 (22.5%)	40 (87.0%) / 6 (13.0%)
<b>Race</b>	Asian	Asian
	51 (57.3%)	29 (63.0%)
	Black or African American	Black or African American
	1 (1.1%)	0
	White	White
	36 (40.4%)	14 (30.4%)
	Unknown	Unknown
	1 (1.1%)	3 (6.5%)
<b>Primary tumor location</b>	Hypopharynx	Hypopharynx
	5 (5.6%)	1 (2.2%)
	Larynx	Larynx
	3 (3.4%)	2 (4.3%)
	Nasopharynx	Nasopharynx
	0	1 (2.2%)
	Oral cavity	Oral cavity
	51 (57.3%)	30 (65.2%)
	Oropharynx	Oropharynx
	24 (27.0%)	9 (19.6%)
	Sinonasal tract	Sinonasal tract
	0	2 (4.3%)
	Other*	Other*
	6 (6.7%)	1 (2.2%)
<b>ECOG</b>	0	0
	20 (22.5%)	13 (28.3%)
	1	68 (76.4%)
	2	1 (1.1%)
	3	0
	4 or more	0
<b>Longest diameter of largest lesion<sup>b</sup></b>	Median (min, max), mm	Median (min, max), mm
	35 (13, 86)	36 (12, 80)
	< 30 mm	< 30 mm
	29 (32.6%)	15 (32.6%)
	≥ 30 mm	≥ 30 mm
	60 (67.4%)	31 (67.4%)
<b>Number of prior lines of therapy<sup>c</sup></b>	1	1
	0 (0.0%)	0 (0.0%)
	2	32 (36.0%)
	3	17 (37.0%)
	4 or more	40 (44.9%)
	18 (39.1%)	

Data are n (%). Abbreviations: PIT = photoimmunotherapy; SD = standard deviation; SOC = standard of care; \* Other tumor locations included: retropharynx, lymph node supraclavicular, submandibular, temple, external ear canal, outer ear, or were unknown. <sup>b</sup> Stratification factor which is centrally evaluated. <sup>c</sup> Treatment lines which counted by investigators and is one of the randomization stratification factors.

### Efficacy

- The median number of ASP-1929 PIT cycles was 3 (range 0-8).
- The confirmed ORR per BICR mRECIST 1.1 are represented in Table 2. ORR was numerically higher with ASP-1929 PIT compared with SOC (25.8% vs 15.2%). DCR was also numerically higher in the ASP-1929 PIT arm than in the SOC arm (68.5% vs 43.5%), indicating greater disease stabilization.
- The Kaplan-Meier plots of PFS and OS are shown in Figure 5. PFS was similar between treatment arms (Figure 5A). Median OS was numerically longer with ASP-1929 PIT than with SOC (15.7 vs 9.6 months) (Figure 5B), suggesting a trend toward improved survival.

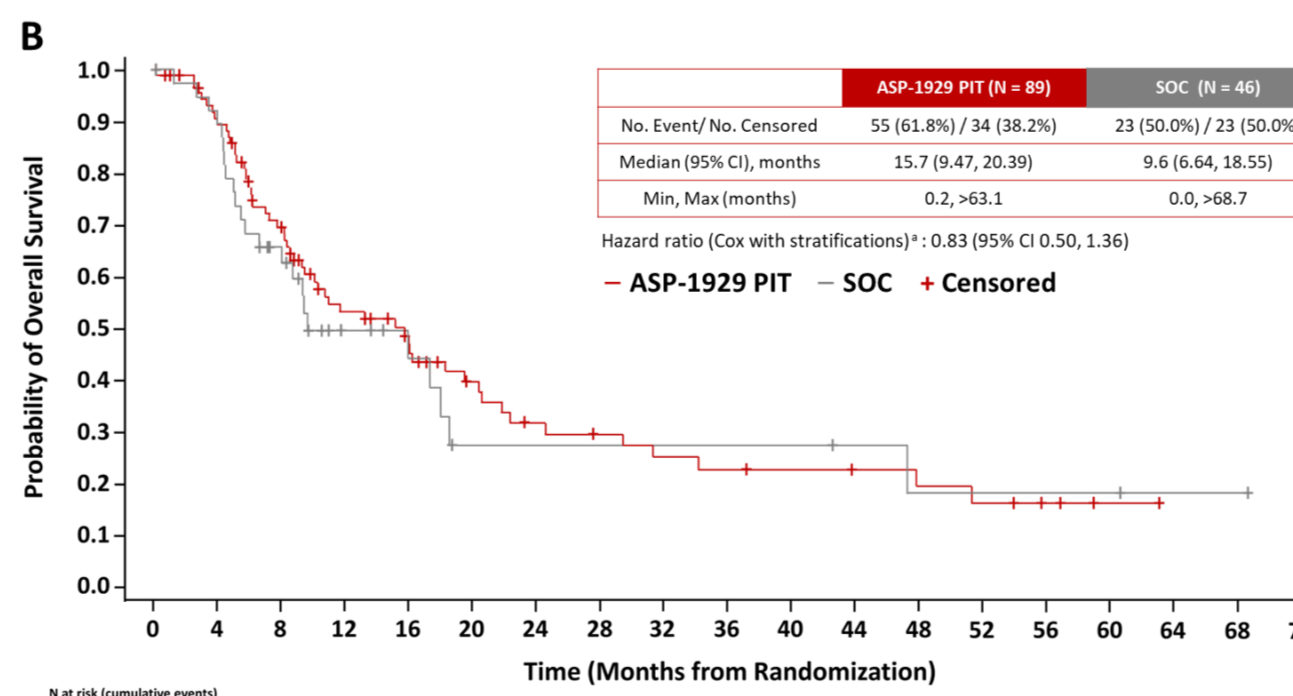
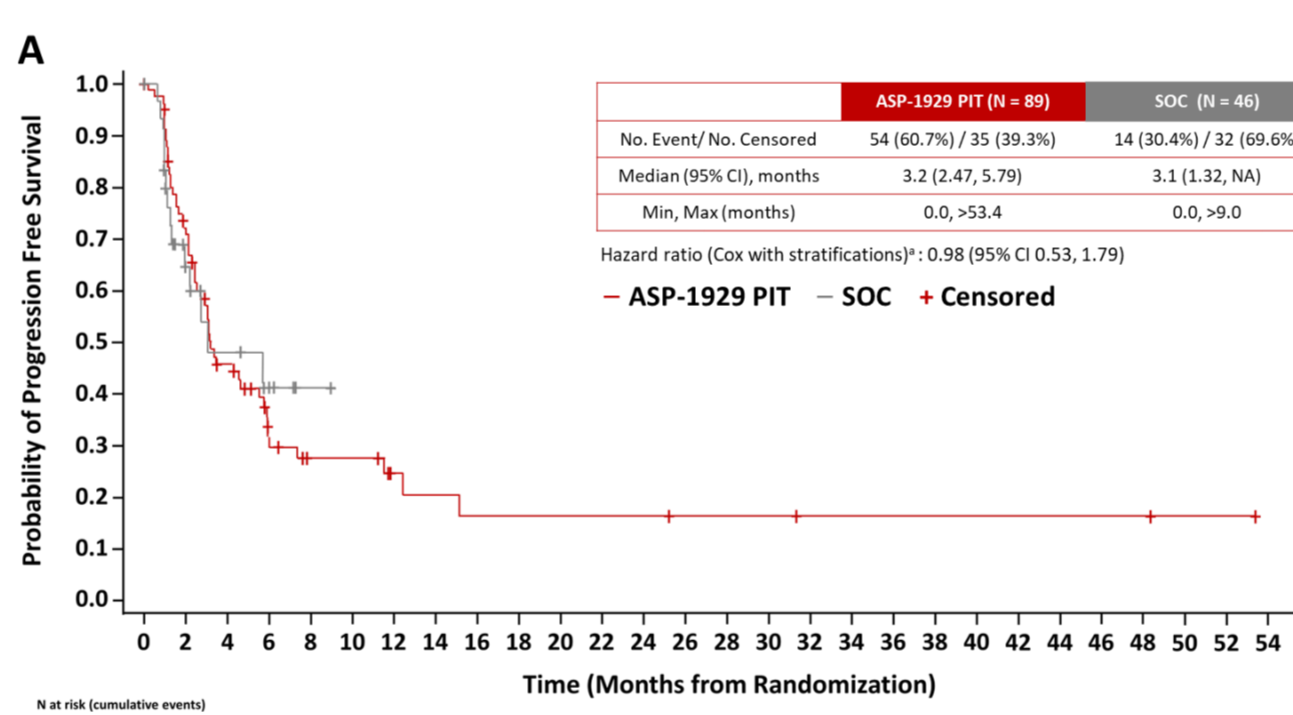
Table 2. ORR per Blinded Independent Central Review

	ASP-1929 PIT (N = 89)	SOC (N = 46)
<b>Best Overall Response (BOR) - confirmed</b>		
CR	6 (6.7%)	2 (4.3%)
PR	17 (19.1%)	5 (10.9%)
SD	38 (42.7%)	13 (28.3%)
PD	19 (21.3%)	8 (17.4%)
NE*	9 (10.1%)	18 (39.1%)
<b>Disease Control Rate (DCR: CR + PR + SD)</b>	61 (68.5%)	20 (43.5%)
<b>Object Response Rate (ORR: CR + PR)</b>	23 (25.8%)	7 (15.2%)

\* NE (not evaluable) was defined as either disease response not being assessable (in one patient) or absence of any post-baseline tumor assessment (in the majority of cases)

Abbreviations: BOR = best overall response; CI = confidence interval; CR = complete response; DCR = disease control rate; NE = not evaluable; ORR = objective response rate; PD = progressive disease; PIT = photoimmunotherapy; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumors; SD = stable disease; SOC = standard of care.

Figure 5. Kaplan-Meier Plot of PFS (A) and OS (B)



<sup>a</sup> Stratified by the stratification factors at randomization (2 vs. ≥3 previous lines of therapy, <30 vs. ≥30mm of longest diameter of largest target lesion). Abbreviations: N = total number of patients; PIT = photoimmunotherapy; SOC = standard of care; NA = not available; CI = confidence interval; Min = minimum; Max = maximum

**References**  
1. Barsouk A, et al. Med Sci (Basel). 2023;11(2):42. 2. Chow LQM. N Engl J Med. 2020;382(1):60-72. 3. Bray F, et al. J Clin. 2024;74:229-263. 4. Khuri FR, et al. N Engl J Med. 2000;343(25):1812-1818. 5. Goodwin WJ Jr. Laryngoscope. 2000;110(3 Suppl 93):1-18. 6. Ridge JA, et al. N Engl J Med. 2016;375:1156-1167. 7. Patel SA, et al. J Clin Oncol. 2016;34(Suppl):4015. 8. Zumsteg ZS, et al. JAMA Oncol. 2017;3(11):1487-1494. 9. Hsu YC, et al. Free Radic Biol Med. 2015;85:24-32. 10. Kishimoto S, et al. Free Radic Biol Med. 2015;85:24-32. 11. Sato K, et al. ACS Cent Sci. 2018;4(11):1559-1569. 12. Cognetti DM, et al. Head Neck. 2021;43(12):3875-3887.

## RESULTS

### Safety

- Grade ≥3 TEAEs occurred more frequently in the ASP-1929 PIT arm than in the SOC arm (58.3% vs 36.4%); however, fewer TEAEs led to dose modification, delay, interruption with PIT (15.5% vs 30.3%) or discontinuation (4.8% vs 9.1%) (Table 3A)
- Adverse events in the ASP-1929 PIT arm were primarily driven by localized and inflammatory reactions, such as pain, swelling, oral pain, dysphagia, and stomatitis, which were mostly low grade and manageable with standard medical care (Table 3B).

Table 3. Adverse Events Overview (A) and Treatment-Emergent Adverse Events ≥10% (B)

	ASP-1929 PIT (N = 84)	SOC (N = 33)
<b>All grade TEAE</b>	81 (96.4)	28 (84.8)
<b>TEAE grade 3 or higher</b>	49 (58.3)	12 (36.4)
<b>TEAE leading to death*</b>	3 (3.6)	2 (6.1)
<b>TEAE related to study treatment*</b>	73 (86.9)	18 (54.5)
<b>Serious Adverse Events (SAE)</b>	36 (42.9)	9 (27.3)
<b>SAE related to study treatment*</b>	14 (16.7)	3 (9.1)
<b>TEAE leading to study treatment discontinuation</b>	4 (4.8)	3 (9.1)
<b>TEAE leading to dose modification, delay, or interruption</b>	13 (15.5)	10 (30.3)

Data are n (%). \* All grade 5 TEAEs in both arms were not related to study treatment. TEAEs leading to death in the ASP-1929 PIT arm included sepsis, coronavirus disease 2019 (COVID-19), and cardio-respiratory arrest (1 patient each). Both TEAEs leading to death in the SOC arm were reported as deaths due to unknown causes. <sup>a</sup> ASP-1929 PIT.

### B

	ASP-1929 PIT (N = 84)	SOC (N = 33)
	All grades	≥ Grade3
Constipation	27.4%	1.2%
Oral pain	19.0%	6.0%
Fatigue	17.9%	2.4%
Nausea	17.9%	0.0%
Application site pain	13.1%	4.8%
Diarrhea	13.1%	0.0%
Dysphagia	13.1%	6.0%
Stomatitis	13.1%	2.4%
Pyrexia	13.1%	0.0%
Swelling face	13.1%	0.0%
Cough	11.9%	0.0%
Insomnia	11.9%	0.0%
Face edema	11.9%	2.4%
Hypertension	11.9%	0.0%
Pneumonia	11.9%	6.0%
Wound complication	11.9%	1.2%
Anemia	10.7%	4.8%
Oropharyngeal pain	10.7%	1.2%
Tumor pain	10.7%	2.4%
Rash	9.5%	0.0%
Vomiting	7.1%	0.0%

Abbreviations: AE = adverse event; N = total number of patients; PIT = photoimmunotherapy; SAE = serious adverse event; SOC = standard of care; TEAE = treatment-emergent adverse event.

### Quality of Life

- ECOG PS improved in 19.1% of patients in the ASP-1929 PIT arm (17/89) versus 0% in the SOC arm.
- Quality of life was assessed using EORTC QLQ-C30 mean change from baseline to best post-baseline in the Safety Analysis Population. No overall negative impact on quality of life was observed with ASP-1929 PIT compared with SOC (Figure 6).
- ASP-1929 PIT was associated with favorable trends in patient-reported quality-of-life outcomes compared with standard of care across key functional domains and global health status/quality of life (Figure 6A).
- ASP-1929 PIT also showed favorable trends toward reduced EORTC QLQ-C30 symptom burden versus standard of care (Figure 6B).

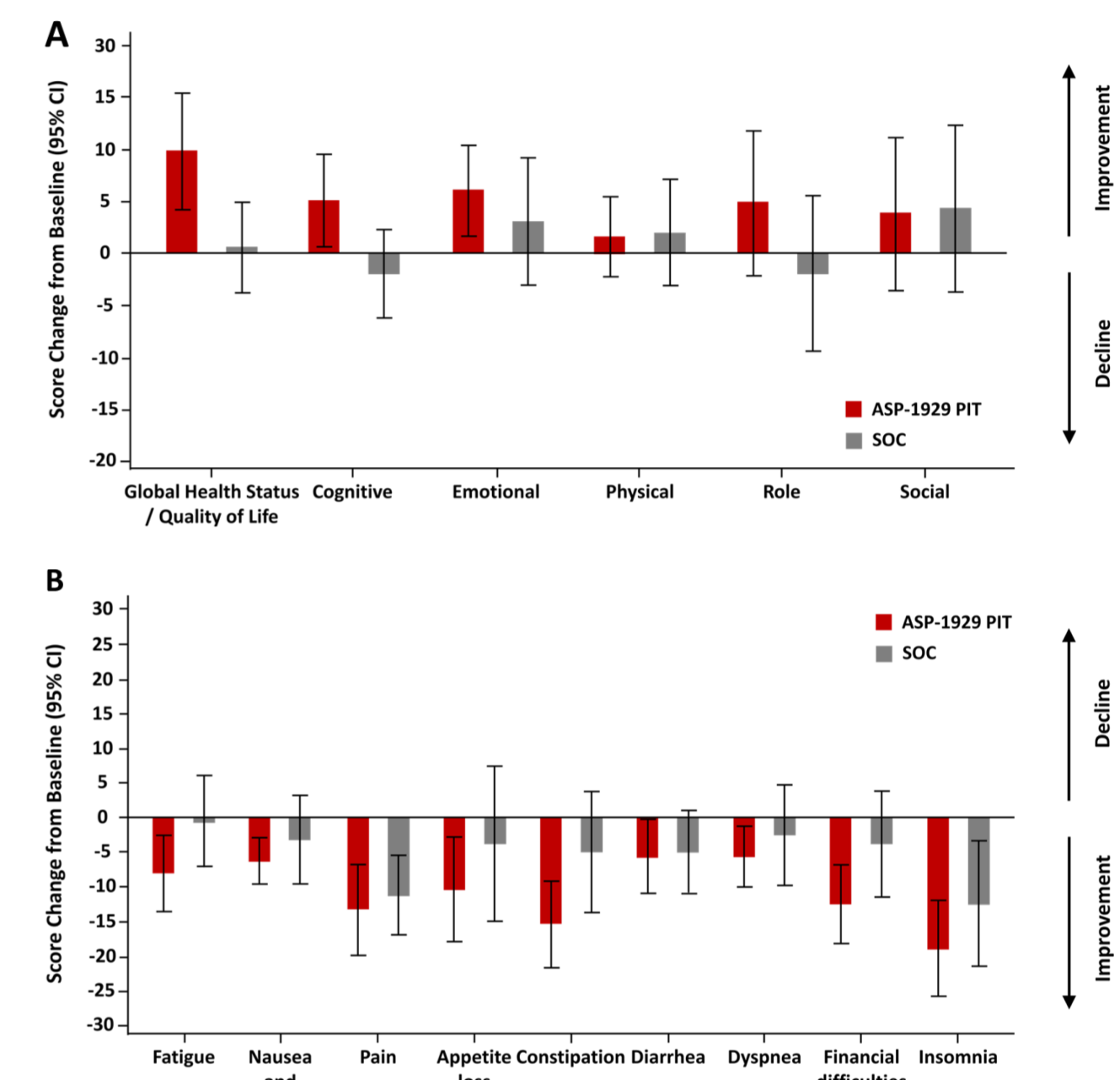
### Acknowledgments

We thank the patients and their families, the investigators and their teams, Rakuten Medical colleagues, clinical research organizations, and vendors. Study sponsored by Rakuten Medical. Presented at 2026 ASCO Annual Meeting, May 29-June 2, 2026, Chicago, IL, USA. ClinicalTrials.gov Identifier: NCT03769506. Contact information: Dr. Rebecca Cheng rebecca.cheng@rakuten-med.com

### Presenting author disclosures:

- Clinical trial PI - Rakuten Medical
- Research contracts: Jazz Pharmaceuticals, Global Cancer Technologies, Thyry Therapeutics, NABORS Industries

Figure 6. Quality of Life EORTC QLQ-C30 Global Health Status and Functional Scales (A) and Symptom Burden (B)



Abbreviations: AE = adverse event; PIT = photoimmunotherapy; SOC = standard of care; C30 = Core 30; EORTC QLQ = European Organization for Research and Treatment of Cancer Quality of Life questionnaire.

Figure 7. Case Photo Pre- and Post-PIT



72-year-old male with left lower lip HNSCC, initially treated with CCRT, followed by multiple systemic therapies (carboplatin/5-FU/methotrexate 16 cycles, epirubicin 3 cycles, cetuximab 15 cycles) for recurrence; disease relapsed again at the same site within 3 months after second-line treatment.

Case results presented are based on early-stage results, and may not necessarily be typical for all patients

## CONCLUSIONS

- The current study is the first to evaluate ASP-1929 PIT in a Phase 3 randomized, comparator-controlled setting.
- Among heavily pretreated patients, trends toward higher ORR, DCR, and OS were observed with ASP-1929 PIT compared with SOC.
- Due to the evolving treatment landscape and a high drop out rate in SOC arm, the resulting limited sample size precluded a valid statistical comparison of efficacy between treatment arms.
- Adverse events observed in the ASP-1929 PIT arm were predominantly low grade and primarily due to local effects of the PIT procedure.
- The preservation of performance status and patient-reported quality of life may suggest that ASP-1929 PIT may deliver clinical benefit without compromising patients' well-being.
- Overall, these findings support the clinical potential of ASP-1929 PIT as a novel therapeutic modality associated with improved tumor response, durable locoregional control, and manageable safety profile for patients with recurrent HNSCC.