

Indirect comparison of amivantamab with real-world therapies in recurrent/metastatic head & neck squamous cell carcinoma after immune checkpoint inhibitor and platinum-based chemotherapy

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Key Takeaway



Amivantamab monotherapy demonstrated statistically significant and clinically meaningful improvements in survival and disease-control outcomes in patients with HPV-unrelated R/M HNSCC after ICI and platinum-based chemotherapy versus real-world therapies from a trial-matched control arm

Conclusions



Baseline characteristics were well balanced between OrigAMI-4 Cohort 1 (amivantamab cohort) and the RW SoC cohort after weighting, which indicates successful adjustment for measured confounders



Amivantamab significantly improved OS compared with RW SoC (12.5 vs 7.7 months, respectively; HR, 0.61; 95% CI, 0.44–0.85; $P=0.003$) in patients with R/M HNSCC after ICI and platinum-based chemotherapy, with 54% versus 35% of patients alive at 12 months



PFS, TTD, and TTNT were also significantly improved in the amivantamab cohort compared with the RW SoC cohort



These data provide clinically meaningful real-world evidence supporting the efficacy of amivantamab monotherapy, including significantly improved OS, in HPV-unrelated R/M HNSCC



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Disclosures

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Introduction

- Prognosis is poor for patients with human papillomavirus (HPV)–unrelated recurrent/metastatic (R/M) head & neck squamous cell carcinoma (HNSCC) after immune checkpoint inhibitor (ICI) and platinum-based chemotherapy, with a median overall survival (OS) of <10 months and a median progression-free survival (PFS) of approximately 4 months,^{1,2} highlighting the limited effective treatments in this setting
- The epidermal growth factor receptor (EGFR) and MET proteins are overexpressed in 80%–90% of R/M HNSCC tumors and are associated with poor prognoses^{3–6}
- Amivantamab is an EGFR–MET bispecific antibody with dual-targeting activity against EGFR and MET and immune cell–directing activity^{7,8}
- Subcutaneous (SC) amivantamab received US Food and Drug Administration Breakthrough Therapy Designation for patients with HPV-unrelated R/M HNSCC after anti–programmed death–(ligand) 1 (PD–[L]1) antibody and platinum-based chemotherapy based on results from Cohort 1 of the OrigAMI-4 study^{9–11}
- To contextualize these results, outcomes in Cohort 1 were compared with a trial-matched real-world standard-of-care (RW SoC) cohort derived from real-world patients treated in clinical practice

Results

Patients

- In Cohort 1 of OrigAMI-4 (amivantamab cohort), 102 patients with R/M HNSCC after ICI and platinum-based chemotherapy received ≥ 1 dose of SC amivantamab¹¹
- A total of 317 patients were identified from the US Flatiron Health Advanced Head & Neck Dataset who met the OrigAMI-4 Cohort 1 criteria (RW SoC cohort; **Figure 1**)
- The most common treatments received in the index LoT after anti–PD–(L)1 antibody and platinum-based chemotherapy in the RW SoC cohort were anti–PD–(L)1 antibody–based therapies (pembrolizumab or nivolumab monotherapy or combination therapies; 26%), EGFR antibody–based combination therapies (21%), and EGFR antibody–based monotherapy (17%)
- Demographic and baseline disease characteristics before ATT weighting for the amivantamab and RW SoC cohorts are shown in **Table 1**

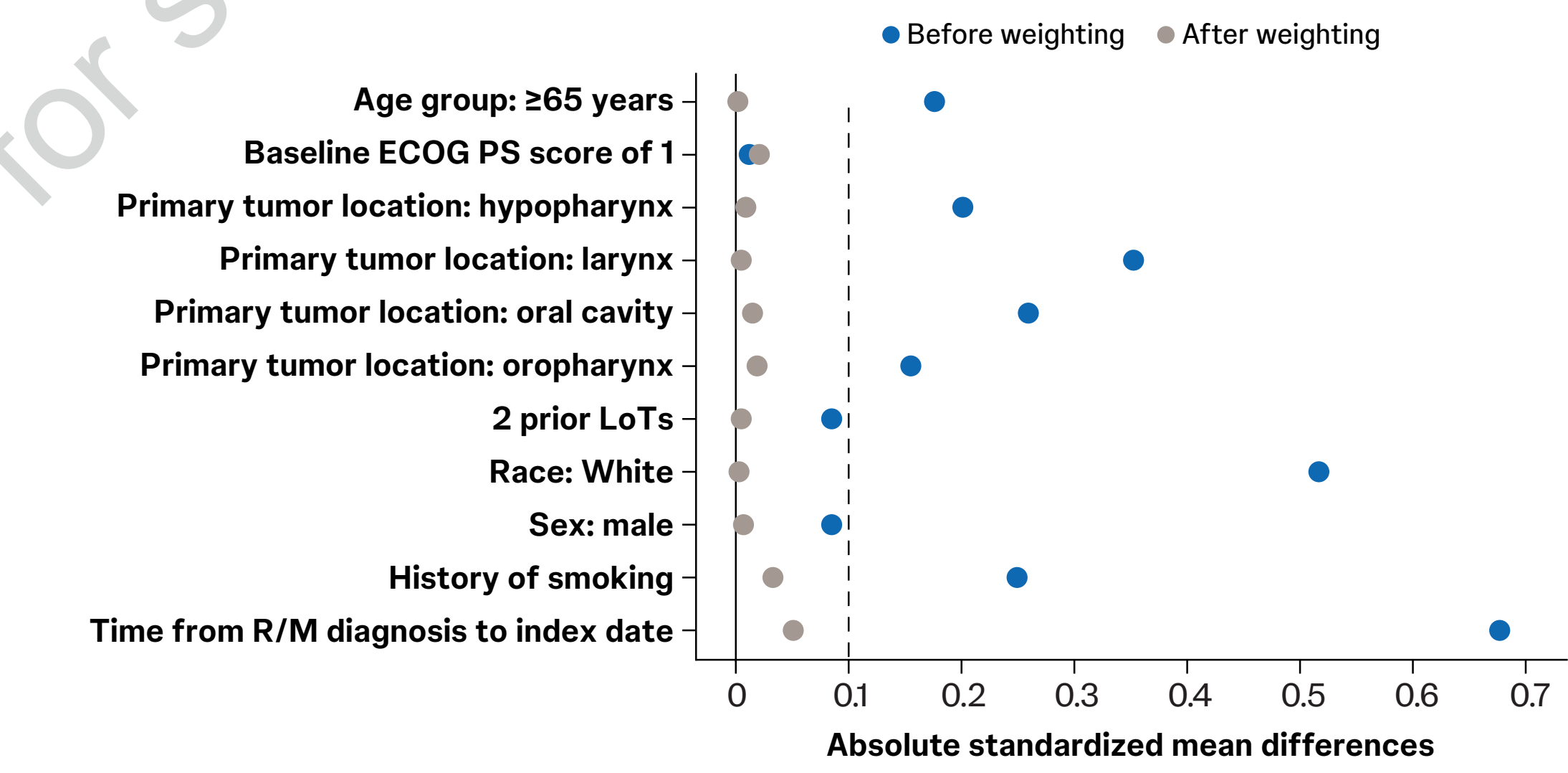
Table 1: Demographic and baseline disease characteristics before ATT weighting

Characteristic, n (%)	Amivantamab (N=102)	RW SoC (N=317)
Age		
Median (Q1–Q3), years	63.0 (57.0–70.0)	66.0 (57.0–73.0)
<65 years	56 (55)	148 (47)
≥ 65 years	46 (45)	169 (53)
Sex		
Male	79 (77)	235 (74)
Female	23 (23)	82 (26)
Race		
Non-White ^a	46 (45)	70 (22)
White	42 (41)	215 (68)
Not reported	14 (14)	32 (10)
ECOG PS score		
0	34 (33)	98 (31)
1	68 (67)	201 (63)
Unknown	0	18 (6)
History of smoking		
Yes	72 (71)	261 (82)
No	30 (29)	56 (18)
Number of prior LoTs		
1	53 (52)	178 (56)
2	49 (48)	139 (44)
Primary tumor site		
Oral cavity	48 (47)	107 (34)
Larynx	24 (24)	121 (38)
Hypopharynx	16 (16)	28 (9)
Oropharynx	14 (14)	61 (19)
Median (Q1–Q3) time from R/M diagnosis to start of index LoT, months	8.9 (3.6–14.2)	10.2 (6.6–16.2)

^aIncludes Asian, Black or African American, and other race.
ATT, average treatment effect on the treated; ECOG PS, Eastern Cooperative Oncology Group performance status; LoT, line of therapy; Q, quartile; R/M, recurrent/metastatic; RW SoC, real-world standard of care.

- Baseline differences between the amivantamab and RW SoC cohorts were substantially reduced after weighting, with all absolute standardized mean differences <0.1 (**Figure 2**)

Figure 2: Baseline covariates before and after ATT weighting



Note: An absolute standardized mean difference <0.1 was the threshold for appropriate weighting.
ATT, average treatment effect on the treated; ECOG PS, Eastern Cooperative Oncology Group performance status; LoT, line of therapy; R/M, recurrent/metastatic.

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Methods

- OrigAMI-4 (ClinicalTrials.gov identifier: NCT06385080) is an open-label, phase 1b/2 study of SC amivantamab, co-formulated with recombinant human hyaluronidase PH20, as a monotherapy and in combination with other standard-of-care therapeutic agents in participants with R/M HNSCC
- This analysis used the US Flatiron Health Advanced Head & Neck Cancer Dataset to construct a trial-matched comparator cohort of patients with HNSCC based on real-world data using key OrigAMI-4 Cohort 1 trial eligibility criteria (**Figure 1**)
- Consistent with Cohort 1, prior anti-EGFR therapy, HPV-positive oropharyngeal carcinoma, and any known p16-positive tumors were exclusionary
- Consistent with OrigAMI-4 Cohort 1 eligibility criteria, all patients had received anti–PD–(L)1 antibody and platinum-based chemotherapy
- The index line was defined as the first subsequent line of therapy (LoT) after anti–PD–(L)1 antibody and platinum-based chemotherapy
- Average treatment effect on the treated (ATT)–weighted inverse probability of treatment weighting (IPTW) was used to balance the distribution of confounders between arms
- OS, investigator-assessed PFS, time to treatment discontinuation (TTD), and time to next treatment (TTNT) were compared using weighted Kaplan-Meier methods, with the Cox proportional hazards model used to estimate hazard ratios (HRs) and confidence intervals (CIs)

Efficacy

- Amivantamab demonstrated significantly improved median OS relative to the RW SoC (12.5 vs 7.7 months, respectively), with a 39% reduction in the risk of death (HR, 0.61; 95% CI, 0.44–0.85; $P=0.003$; **Figure 3**)
 - At 12 months, 54% versus 35% of patients were alive
- OS favored amivantamab relative to the RW SoC across all subgroups (**Figure 4**)
- Median investigator-assessed PFS was significantly prolonged with amivantamab relative to the RW SoC (6.8 vs 3.7 months, respectively), with a 44% reduction in the risk of disease progression or death (HR, 0.56; 95% CI, 0.42–0.74; $P<0.001$; **Figure 5**)
 - At 12 months, 23% versus 15% of patients were alive and progression-free
- Median TTD (6.8 vs 3.6 months, respectively; HR, 0.53; 97.5% CI, 0.40–0.70; $P<0.001$; **Figure 6A**) and median TTNT (8.0 vs 4.5 months; HR, 0.52; 97.5% CI, 0.39–0.69; $P<0.001$; **Figure 6B**) were also significantly prolonged relative to the RW SoC

Figure 3: OS

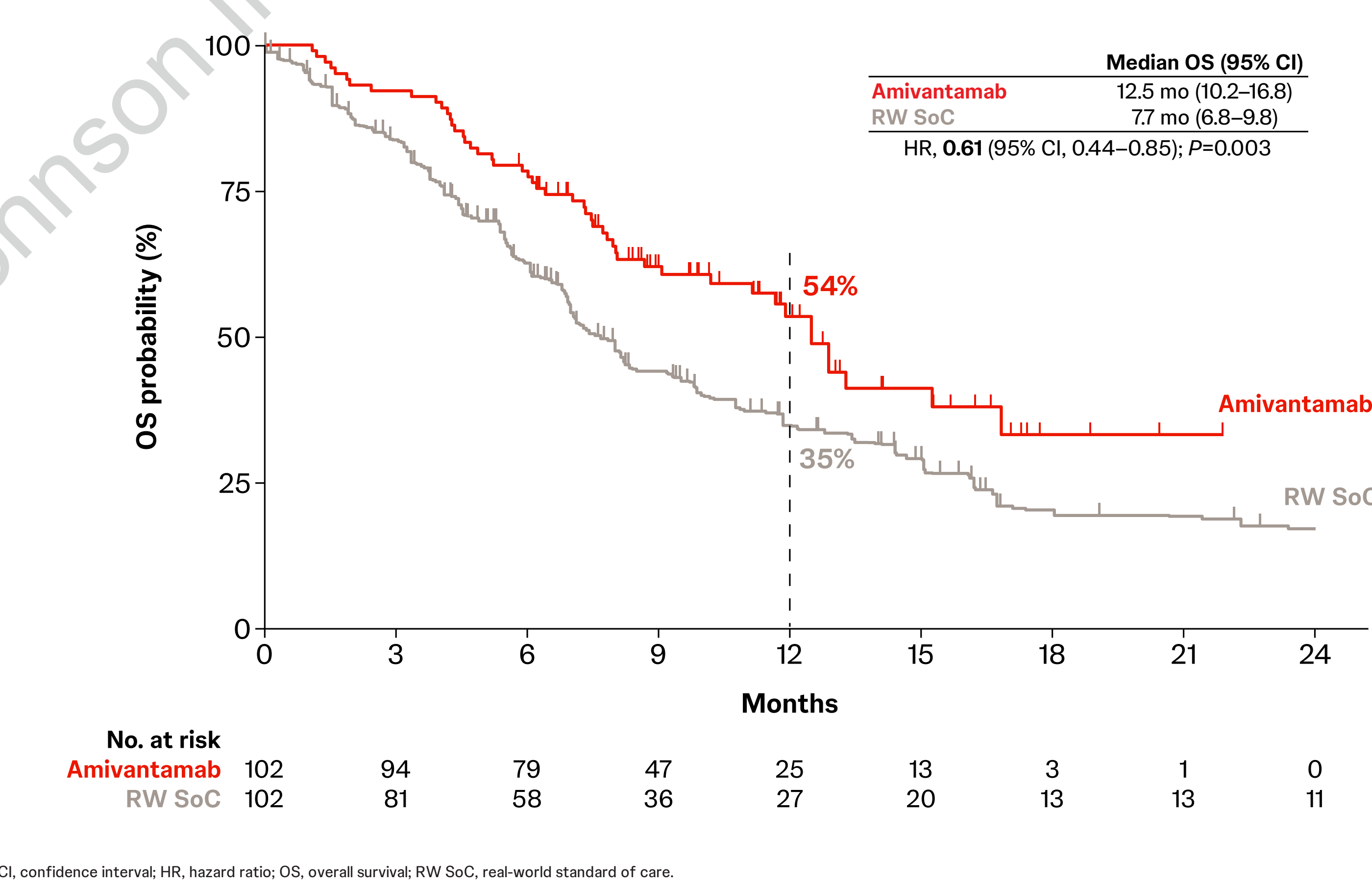
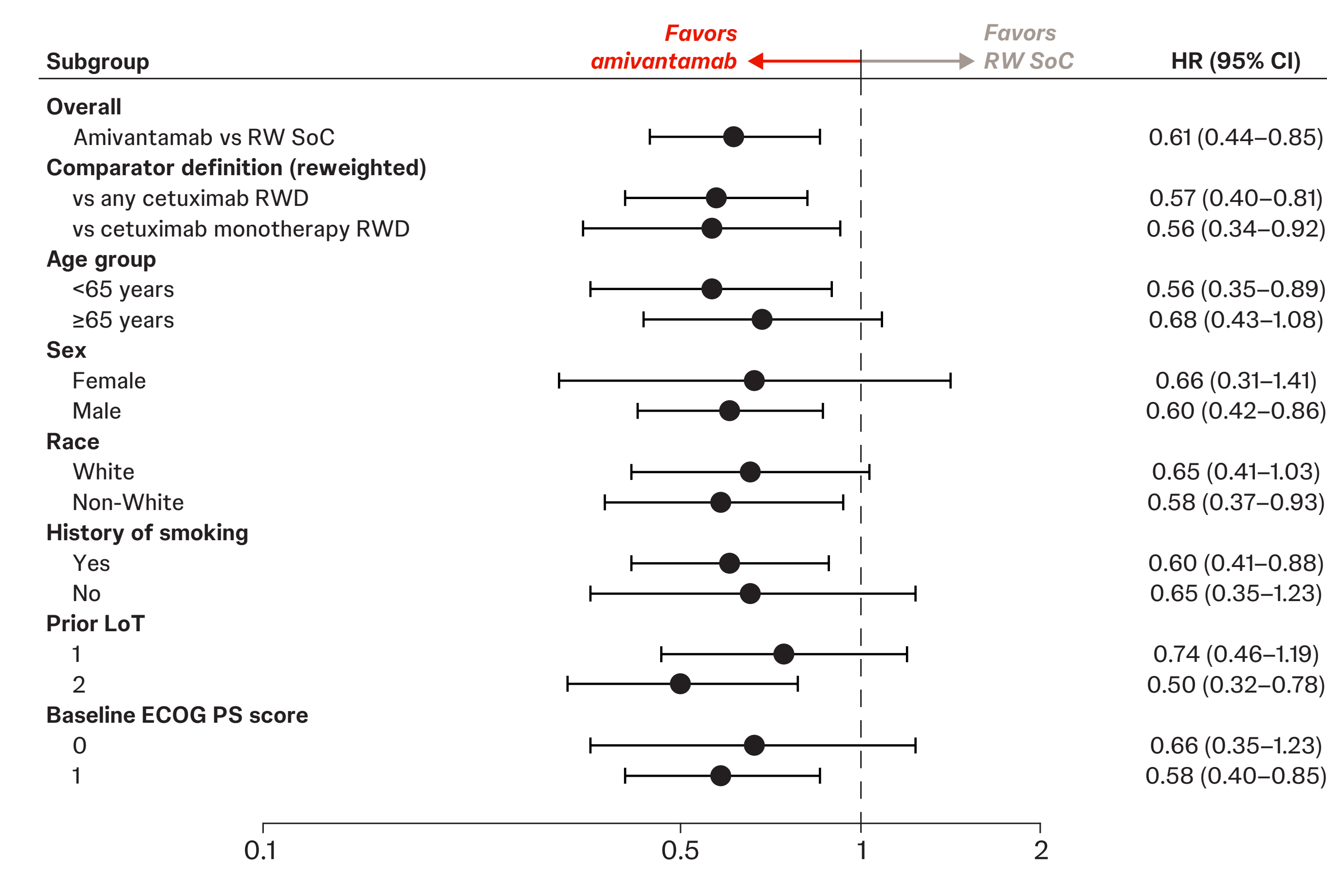
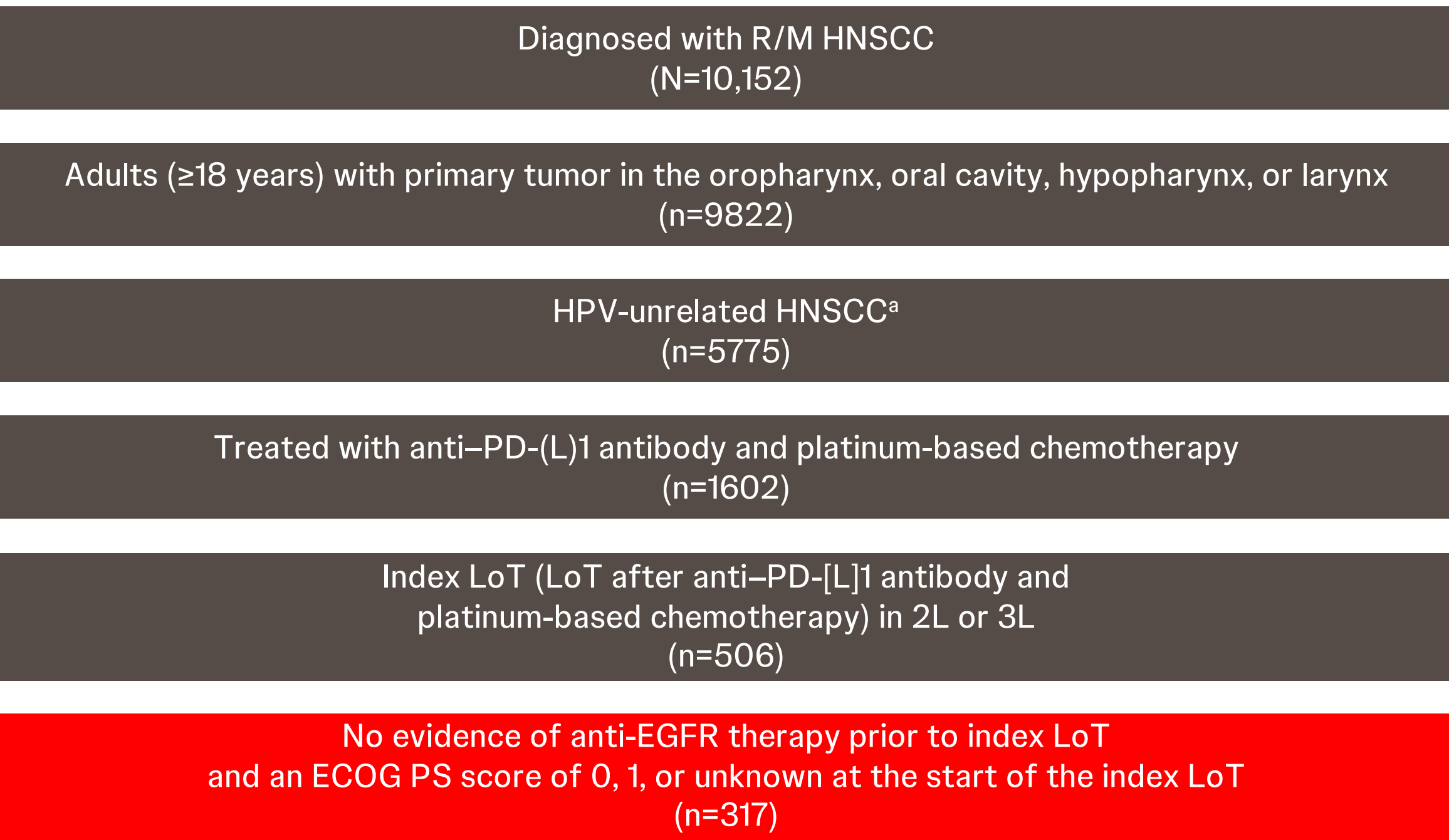


Figure 4: Subgroup analysis of OS



CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; LoT, line of therapy; OS, overall survival; RWD, real-world data; RW SoC, real-world standard of care.

Figure 1: Study population derivation



*Including oral cavity, hypopharynx, larynx, or p16-negative oropharynx primary tumors.
2L, second-line; 3L, third-line; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HNSCC, head & neck squamous cell carcinoma; HPV, human papillomavirus; LoT, line of therapy; PD–(L)1, programmed death–(ligand) 1; R/M, recurrent/metastatic.

Figure 5: PFS

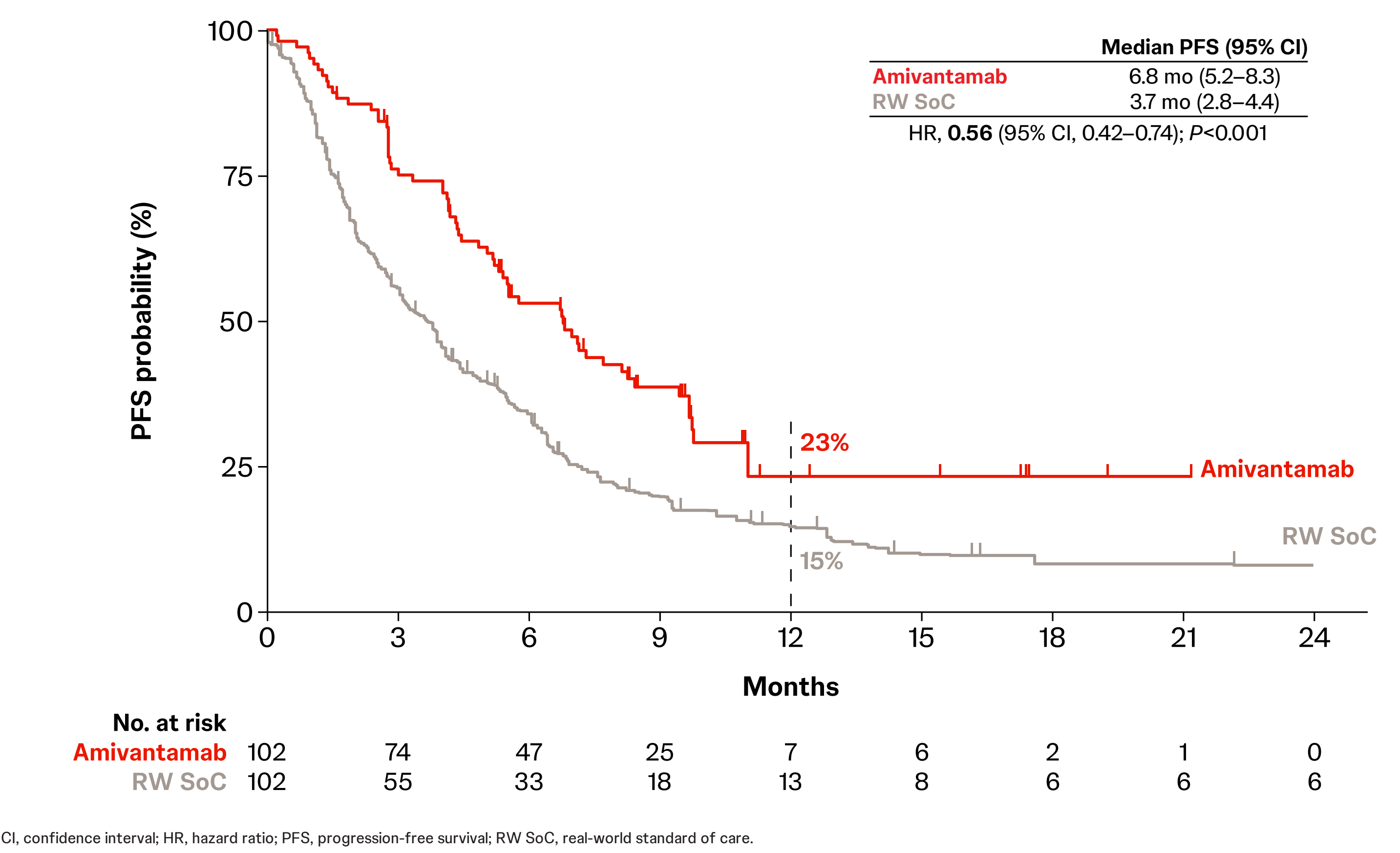


Figure 6: (A) TTD and (B) TTNT efficacy outcomes

