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Real-world treatment patterns and overall survival in recurrent/metastatic head and neck squamous cell carcinoma following treatment with immune checkpoint inhibitor and platinum-based chemotherapy

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Key Takeaway

Real-world overall survival (rwOS) is poor in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) following treatment with immune checkpoint inhibitor and platinum-based chemotherapy

Conclusions

Over 50% of patients with R/M HNSCC did not receive treatment after immune checkpoint inhibitor and platinum-based chemotherapy

Among patients with R/M HNSCC who were able to receive subsequent therapy following immune checkpoint inhibitor and platinum-based chemotherapy, rwOS was 7.8 months

Outcomes were worse for patients with HPV-unrelated R/M HNSCC (rwOS HR, 0.85; *P*=0.04)

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Introduction

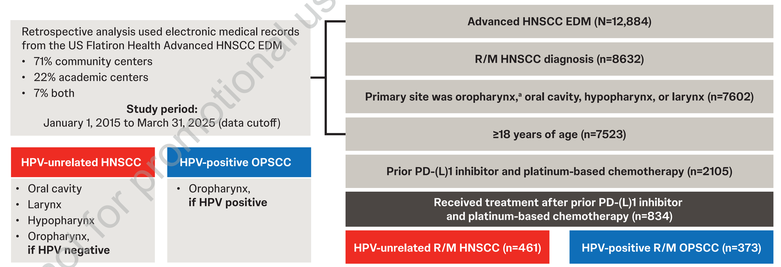
- Treatments for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) include immune checkpoint inhibitor (ICI) monotherapy, ICI + platinum-based chemotherapy, and cetuximab + platinum-based chemotherapy[1,2]
- Most patients will experience disease progression, with poor survival and limited therapeutic options in both first- and later-line settings[3–6]
  - Median overall survival (OS) with single-agent cetuximab after ICI and platinum-based chemotherapy was 8.6 months[6]
- Real-world evidence on treatment patterns and survival outcomes in R/M HNSCC after ICI and platinum-based chemotherapy is limited

We characterized real-world treatments and survival outcomes in patients with R/M HNSCC following treatment with ICI and platinum-based chemotherapy

Methods

- This retrospective analysis used electronic medical records from the US Flatiron Health Advanced Head and Neck Squamous Cell Carcinoma (HNSCC) EDM
- All identified patients had R/M HNSCC and had received prior programmed death-(ligand) 1 (PD-[L]1) inhibitor and platinum-based chemotherapy (**Figure 1**)
- Demographics, baseline disease characteristics, and treatment patterns were analyzed descriptively
- Kaplan-Meier method was used to evaluate real-world overall survival (rwOS), defined as time from index date (first date of treatment after PD-[L]1 inhibitor and platinum-based chemotherapy) until date of recorded death
- Human papillomavirus (HPV)–positive oropharyngeal squamous cell carcinoma (OPSCC) was evaluated separately, based on its better prognosis and differing disease biology relative to HPV-unrelated R/M HNSCC[2]

Figure 1: Real-world attrition



[a]Oropharynx tumors required an HPV test for inclusion.
HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; OPSCC, oropharyngeal squamous cell carcinoma; PD-(L)1, programmed death-(ligand) 1; R/M, recurrent/metastatic.

Results

Patients

- From January 2015 to March 2025, 2105 patients with R/M HNSCC were identified from the Flatiron database as previously treated with PD-(L)1 inhibitor and platinum-based chemotherapy (index line; **Figure 1**)
  - 1271 (60%) patients did not receive a subsequent line of therapy; among these, 875 (69%) patients died
  - 834 (40%) patients received a subsequent line of therapy after PD-(L)1 inhibitor and platinum-based chemotherapy and were eligible for analysis (2L+ R/M HNSCC population)

Demographic and baseline disease characteristics

- Subgroups were generally consistent with the overall patient population of R/M HNSCC (**Table 1**)
- Higher observed rates of HPV-positive OPSCC reflect enrichment for patients with more favorable prognosis who survive to receive subsequent lines of therapy, as evidenced by increasing HPV-positive proportions with greater lines of therapy in this longitudinal cohort (analysis not shown)
  - Notably, 18% of patients had an unknown HPV status

Table 1: Demographic and baseline disease characteristics

Characteristic, n (%)	All 2L+ R/M HNSCC (n=834)	2L+ HPV-unrelated R/M HNSCC[a] (n=461)	2L+ HPV-positive R/M OPSCC (n=373)
Median (range) age, years	66 (33–85)	66 (39–85)	66 (33–85)
Male / female	685 (82) / 149 (18)	332 (72) / 129 (28)	353 (95) / 20 (5)
Race			
White	587 (70)	313 (68)	274 (73)
Black or African American	47 (6)	33 (7)	14 (4)
Asian	13 (2)	12 (3)	1 (<1)
Other	107 (13)	59 (13)	48 (13)
Not reported	80 (10)	44 (10)	36 (10)
Smoking status			
History of smoking	609 (73)	382 (83)	227 (61)
No history of smoking	225 (27)	79 (17)	146 (39)
Primary tumor site			
Oropharynx	459 (55)	86 (19)	373 (100)
Larynx	171 (21)	171 (37)	0
Oral cavity	152 (18)	152 (33)	0
Hypopharynx	52 (6)	52 (11)	0
HPV status			
HPV positive	373 (45)	0	373 (100)
HPV negative	309 (37)	309 (67)	0
Unknown	152 (18)	152 (33)	0
ECOG PS score			
0	217 (26)	107 (23)	110 (29)
1	427 (51)	232 (50)	195 (52)
2+	143 (17)	94 (20)	49 (13)
Unknown	47 (6)	28 (6)	19 (5)
No. of prior lines in the R/M setting			
1	295 (35)	163 (35)	132 (35)
2	411 (49)	232 (50)	179 (48)
3+	128 (15)	66 (14)	62 (17)
Locoregional recurrence	288 (35)	212 (46)	76 (20)
Median (range) time from R/M diagnosis to start of index line therapy, days	398 (45–3520)	363 (45–3520)	437 (56–3320)

[a]Included HPV-negative OPSCC and primary tumors of the hypopharynx, larynx, and oral cavity irrespective of HPV status.
2L+, second line or later; ECOG PS, Eastern Cooperative Oncology Group performance status; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; OPSCC, oropharyngeal squamous cell carcinoma; R/M, recurrent/metastatic.

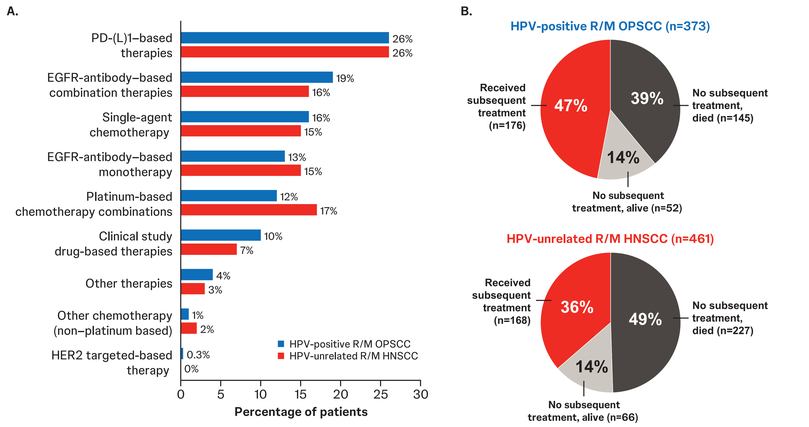
Treatment patterns

- Most common regimens in the index line of therapy included (**Figure 2A**):
  - PD-(L)1–based therapies (26%)
  - Anti-epidermal growth factor receptor (EGFR)–based therapies (31%)
    - Combination therapies (17%)
    - Monotherapy (14%)
- Few patients were treated in a clinical trial (≤10%)
- Among patients who received an index line of therapy (**Figure 2B**):
  - 39% with HPV-positive R/M OPSCC died prior to receiving another line of therapy
  - 49% with HPV-unrelated R/M HNSCC died prior to receiving another line of therapy

Real-world overall survival

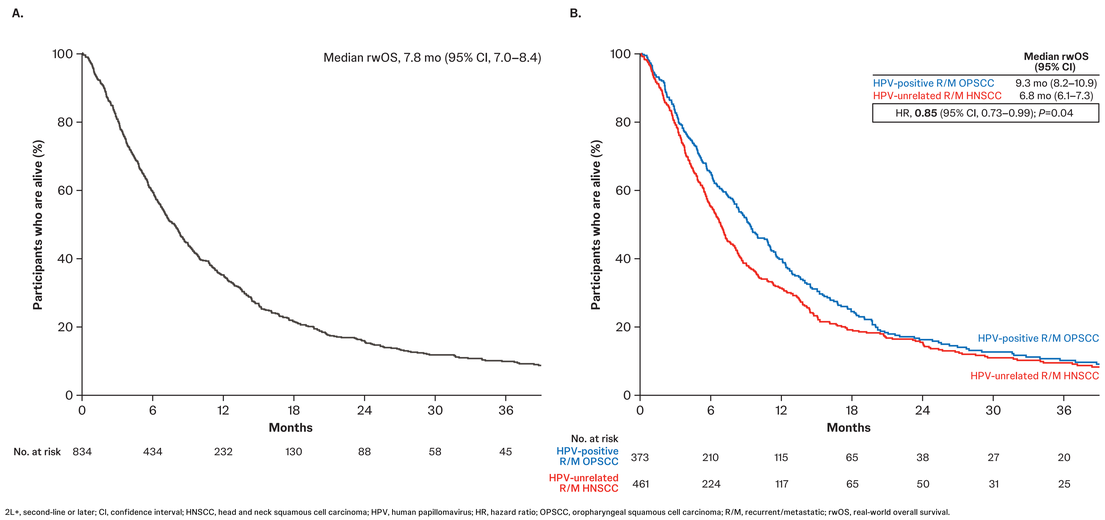
- Among the total 2L+ R/M HNSCC population, rwOS was only 7.8 months (95% CI, 7.0–8.4; **Figure 3A**)
- Median rwOS was significantly longer for HPV-positive R/M OPSCC versus HPV-unrelated R/M HNSCC (HR, 0.85; 95% CI, 0.73–0.99; *P*=0.04; **Figure 3B**)

Figure 2: Treatment patterns including (A) index line of therapy[a] and (B) subsequent therapy



Note: some values may not sum to 100% due to rounding. [a]First line of therapy after PD-(L)1 inhibitor and platinum-based chemotherapy.
HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; OPSCC, oropharyngeal squamous cell carcinoma; PD-(L)1, programmed death-(ligand) 1; R/M, recurrent/metastatic.

Figure 3: rwOS in the (A) overall 2L+ R/M HNSCC population and (B) by subgroup



2L+, second-line or later; CI, confidence interval; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; HR, hazard ratio; OPSCC, oropharyngeal squamous cell carcinoma; R/M, recurrent/metastatic; rwOS, real-world overall survival.

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