

In Reference to *Primary site surgical resection in cM1 oral cavity squamous cell carcinoma*

Dear Editor,

We applaud Patel and colleagues for their study investigating the impact of primary site surgical resection on overall survival (OS) in patients diagnosed with clinically distant metastatic (cM1) oral cavity squamous cell carcinoma (OCSCC).¹ The study included 278 patients: 139 (50.0%), 80 (28.8%), 25 (9.0%), and 34 (12.2%) treated with chemotherapy (CT), chemoradiotherapy (CRT), surgical resection + adjuvant chemotherapy (S-CT), and surgical resection + adjuvant chemoradiotherapy (S-CRT), respectively. Respective 5-year OS rates were 9.4%, 15.2%, 8.3%, and 23.8% ($p < .001$), indicating that surgical resection was beneficial only when combined with CRT. While the present study provides valuable insights into the treatment outcomes of cM1 OCSCC patients, addressing two critical concerns would ensure a more comprehensive understanding of Patel and colleagues' findings.¹

First, the study findings indicated that despite a high incidence of positive surgical margins (a significant adverse prognostic factor) S-CRT was linked to significantly improved OS rates compared to the alternative strategies of CT, CRT, and S-CT. Nevertheless, the 5-year OS rates of 9.4% for CT and 8.3% S-CT groups are nearly equivalent and substantially inferior to the 15.2% observed in the CRT group, suggesting that the principal factor influencing outcomes is the incorporation of radiotherapy with CT, namely definitive CRT.² Although the authors provide no comparative patient and disease characteristics for all four treatment regimens, the notably superior outcomes achieved in the CRT groups were most likely despite the accumulation of unfavorable prognostic variables in these groups, as can be anticipated from tab. 1 of the original manuscript.¹ For example, therapy in a nonacademic center, high-grade histology, T3-4 tumors, N1-3 disease, and pathologic extra-nodal extension all disadvantage the non-surgical groups.


And second, S-CRT resulted in the best 5-year OS rates (23.8%) even when compared to CRT (15.2%). However, it remains uncertain whether the two cohorts possessed comparable tumor and patient characteristics, including comorbidities that could serve as competing risk factors for mortality, mainly since OS is the designated primary endpoint rather than disease-specific survival.³ However, more precise comparative data are needed for definitive conclusions because selection biases favoring surgical groups are a common finding in

retrospective studies. Due to the common occurrence of selection biases favoring surgical studies in retrospective studies.⁴ Therefore, to prevent highly toxic and futile therapies, we recommend using propensity score matching methods to balance the confounding variables between groups until the results of well-designed, large-scale, randomized clinical trial data become available.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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