



Neoadjuvant Immunotherapy for Oral Cavity Squamous Cell Carcinoma (OCSCC)

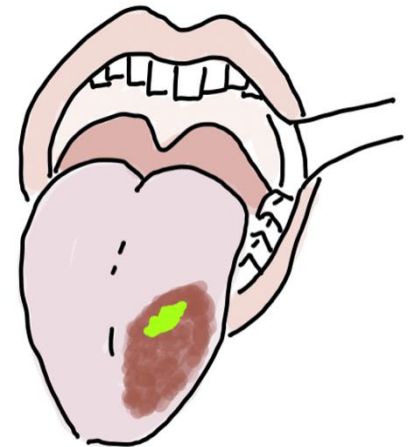
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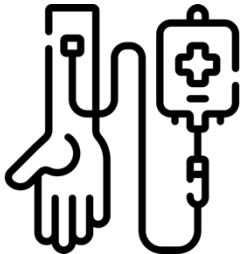
Poor Outcomes of OCSCC



- 5-year mortality $\sim 50\%$ ^{1,2}



- Delayed diagnosis: asymptomatic or benign-appearing lesions^{3,4}
- Often presents at late stage with early regional metastases^{1,5}
- Recurrence: 20-32%^{6,7}

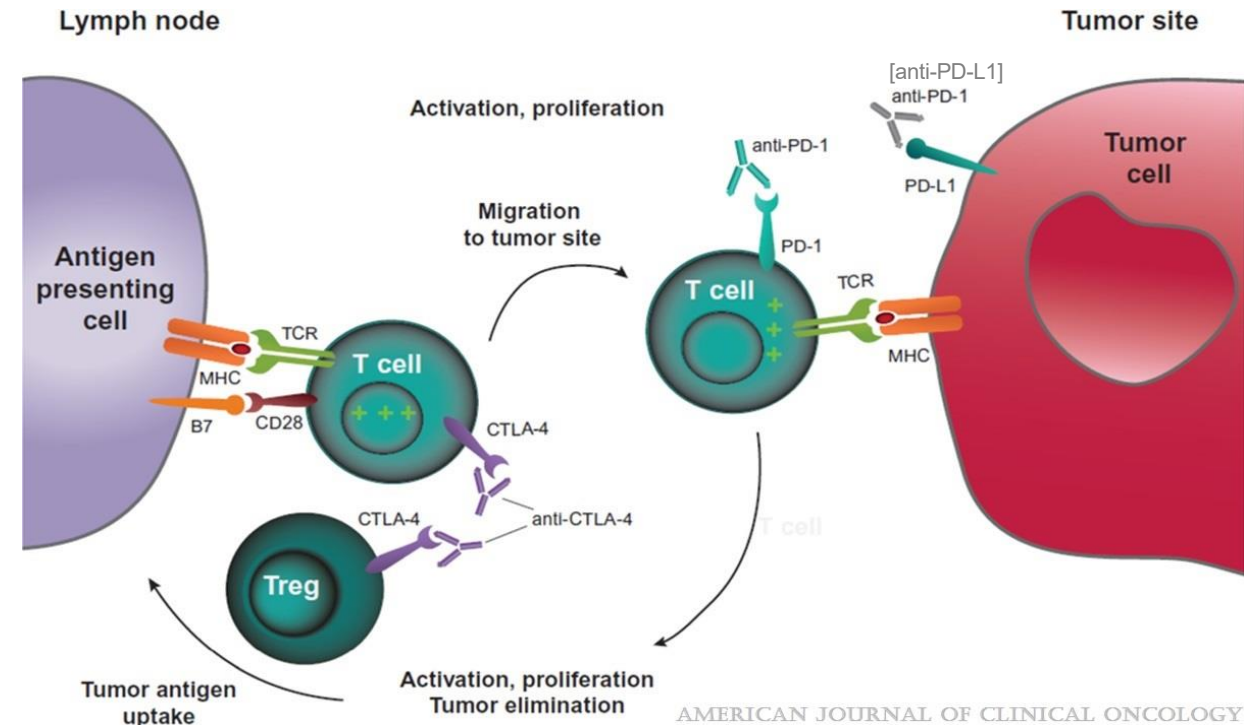


- Need for novel treatment beyond surgery, radiation, and chemotherapy.⁸





Immune Checkpoint Inhibitors (ICIs)

	CTLA-4i	PD-1i [PD-L1i]
Examples	Ipilimumab (Yervoy)	Pembrolizumab (Keytruda) Nivolumab (Opdivo) Toripalimab (Loqtorzi) [Durvalumab (Imfinzi)]
Timing	Early	Late
Mechanism	-> T-cell priming - Treg-cells	Restores antitumor T cells from quiescence
Primary Location ⁹	Lymph nodes	Peripheral tissue (Tumor)



Buchbinder EI, Desai A. CTLA-4 and PD-1 Pathways: Similarities, Differences, and Implications of Their Inhibition. *Am J Clin Oncol*. 2016;39(1):98-106.
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Neoadjuvant immunoradiotherapy results in high rate of complete pathological response and clinical to pathological downstaging in locally advanced head and neck squamous cell carcinoma

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CLINICAL TRIALS: IMMUNOTHERAPY | MAY 15 2024

A Phase II Open-Label Randomized Clinical Trial of Preoperative Durvalumab or Durvalumab plus Tremelimumab in Resectable Head and Neck Squamous Cell Carcinoma

Chang Gon Kim ¹; Min Hee Hong ¹; Dahee Kim ¹; Brian Hyohyoung Lee ¹; Hyunwook Kim ¹; Chan-Young Ock ¹; Geoffrey Kelly ¹; Yoon Ji Bang ¹; Gamin Kim ¹; Jung Eun Lee ¹; Chaeyeon Kim ¹; Se-Heon Kim ¹; Hyun Jun Hong ¹; Young Min Park ¹; Nam Suk Sim ¹; Heejung Park ¹; Jin Woo Park ¹; Chang Geol Lee ¹; Kyung Hwan Kim ¹; Goeun Park ¹; Inkyung Jung ¹; Dawoon Han ¹; Jong Hoon Kim ¹; Junha Cha ¹; Insuk Lee ¹; Mingu Kang ¹; Heon Song ¹; Chiyeon Oum ¹; Seulki Kim ¹; Sukjun Kim ¹; Yoojoo Lim ¹; Seunghee Kim-Schulze ¹; Miriam Merad ¹; Sun Ock Yoon ¹; Hyun Je Kim ¹; Yoon Woo Koh ¹; Hye Ryun Kim ¹

Neoadjuvant immunochemotherapy for locally advanced resectable oral squamous cell carcinoma: a prospective single-arm trial (Illuminate Trial)

Yingying Huang, PhD, MD^a, Jingjing Sun, MD^b, Jun Li, MD^a, Dongwang Zhu, PhD, MD^a, Minjun Dong, MD^c, Shengjin Dou, MD^a, Yong Tang, MD^d, Wentao Shi, MD^a, Qi Sun, MD^c, Tongchao Zhao, PhD, MD^a, Zhihang Zhou, PhD, MD^a, Xinyu Zhou, MD^a, Ying Liu, PhD, MD^a, Jiang Li, PhD, MD^b, Guopei Zhu, PhD, MD^a, Ding Zhang, MD¹, Yanan Chen, MD¹, Qi Zhu, PhD, MD^{a,d,*}, Wutong Ju, PhD, MD^{a,*}, Laiping Zhong, PhD, MD^{a,d,g,h,i,*}

CLINICAL TRIALS: IMMUNOTHERAPY | OCTOBER 01 2020

Neoadjuvant and Adjuvant Pembrolizumab in Resectable Locally Advanced, Human Papillomavirus–Unrelated Head and Neck Cancer: A Multicenter, Phase II Trial

Ravindra Uppaluri ¹; Katie M. Campbell ¹; Ann Marie Egloff; Paul Zolkind; Zachary L. Skidmore ¹; Brian Nussenbaum ¹; Randal C. Paniello ¹; Jason T. Rich; Ryan Jackson; Patrik Pipkorn ¹; Loren S. Michel; Jessica Ley; Peter Oppelt; Gavin P. Dunn; Erica K. Barnell ¹; Nicholas C. Spies; Tianxiang Lin; Tiantian Li; David T. Mulder; Youstina Hanna; Iulia Cirian ¹; Trevor J. Pugh ¹; Tenny Mudianto; Rachel Riley; Liye Zhou; Vickie Y. Jo; Matthew D. Stachler; Glenn J. Hanna; Jason Kass; Robert Haddad; Jonathan D. Schoenfeld ¹; Evisa Gjini ¹; Ana Lako; Wade Thorstad; Hiram A. Gay; Mackenzie Daly; Scott J. Rodig; Ian S. Hagemann ¹; Dorina Kallogjeri; Jay F. Piccirillo ¹; Rebecca D. Chernock; Malachi Griffith ¹; Obi L. Griffith ¹; Douglas R. Adkins

JAMA Oncology | **Original Investigation**

Neoadjuvant Nivolumab or Nivolumab Plus Ipilimumab in Untreated Oral Cavity Squamous Cell Carcinoma A Phase 2 Open-Label Randomized Clinical Trial

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Neoadjuvant Immunotherapy (NI) for OCSCC

- Early trial data show:
 - Safety¹⁰⁻¹³
 - Favorable pathologic response and tumor downstaging in neoadjuvant and other settings^{8,14-17}
 - No overall survival data for NI (but improved in metastatic and recurrent)¹⁸⁻²⁰
- Current NI findings limited by small samples or lack of long-term follow-up



Hypothesis

Neoadjuvant immunotherapy improves overall survival without worsening postoperative outcomes after non-metastatic OCSCC definitive resection.





Methods



Cohort

- Adults from National Cancer Database (NCDB)
- Curative-intent OCSCC surgery with neck dissection without prior radiation or distant metastases

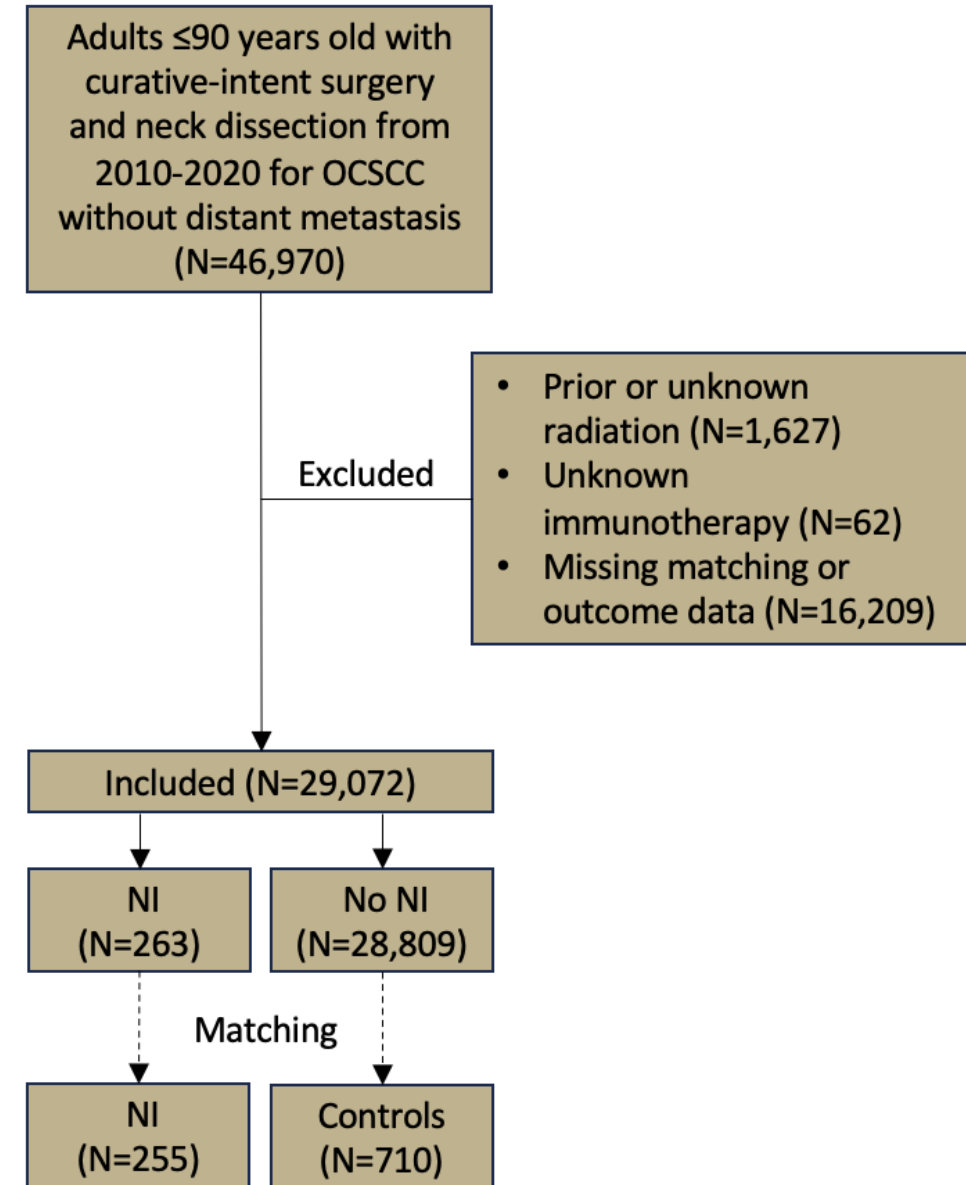
Analysis

- 1:3 matched patient cohorts (NI vs no NI)
- Chi-square / Wilcoxon rank-sum tests for demographics and postoperative outcomes by NI
- Kaplan-Meier and Cox proportional-hazards analyses



Outcomes

- Postoperative:
 - 30-day mortality
 - Unplanned 30-day readmission
 - Length of stay (LOS)
 - Positive surgical margins
 - Days to post-op radiation
- Overall survival (OS)

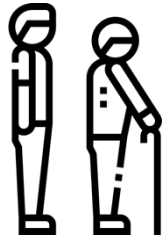




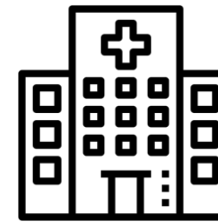
NI Patient Characteristics

Total cohort: 29,072; NI: 263 (0.9%)

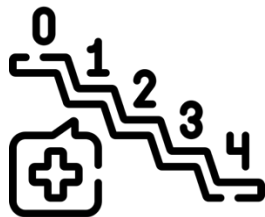
Compared to no NI, patients with NI were more likely to be:



Younger (62 yrs vs 64 yrs, $p < .001$)

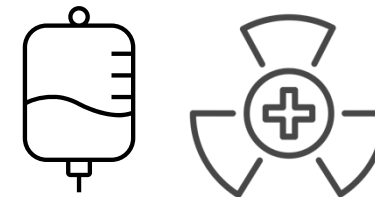


At academic centers (93.2% vs 73.2%, $p < .001$)
with top quartile case volume (67.7% vs 40.0%, $p < .001$)



More advanced stage

- cT4 (56.7% vs 27.3%, $p < .001$)
- cN2–3 (51.0% vs 20.8%, $p < .001$)



Administered neoadjuvant chemo (30.0% vs 1.1%, $p < .001$)
and post-op radiation (74.5% vs 47.8%, $p < .001$)



Postoperative Outcomes

- No significant outcome differences between NI and no NI

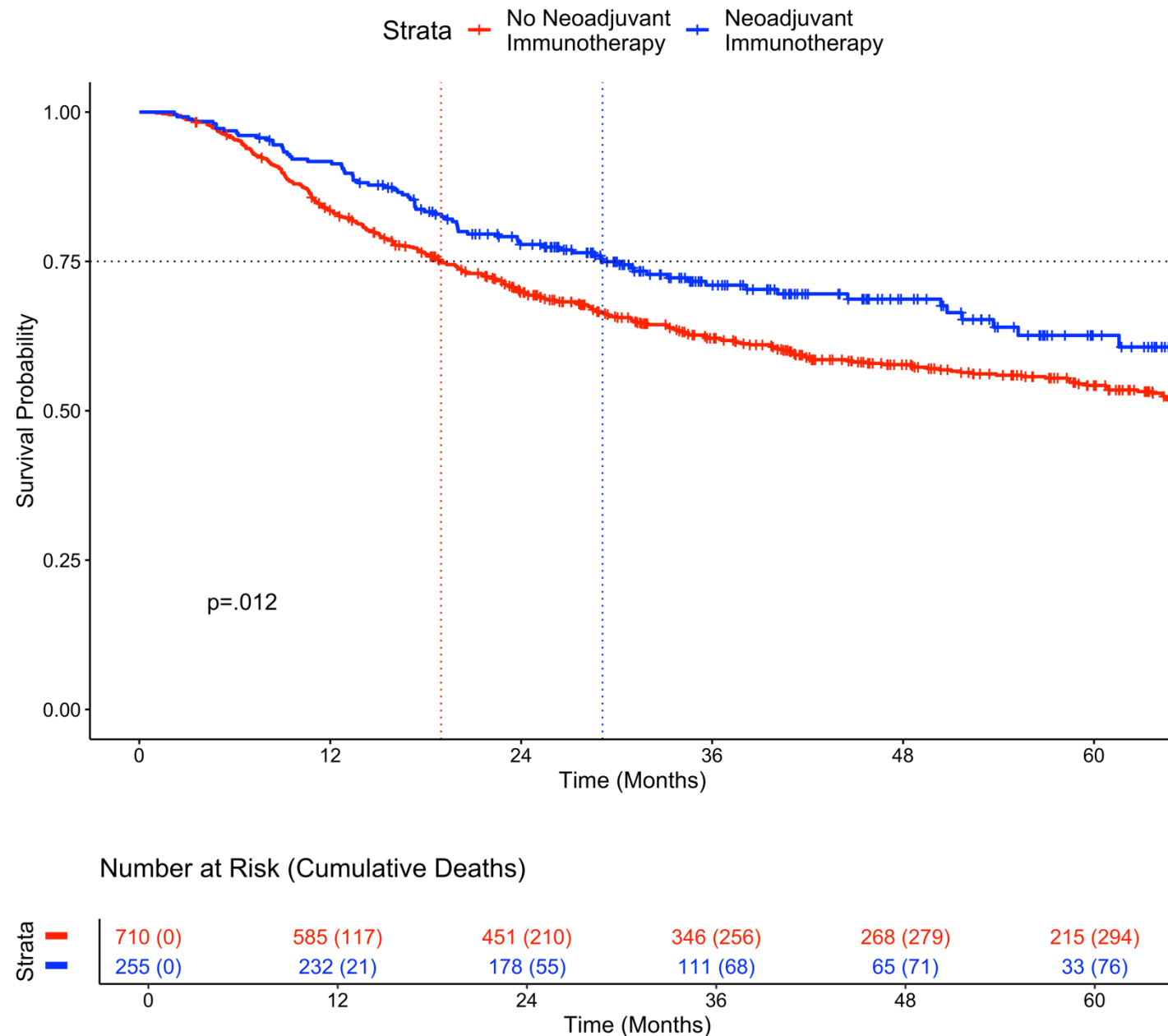
Outcome	NI (N=255)	No NI (N=710)	P Value
30-Day Mortality	3 (1.2%)	6 (0.8%)	.705
Unplanned 30-Day Readmission	11 (4.3%)	38 (5.4%)	.517
Hospital LOS (days), median [IQR]	8 [6-11]	8 [6-12]	.994
Positive Margin	27 (10.6%)	103 (14.5%)	.116
Days from Surgery to Postoperative Radiation, median [IQR]	49 [42-61]	52 [42-62]	.296

IQR: Interquartile range



Overall Survival

- NI was associated with improved OS.
- 5-year expected OS probability
 - NI: 60.0%
 - No NI: 55.8%
- Number needed to treat = 24





Cox Proportional Hazards

- NI was independently associated with improved OS.
- Covariates associated with
 - Improved OS:
 - Adjuvant chemo
 - Worse OS:
 - Higher clinical N stage
 - Neoadjuvant chemo
 - Post-op radiation

Variable	Hazard Ratio (95% Confidence Interval)	P Value
Age	1.01 (1.00-1.02)	.113
Female Sex (vs Male)	0.94 (0.77-1.16)	.585
Race (vs White)		
Black	1.18 (0.76-1.86)	.462
Other	0.88 (0.48-1.62)	.689
Insurance		
Private/Managed Care	0.78 (0.45-1.33)	.356
Medicaid	1.31 (0.72-2.37)	.374
Medicare/Other Government	1.15 (0.65-2.02)	.629
Research/Academic Facility	0.98 (0.67-1.43)	.918
Top Quartile Facility Case Volume	1.18 (0.93-1.49)	.162
Charlson-Deyo Comorbidity Index (vs 0)		
1	1.2 (0.94-1.54)	.149
2+	1.35 (0.98-1.84)	.064
Clinical T Stage (vs cT1)		
cT2	0.81 (0.46-1.41)	.456
cT3	1.04 (0.58-1.85)	.901
cT4	1.19 (0.70-2.02)	.516
Clinical N Stage (vs cN0)		
cN1	1.22 (0.89-1.66)	.212
cN2-cN3	1.64 (1.30-2.09)	<.001
Neoadjuvant Immunotherapy	0.66 (0.51-0.84)	.001
Neoadjuvant Chemotherapy	1.44 (1.12-1.85)	.005
Adjuvant Chemotherapy	0.66 (0.51-0.84)	.001
Postoperative Radiation	1.34 (1.04-1.72)	.021



Discussion / Conclusion



- **Limitations**

- Retrospective
- Lack of specific adverse event data in NCDB
- Potential clinical trial enrollment bias



- NI patients were more often
 - Younger
 - At high-volume academic centers
 - Higher-stage
 - Administered neoadjuvant chemo and post-op radiation



- NI was associated with improved OS.
 - No increase in surgical risk
- Though not yet standard of care, the OS benefit of NI may facilitate more effective individualized cancer care.



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Thank you!

Questions?

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