



# Neoadjuvant Immunotherapy for Oral Cavity Squamous Cell Carcinoma (OCSCC)

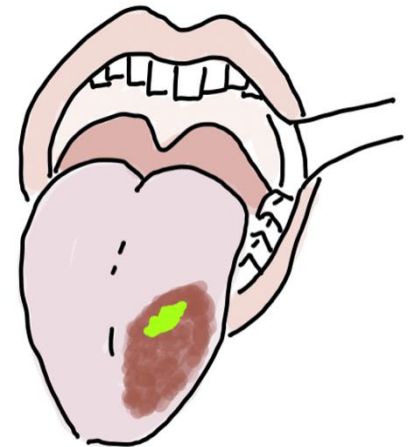
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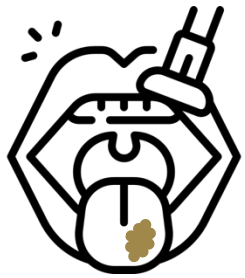




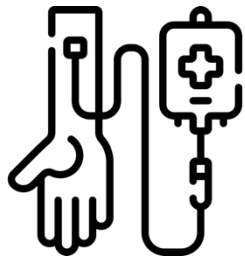
# Poor Outcomes of OCSCC



- 5-year mortality ~50%<sup>1,2</sup>



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





- Need for novel treatment beyond surgery, radiation, and chemotherapy.<sup>8</sup>

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AMERICAN JOURNAL OF CLINICAL ONCOLOGY

## Neoadjuvant immunoradiotherapy results in high rate of complete pathological response and clinical to pathological downstaging in locally advanced head and neck squamous cell carcinoma

Rom Leidner <sup>1,2</sup> Marka Crittenden,<sup>1,2,3</sup> Kristina Young,<sup>1,2,3</sup> Hong Xiao,<sup>4</sup> Yaping Wu,<sup>4</sup> Marcus A Couey,<sup>1</sup> Ashish A Patel,<sup>1,5</sup> Allen C Cheng,<sup>5</sup> Amber L Watters,<sup>1</sup> Carlo Bifulco,<sup>1,2,4</sup> George Morris,<sup>2</sup> Lessli Rushforth,<sup>2</sup> Shorin Nemeth,<sup>1</sup> Walter J Urba,<sup>1,2</sup> Michael Gough <sup>1,2</sup> R Bryan Bell <sup>1,2</sup>

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

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

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

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

Jonathan D. Schoenfeld, MD, MPH; Glenn J. Hanna, MD; Vickie Y. Jo, MD; Bhupendra Rawal, MS; Yu-Hui Chen, MS; Paul S. Catalano, ScD; Ana Lako, PhD; Zoe Ciantra, BS; Jason L. Weirather, PhD; Shana Criscitiello, BA; Adrienne Luoma, PhD; Nicole Chau, MD; Jochen Lorch, MD, MS; Jason I. Kass, MD, PhD; Donald Annino, MD, DMD; Laura Goguen, MD; Anupam Desai, MD; Brendan Ross, BS; Hina J. Shah, MD; Heather A. Jacene, MD; Danielle N. Margalit, MD, MPH; Roy B. Tishler, MD, PhD; Kai W. Wucherpfennig, MD, PhD; Scott J. Rodig, MD, PhD; Ravindra Uppaluri, MD, PhD; Robert I. Haddad, MD

## Neoadjuvant Immunotherapy (NI) for OCSCC

- Early trial data show:
  - Safety<sup>10-13</sup>
  - Favorable pathologic response and tumor downstaging in neoadjuvant and other settings<sup>8,14-17</sup>
  - No overall survival data for NI (but improved in metastatic and recurrent)<sup>18-20</sup>
- Results 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

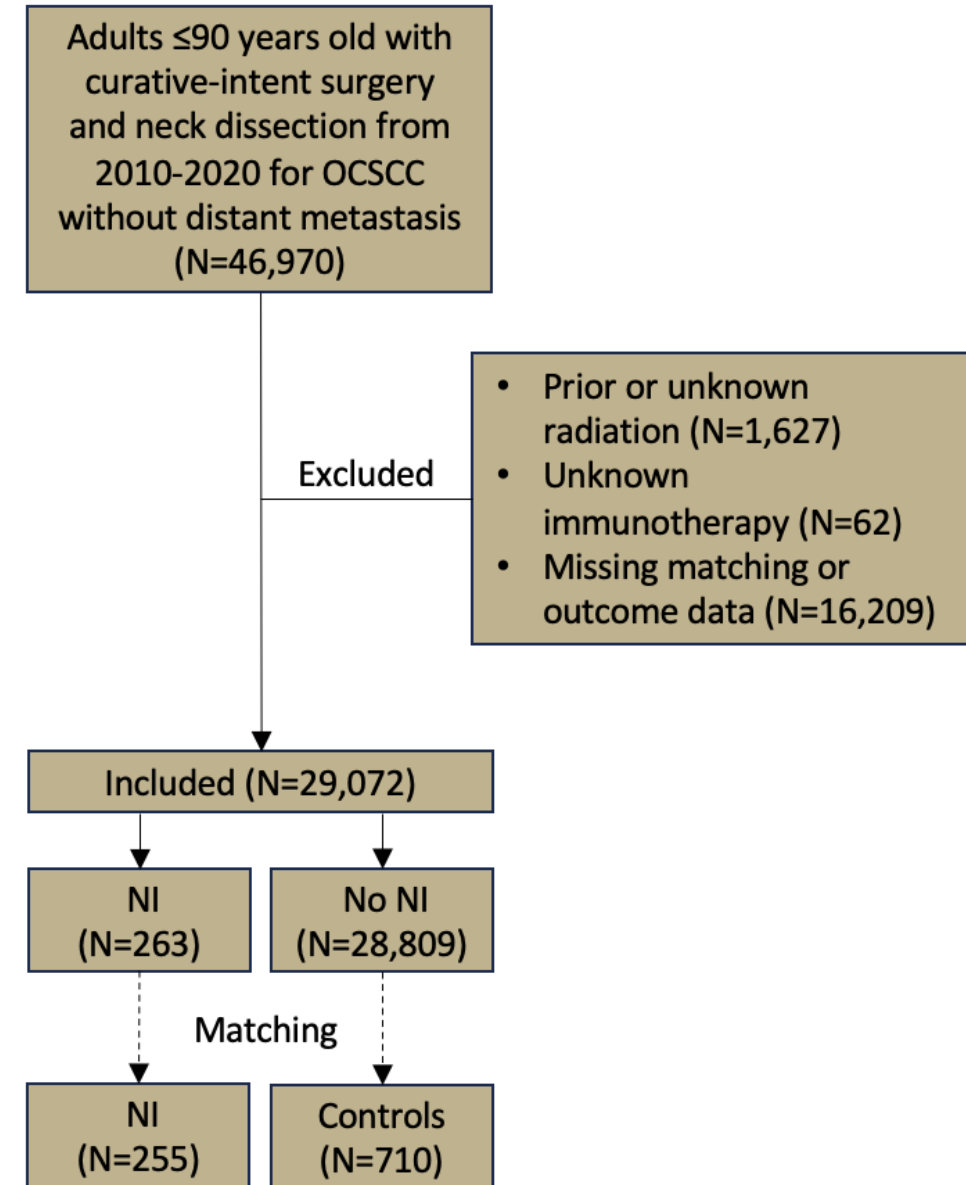
## Analysis

- 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)

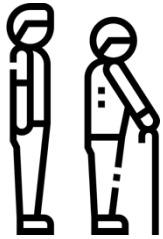




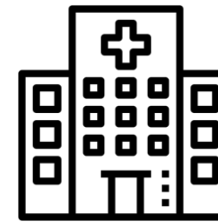
# NI Patient Characteristics

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

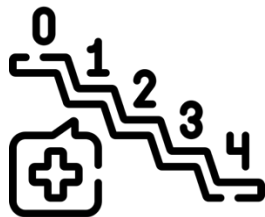
Compared to no NI, patients with NI were more likely to be:



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

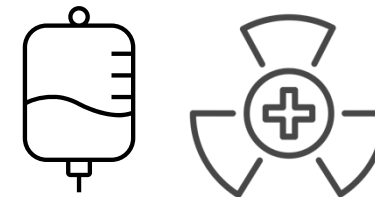


At academic centers (93.2% vs 73.2%,  $p < .001$ )  
with top quartile case volume (67.7% vs 40.0%,  $p < .001$ )



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

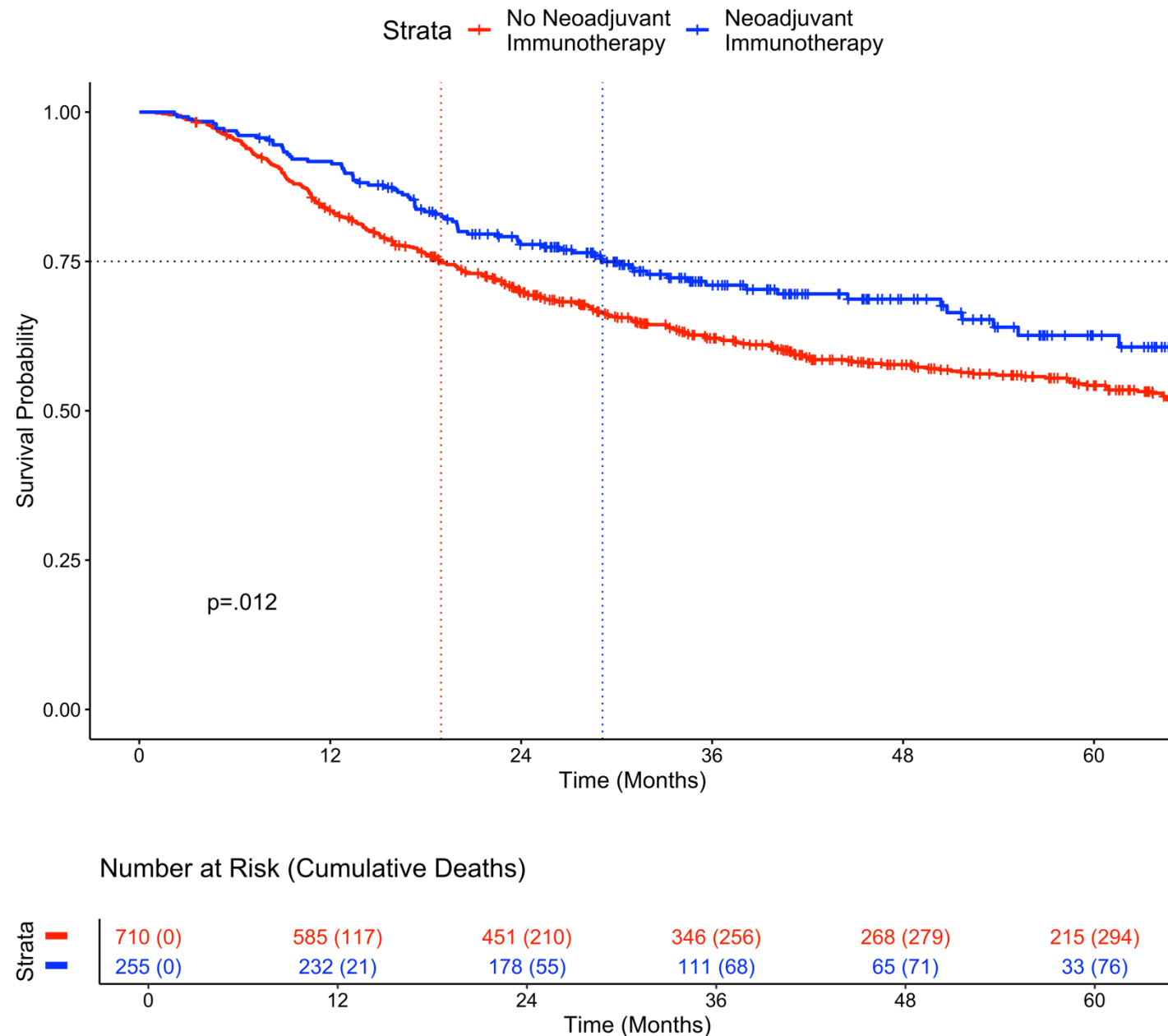
IQR: Interquartile range





# Overall Survival

- NI was associated with improved OS.
- 5-year expected OS:
  - 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
<b>cN2-cN3</b>	<b>1.64 (1.30-2.09)</b>	<b>&lt;.001</b>
<b>Neoadjuvant Immunotherapy</b>	<b>0.66 (0.51-0.84)</b>	<b>.001</b>
<b>Neoadjuvant Chemotherapy</b>	<b>1.44 (1.12-1.85)</b>	<b>.005</b>
<b>Adjuvant Chemotherapy</b>	<b>0.66 (0.51-0.84)</b>	<b>.001</b>
<b>Postoperative Radiation</b>	<b>1.34 (1.04-1.72)</b>	<b>.021</b>



# Discussion / Conclusion



- **Limitations**

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



- **NI patients were**

- Younger
- Higher-stage
- More often 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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**COSM Poster**

