SCHOOL OF MEDICINE
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Neoadjuvant Immunotherapy for Oral Cavity Squamous Cell Carcinoma (OCSCC)

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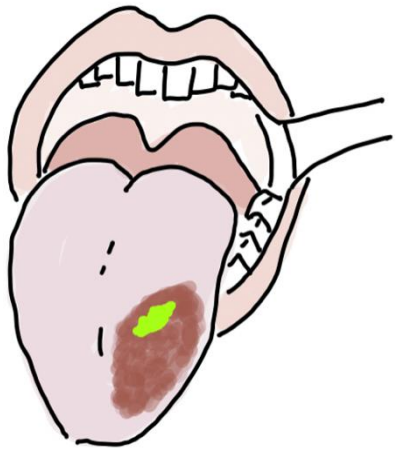

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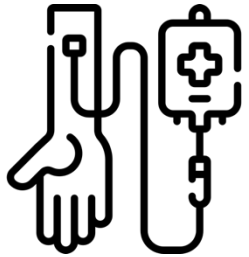
Poor Outcomes of OCSCC

- 5-year mortality ~50%[1,2]

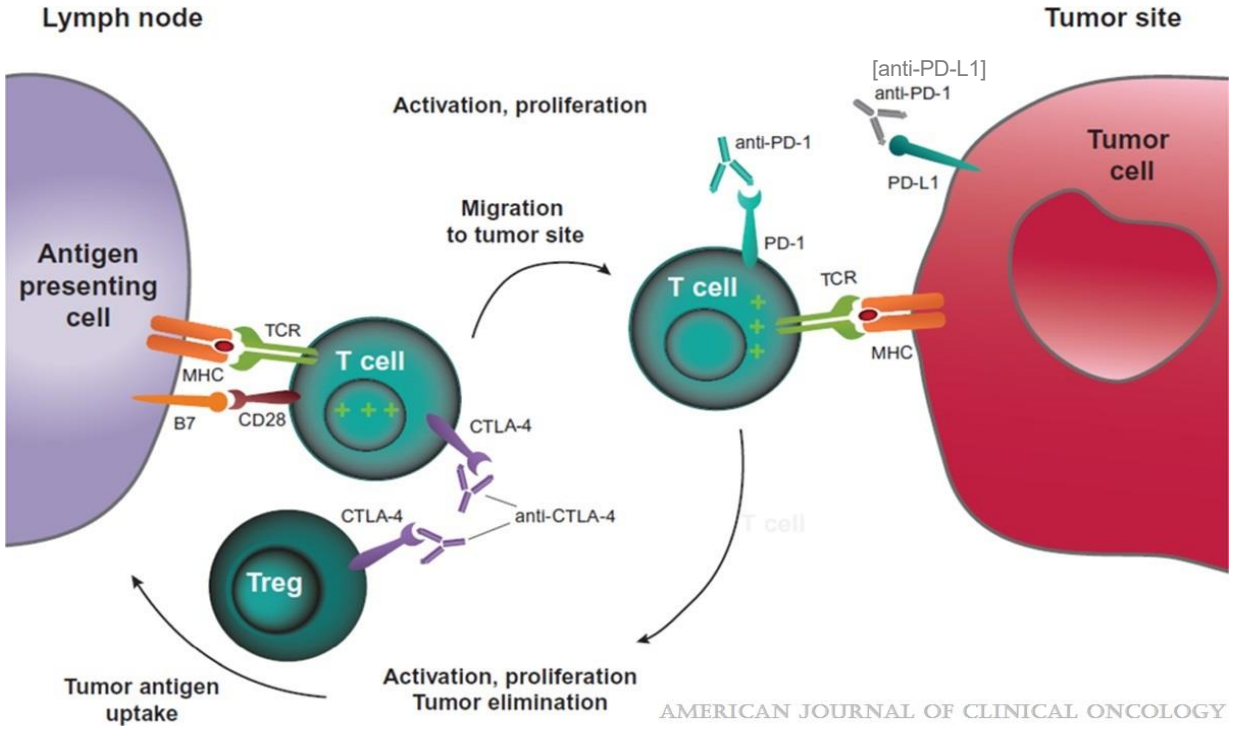
- Delayed diagnosis: asymptomatic or benign-appearing lesions[3,4]
- Often presents at late stage with early regional metastases[1,5]
- Recurrence: 20-32%[6,7]



- 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)



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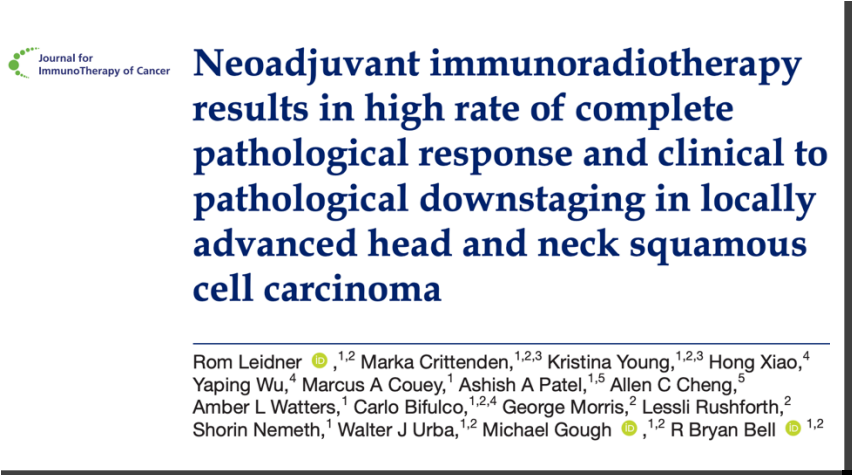
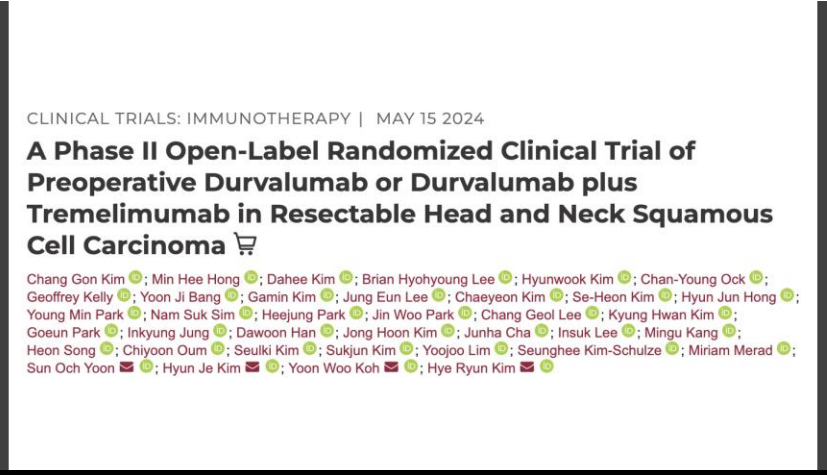
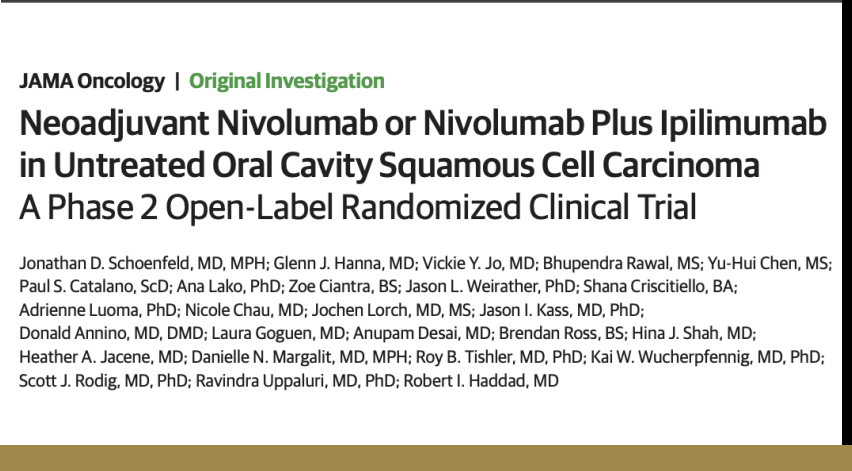






Neoadjuvant Immunotherapy (NI) for OCSCC

- Early trial data show:
  - Safety[10-13]
  - 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]
- 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

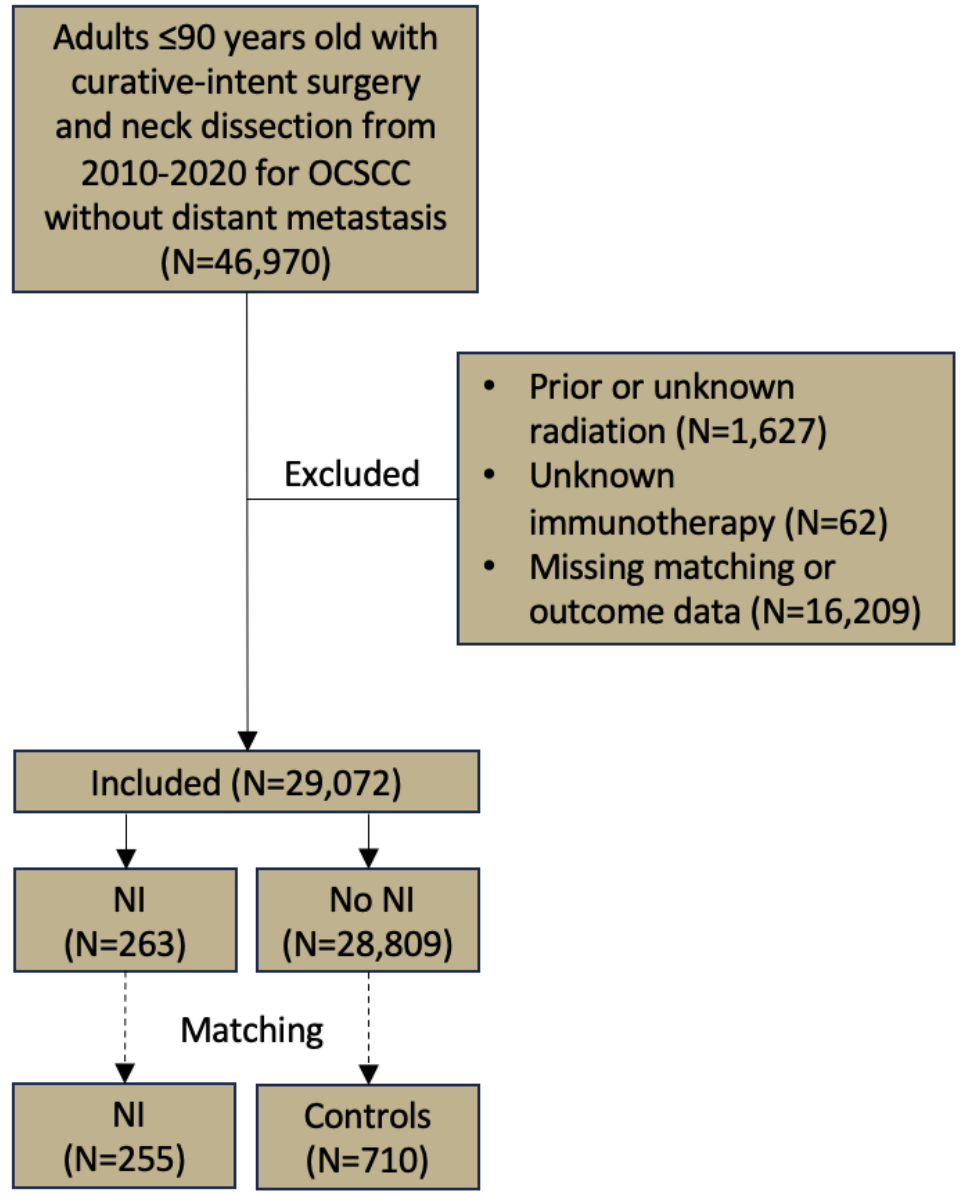
- Adults from National Cancer Database (NCDB)
- Curative-intent OCSCC surgery with neck dissection without prior radiation or distant metastases

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

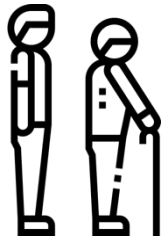
- Postoperative:
  - 30-day mortality
  - Unplanned 30-day readmission
  - Length of stay (LOS)
  - Positive surgical margins
  - Days to post-op radiation
- Overall survival (OS)



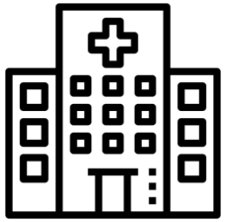
NI Patient Characteristics

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

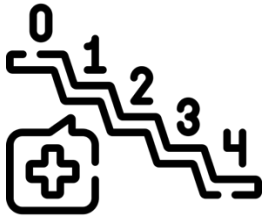
Compared to no NI, patients with NI were more likely to be:



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

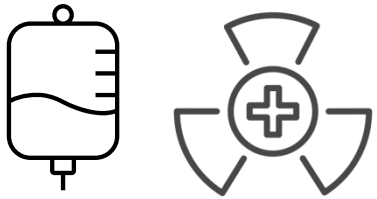


At academic centers (93.2% vs 73.2%, p<.001)
with top quartile case volume (67.7% vs 40.0%, p<.001)



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

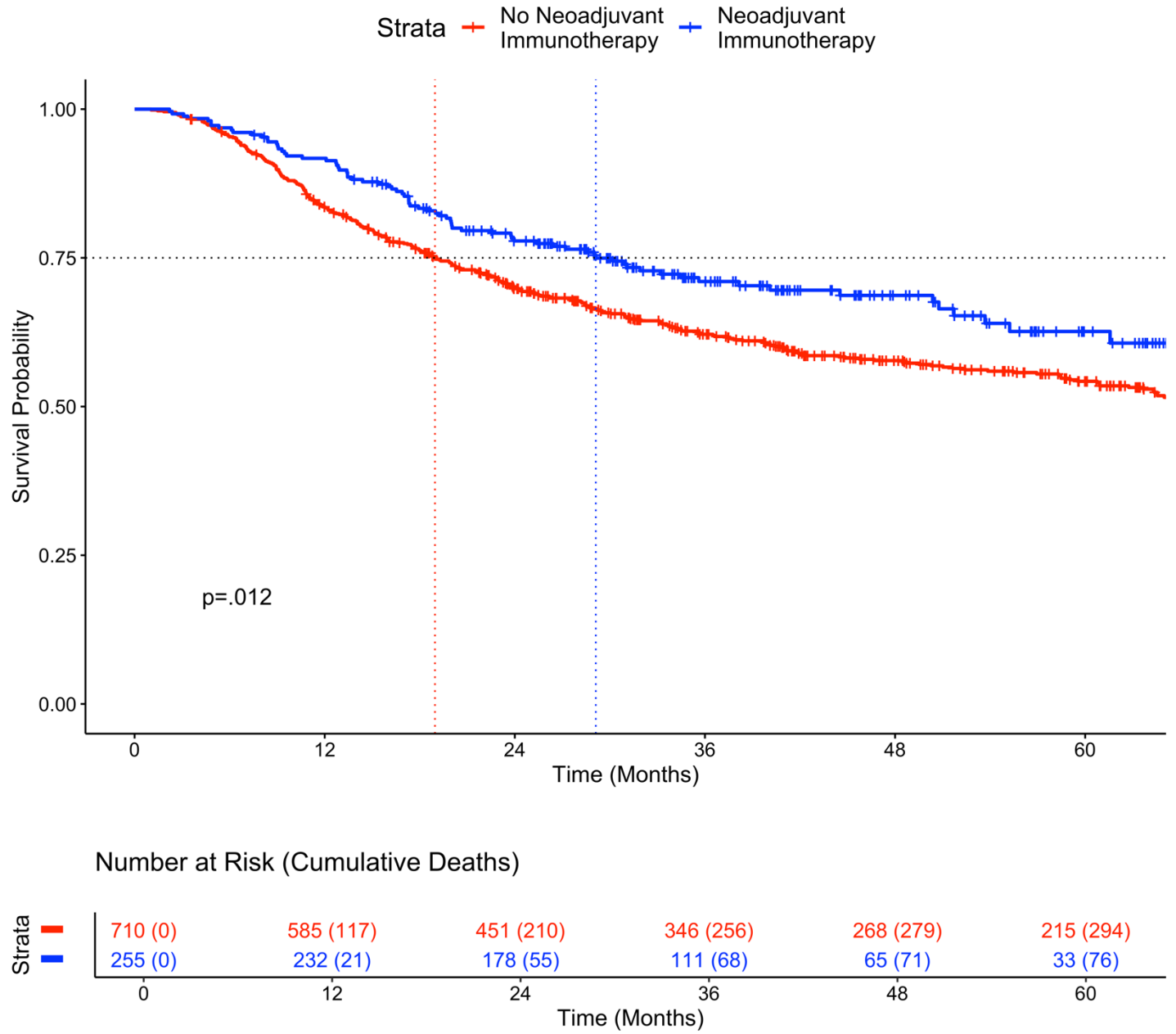
- No significant outcome differences between NI and no NI

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
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
  - 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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