

# Adjuvant Chemotherapy Does Not Improve Overall Survival in Positive Surgical Margin Oral Cavity Cancer Patients Without Extranodal Extension

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## Introduction

- National Comprehensive Cancer Network Guidelines recommend adjuvant chemoradiotherapy (CRT) for oral cavity squamous cell carcinoma (OCSCC) patients with positive margins and/or extranodal extension (ENE) based on two landmark clinical trials: EORTC 22931<sup>1</sup> and RTOG 95-01<sup>2</sup>.
- However, both trials included only a small minority of patients with positive margins and no ENE.
- Objective:** Determine if postoperative CRT is associated with an overall survival (OS) difference compared to radiotherapy (RT) alone in patients with stage III-IV OCSCC with positive margins, with and without ENE.

## Methods

- Population:** National Cancer Database (NCDB) OCSCC surgery patients
- Statistical Analysis:**
  - 3:1 and 1:1 propensity matching of patients by CRT with and without ENE, respectively
  - Kaplan-Meier survival analyses
  - Cox proportional-hazards analyses
- Covariates:**
  - Age
  - Charlson-Deyo Comorbidity Index
  - Pathologic T/N stage
  - Lymphovascular invasion (LVI)
- Primary Outcome:** OS

Adults ≤90 years old with curative-intent open surgery and neck dissection from 2018-2021 for Stage III-IV OCSCC with positive margins without distant metastasis (N=1,909)

Excluded

- Unknown ENE (N=588)
- Prior radiation (N=39)
- No postoperative radiotherapy (N=355)
- Unknown AC (N=17)
- Neoadjuvant chemotherapy (N=6)
- LVI unknown (N=44)
- Unknown OS (N=226)

Included (N=634)

ENE (N=369)

No ENE (N=265)

CRT (N=309)

RT Alone (N=60)

CRT (N=146)

RT Alone (N=119)

CRT (N=130)

RT Alone (N=52)

CRT (N=96)

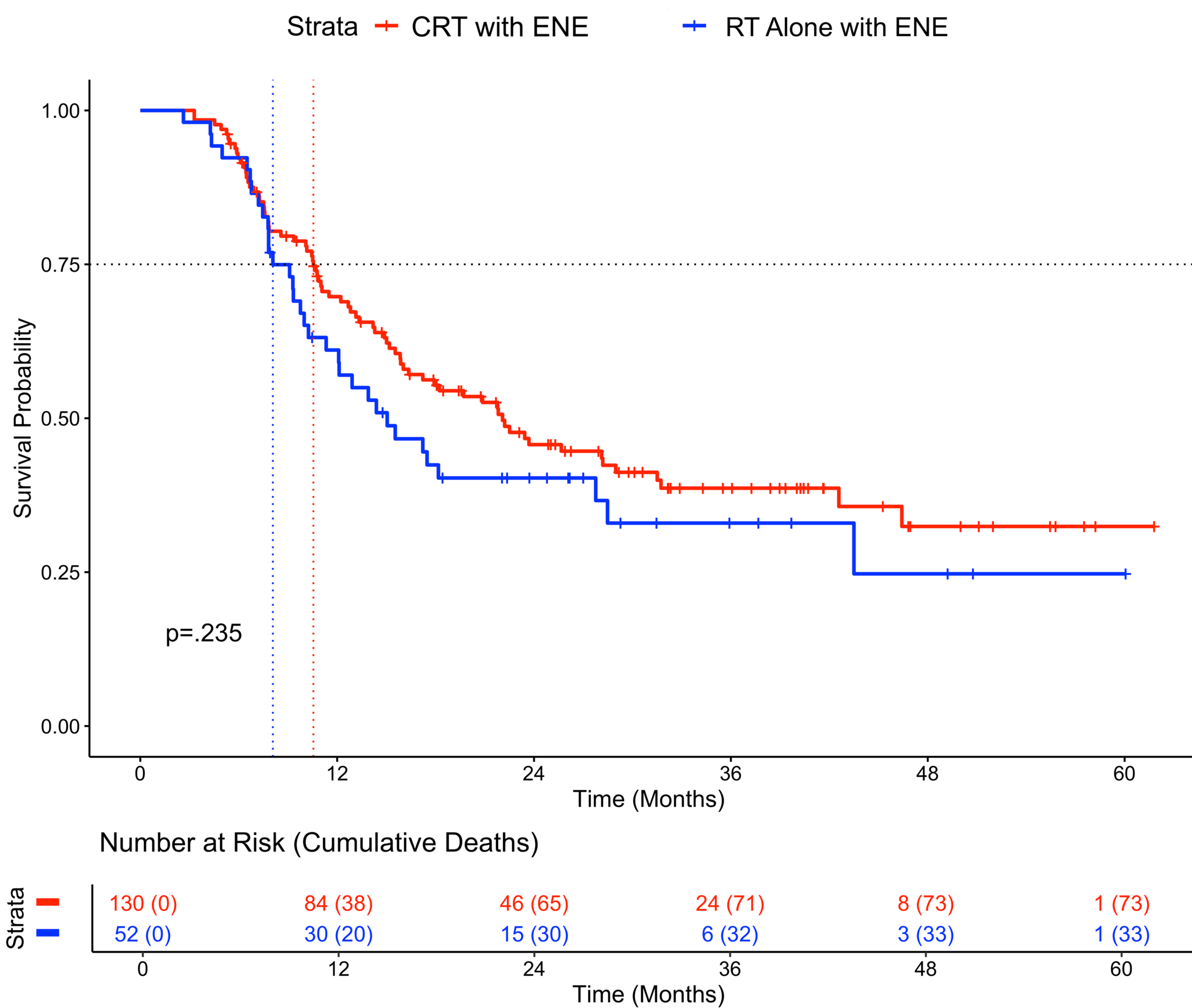
RT Alone (N=96)

3:1 Matching

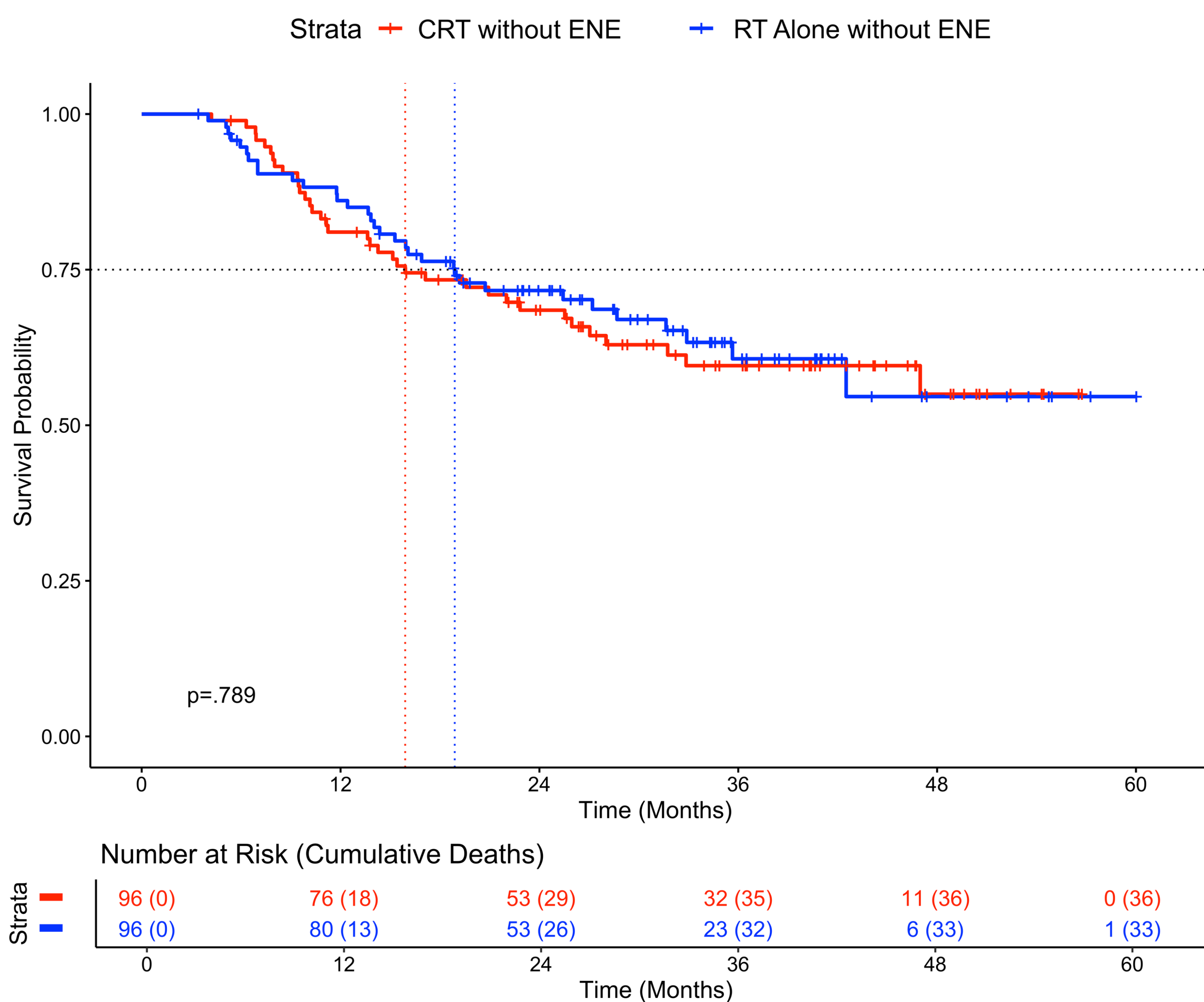
1:1 Matching

## Results

**Figure 1. Kaplan-Meier Survival Analysis by Postoperative Therapy with and without Extranodal Extension**



For OCSCC with ENE, CRT exhibited a non-significant trend toward improved OS on Kaplan-Meier analysis.



For OCSCC without ENE, CRT was not associated with improved OS on Kaplan-Meier analysis.

**Table 2. Multivariable Cox Proportional-Hazards Analysis Results with and without Extranodal Extension**

	OCSCC with ENE	HR	95% CI	P Value	OCSCC without ENE	HR	95% CI	P Value
Age		1.02	1.00-1.04	.079	Age	1.01	0.99-1.03	.339
Any Comorbidity		0.99	0.65-1.51	.955	Any Comorbidity	1.18	0.72-1.94	.500
pT3-pT4 (vs pT1-pT2)		1.52	0.85-2.74	.160	pT3-pT4 (vs pT1-pT2)	1.60	0.83-3.06	.159
<b>pN3 (vs pN1-pN2)</b>		<b>2.13</b>	<b>1.19-3.81</b>	<b>.011</b>	pN3 (vs pN0-pN2)	2.98	0.90-9.83	.073
LVI		1.28	0.85-1.94	.234	<b>LVI</b>	<b>1.76</b>	<b>1.09-2.84</b>	<b>.022</b>
CRT (vs RT Alone)		0.79	0.52-1.21	.280	CRT (vs RT Alone)	1.03	0.64-1.66	.903

CRT was not independently associated with improved OS after controlling for matching variables.

## Discussion / Conclusion

- Limitations:** Missing NCDB pathologic data and small sample with ENE treated with RT alone
- Postoperative CRT (vs RT alone) for positive margin OCSCC without ENE exhibited no OS difference.
- For OCSCC patients without ENE, potential benefits of CRT may not outweigh increased toxicity.

## References

- Bernier J, Domenge C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med.* 2004;350(19):1945-1952.
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