

# Real-World Cancer Recurrence and Overall Survival Outcomes in Muscle-Invasive Bladder Cancer (MIBC) Patients Treated With Radical Cystectomy (RC): A Retrospective Surveillance, Epidemiology, and End Results-Medicare Study

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## Introduction

- For patients with muscle-invasive bladder cancer (MIBC), radical cystectomy (RC) with pelvic lymph node dissection (PLND) remains the standard treatment<sup>1</sup>
  - However, despite RC, many patients experience disease recurrence due to micrometastases present at the time of resection<sup>2</sup>
- Limited real-world data exist on cancer recurrence and overall survival (OS) in radically resected MIBC, especially by disease stage or treatment received

## Objectives

- To evaluate treatment patterns, disease recurrence, and OS in patients with MIBC treated with RC in the United States

## Methods

### Study design

- This retrospective, observational study used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database (2007–2020)
- The index date was the date of RC for the overall analyses and for subgroups defined by stage and treatment
- The index date was 30 days before the date of recurrence for the recurrence subgroup, and the index date was selected and assigned based on the beta distribution of time between RC and recurrence for patients without recurrence
- The baseline period was the 12 months before the index date, and the follow-up period was the time from the index date until the earliest of end of data availability, end of Medicare coverage, or death

### Study population

- Eligible patients with MIBC were age ≥65 years, had RC with or without PLND, and had continuous enrollment in Medicare Parts A, B, and D for ≥12 months prior to and ≥1 month after index. Patients with prior partial cystectomy, radiation therapy, or other cancers and patients with secondary malignancies prior to or within 60 days of RC were excluded
- Patients were analyzed overall, by disease stage, by treatment received, and by recurrence:
  - Stratifications by stage at diagnosis of MIBC: 1) T2N0M0, 2) T3-T4N0M0, and 3) T1-T4N1M0
  - Stratifications by treatment received: 1) neoadjuvant therapy (NAD) only, 2) adjuvant therapy (AD) only, 3) both NAD and AD, and 4) surgery alone (ie, received neither NAD nor AD)
  - Stratifications by recurrence after RC: 1) recurrence, defined as first diagnosis for metastatic disease, initiation of radiation therapy ≥180 days after the end of primary treatment episode, and/or systemic treatments for advanced bladder cancer after RC, and 2) no recurrence

### Study outcomes

- Treatment patterns, summarized over time from 2007–2009, 2010–2012, 2013–2015, 2016–2018, and 2019–2020 in the overall population
- Time to recurrence was summarized in the overall population and by stage and treatment cohorts and was defined as time from index date to recurrence
- OS was described in all populations and was defined as time from index date to death due to any cause

### Statistical analyses

- Continuous variables were summarized using means and standard deviations (SDs); categorical variables were summarized using frequency counts and percentages
- Time to event analyses were conducted using the Kaplan-Meier method, with the median time to event and associated 95% confidence intervals (CIs) reported
- OS was compared between patients with and without recurrence using Cox proportional hazards models adjusting for key baseline characteristics

## Results

### Patient characteristics

- 1,149 patients, with a median follow-up of 2.6 years, were included in the overall radically resected MIBC study population
  - 692 (60.2%) had T2N0M0, 364 (31.7%) had T3-T4N0M0, and 93 (8.1%) had T1-T4N1M0 disease
  - When stratified by treatment, 390 (33.9%) had NAD only, 117 (10.2%) had AD only, 26 (2.3%) had both NAD and AD, and 616 (53.6%) received surgery alone
  - The recurrence analysis included 1,105 patients, with 503 (45.5%) in the recurrence cohort and 602 (54.5%) in the non-recurrence cohort
- Patient demographic and clinical characteristics are summarized in **Table 1** for the overall population

### References

- Kaczmarek K. *Cancers (Basel)*. 2023.
- Stein JP. *J Clin Oncol*. 2001.

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### Acknowledgement and disclaimer

The collection of cancer incidence data used in this study was supported by the California Department of Public Health pursuant to California Health and Safety Code Section 103885; Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries, under cooperative agreement 1NU58DP007156; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN2612018000321 awarded to the University of California, San Francisco, contract HHSN2612018000151 awarded to the University of Southern California, and contract HHSN2612018000091 awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the author(s) and do not necessarily reflect the opinions of the State of California, Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors.

Table 1. Demographic and clinical characteristics of patients with MIBC treated with RC

	Overall N=1,149
<b>Demographic characteristics</b>	
Age at RC (years), mean ± SD	74.2 ± 5.7
Time from MIBC diagnosis to RC (months), mean ± SD	3.6 ± 2.4
Male, n (%)	859 (74.8)
White race, n (%)	989 (86.1)
Year of RC, n (%)	
2007 - 2011	383 (33.3)
2012 - 2016	502 (43.7)
2017 - 2020	264 (23.0)
<b>Clinical characteristics at MIBC diagnosis</b>	
TNM stage, <sup>1</sup> n (%)	
T2N0M0	692 (60.2)
T3-T4N0M0	364 (31.7)
T1-T4N1M0	93 (8.1)
Histology type, n (%)	
Urothelial carcinoma	702 (61.1)
Papillary urothelial carcinoma	409 (35.6)
Spindle cell carcinoma	28 (2.4)
Tumor size (mm) <sup>2</sup> , mean ± SD	41.4 ± 21.8
<b>Comorbidities during baseline period</b>	
CCI, mean ± SD	1.6 ± 1.6
Comorbidities, n (%)	
Hypertension	946 (82.3)
Chronic pulmonary disease	428 (37.2)
Peripheral vascular disease	370 (32.2)
Renal disease	275 (23.9)
Diabetes without chronic complication	263 (22.9)
Cerebrovascular disease	222 (19.3)
Congestive heart failure	200 (17.4)
Liver disease, mild	199 (17.3)
Myocardial infarction	158 (13.8)
Diabetes with chronic complication	148 (12.9)
Any proxy for cisplatin contraindications <sup>3</sup> , n (%)	505 (44.0)
Cardiac disease	292 (25.4)
Renal insufficiency	205 (17.8)
Sensorineural hearing loss	78 (6.8)
Peripheral neuropathy	76 (6.6)

CCI, Charlson Comorbidity Index; MIBC, muscle-invasive bladder cancer, RC: radical cystectomy, SD: standard deviation.

<sup>1</sup>171 patients with stage 2 disease had incomplete TNM information and were assumed to have T2N0M0 disease.

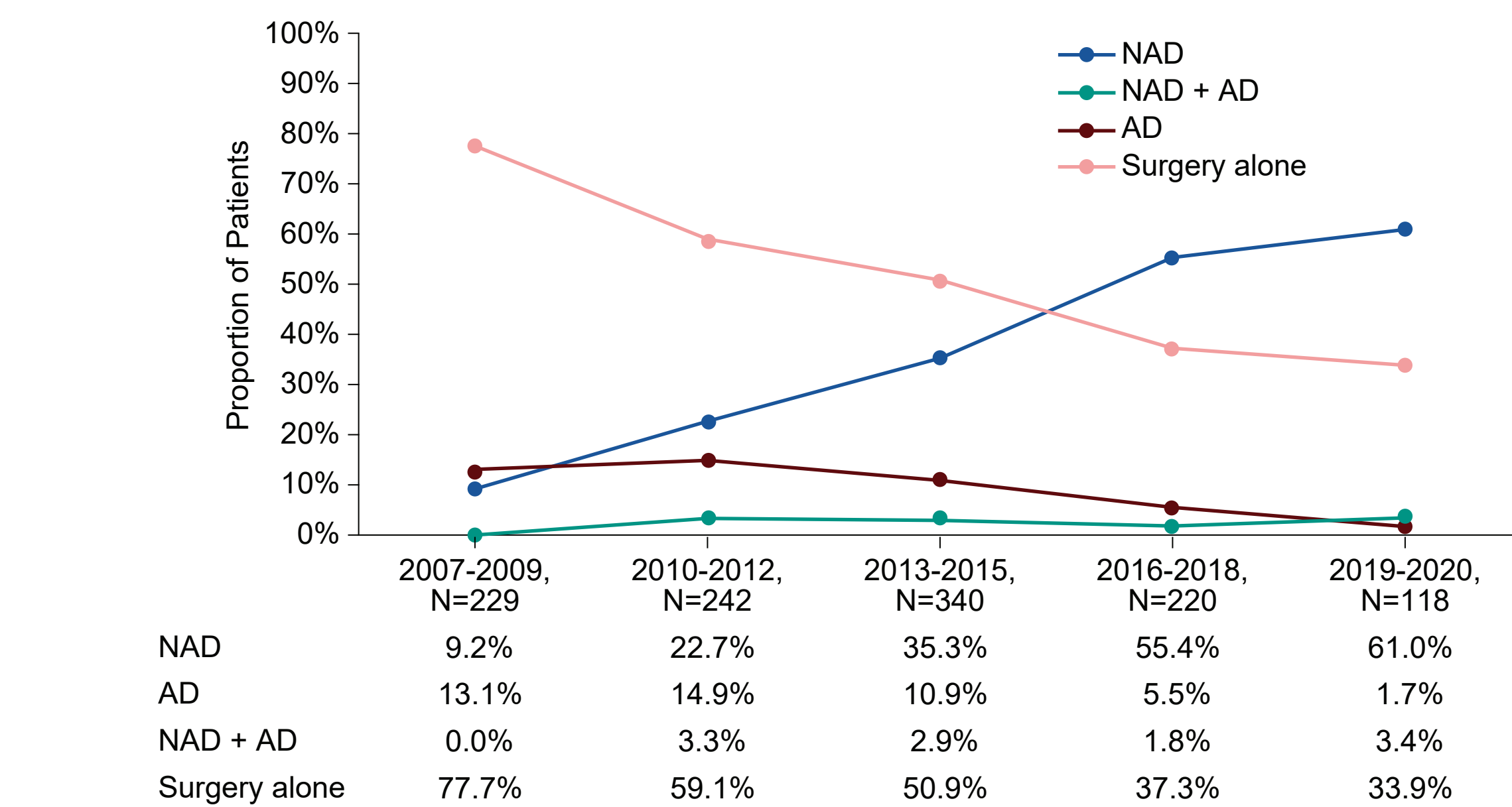
<sup>2</sup>Tumor size was summarized among 855 patients with complete information on tumor size.

<sup>3</sup>Specific conditions listed under cisplatin contraindications are further described in Nyame YA, Holt SK, Diamantopoulos LN, et al. Social and clinical correlates of neoadjuvant chemotherapy in medicare beneficiaries with muscle invasive bladder cancer from 2004-2015. *Urology*. 2021;149:154-160. doi:10.1016/j.urology.2020.12.020

### Treatment patterns

- Over time, the proportion of patients who received surgery alone decreased from 77.7% (2007–2009) to 33.9% (2019–2020) while the use of NAD only increased from 9.2% (2007–2009) to 61.0% (2019–2020) (**Figure 1**)
  - The use of AD only remained low over time, ranging from 13.1% (2007–2009) to 1.7% (2019–2020)
- Among the 416 patients who initiated NAD, most (87.5%) received a cisplatin-based regimen (**Figure 2**)
- For AD (n=143), 44.1% received a cisplatin-based regimen, 37.8% received a non-cisplatin-based regimen, and 18.2% received radiation therapy (**Figure 3**)

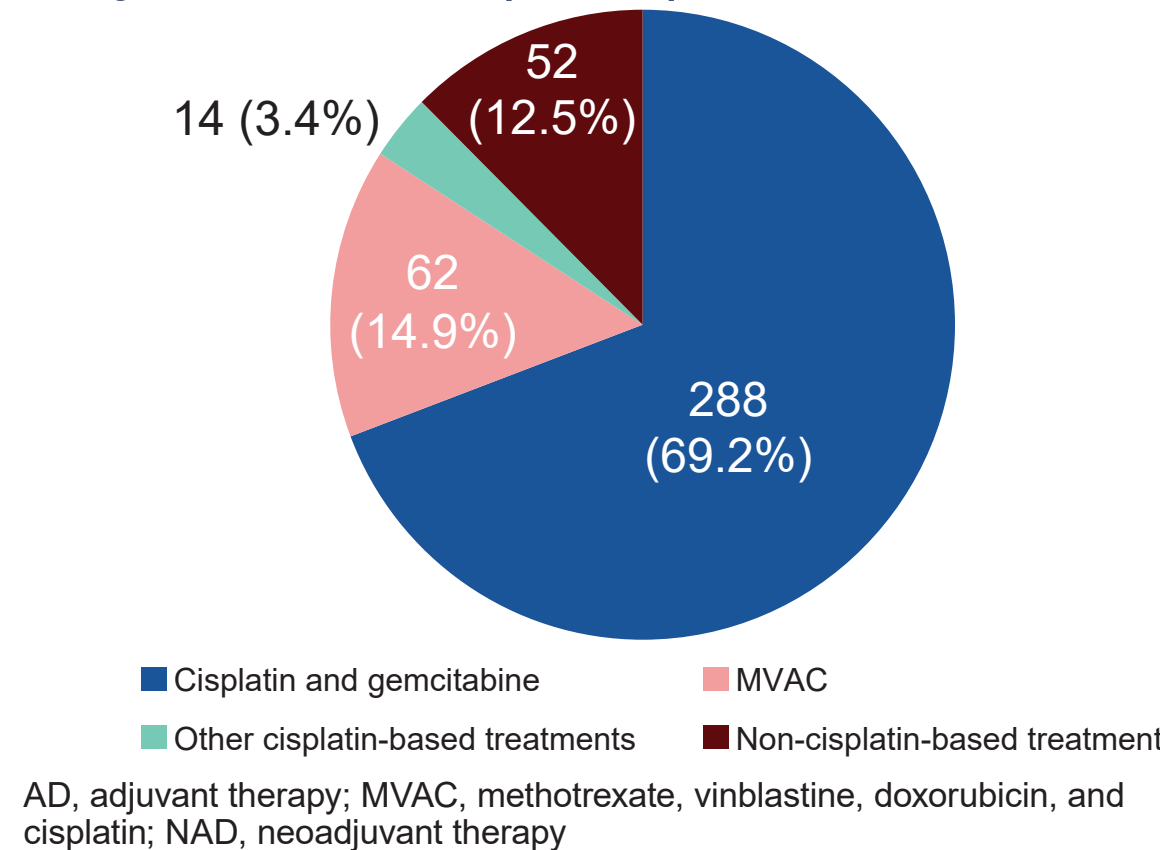
Figure 1. Trends in treatment patterns among patients with MIBC treated with RC



AD, adjuvant therapy; MIBC, muscle-invasive bladder cancer; NAD, neoadjuvant therapy; RC, radical cystectomy.

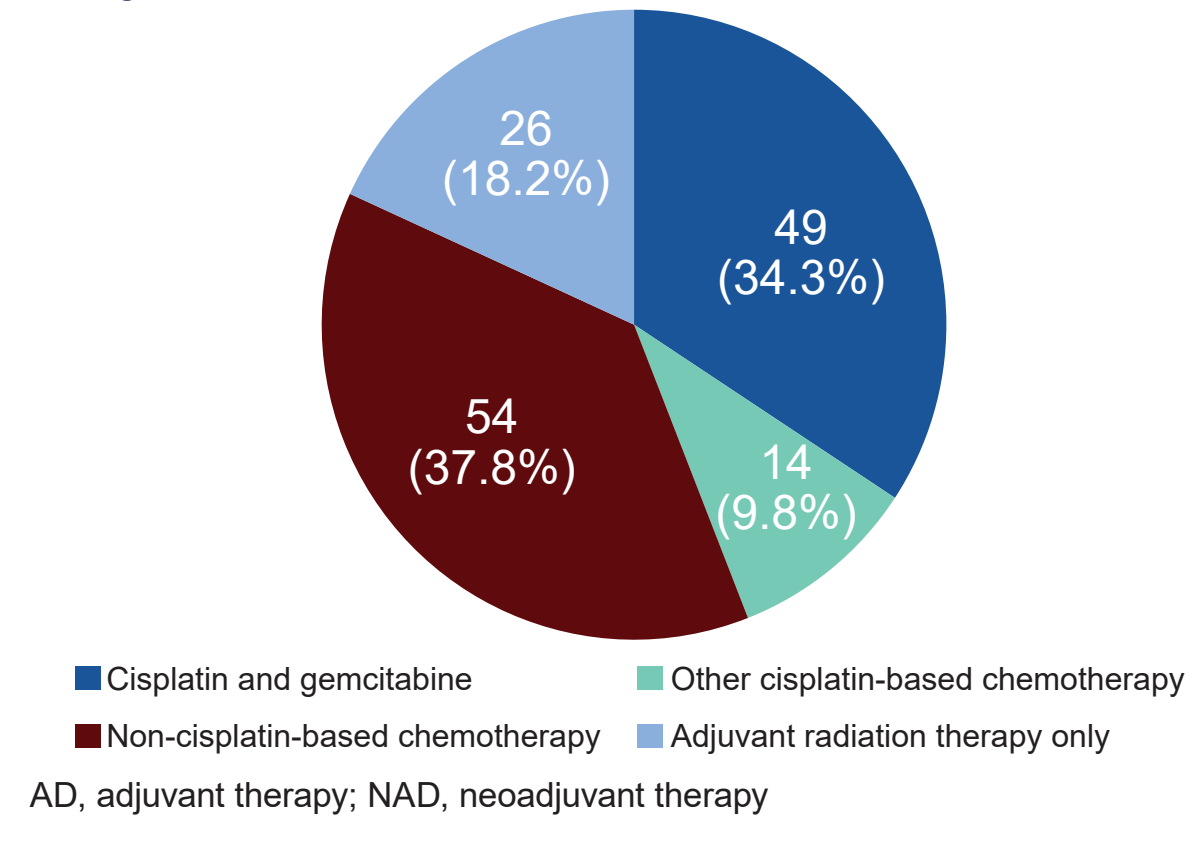
The year in the figure represents the year of RC.

Figure 2. Distribution of NAD among patients with MIBC who received NAD only or NAD + AD (N=416)



AD, adjuvant therapy; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; NAD, neoadjuvant therapy

Figure 3. Distribution of AD among patients with MIBC who received AD only or NAD + AD

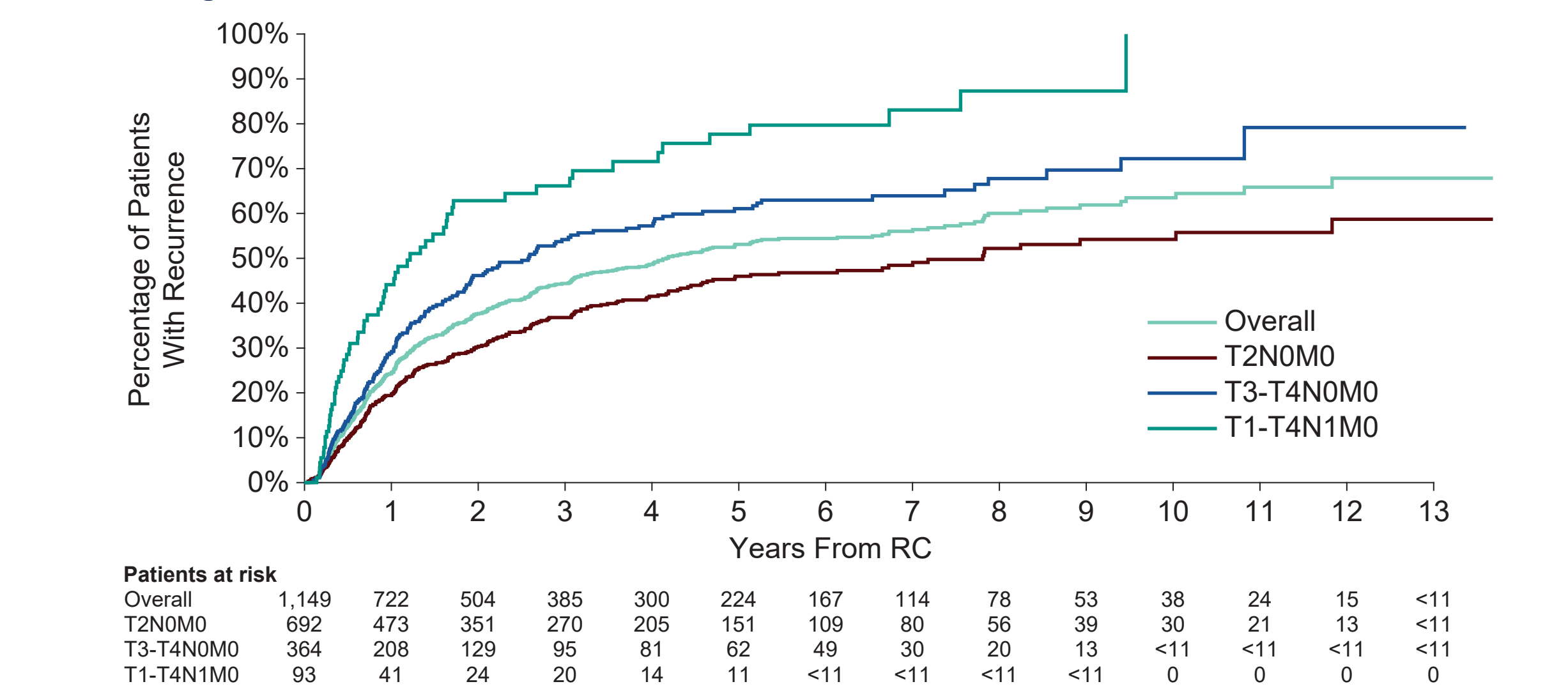


AD, adjuvant therapy; NAD, neoadjuvant therapy

### Recurrence

- The overall 5-year recurrence rate was 53.1%, and was 46.0% for T2N0M0 disease, 61.1% for T3-T4N0M0 disease, and 77.7% for T1-T4N1M0 disease (**Figure 4**)
- The 5-year recurrence rate was 51.4% for those who received surgery alone, 47.6% for those who received NAD only, and 69.3% for those who received AD only. The 5-year recurrence rate for those who received NAD and AD was unavailable due to small sample size (**Figure 5**)

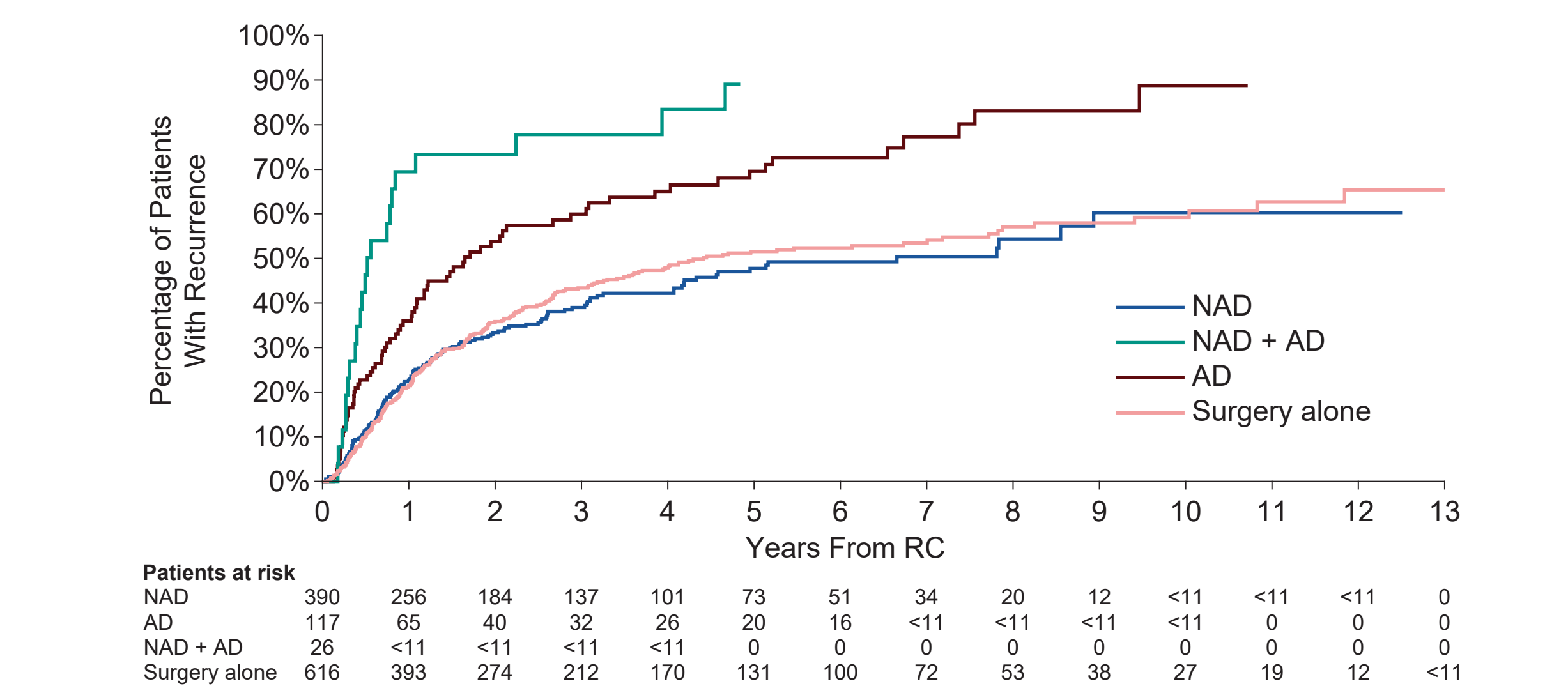
Figure 4. Time to recurrence among patients with MIBC treated with RC, overall and by disease stage



		Recurrence rate													Censored, n (%)		Median time to recurrence [95% CI] (years)
Cohort	Total N	1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year	11-year	12-year	13-year			
Overall	1,149	24.3%	37.6%	44.4%	48.6%	53.1%	54.4%	56.0%	60.0%	61.9%	63.5%	65.9%	67.9%	67.9%	430 (56.2%)	4.2 [3.3, 5.1]	
T2N0M0	692	19.4%	30.2%	36.8%	41.5%	46.0%	46.8%	48.4%	52.2%	54.2%	54.2%	55.8%	58.7%	58.7%	430 (62.1%)	7.8 [5.0, 11.8]	
T3-T4N0M0	364	28.9%	46.2%	54.2%	57.2%	61.1%	63.0%	63.9%	67.8%	69.7%	72.2%	79.2%	79.2%	184 (50.9%)	2.6 [1.9, 3.3]		
T1-T4N1M0	93	44.1%	62.8%	66.2%	71.6%	71.6%	77.7%	79.7%	83.1%	87.3%	100.0%	-	-	-	32 (34.4%)	1.2 [0.8, 1.7]	

CI, confidence interval; MIBC, muscle-invasive bladder cancer, RC: radical cystectomy.

Figure 5. Time to recurrence among patients with MIBC treated with RC, stratified by treatment received



		Recurrence rate													Median time to recurrence [95% CI] (years)	
Cohort	Total N	1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year	11-year	12-year	13-year	Censored, n (%)	
NAD	390	22.3%	33.3%	38.9%	42.0%	47.6%	49.1%	50.3%	54.2%	60.1%	60.1%	60.1%	-	-	238 (61.0%)	6.7 [4.2, -]
AD	117	35.9%	53.6%	59.7%	64.9%	69.3%	72.4%	77.1%	82.8%	82.8%	88.5%	-	-	-	41 (35.0%)	1.7 [1.1, 2.9]
NAD + AD	26	69.2%	73.1%	77.6%	83.2%	-	-	-	-	-	-	-	-	-	<11 (<42.3%)	0.5 [0.4, 0.9]
Surgery alone	616	21.0%	35.5%	43.2%	47.8%	51.4%	52.2%	53.3%	56.9%	57.8%	59.0%	62.5%	65.2%	65.2%	363 (58.9%)	4.4 [3.4, 7.7]

AD, adjuvant therapy; CI, confidence interval; MIBC, muscle-invasive bladder cancer; NAD, neoadjuvant therapy; RC, radical cystectomy.

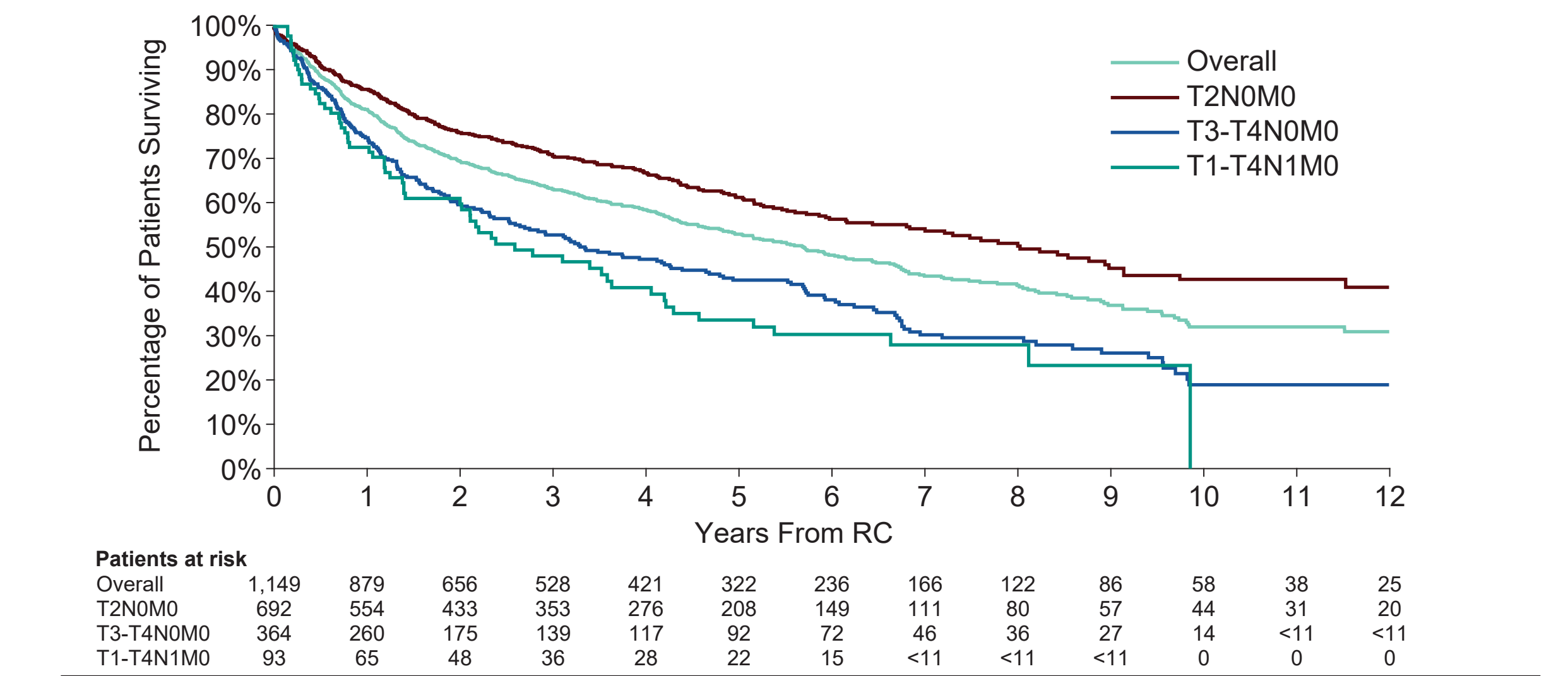
### Overall survival

- The overall 5-year OS rate was 53.0%, and was 61.3% for T2N0M0 disease, 42.6% for T3-T4N0M0 disease, and 33.8% for T1-T4N1M0 disease (**Figure 6**)
- The 5-year OS rate was 48.2% for those who received surgery alone, 66.9% for those who received NAD only, 42.0% for those who received AD only, and 38.0% for those who received both NAD and AD (**Figure 7**)
- Patients who experienced recurrence during the follow-up period had a significantly lower 5-year OS compared to those without recurrence (29.3% vs 56.6%; hazard ratio = 1.88, 95% CI 1.54–2.28,  $P<0.001$ ) (**Figure 8**)

### Strengths and limitations

- To the best of our knowledge, the present study is among the first to quantify clinical outcomes associated with recurrence by disease stage or by treatment group among patients with MIBC treated with RC using real-world, SEER-Medicare data
- However, results should be interpreted in the context of some limitations:
  - The population was aged ≥65 years; therefore, the results may not reflect outcomes among a younger patient population
  - The administrative claims data lacked specific codes to directly identify MIBC recurrence; potential coding inaccuracies may have introduced misclassification bias or misidentification. To address this, we applied an algorithm using procedure, diagnosis, and drug codes, validated through clinical consultation for accuracy
  - This study included descriptive comparisons between disease stages and treatment groups, without adjustment for confounding variables, which should not be interpreted causally

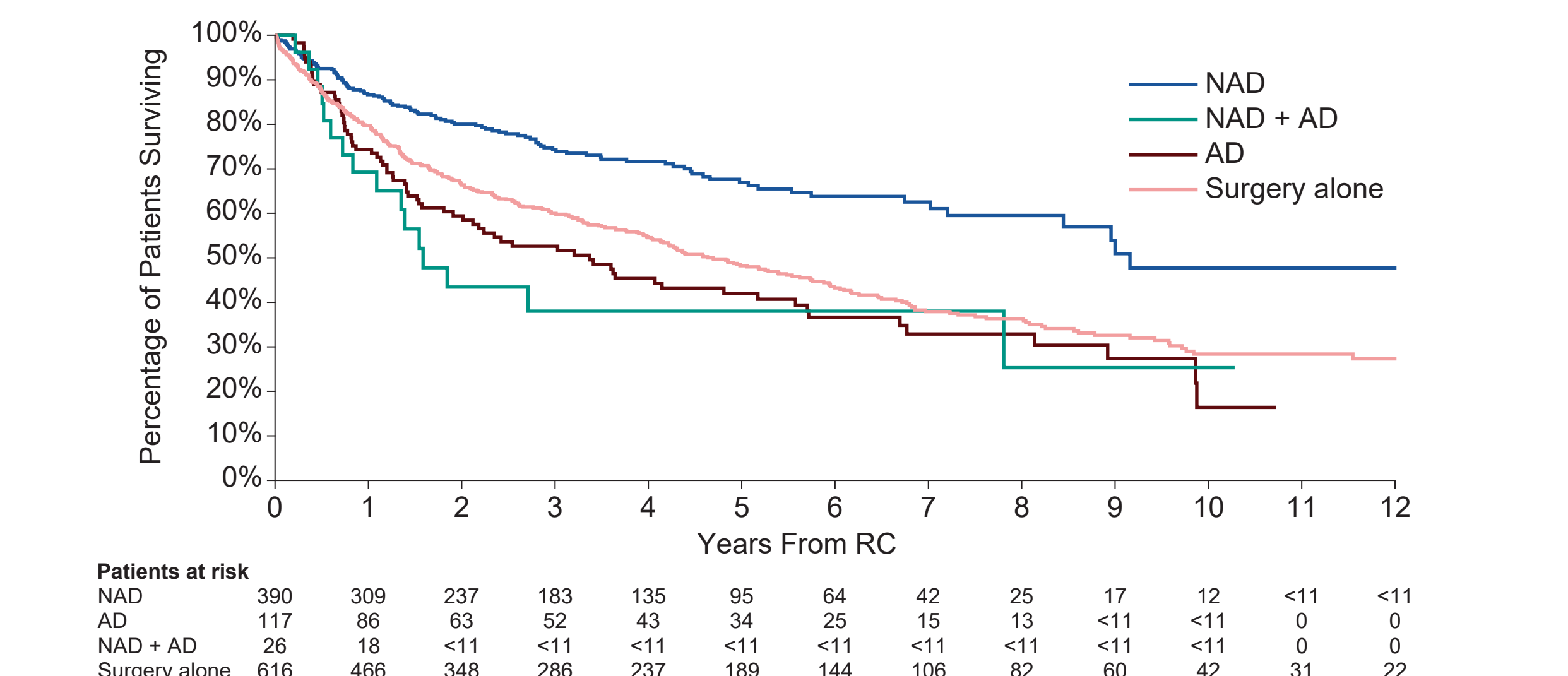
Figure 6. Overall survival among patients with MIBC treated with RC, overall and by disease stage



Cohort	Total N	OS rate												Censored, n (%)	Median OS (95% CI) (years)
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year	11-year	12-year		
Overall	1,149	81.2%	69.6%	63.4%	58.5%	53.0%	48.3%	43.8%	41.8%	36.9%	32.0%	32.0%	31.0%	610 (53.1%)	5.7 (5.0, 6.6)
T2N0M0	692	85.8%	76.0%	71.0%	66.9%	61.3%	56.4%	54.2%	50.9%	45.3%	42.8%	42.8%	41.0%	429 (62.0%)	8.0 [6.8, 9.1]
T3-T4N0M0	364	74.8%	59.7%	52.8%	47.3%	42.6%	38.2%	30.3%	29.6%	26.1%	18.9%	18.9%	18.9%	148 (40.7%)	3.4 [2.5, 4.7]
T1-T4N1M0	93	72.7%	61.1%	48.1%	40.9%	33.6%	30.3%	28.0%	28.0%	23.3%	-	-	-	33 (35.5%)	2.6 [2.0, 4.2]

CI, confidence interval; MIBC, muscle-invasive bladder cancer; OS: overall survival; RC, radical cystectomy.

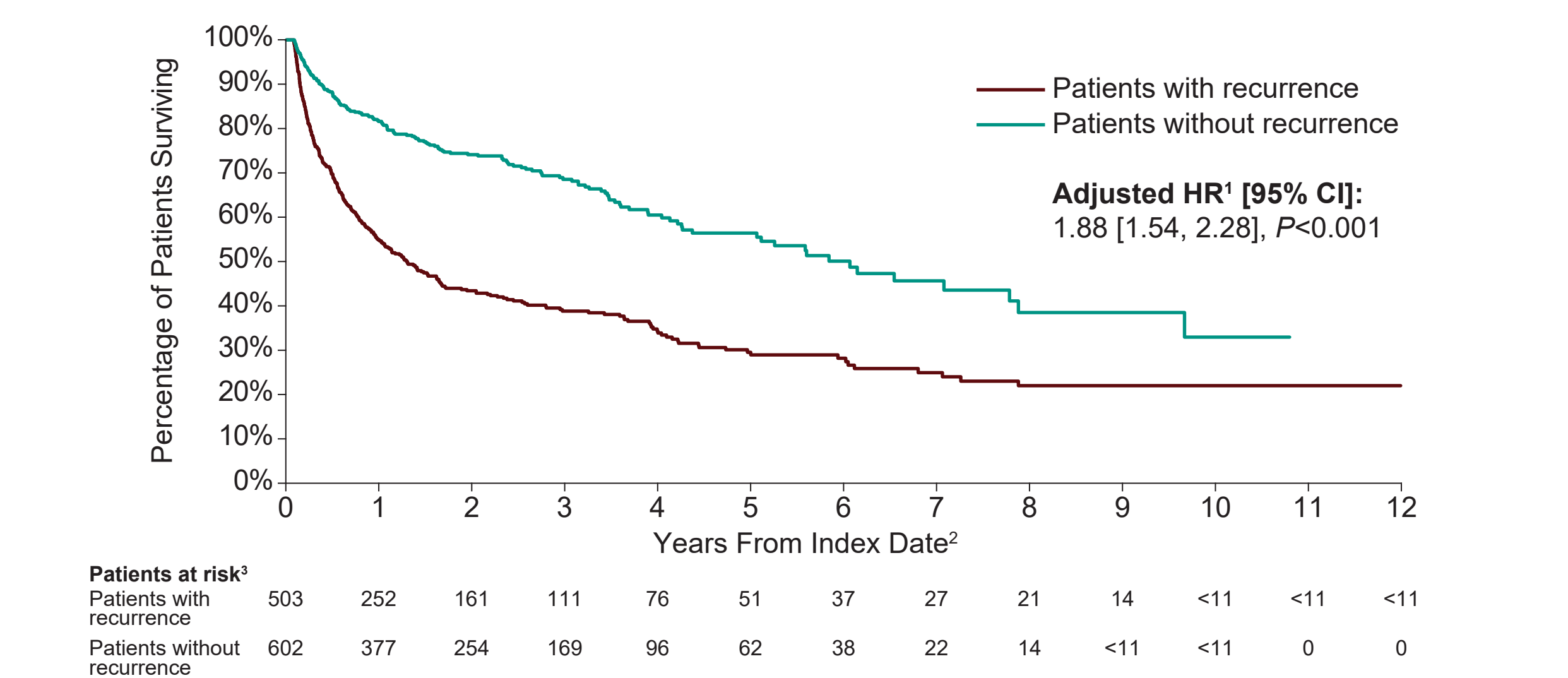
Figure 7. Overall survival among patients with MIBC treated with RC, stratified by treatment received



		OS rate												Censored, n (%)		Median OS [95% CI] (years)
Cohort	Total N	1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year	11-year	12-year			
NAD	390	80.7%	80.0%	74.3%	71.7%	66.9%	63.8%	62.5%	59.5%	50.9%	47.8%	47.8%	47.8%	276 (70.8%)	9.1 [8.4, -]	
AD	117	74.3%	59.4%	52.6%	45.4%	42.0%	36.7%	32.9%	32.9%	27.3%	16.4%	-	-	43 (36.8%)	3.4 [1.9, 5.2]	
NAD + AD	26	69.2%	43.4%	38.0%	38.0%	38.0%	38.0%	25.3%	25.3%	25.3%	25.3%	-	-	<11 (<42.3%)	1.6 [0.8, -]	
Surgery alone	616	79.7%	66.4%	60.0%	54.5%	48.2%	43.3%	37.9%	36.3%	32.6%	28.4%	28.4%	27.3%	281 (45.6%)	4.6 [4.0, 5.6]	

AD, adjuvant therapy; CI, confidence interval; MIBC, muscle-invasive bladder cancer; NAD, neoadjuvant therapy; OS: overall survival; RC, radical cystectomy.

Figure 8. Overall survival among patients with MIBC treated with RC, stratified by recurrence status



		OS rate												Censored, n (%)	Median OS [95% CI] (years)
Cohort	Total N	1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year	11-year	12-year		
Patients with recurrence	503	55.1%	43.7%	39.1%	34.2%	29.3%	28.5%	25.3%	22.4%	22.4%	22.4%	22.4%	22.4%	191 (38.0%)	1.3 [1.0, 1.7]
Patients without recurrence	602	81.7%	74.2%	68.7%	60.7%	56.6%	50.3%	45.9%	38.8%	38.8%	33.2%	-	-	418 (69.4%)	6.1 [5.1, 7.9]

CI, confidence interval; HR, hazard ratio; MIBC, muscle-invasive bladder cancer; OS: overall survival; RC, radical cystectomy.

<sup>1</sup>The Cox proportional hazards model adjusted for age at diagnosis, time from initial MIBC diagnosis to RC, gender, race, ethnicity, region, TNM stage at diagnosis, hypertension during baseline, year of index, Quan-Charlson Comorbidity Index score during baseline, any cisplatin contraindications, any inpatient