

# Survival Rates and Health Care Costs for Patients With Advanced Bladder Cancer Treated and Untreated With Chemotherapy

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## Abstract

**The objective of this retrospective cohort study was to estimate survival and health care costs for patients with stage IV bladder cancer. Approximately two thirds of patients were not treated with systemic chemotherapy. Patients who received chemotherapy had a longer median survival rate, fewer per-patient–per-month health care visits, and lower per-patient–per-month costs than patients not treated with systemic chemotherapy.**

**Background:** Systemic chemotherapy has long been the standard of care for advanced bladder cancer, but its cost implications are poorly understood. The objective of this analysis was to estimate survival and health care costs for patients with stage IV bladder cancer who did or did not receive chemotherapy. **Patients and Methods:** This was a retrospective cohort study of patients identified in the Surveillance, Epidemiology, and End Results–Medicare database with a new primary diagnosis of stage IV bladder cancer between January 2007 and December 2011. Survival and health care visits and costs following the date of diagnosis were determined for treated and untreated patients. Costs were expressed in 2016 US dollars. **Results:** A total of 1215 patients were diagnosed with stage IV bladder cancer, of whom 411 (33.8%) were treated with chemotherapy and 804 (66.2%) were untreated. Median overall survival was 10 months longer for treated than for untreated patients: 13.2 (95% confidence interval, 12.3–14.1) months versus 3.2 (95% confidence interval, 3.0–3.5) months. Treated patients had fewer per-patient–per-month (PPPM) health care visits than untreated patients (7.5 vs. 10.2,  $P < .01$ ) and lower total PPPM health care costs (\$10,707 vs. \$18,935). Overall mean total lifetime costs were greater for treated than for untreated patients (\$139,893 vs. \$66,829,  $P < .05$ ), which was driven by an approximate 4-fold increase in life expectancy for the treated patients. **Conclusion:** Approximately two thirds of patients diagnosed with stage IV bladder cancer were not treated with systemic chemotherapy. Increasing the percentage of treated patients in this population could potentially extend overall survival while simultaneously lowering PPPM costs.

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## Introduction

The incidence rate of urinary bladder cancer in the United States is 19.8 cases per 100,000 individuals (data for 2010–2014).<sup>1</sup> The incidence is much higher in individuals aged  $\geq 65$  years than in those aged  $< 65$  years (122 vs. 5.1 per 100,000) and in men than

in women (34.9 vs. 8.4 cases per 100,000).<sup>1</sup> At diagnosis, the distribution of cases is 85% in situ or localized and about 4% distant (data for 2007–2013).<sup>1</sup> The 5-year survival rate is approximately 5% for those diagnosed with distant disease.<sup>1</sup> Platinum-based combination chemotherapy has historically been the standard of care for first-line treatment of advanced bladder cancer.<sup>2</sup> There is, however, little information about chemotherapy treatment of patients diagnosed with advanced bladder cancer outside the clinical trial setting.

The objective of this study was to describe survival rates and the costs of care after a diagnosis of advanced bladder cancer for patients who received or did not receive chemotherapy in the clinical practice setting.

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# Bladder Cancer and Chemotherapy

## Methods

### Study Description

Details of the study design are provided elsewhere.<sup>3</sup> Briefly, this was a retrospective cohort study of patients identified in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database. Patients with a new advanced bladder cancer diagnosis on a date (the index diagnosis date) between January 1, 2007, through December 31, 2011, were followed until the earliest of the following: date of death, end of health maintenance organization (HMO) enrollment, last known date of follow-up in the SEER-Medicare database, or end of the study period (December 31, 2013). No minimum or maximum duration of follow-up was required for the analysis. Survival, health care visits, and costs for treated and untreated patients were determined.

### Study Sample

Patients were eligible for inclusion if they were aged 65 years or older; had a new primary diagnosis of stage IV bladder cancer with tumor, node, metastasis classification system staging as T4b, N0, M0, any T, N1-N3, M0, or any T, any N, M1; and had continuous enrollment in Medicare Part A and Part B with no HMO enrollment during the study period. Patients were excluded if they had a concomitant or history of a malignancy other than bladder cancer.

Treated patients were those who were treated with cisplatin-based, carboplatin-based, or non-platinum-based cytotoxic chemotherapy regimens. Untreated patients did not receive systemic chemotherapy. Chemotherapy regimens were identified using Healthcare Common Procedures Coding System or National Drug Code numbers for specific agents categorized as carboplatin-based regimens, cisplatin-based regimens, and non-platinum-based regimens.

### Study Variables

The outcomes of interest were survival and health care visits and costs for treated and untreated patients. Health care visits and costs were determined during the follow-up period. Health care visits and costs were categorized as bladder cancer related, adverse event (AE) related, or other. Bladder cancer-related visits and costs were those with an International Classification of Diseases (ICD)-9 codes indicating bladder cancer (ICD codes 188.x, 189.1-189.3, 233.7, 236.7, and 239.4) as the primary diagnosis. AE-related visits and costs were those with a primary claim for an AE of interest. AEs of interest were those occurring of severity grade 3/4, and with an incidence  $\geq 5\%$  as reported in the US prescribing information for drugs used in 1L and 2L treatment of bladder cancer. AEs of interest that required resource use, and were not only laboratory investigations (based on the Common Terminology Criteria for Adverse Events description and clinical input), were chosen for inclusion in this study. Other visits and costs were those without a primary diagnosis of bladder cancer or AEs.

Health care visits and costs were further classified by setting of care: outpatient, emergency, inpatient, skilled nursing facility, and hospice. Health care costs were also categorized by payer. Medicare Claims divides payments into 3 categories: (1) Medicare payments, (2) primary payer payments (referred to as “other payer” in this study), and (3) patient copay/deductible payments (referred to as

“patient payment” in this study). The primary payer or “other payer” represents any other insurance company that the patient receives insurance from besides Medicare.

### Data Analysis

This was a descriptive analysis. All analyses were stratified by patient group (treated and untreated). Patient demographic and clinical characteristics at baseline, defined as the 6-month period before the index diagnosis date, were presented as means and standard deviations for continuous variables, and numbers and percentages for categorical variables. Differences between treated and untreated patients were assessed by *t* tests for continuous variables and the chi-square or Fisher exact tests for categorical variables. The significance threshold was set at .05. The Kaplan-Meier method was utilized to evaluate time-to-event outcomes from the index diagnosis date. Survival from the index diagnosis date was expressed as a median and as a survival rate (percentage survival) at 1, 2, and 3 years. Health care visits and costs were reported as averages as well as per-patient-per-month (PPPM) values, to account for variable durations of follow-up. PPPM values were calculated as the total value divided by the patient-specific days in the follow-up period multiplied by 30. Costs are reported in 2016 US dollars.

Data were coarsened in order to conform with the Centers for Medicare and Medicaid Services Cell Size Suppression Policy, which sets the minimum threshold for the display of Centers for Medicare and Medicaid Services data. The policy specifies that no cell containing a value of 1 to 10 patients can be reported directly and no cell can be reported that allows a value of 1 to 10 to be derived from other reported cells or information.

## Results

### Patient Characteristics

A total of 1215 patients with advanced bladder cancer were included in this analysis, of whom 411 (33.8%) were treated with chemotherapy and 804 (66.2%) were untreated (Table 1). Treated patients were, on average, younger than untreated patients (mean age 74.5 vs. 79.9 years,  $P < .01$ ), included a greater percentage of male subjects (70.6% vs. 58.6%,  $P < .01$ ), and had fewer distant metastases (61.3% vs. 68.9%,  $P < .01$ ). The distributions of race, region, and setting were not significantly different between the treated and untreated patients.

### Survival

Figure 1 shows the Kaplan-Meier curves for survival from the index diagnosis date. Median survival from index diagnosis date for treated and untreated patients was 13.2 and 3.2 months, respectively (Table 2). Survival rates at 1, 2, and 3 years for treated and untreated patients were 56.5% versus 12.9%, 25.6% versus 6.0%, and 15.5% versus 4.7%, respectively ( $P < .05$  for all comparisons; Table 2).

### Health Care Visits

Treated and untreated patients reported 7.5 and 10.2 health care visits PPPM (Table 3). Most visits were in the outpatient setting: 6.9 and 8.8 visits PPPM for treated and untreated patients, respectively. Bladder cancer-related visits accounted for the most

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