Poster number: PCN134

Humanistic Consequences of Preventable Bladder Tumor Recurrences in Non-Muscle Invasive Bladder Cancer

Daniel Barocas, MD, MPH[1]; Denise Globe[2], PhD, Danielle Colayco, PharmD, MS[2]; Amanda Gilmore, PhD, MPH[3]; Thomas Bramley, RPh, PhD[3]

[1]Nashville,TN; [2]Allergan, Inc., Irvine, CA; [3]Xcenda LLC, Palm Harbor, FL

ABSTRACT

OBJECTIVES: Bladder cancer is a common malignancy with ~70,500 incident cases per year in the US; 70% present as non-muscle invasive bladder cancer (NMIBC). Perioperative instillation of chemotherapy after transurethral resection of the bladder (TURBT) can reduce the risk of recurrence. Our objective was to estimate the loss of quality-adjusted life years (QALY) due to unnecessary recurrences for patients not receiving perioperative chemotherapy (PC).

METHODS: A decision-tree model estimated the loss of QALYs following recurrence in NMIBC patients not receiving PC. Therapy utilization rates were obtained from a chart review study of 1,010 NMIBC patients treated by 259 US urologists. In this sample, 17% of patients received PC after the initial TURBT and 27% received perioperative therapy after the first recurrence. In addition, 48.6% received induction therapy with BCG (85%) or mitomycin-C (MMC, 15%) after the first recurrence. The estimated 2-year recurrence rates in NMIBC patients were 53% with TURBT alone and 36% with TURBT and PC. QALY estimates were obtained from literature with disutilities of -0.10 for each resection, -0.026 for BCG therapy, and an assumed -0.01 for MMC therapy.

RESULTS: According to estimates, 49,350 new cases of NMIBC are expected in the US in 2010; 100% utilization of PC would result in avoidance of 6,962 bladder tumor recurrences. The model estimates that 911 QALYs are lost over a two-year time period from preventable recurrences. This equates to 0.02 QALYs for all patients undergoing TURBT. An estimate of disutility at the first recurrence indicates a gain of nearly 47 quality-adjusted days per avoidable recurrence and ~8 days per new NMIBC case if intravesical PC was utilized.

CONCLUSIONS: A substantial number of QALYs are lost each year due to underuse of intravesical PC. Increased use of PC could reduce the humanistic burden of unnecessary recurrences in NMIBC.

OBJECTIVES

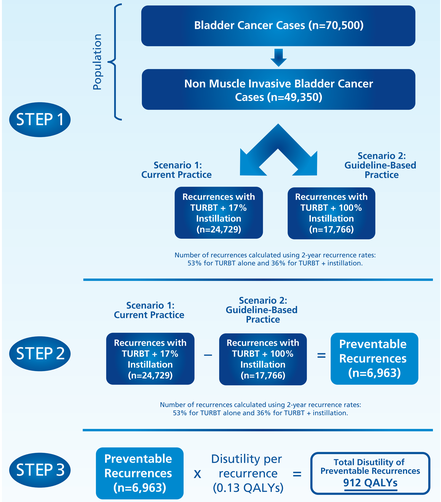
- Bladder cancer is one of the most common malignancies in the United States, with an estimated 70,530 new cases and a projected 14,680 deaths in 2010 (Jemal 2010), and an estimated prevalence of 535,236 persons in 2007 (Altekruse 2010).
- Approximately 70% of newly diagnosed cases of bladder cancer are non-muscle invasive (Pashos 2002).
- Bladder cancer and its treatments are associated with marked decrease in patient quality of life (Reeve 2009), indicating that efforts to reduce tumor recurrences could have humanistic consequences.
- Treatment guidelines recommend adjuvant intravesical chemotherapy for NMIBC patients to reduce the risk of tumor recurrence (Nieder 2005, AUA 2007, Babjuk 2009). However, the use of immediate intravesical chemotherapy remains inappropriately low, with estimates ranging from 0.33% to 27% (Madeb 2009, NCI 2010). This may result in a substantial number of preventable NMIBC recurrences and, thus, have significant humanistic implications.
- This study sought to develop a decision analytic model to estimate the humanistic burden associated with these preventable bladder tumor recurrences.

METHODS

Model Overview

- A decision analytic model was built using Microsoft Excel 2007 software to estimate the utility loss associated with preventable bladder cancer recurrences (Figure 1).
- The perspective adopted was that of the US health care system.
- The time horizon of two years was utilized, and discounting was not applied.
- Humanistic outcomes were measured in quality-adjusted life years (QALYs).

Figure 1: Model Schematic



Population At-Risk

- An estimated 70,500 new cases of bladder cancer was multiplied by 70% (Witjes 2008) to obtain an estimated annual incidence of 49,000 cases of NMIBC.

Preventable Recurrences

- Based on a chart review study of 1,010 NMIBC patients (from 259 US urologists) the estimated utilization rate of post-TURBT intravesical chemotherapy was 17% (Cookson 2011).
- The recurrence rate for TURBT alone was 53% versus 36% for TURBT plus immediate intravesical chemotherapy (Table 1). Recurrence rates were obtained from a 502 patient trial.
- The model assumed that all patients received MMC, since it accounts for over 80% of immediate intravesical chemotherapy after TURBT (Cookson 2011)

Table 1: Model population parameters

Parameter	Value	Source
Bladder cancer cases (#)	70,500	Jemal 2010
NMIBC (%)	70%	Witjes 2008
Not receiving post-operative instillation (%)	83%	Data on file
Recurrence rate for TURBT alone	53%	Tolley 1996
Recurrence rate for TURBT plus immediate intravesical chemotherapy	36%	Tolley 1996

Utility / Disutility Estimates for Preventable Recurrences

- According to the chart review, 27% of patients with a recurrence received a single instillation of MMC; 41% of patients received BCG induction; and 7% of patients received MMC induction.
- It was assumed that on average, patients on induction would receive a total of 6 instillations.
- It was estimated that 26.6% of those receiving BCG induction/maintenance would experience a complication (Kulkarni 2009).
- The utility loss associated with treatments for recurrence was measured in QALYs.

Table 2: Treatment utility parameters

Parameter	Value	Source
TURBT utility loss (QALYs)	0.1	Kulkarni 2009
BCG induction utility loss (QALYs)	0.02	Kulkarni 2009
BCG induction complication utility loss (QALYs)	0.2	Kulkarni 2009
MMC induction utility loss (QALYs)	0.01	Assumption

- The total utility loss was calculated by multiplying the number of preventable recurrences by the utility loss associated with a single recurrence.

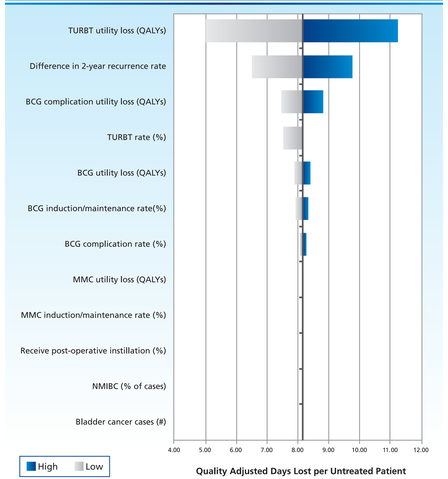
Sensitivity Analysis

- One-way sensitivity analyses were performed using the following key model inputs: population, utilization, and utility parameters.
- All base case model parameters were varied by +/- 10% with the exception of the difference in 2-year recurrence rate and utilities.
- Given the uncertainty in the patient utilities, which were estimated based on comparable health state utilities, we varied the utilities by +/-50%.
- Results were plotted in a tornado diagram to illustrate the impact of the range of tested values on quality adjusted days per untreated patient.

RESULTS

- The model estimates that approximately 41,000 patients diagnosed with NMIBC in 2010 did not receive an immediate post-operative instillation of chemotherapy.
- If treatment guidelines were followed, it is estimated that 6,963 NMIBC recurrences would be prevented annually.
- These preventable recurrences result in 0.13 QALYs lost per recurrence, which is equivalent to approximately 48 quality adjusted life days per recurrence.
- At the population level this amounts to 912 quality adjusted life years lost annually.
- Among those patients who fail to receive a post-operative instillation this translates into an expected utility loss of 0.022 years or 8.1 days.
- Results were most sensitive to the following parameters: TURBT utility loss, difference in 2-year recurrence rate, BCG complication utility loss, and TURBT rate (Figure 2).
- Over the entire range of tested values there was a net loss of quality adjusted days per untreated patient.

Figure 2: One-Way Sensitivity Analysis: Humanistic Analysis



CONCLUSIONS

- A substantial number of QALYs are lost each year due to underuse of intravesical PC.
- Improved compliance with treatment guidelines from increased use of perioperative intravesical chemotherapy can reduce the humanistic burden of NMIBC.

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Presented at: ISPOR 16th Annual International Meeting, May 21-25, 2011, Baltimore, MD, USA

Research funded by: Allergan, Inc