

Sex differences in the effectiveness of intravesical BCG for non-muscle invasive bladder cancer

Introduction

- Non-muscle invasive bladder cancer (NMIBC) represents the vast majority of bladder cancer cases, of which virtually all are urothelial carcinoma (UC).
- The incidence of UC of the bladder is lower in women but they tend to present with more aggressive and advanced disease.
- Intravesical Bacillus-Calmette Guérin (BCG) reduces the risk of recurrence and progression for NMIBC
- Whether differences exist in the response to BCG between men and women remains incompletely understood, with conflicting results reported in the literature.

Objective

- Using a large, population-based cohort at a single institution, we seek to define whether there exist differences between men and women in response to intravesical BCG treatments. Outcomes evaluated include recurrence, progression and treatment completion (tolerability).

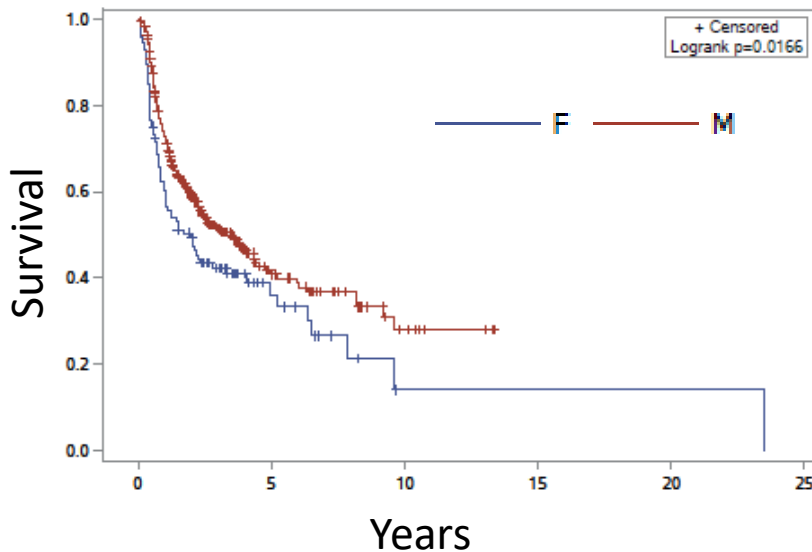
Patients and Methods

- Retrospective single-institution cohort study
- Patients included received intravesical BCG for urothelial carcinoma at the Hôtel-Dieu de Québec Hospital in the CHU de Québec center from 2009 to 2019.
- Patients who received BCG were identified from pharmacy records with medical chart review to obtain clinical characteristics and outcomes
- Tolerability was defined according to the completion of BCG prescribed
- Progression was defined as an increase in grade or stage; that is, the new development of a high-grade pathology or an increase in pathologic stage.
- Outcomes of recurrence and progression were compared using Kaplan-Meier and cox regression analysis adjusted for T-stage, grade (low grade vs high grade), tumor size (<3cm vs ≥3cm), smoking status (Yes vs No), age, presence of carcinoma in situ (CIS) and BCG received (>6 treatments vs <6 treatments)

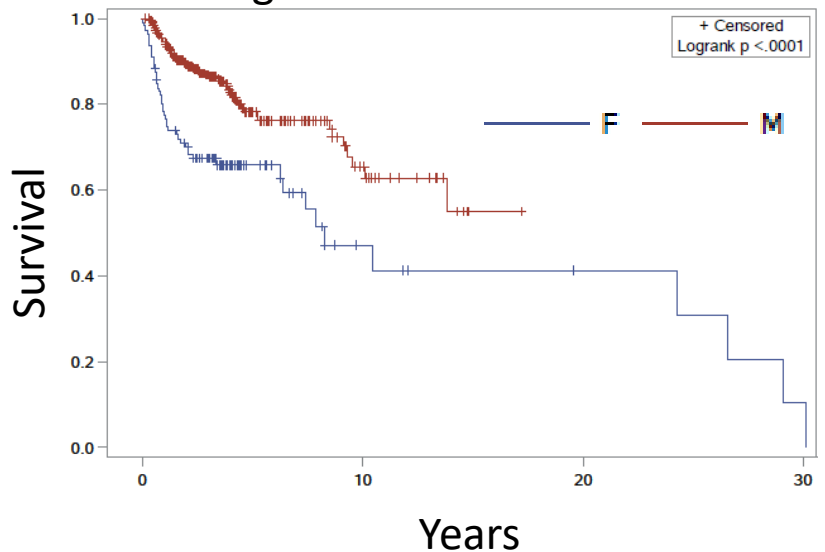
Results

- 417 men and 112 women were treated with intravesical BCG treatments during the years 2009-2019
- The median follow-up for all patients was 3.7 years
- Among these patients, 206 men (49.4%) and 40 women (35.7%) had recurrences demonstrated on pathology
- Kaplan-Meier analysis demonstrate that women have a greater risk of recurrence ($p=0.017$) and progression ($p<0.001$)
- On multivariable cox regression analysis women had a higher risk of recurrence (HR=1.67) and progression (HR=2.96) when adjusting for T-stage, grade, tumor size, smoking status, age, presence of CIS and receipt of at least 6 BCG instillations.
- Completion of at least 6 induction + 9 maintenance BCG instillations occurred more commonly in women (45%) than men (31%).

Recurrence-free survival



Progression-free survival



	Male (vs Female)	Female (vs Male)	p-value
Adjusted HR for Recurrence (95% CI)	0.60 (0.44-0.82)	1.67 (1.21-2.27)	0.0014
Adjusted HR for Progression (95% CI)	0.34 (0.22-0.53)	2.96 (1.89-4.55)	<0.0001

Discussion

- Strengths of our study include a large cohort of patients at a single centre providing care for the entire city and referral region in a universal health-care system.
- Limitations include the non-consecutive nature of these patients, with the highest capture rate in 2017 due to shifting pharmacy record keeping practice patterns over time. A full review of the remaining patients is underway.
- These results suggest increased vigilance is needed for follow-up of female patients.
- Further research is needed to understand the biological reasons behind these results and develop novel treatment approaches.

Conclusions

- Female patients have a higher risk for both recurrence and progression following intravesical BCG treatment compared to male.
- These results occurred despite full intravesical BCG protocols being better tolerated by female patients