



Prevention and Management of Intravesical BCG-related Lower Urinary Tract Symptoms with Prophylactic Pentosan Polysulphate in Patients with Non-Muscle-Invasive Bladder Cancer: A Randomized Controlled Trial

Samer Shamout, Simon Tanguay, Maurice Anidjar, Lysanne Campeau

CQI Research Grant 2017

INTRODUCTION

- **Bacillus Calmette-Guerin (BCG)** remains the most effective prophylactic treatment of intermediate and high-risk non-muscle invasive bladder cancer.
- **30 to 60%** of bladder cancer patients experienced systemic and local adverse events of variable severity following intravesical BCG therapy
- **Only 16 to 29%** of patients completed all the three-year BCG treatment regimen.
- Guidelines recommend medications, such as oxybutynin phenazopyridine, and propantheline bromide for short term symptomatic relief.
- **Pentosan Polysulphate (PPS)** is an oral medication with unique analgesic properties used to relieve bladder pain and discomfort related to conditions of bladder inflammation (Interstitial Cystitis / Bladder pain syndrome).
- **Pentosan Polysulphate** acts by replacing the mucus in the glycosaminoglycan layer of damaged urothelium in the bladder.

OBJECTIVES

Hypothesis:

Concomitant administration of oral PPS and intravesical BCG can prevent and decrease BCG-related LUTS.

Primary Objective:

1. Determine the efficacy and safety of co-administration of Pentosan Polysulphate (100mg) versus placebo administered orally thrice daily for 6 weeks in preventing BCG-related LUTS in adult subjects with a diagnosis of NMIBC.

2. Assess the impact of this intervention on Health-related quality of life in bladder cancer patients.

Secondary Objectives:

1. Evaluate the efficacy of BCG therapy following co-administration of PPS in patients with a diagnosis of NMIBC.
2. Identify the predisposing factors to developing BCG-related LUTS based on clinical, demographic and voiding parameters.

METHODS / INTERVENTIONS

Study Design

- Phase 2, double-blind, randomized, placebo-controlled, parallel-group study
- Multicentre trial involving two partner sites: (Jewish General Hospital, McGill University Health Centre)

Outcomes

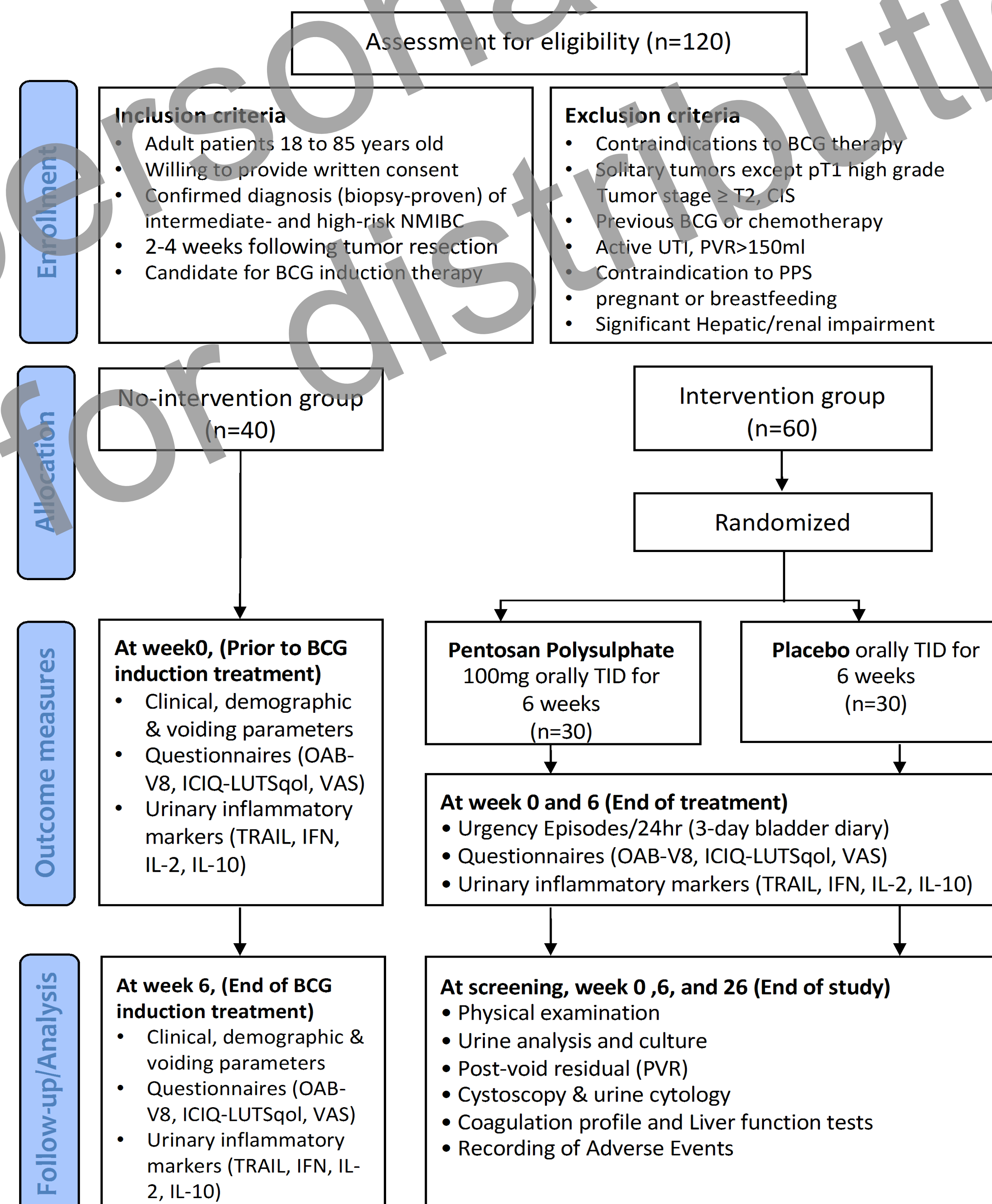
Primary outcomes (change from baseline to end of treatment):

- Mean change in number of urgency episodes/24hr (3-day bladder diary)
- Mean change in ICIQ-LUTSqol score
- Mean change in OAB-V8 score

Secondary outcomes (change from baseline to end of treatment):

- Mean change in VAS score
- Mean change in urinary inflammatory markers (TRAIL, IFN, IL-2, IL-10)
- Cystoscopy and urine Cytology at 3 and 6 months

STUDY FLOW DIAGRAM



PATIENT IMPACT

- Improve patient experience by identifying predictor markers rendering patients at higher risk of developing BCG-related LUTS.
- This will guide patient counselling before treatment to inform them about associated risks and benefits of the BCG treatment.
- We will determine the role of prophylactic PPS to prevent these LUTS from occurring, particularly if patients are considered at higher risk, and therefore improve patient experience.
- The improvement measurements are validated in the assessment of lower urinary tract symptoms related to BCG therapy (voiding diary and OAB-V8) and their quality of life (ICIQ-LUTSqol).

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TRANSLATION ACROSS THE RCN

- The proposed study will provide evidence to guide larger scale studies that may change our practice. Evidence-based treatment intervention (Pentosan Polysulphate) will help to improve bladder cancer patients' quality of life and optimize the effectiveness of BCG treatment.
- This can effectively reduce patient hospital stay and outpatient visits and hence, treatment related cost. Moreover, it will minimize the burden of bladder cancer-treatment-related adverse events in Quebec.
- The proposed study is completely aligned with the MSSS and Direction generale de cancerologie, as it will continue to give highest quality care to NMIBC patients with BCG treatment, as it currently is recommending.
- The study will identify predictive marker to improve informed consent and direct prophylactic measure to avoid complications such as BCG related LUTS.