



# Lowered HbA1c in Individuals with Long-term Type 1 Diabetes Undergoing BCG Bladder Cancer Therapy



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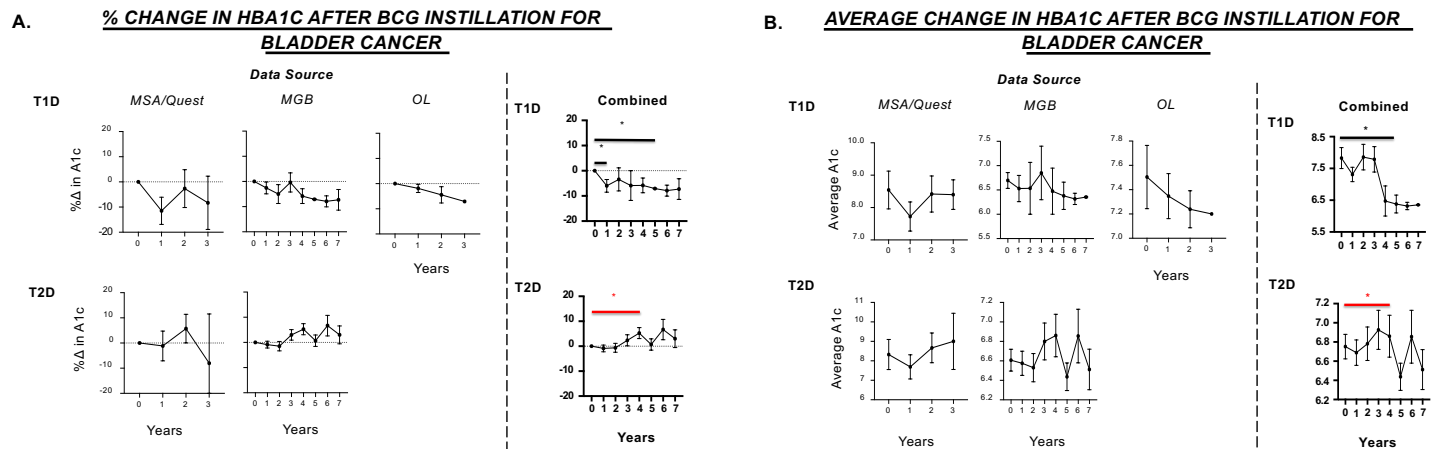
## INTRODUCTION

- A double-blind Phase I clinical trial and open-label trial have shown that adults with type 1 diabetes (T1D) receiving repeat bacillus Calmette-Guérin (BCG) vaccinations experience statistically significantly lowered HbA1c values over a multi-year time course
- BCG has also been used in the United States and Europe for early-stage bladder cancer, administered commonly as 6 intravesical doses for 6 weeks
- We investigated whether intravesical instillation of BCG for bladder cancer might improve blood sugar levels in those with comorbid T1D or type 2 diabetes (T2D)

## METHODS

- We retrospectively analyzed three large patient databases in the United States to assess BCG's year-by-year impact on HbA1c in subjects with documented T1D (N=19) or T2D (N=106) who underwent BCG therapy for bladder cancer: Management Sciences Associates/Quest Diagnostics (MSA): N=263 million adults, Massachusetts General Brigham (MGB): N=6.5 million adults, Optum Labs (OL): N=45 million adults
- No patients had a history of BCG treatment/vaccination other than for bladder cancer.

## RESULTS



**Fig 1. BCG therapy in adults with comorbid diabetes and bladder cancer was associated with multi-year and stable lowering of HbA1c in T1D, but not in T2D.** (N for each dataset: T1D: MSA=9, MGB=4, OL=6; T2D: MSA=9, MGB=97, OL=0) **(A.) Lower HbA1c in T1D, but not T2D, post-BCG treatment for bladder cancer.** In T1D, all three datasets show a reduction in HbA1c values (% change in HbA1c post-BCG instillation) and a near 10% decrease in HbA1cs at differing time points. The combined T1D data shows a statistically significant decrease in HbA1c at Year 1 and Year 5 post-BCG ( $p = 0.0304, 0.0136$ ). In T2D, MSA data shows no change and MGB data shows an increase in HbA1c values post-BCG instillation. The combined T2D data indicates a significant increase in Year 4 after BCG instillation ( $p = 0.0223$ ). **(B.) Decreasing trends in average HbA1c for T1D, but not T2D.** In T1D, lower HbA1cs are seen in all three databases for subjects treated with BCG for bladder cancer. When all three T1D datasets were combined, a Student's paired t-test showed significance when comparing year 0 to year 5 ( $p = 0.0133$ ). In T2D, the trend is in an upwards direction post BCG instillation, a significant increase when comparing year 0 to year 4 ( $p = 0.0460$ ).

## CONCLUSIONS

- Elderly patients with longstanding T1D who received high-dose intravesical BCG therapy as bladder cancer treatment show a gradual lowering of HbA1c, which is not seen in those with T2D, likely due to metformin's interference in BCG's ability to change glycolysis pathways
- High-dose intravesical BCG therapy may contribute towards a drop in HbA1c values in T1D, consistent with interventional trials of the BCG vaccine in longstanding T1D