



## Repeat BCG Vaccinations For The Treatment of Pediatric Type I Diabetes

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### OVERVIEW:

- Double-blind placebo controlled study
- 150 participants with a 1:1 ratio of BCG to placebo treatment
- Ages 12-17 (must be < 18 for first injection)
- Two injections administered at MGH spaced 4 weeks apart
- Five years of twice yearly follow-up visits at MGH or NYU

### PARTICIPATION CRITERIA:

- Diagnosed with type 1 diabetes  $\geq$  two years with at least one positive autoantibody
- Average HbA1c between 7.0 – 9.0% within three months prior to enrollment
- No diabetic complications
- No prior BCG vaccination or history of TB
- Born in the United States
- Currently on or willing to use a CGM
- Not immunosuppressed for any reason including HIV or medications

More information and a complete list of participation criteria can be found on [clinicaltrials.gov](https://clinicaltrials.gov) (NCT05180591).

### HOW TO GET INVOLVED or LEARN MORE:

For patients at NYU Langone, talk to your endocrinologist for more information and to be screened for participation.

All other inquiries can be directed to Dr. Faustman's Immunobiology Laboratory at:

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Charlestown, MA 02129

Email: [diabetestrial@partners.org](mailto:diabetestrial@partners.org)  
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### BCG AND TYPE 1 DIABETES

Over the last two decades, the Immunobiology Lab at Massachusetts General Hospital (MGH) has been investigating the potential of the generic bacillus Calmette-Guérin vaccine (BCG) to reverse various forms of autoimmunity, including type 1 diabetes. BCG is one of the oldest, safest, most affordable medicines ever developed, and has historically been given to protect against tuberculosis. Introduced in 1921, BCG is considered to be extremely safe, is on the World Health Organization's List of Essential Medicines, and is given to roughly 180 million children per year globally. BCG is also one of the most affordable medicines, costing less than a dollar per dose in many parts of the world.

In a Phase I clinical trial conducted at MGH, two injections of BCG showed significant efficacy in changing the primary biomarkers in established type 1 diabetes. The vaccine showed potential to significantly lower blood sugars without a high incidence of hypoglycemia, resulting in a lower insulin requirement and easier diabetes management.



## NOVEL MECHANISMS WITH A VERY OLD HISTORY

The relationship between the increased incidences of allergy and autoimmune disease and the decline in chronic infections in modern societies has been well documented and is often described in the context of the “Hygiene Hypothesis” or the “Old Friends Hypothesis.” These theories suggest that infectious diseases, in general, and life long bacterial exposure, in particular, may play a beneficial immunoregulatory role, including by inducing a cytokine called tumor necrosis factor (TNF) and potentially by upregulating a population of protective T cells called Tregs and killing the “bad” cytotoxic T cells. As societies have become cleaner, more urban, and less agricultural, there has been a reduction in infections and exposures coincident with an increase in the incidence of allergy and autoimmunity. It has been suggested that BCG may replace the impact of immunomodulating bacterial exposures lost in the move to cleaner societies. Epidemiological studies have also examined the impact of BCG vaccination to prevent type 1 diabetes. In Turkish children, at least two doses had a protective effect against type 1 diabetes development.

### FREQUENTLY ASKED QUESTIONS

#### **Is this trial to show prevention or delayed onset of type 1 diabetes?**

Although many trials in pediatric type 1 diabetes are focused on new onset children, BCG shows potent efficacy in people with established diabetes. There is compelling evidence that multiple doses of the right strain of BCG could delay and possibly prevent type 1 diabetes, but this trial is designed to prove that two doses of BCG can help children that have had type 1 diabetes for at least 2 years.

#### **What do you hope to demonstrate with the trial?**

The adults in the Phase I trial lived with type 1 diabetes for an average of 18 years and showed significant and long-term lowering in blood sugars. Our hope is that younger patients will benefit from similar improved glucose control through BCG vaccination. BCG can correct the underlying immune imbalance at the root of type 1 diabetes, and has the potential to reverse the disease.

#### **What are the key outcomes you will be measuring?**

In addition to blood sugar as measured by HbA1c, we will track changes in insulin requirements and the ability of the body to procure its own insulin as measured by c-peptide from the pancreas.

#### **Will the children in the trial be required to change their standard care?**

Children enrolled in the trial will be asked to use a continuous glucose monitor (CGM), but not otherwise asked to change their standard of care.

#### **What are the risks of participating in the trial?**

BCG has been administered millions of times with an incredible safety profile. There is also a large body of evidence that BCG can protect children from various infectious diseases.

#### **Why is the trial five years?**

Previous BCG studies in multiple sclerosis and type 1 diabetes have demonstrated that the vaccine’s clinical effect can take up to three years. The goal of the trial is to show a long-term, durable response.

#### **What are other possible benefits of BCG?**

Global studies suggest BCG protects from other autoimmune diseases such as multiple sclerosis. In addition to tuberculosis, BCG protects humans from other viral and bacterial infections, and possibly COVID-19.