

Faustman Lab Frequently Asked Questions

What is the significance of HbA1c?

HbA1c refers to glycated hemoglobin and is a measure of the overall picture of average blood sugar levels over a period of months. HbA1c is clinically important because higher HbA1c is directly correlated with greater risks of developing diabetes-related complications such as blindness, heart attacks, strokes, renal failure, etc. A significant lowering in HbA1c is a primary endpoint for diabetes clinical trials.

What is the primary marker for the BCG study?

. m the starting values and on average, levels to 6.1%, a low value close to the normal range.

What was the patient study group? What are you studying? Why is it unique?

All of the reported patients were adults with existing type 1 diabetes (for at least two years) and many patients had diabetes for over a decade at time of enrollment. For this study, we are testing the ability of the BCG vaccines to lower HbA1c to the normal range. This data would be unique to show a durable effect in patients with established disease.

What is effect of the BCG Vaccine on the immune system?

BCG has been known for over 30 years to boost a cytokine called TNF. TNF is beneficial in autoimmune diseases by directly eliminating the self-reactive white blood (the autoreactive T cells that attack the pancreas) as well as inducing beneficial immune cells called regulatory T cells (Tregs). BCG resets the immune system back to normal immunoregulation. Furthermore the data in the paper reports the BCG organism is able to do this at the DNA level of the host perhaps explains why limited vaccines can have such a durable clinical effect.

How safe is the BCG vaccine and what is the BCG vaccine?

The BCG vaccine is a >100-year-old vaccine, originally developed and used today on a global basis as a preventive therapy for tuberculosis in high risk countries. Over 3 billion people have received this vaccine, typically at birth, on a global level for over 100 years. The BCG vaccine via the World Health Organization is heralded as the safest vaccine in the history of the world. The BCG vaccine is a safe derivative of a strain of a mycobacteria organism. Interesting, this organism for over 100,000 years co-evolved with humans but with cleaner modernized human cultures, this organism is typically not found within humans. This has led many to believe the Hygiene Hypothesis of why autoimmune diseases and allergies are on the rise in civilized countries i.e. humans may have lost their evolutionary advantages of living with safe versions of mycobacteria.

What are the disadvantages of repeat BCG vaccines and who might not qualify?

Like any live attenuated vaccine, the BCG vaccine cannot be given to someone on immunosuppressive therapy nor to anyone on high dose steroids. The vaccine requires a normal immune system to be effective and safe. Similar to the original disease process of autoimmunity, which is known to take a number of years to develop, the BCG vaccine in both type 1 diabetic trials and multiple sclerosis trials takes a number of years for a visible clinical

effect (lowering of HbA1c or changes in brain disease activity) but the clinical effect in autoimmune human trials appears to be durable and long lasting beyond five year observation periods.

How can more trials be done with BCG in type 1 diabetic subjects so more people can participate?

The rate these trials forward as well as expanding these trials into more type 1 diabetic subjects is limited by money since formal clinical trials are expensive with FDA oversight are expensive. Donations are sincerely appreciated, and more information can be gained from diabetestrial@partners.org.

How do I get enrolled in BCG clinical trials?

Please register at diabetestrial@partners.org

Have pediatric trials started so children can benefit from BCG?

Not yet. If we raise money for these trials, we will start these trials. As above, BCG is typically in global 3rd world countries administered at birth, so safety is not an issue for future pediatric clinical trials. We do know that one vaccine at birth of BCG, a time period prior to the start of autoimmunity, is not protective.

What is the status of the Phase II BCG clinical trials that are ongoing?

The FDA approved Phase II clinical trial is fully enrolled (100 BCG and 50 placebo). All of the subjects have been enrolled for at least one year and have received at least two doses of the BCG vaccine.

Do you recommend all type 1 diabetics take BCG now?

We do not recommend that anyone take BCG for diabetes nor do we recommend any “off label” use of BCG. These results are reports from clinical trials and should not be confused with approval from the FDA.

Can BCG prevent type 1 diabetes?

There are interesting studies looking at historic effects of multiple doses of BCG on type 1 incidence in Turkey and Greece. Large pediatric trials are also underway in Australia and Denmark to look at the impact of this drug as it relates to resetting the immune system for allergies and prevention of other infectious diseases. The question is not answered yet, but there is growing evidence.

How many patients are involved in the BCG clinical trial programs?

The MGH clinical trial program has been underway for almost ten years. There have been hundreds of patients (diabetic and control) involved in treated and reference groups for the in vitro and in vivo studies. To date more than 120 patients with existing type 1 diabetes have been treated with at least two doses of BCG. Nine of those patients have been followed for more than five years.

What other clinical lessons have been learned from the BCG trial program?

As we moved from mice studies to human clinical trials there were a number of key steps we needed to make including how to measure the death of auto-reactive T-cells, the induction of beneficial T cells called Treg cells and the clinical significance of low level of continued insulin secretion as measured by C-peptide on diabetes outcomes.

Are there any active trials enrolling?

Yes. We have eight clinical trials underway. Not only are we studying type 1 diabetic subjects long term for the durability of the BCG clinical effects but have many human studies ongoing on biomarker development, formal Phase II clinical trials, BCG strain comparison trials, drug stability studies with different BCG formulation formats, systemic glucose utilization studies with radiographic study and soon expanded studies into additional autoimmune diseases. Pending funding and FDA approval, MGH is planning several trials including pediatric trials and trials in broader selections of long term diabetics.

Who funds these clinical trials in type 1 diabetes or other autoimmune diseases trials?

For all the global trials ongoing with BCG at MGH for new autoimmune, allergic and infectious indications, the funding comes from the public as philanthropic contributions. The trials do not currently have support from industry.

Why are there not more type 1 diabetics being treated with BCG and how do I get into a BCG clinical trial?

Financial support drives the number of clinical trials. All type 1 diabetic subjects interested should email us to get registered and for follow up since as grant money and public donations are received we then will be able to expand these studies.

Will BCG work in other autoimmune diseases?

The potential in multiple sclerosis is well documented. We don't know if BCG will reverse other forms of autoimmunity. We are looking at fibromyalgia right now and it would be interesting to see if other autoimmune diseases would respond to BCG.

How does the Phase I BCG treatment regimen differ from the ongoing Phase II BCG clinical trial study design?

The Phase II clinical patients all received two doses of BCG in the first year and are receiving one dose of BCG per year for the following four years.

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When will BCG be approved for type 1 diabetes?

We do not know yet.

Will BCG be viable for everyone with type 1?

Our trials so far involve adult patients with established type 1 diabetes (at least two years disease duration and in many cases more than 15 years duration). How BCG works in pediatric patients, how BCG works in new onset subjects and how BCG works in type 1 subjects with more than two decades of disease will be something we are hoping to study in trials soon.

Does BCG work for type 2 diabetes?

There is growing evidence that BCG may play a role in metabolic disease including type 2 diabetes. That data is extremely early but a mechanism we are definitely interested in exploring.

Could BCG be combined with other therapies?

How to improve and compliment the immunoregulatory effect of BCG will be one of the great questions we hope the diabetes community will help us answer. We believe we have demonstrated a mechanism and new basis for beginning a novel type 1 diabetes therapy. Complimentary interventions that spur regeneration of insulin producing cells or long lasting/low level insulin dosing options are all very interesting.

Questions for Patients Calling the Lab

Can I get BCG now?

No. BCG is not approved by the FDA for the treatment or prevention of type 1 diabetes. Access to BCG is only in a clinical trial format.

Can I get enrolled in a clinical trial using BCG?

We are currently enrolling multiple clinical trials. We recommend you email the lab to see if you might be eligible: DiabetesTrial@partners.org

How do I donate to this program and who supports this work?

To date this work has relied almost entirely on donations from individuals and family foundations. Donations are critical to sustaining and growing the clinical trial program.

Is Boston the only US site where the diabetes trials are occurring with BCG?

Yes, Boston is currently the only site for BCG clinical trials in the US.

If I have had diabetes for a long time (10 years) am I still eligible to participate?

Yes. We are looking at conducting clinical trials in patients with longstanding disease.

I have one or more autoimmune diseases. Can BCG help my other autoimmune diseases?

We know there is a clinical effect in multiple sclerosis and there are studies ongoing in Italy. We are conducting a study using BCG in fibromyalgia right now. We may begin trials in other autoimmune diseases.

Globally, but not in the US, there are many different strains of the BCG vaccine. Are they all the same?

No BCG strains are very different, and it is known that many strains of BCG are not efficacious in autoimmune diseases.