

Updates

Fall 2014



MASSACHUSETTS
GENERAL HOSPITAL



HARVARD
MEDICAL SCHOOL

from the Faustman Laboratory at Massachusetts General Hospital

A Note from Dr. Faustman

As we head into fall, we are putting the final touches on the Phase II BCG human clinical trial in type 1 diabetes, including the final regulatory approvals. The human studies protocols have already been successfully reviewed by the many committees at Massachusetts General Hospital, which was a large accomplishment this year.

We are hopeful that the first group of long term type 1 diabetics will receive BCG this year. We will follow all participants for five years, which will require over 30 visits to our facility in Boston. The length of follow up for this study was based on follow-up data from the Phase I BCG trial in long-term diabetics and on data from trials testing BCG in multiple sclerosis, which have shown that the therapeutic effects of treatment may be more pronounced over time.

As you may be aware from following our work, the pancreatic function of most people with type 1 diabetes decays over years; therefore, people with longstanding type 1 diabetes aren't all just "the same." They will be at different stages of insulin loss—which has relevance to our Phase II study. In our study, we want to better understand how these different groups of patients—as defined by how much insulin they are still producing—will respond to BCG, so that we can figure out

how best to treat them. This means that participants in our clinical trials will be divided into subgroups based on the amount of C-peptide (the protein that is a marker of insulin production) their pancreases are producing. We will first look at participants with a very small amount of C-peptide production—typically those who have been living with type 1 diabetes for about 15 to 20 years. We do anticipate having future groups, including a group with no detectable C-peptide production. The timeframe for when we begin planning for future groups will depend on our resources, but we encourage everyone who is interested, regardless of the duration of your diabetes, to register for possible participation in future studies. Please email the lab at diabetestrial@partners.org.

If you are already in our clinical trial database, you will automatically be screened each time we finalize selection criteria for a group. However, we do notice that information, and especially email addresses, does change over the passage of time, so please drop us a line to update or confirm your information anytime – we do not mind repeat messages.

On a global level, interest in the BCG vaccine for prevention and treatment of diverse autoimmune diseases and allergies has expanded



over the past three years. We are no longer alone in advocating for the advancement of clinical trials using the safe BCG vaccine to modulate the immune response in these conditions. There are now at least seven global trials using BCG for the prevention or treatment of autoimmunity and allergic conditions, including our type 1 diabetes trials as well as trials in multiple sclerosis, Sjögren's syndrome, and eczema. In this coming year, we hope to again bring these diverse researchers together at the next meeting of the BCG and Autoimmunity Working Group so that we can all share our respective knowledge on using the BCG vaccination for exciting new purposes.

Thank you for all of your support!

Sincerely,

Denise L. Faustman, MD, PhD

Now Recruiting

We are currently recruiting type 1 diabetic participants who:

- are over 18 years old; and
- have had type 1 diabetes for less than 20 years.

If you are interested and fit this criteria, please email diabetestrial@partners.org (Subject line: *Faustman Lab Research Interest*) or call 617-726-4084.

For new patients and those that have not donated blood samples to the Faustman lab in over a year, we will schedule you for a 30 minute screening visit to donate a blood sample at our facility in Boston. Data collected may be used for eligibility screening for Phase II studies.

If you have previously filled out paperwork or donated a blood sample, we encourage you to email us your interest in participating at this time, along with any updates to your email, mailing address or phone number. *Due to the typically strong response we get from these requests, please allow us a few weeks to respond to your call or email.*

For those that do not fit the criteria but are interested in participating in the research, we still encourage you to register your interest, as we may be seeking patients with longer durations of diabetes at a later date.

Help Us Reach Our Funding Goal

We now have over \$18.4 million raised for the Phase II clinical trial.

To find out how you can help us reach our \$25.2 million goal, please see “How You Can Help” on the last page of this newsletter.

BCG and Autoimmunity Working Group

Last October, the Faustman Lab convened an international group of researchers (now called the “BCG and Autoimmunity Working Group”) in London to discuss how BCG or similar immune boosting strategies may prevent or reverse type 1 diabetes, multiple sclerosis, Sjögren’s syndrome, celiac disease and other autoimmune conditions. A book based on the conference proceedings, called “The Value of BCG and TNF in Autoimmunity” was published by Elsevier this spring. With contributions from each of the conference participants, the book—which is geared towards a scientific research audience—is a collection of the data on using BCG or similar approaches in autoimmunity. A follow up meeting is being planned for 2015.



A book was published based on the meeting proceedings.

EASD Meeting

In mid-September, Dr. Faustman presented new data at the European Association for the Study of Diabetes (EASD) meeting in Vienna, showing that even producing a little bit of insulin can help protect people with type 1 diabetes from diabetic complications compared with no or extremely low level insulin production. In the future, this might lead to better care for patients who are most at risk of long-term complications, as well as clinical trial designs that focus on the most at-risk patients. You can watch a webcast of the presentation, “Low levels of C-peptide production protect from complications and improve HbA1c control in longstanding type 1 diabetes,” here: <http://www.easdvirtualmeeting.org/resources/18851>.

What was also exciting at EASD was the number of presentations focused on long-term insulin production in people with type 1 diabetes. Previously, the Faustman Lab and a research group from the UK independently demonstrated that many people with longstanding type 1 diabetes actually do produce some insulin, even many years after diagnosis. At this year’s EASD meeting, we were pleased to see at least three presentations that continue to expand on these findings:

- Timothy McDonald (UK) – “Most people with long duration of type 1 diabetes are insulin microsecretors and produce their own endogenous insulin,” Abstract #510.
- Gonca Tamer (Turkey) – “Functioning beta cells in type 1 diabetes may not be as low as it is presumed,” Abstract #449.
- Polly Bingley (UK) – “Residual beta cell function in long-standing childhood onset type 1 diabetes,” Abstract #450.

As a field, we need to bring innovations to all people with type 1 diabetes—from the newly diagnosed to those who have had diabetes for decades. Therefore, it is very encouraging to see this interest in longstanding type 1 diabetes!



BCG in Multiple Sclerosis

At the end of 2013, Italian researcher Giovanni Ristori, MD, PhD, and his team at Sapienza University in Rome reported the results of their five-year, double-blind, Phase II clinical trial in which they administered the BCG vaccine to patients with early signs of multiple sclerosis (MS). The results showed that, compared to placebo, a single dose of BCG halved the rate at which patients progressed to full-blown MS. BCG-vaccinated patients had fewer brain lesions (a sign of MS) and were more likely to be symptom-free than patients who received the placebo. The full study was published in the January 2014 issue of *Neurology*.

This work is exciting because it demonstrates the long-term efficacy of a single injection of BCG. It also helps to substantiate and confirm our lab’s work in type 1 diabetes. We continue to remain in close communication with Dr. Ristori and his team to share research findings and best practices from our respective studies. Dr. Ristori’s group is currently planning Phase III trials in MS.

Frequently Asked Questions

How can I register to potentially participate in this research?

Please email diabetestrial@partners.org with your name, current mailing address, phone number, and Email, even if you have previously sent in your information, as we find that people’s contact information changes frequently. The clinical trial coordinators will email you to confirm that you are registered in our database, or they will send you forms to register if you are not yet in the database. You can also visit www.faustmanlab.org and find the forms (called “patient information forms”) under the “Clinical Trials” tab.

About the Type 1 Diabetes Reversal Trials at MGH

Led by Dr. Denise Faustman at Massachusetts General Hospital (MGH), the BCG Human Clinical Trial Program is testing Bacillus Calmette-Guérin (BCG), an inexpensive generic drug, as a treatment for longstanding type 1 diabetes. In the Phase I human study, BCG was administered to adults who had been living with type 1 diabetes for an average of 15 years. This treatment not only helped eliminate the defective T cells that mistakenly attack and destroy the insulin-producing cells of the pancreas, it also temporarily restored the ability of the pancreas to produce small amounts of insulin. A Phase II study is now beginning to enroll patients. The goal of the Phase II study is to identify the drug dose and schedule that will put advanced type 1 diabetes into remission and help prevent diabetic complications.

Our Inspiration



One of the fundraisers for our lab this year was held outside under this beautiful tree. Amanda, an Essentrics teacher in Ottawa whose daughter has type 1 diabetes, held all of her summer classes outdoors, and donated the proceeds to our research. Thank you to Amanda, and to all of you who were able to devote the time and energy to supporting this research.

Seeking more information about this type 1 diabetes research?
Visit www.faustmanlab.org.

Have questions about participating in the research?
Email: DiabetesTrial@partners.org.

How You Can Help

Please consider making a tax-deductible donation today to sustain the momentum of this type 1 diabetes research program. Every gift makes a difference for patients ... today and tomorrow.

1. To make a secure online donation, please visit www.faustmanlab.org and click on "Support."
2. You may make a gift by check (**payable to "Massachusetts General Hospital"**) and mail your check to:

*Diabetes Clinical Trial
c/o Dr. Denise Faustman
Immunobiology Laboratory
Massachusetts General
Hospital-East
Building 149, 13th Street, CNY-3601
Charlestown, MA 02129*

On the memo line of your check, please write: "Type 1 diabetes research."

Thank you for joining us in the fight against diabetes!

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