

Updates

Winter 2011



MASSACHUSETTS
GENERAL HOSPITAL



HARVARD
MEDICAL SCHOOL

from the Faustman Laboratory at Massachusetts General Hospital

Moving Forward into Phase II

A Note from Dr. Faustman

As year end approaches and we begin planning the Phase II human clinical trial in type 1 diabetes, it's a nice time to look back at all of our progress.

We've come a long way since 2001, when we first announced we could reverse type 1 diabetes—in mice. Today, all of our type 1 diabetes work is in humans. In fact, we no longer even have mice at the lab! Our success, which includes bringing a generic drug successfully through Phase I testing, is the fruition of over 20 years of research—research that has helped to redefine how we look at the treatment of this disease.

One of the things that makes our trials so unique is that we are testing a new treatment approach for people who have been diabetic for many years. This is unlike other type 1 diabetes trials, which tend to look at ways to prevent or delay type 1 diabetes, or to focus only on those who have just been diagnosed. While necessary, those trials leave out a whole population of people who have been living with the disease for a long time.

In our studies, we are trying to address one of the underlying causes of type 1 diabetes: the autoimmune attack on the pancreas. In our experiments in end-stage diabetic mice, stopping this attack allowed the pancreas to regenerate and restored blood sugars to normal, even in late-stage disease.

This approach also seems to work in humans. As we saw in the Phase I BCG trial, participants began to briefly produce small amounts of insulin when we interrupted the autoimmune attack. In Phase II, we will work to refine our dosing and identify how frequently patients would need to be treated to sustain these effects.

We hope that our efforts will translate into a treatment that can put type 1 diabetes into remission, sparing people with type 1 diabetes the need to so frequently monitor glucose levels or administer insulin—also better protecting them against dangerous fluctuations in blood glucose levels that cause both short- and long-term complications.



We also want the treatment to be affordable for patients here in the U.S. and worldwide. This is why we are so happy to find such a promising generic drug to test in these studies. If our trials demonstrate that BCG is an effective diabetes treatment, we hope that its approval would not only have a tremendous impact on the health of people living with type 1 diabetes, but also reduce diabetes-related healthcare costs, which are so burdensome on families.

Thank you so much for supporting these human clinical trials to reverse diabetes! Happy Holidays!

Sincerely,

Denise L. Faustman, MD, PhD

Phase I Success

BCG Vaccination Eliminates Defective T Cells, Briefly Turns Pancreas Back On

This summer, new data from the Phase I BCG Human Clinical Trial was presented at the American Diabetes Association's annual scientific conference. This trial, which is part of the *Cure Diabetes Now* program at Massachusetts General Hospital, was the first step in testing the inexpensive generic drug BCG (*Bacillus Calmette-Guérin*) as a treatment for advanced type 1 diabetes.

The Phase I data showed that study participants—who had been living with type 1 diabetes for 15 years, on average—had positive responses to BCG treatment, even at relatively low doses.

In the study, we saw that BCG treatment could eliminate the disease-causing T cells (the ones that attack and kill the insulin-secreting cells of the pancreas). We also saw early signs that the pancreas was starting to produce insulin again—at least briefly—after years of dormancy in those

who received treatment.

Together, these data show the potential of BCG treatment or a similar therapy to turn the pancreas “back on”, even in people who have had type 1 diabetes for more than a decade. This exciting news was covered in media outlets from *The Wall Street Journal* to the *Los Angeles Times*.

The Phase I safety data, released in June 2010, had previously shown that there were no serious or unexpected adverse effects from low-dose, repeated BCG vaccination (two vaccinations spaced four weeks apart).

A Phase II study will be conducted to both expand on these findings in a larger group of patients and to identify the drug dose and schedule needed to maintain a sustained response.

Phase II Study Kicks Off \$8.5 Million Raised

The first fundraising goal for the Phase II trial was met this summer: \$8.5 million, or one-third of the needed funding, which is enough to support the first year of work.

Early work is now underway.

In the Phase II study, which will include a larger number of participants than Phase I, we will look for the optimal dose of BCG and investigate how frequently it would need to be given to be a functional and sustained type 1 diabetes treatment—one that halts the autoimmune attack on the pancreas and, hopefully, allows some level of insulin production to begin again, as we saw in the Phase I study.

Our trial team has begun taking many of the required steps that will lead up to patient enrollment. Some of the key steps include: working on trial design, submitting regulatory documents to the FDA, setting up a data safety monitoring board, determining the criteria for patient selection, further refining the methods for monitoring drug efficacy, and identifying which outcome measures will be used to determine whether the trial is a success. With these steps in place—along with the funds to support the study beyond year one—patient enrollment may begin as early as the end of 2012.

Faustman Lab in the News!

The results of the Phase I trial were featured in many news outlets this summer, including *The Wall Street Journal* (“Drug Offers Hope in Diabetes Study”), the *Los Angeles Times* (“Research Shows Promise in Reversing Type 1 Diabetes”), *United Press International* (“Cure for Type 1 Diabetes?”), and *Bloomberg* (“Generic Tuberculosis Medicine Shows Promise for Reversing Type 1 Diabetes”). Want to read more? Please visit our website www.faustmanlab.org and click on “News.”



Building Better Tools

New Machinery for Clinical Trial Monitoring

In type 1 diabetes, a defective subpopulation of white blood cells is responsible for mistakenly attacking and destroying the pancreatic cells that produce insulin. The ability to easily isolate and count these “bad” white blood cells in a given blood sample is important for type 1 diabetes research. With this ability, we can see whether the treatments we are testing in clinical trials specifically eliminate the unwanted cells.

For this reason, designing and

building better tools for white blood cell isolation has been a major focus in our lab since 2003. To achieve this, we assembled an interdisciplinary team of biologists and engineers to design and build cell isolation machinery. We then extensively tested the machinery to show that it was more accurate and precise than existing methods of separating white blood cells for research. We also automated the technology so that the process would be efficient.

This year, we shared a detailed description of this machinery with the larger scientific community in our paper, “Novel Automated Blood Separations Validate Whole Cell

Biomarkers,” which was published in the online journal *PLoS ONE*.

This is the same machinery we used in the Phase I study to monitor the effects of BCG vaccination on the “bad” white blood cells in people with type 1 diabetes. With it, we were able to see, week by week, that BCG treatment selectively killed the defective white blood cells.

This technology will continue to be instrumental as we move into the Phase II human clinical trial and look at different doses of BCG, different intervals between doses, and different patient groups with type 1 diabetes.

Awards

Dr. Faustman Honored at “Laughter Is the Best Medicine” Event

This summer, Dr. Faustman was honored by Partnership for Cures with the “2011 George and Judith Goldman Angel Award” for her research to find an effective treatment for type 1 diabetes using a generic drug.

The award was presented at the Partnership for Cures “Laughter Is the Best Medicine” event. Partnership for Cures and its funding partners are longtime supporters of the Faustman Lab’s research.



Dr. Denise Faustman with Partnership for Cures President, Dr. Bruce Bloom, at the “Laughter Is the Best Medicine” event.

Leadership Role for Iacocca Foundation

Foundation Resumes Commitment to BCG Clinical Trial Program

The Iacocca Foundation, which played a key role in helping to fund the Phase I study, has committed to a leadership role for the Phase II clinical trial. The renewed commitment from the Iacocca Foundation, along with the support of other philanthropic organizations and donations from thousands of individual supporters, has helped the Faustman Lab raise over \$8.5 million for the Phase II trial to date.

The Iacocca Foundation is also calling on other donors to help raise the total \$25.2 million needed to fully fund the Phase II program.

“We have supported this work since the mouse studies that first showed the reversal of longstanding diabetes. The Iacocca Foundation has made a significant gift to the MGH to help start the Phase II trial and we hope that others will join us,” said Kathryn Iacocca Hentz, President of the Iacocca Foundation.

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 advanced type 1 diabetes. In the recently completed Phase I 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. The next step, a Phase II study, is currently being planned, with the goal of identifying the drug dose and schedule that will put advanced type 1 diabetes into remission.

Looking for more information about this type 1 diabetes research?
Please visit www.faustmanlab.org.

Have questions about participating in future studies?
Please 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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