

Juvenile Diabetes Cure Alliance

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Update of Type 1 Human Clinical Trials That Target a Practical Cure

Conclusions:

- Of the 329 type 1 human clinical trials that we examined, only six have the potential to deliver a Practical Cure.
- This number has increased by just one since our last review in December 2011.
- Practical Cure projects continue to represent a very small fraction of the total number of type 1 human clinical trials. It does not appear that Practical Cure research is a priority for the key funders of research.
- Even though there are just six potential Practical Cures in human trials, they are not fully funded, which slows their completion.

Organizations of Focus:

American Diabetes Association (ADA)

Diabetes Research Institute Foundation (DRIF)

JDRF

Joslin Diabetes Center (Joslin)

Our Mission:

To direct donor contributions to the charitable organizations that most effectively fund research with the goal of delivering a type 1 Practical Cure by 2025.

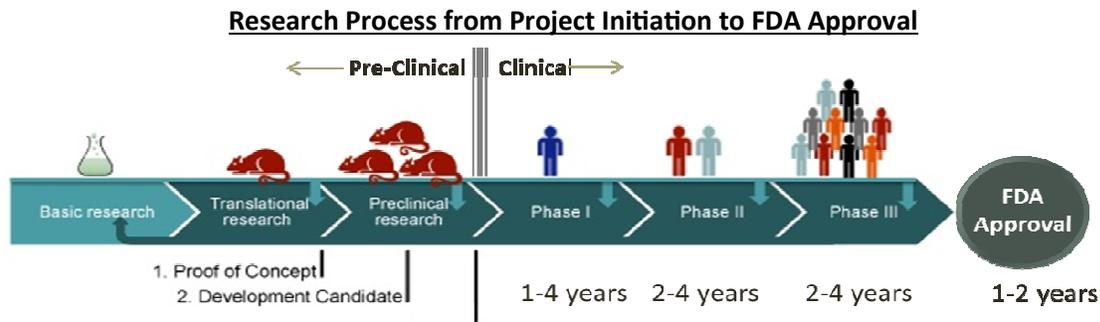
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Update of Type 1 Human Clinical Trials That Target a Practical Cure

This report analyzes the human clinical trials that target a Practical Cure for type 1 diabetes. The number of research projects that have reached this stage of development is one measure of tangible progress toward a cure for individuals who are now living with type 1. It also helps to put into perspective the importance that key funders of type 1 research place on Practical Cure development.

Any research that will yield a cure for type 1 must successfully pass through several stages of testing. The successive stages are: basic research, translational research, pre-clinical testing on animals, and finally clinical testing on humans. Human clinical trials include three increasingly stringent levels of testing, known as Phase I, Phase II, and Phase III. Phase I focuses primarily on the safety of the treatment that is being studied. Phase II and Phase III assess the treatment's efficacy and gather additional safety data. Once a treatment has successfully completed Phase III testing, the U.S. FDA must review the research results and approve it for use before a potential cure can become commercially available in the United States.

The chart below depicts the various stages of research along with the estimated number of years necessary to successfully complete each stage.



Source: California Institute for Regenerative medicine; JDCA estimates; with contributions from Joshua Levy

Research that has already entered human clinical trials has the potential to complete the testing process in fifteen years or less. If any such research targets a Practical Cure, it offers the soonest possible chance to deliver a cure to those now living with type 1, though success cannot be guaranteed. We believe a Practical Cure is possible in our lifetime, whereas an idealized cure, which would return a person to the state they were in prior to type 1, would require many more generations to develop. To qualify as a Practical Cure, a treatment must satisfy the following outcomes:

Practical Cure Definition



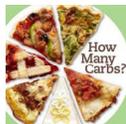
Minimal Monitoring

- ✓ Does not require blood glucose monitoring beyond once a week
- ✓ Keeps A1C levels between 5 and 7



Sleep Worry Free

- ✓ Allows patients to sleep care free



Free Diet

- ✓ Does not restrict a patient's diet
- ✓ Does not require carb counting



- ✓ Best case: Zero side effects
- ✓ Acceptable: Insignificant side effects



Reasonable Meds

- ✓ If pharmacological, an easily managed regime



Fast Recovery

- ✓ If surgical, less than 72 hours recovery

The JDCA examined the U.S. government’s database of human clinical trials to determine if any are targeting a Practical Cure outcome.¹ **There are 329 human clinical trials related to type 1 diabetes that are about to begin or are now underway, which compares to 332 trials when we last examined the trial universe in late 2011. Of these 329, just six have the potential to deliver a Practical Cure**, which is essentially unchanged from last year when we found only five such research projects.² **These six human trials provide tangible evidence that there are research approaches that can potentially deliver a Practical Cure.** Our updated 2012 list includes four of the five projects that were on our 2011 list; one trial from last year’s list was terminated due to unsatisfactory results. In addition, there are two new projects. The six trials are listed in the following table:

Practical Cure Research Projects in Human Clinical Trials

| Project Name | Description | Location |
|----------------------------------|--|---|
| DIABECCELL | Transplanted porcine islets that are micro-encapsulated |  |
| Monolayer Cellular Device | A beta cell encapsulation approach that uses human islets |  |
| ATG/GCSF | Drug combination aimed at stopping both the autoimmune attack and stimulating growth of beta cells |  |
| Sitagliptin/Lansoprazole | Drug combination aimed at stopping both the autoimmune attack and stimulating growth of beta cells |  |
| BCG | Drug that kills disease-causing autoimmune cells and restores pancreatic beta-cell function through regeneration |  |
| Stem Cell Educator | An individual’s blood is treated with stem cells which has the effect of reversing autoimmunity and stimulating beta cell growth |  |

Source: JDCA Research

How do these projects propose to cure type 1 diabetes?

DIABECCELL and the Monolayer Cellular Device both involve islet transplantation.³ Islets that contain insulin-producing beta cells are surgically implanted in the patient’s body through a minimally invasive procedure. The implanted islets are encapsulated within a protective barrier that shields them from an immune system attack, which frees patients from the harsh immunosuppressive drugs that are otherwise necessary to islet transplantation. DIABECCELL is in Phase II trials in New Zealand and Argentina and is already approved in Russia. The Monolayer Cellular device is currently in a Phase I trial in Belgium.

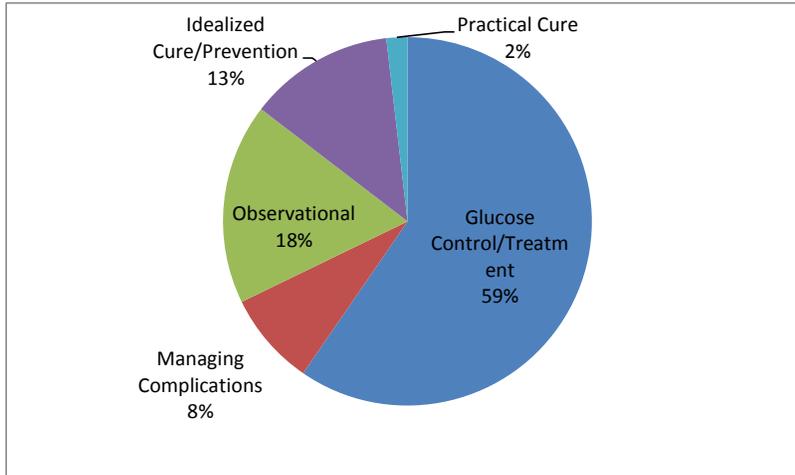
ATG/GCSF and Sitagliptin/Lansoprazole are drug combinations.⁴ They pair a drug designed to inhibit an immune system attack with another drug designed to stimulate the growth of beta cells. This two-part approach addresses the need to both suppress the immune system and regenerate insulin-producing beta cells. Phase I human clinical trials for both projects are being conducted in the United States.

BCG is a single drug that addresses both autoimmunity and beta cell regeneration.⁵ This research has completed a Phase I study in the U.S.

The last project on the list, the Stem Cell Educator, involves a completely different approach. The Educator uses stem cells to treat a patient’s blood with the effect of reversing autoimmunity and stimulating beta cell regeneration.⁶ The treatment takes place outside of the patient’s body; no stem cells are introduced into the patient. This research has Phase II study locations in China and Spain.

These six Practical Cure trials account for just 2% of all human clinical trials related to type 1, meaning that 98% target some other outcome, most of which are not targeting a cure. The other 323 human trials pursue a wide range of objectives, including glucose control/better treatments, managing complications, general observational studies, and idealized cure efforts. **On the whole, the type 1 research projects that are in human clinical trials are extremely skewed toward projects without the potential to cure established diabetics in the next fifteen years.** The following chart depicts the breakdown of the 329 type 1 human clinical trials.

2012 Human Clinical Trials by Major Category



Source: www.clinicaltrials.gov; JDCA Research

Cure trials represent a clear minority, while trials targeting glucose control/treatment, complications, and observational studies represent 85% of the total. The fact that the vast majority of human trials do not target a cure is more concerning due to the recent trend in human trials whereby cure and prevention studies have decreased as a percentage of the total. The table below shows the year-over-year change in the number of trials in the major categories depicted above.

Number of Human Clinical Trials by Major Category

| | 2011 | 2012 | Change |
|---------------------------|------|------|--------|
| Glucose Control/Treatment | 184 | 196 | 12 |
| Managing Complications | 23 | 27 | 4 |
| Observational | 67 | 58 | -9 |
| Idealized Cure/Prevention | 53 | 42 | -11 |
| Practical Cure | 5 | 6 | 1 |
| Total | 332 | 329 | -3 |

Source: www.clinicaltrials.gov; JDCA Research

The total number of idealized cure, prevention, and observational trials decreased from 2011 to 2012. The trials targeting better treatments and managing complications increased in number and as a percentage of the total. Practical Cure studies were essentially unchanged. A greater number of human clinical trials that target a Practical Cure is necessary in order to have a reasonable chance of developing a cure in the near future.

Even though there are only a handful of human clinical trials that are pursuing a Practical Cure, they are not fully funded, which delays any potential progress. Practical Cure research in the pre-clinical phase of development needs funding in order to advance to human clinical trials. It becomes increasingly challenging for the researchers to secure the financing necessary to complete each stage of research development. Insufficient funding is a very real roadblock.

If a Practical Cure is to be developed in the next fifteen years, this area of research needs increased funding at all stages of development. **The major non-profits direct only three cents of every type 1 cure research dollar to Practical Cure research.**⁷ Supporting such projects does not appear to be a priority for the major diabetes non-profits. As we have illustrated in previous reports, donors can influence the non-profits' priorities and improve the prospects of cure development by stipulating that their donations be used only for research that targets a Practical Cure.⁸

Summary

Practical Cure research seeks an outcome that would provide established type 1 diabetics with a cure-like lifestyle in the near future. The JDCA examined 329 type-1-related projects that have advanced through pre-clinical development to being tested in humans. Our analysis indicates that only six projects, or just two percent of the total type 1 research in human clinical trials, target a Practical Cure. The six trials reflect a net addition of just one project since the JDCA's analysis a year ago; one project was deleted from last year's total and two projects were added.

The non-profits can originate and drive more Practical Cure projects into human clinical trials if they prioritize this area of research. In addition, donors can help by stipulating that their contributions be directed to Practical Cure research. Stipulated donations ensure that Practical Cure projects receive more funding so that they are better able to advance through pre-clinical and clinical trials. Directing greater funding to this area of research will increase the chances of achieving a cure in our lifetime.

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Endnotes

1. The ClinicalTrials.gov database, a service of the U.S. National Institutes of Health, is located at <http://clinicaltrials.gov>

2. JDCA report, "Type 1 Clinical Trials That Target a practical Cure," dated January 11, 2012.

3. For a record of the DIABECCELL trial: "Open-label Investigation of the Safety and Effectiveness of DIABECCELL(R) in Patients With Type I Diabetes Mellitus," see: <http://clinicaltrials.gov/show/NCT00940173>

For a record of the Monolayer Cellular Device trial, "Safety and Efficacy Study of Encapsulated Human Islets Allograft Transplantation to Treat Type 1 Diabetes," see: <http://clinicaltrials.gov/show/NCT00790257>

4. For a record of the ATG/GCSF trial, "Reversing Type 1 Diabetes After it is Established," see: <http://clinicaltrials.gov/show/NCT01106157>

For a record of the Sitagliptin/Lansoprazole trial, "Combination Therapy With Sitagliptin and Lansoprazole to Restore Pancreatic Beta Cell Function in Recent-Onset Type 1 Diabetes (REPAIR-T1D)," see: <http://clinicaltrials.gov/show/NCT01155284>

5. For a record of the BCG trial, "Determination of Dosing and Frequency of BCG Administration to Alter T-Lymphocyte Profiles in Type I Diabetics," see: <http://clinicaltrials.gov/show/NCT00607230>

6. For a record of the Stem Cell Educator trial, "Stem Cell Educator Therapy in Type 1 Diabetes," see: <http://clinicaltrials.gov/show/NCT01350219>

7. JDCA Research

8. JDCA Reports: "What Can Donors Do Today to Drive Practical Cure Development?" dated November 30, 2012, and "State of the Cure," dated November 19, 2012.

Analyst Certification

The JDCA analyst responsible for the content of this report certifies that with respect to each organization covered in this report: 1) the views expressed accurately reflect his own personal views about the organizations; and 2) no part of his compensation was, is, or will be, directly or indirectly, related to the specific views expressed in this research report.

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