What is this research study about?

You are being asked to be in this study because you are at increased risk of getting type 1 diabetes. You have already been assigned to a treatment group and have completed the initial two week treatment phase of the study. This phase of the study is being done to monitor you for possible development of type 1 diabetes.

People get type 1 diabetes because their immune system, the part of the body which helps fight infections, mistakenly attack cells (beta cells) that produce insulin in your body. As the immune system destroys these cells, the ability to produce insulin decreases and diabetes develops.

The goal of this study is to see if a study treatment called teplizumab can help delay or prevent type 1 diabetes. Studies have shown teplizumab can help to preserve insulin secretion after diagnosis in people with newly diagnosed type 1 diabetes.

If you want to learn more about this study, you are welcome to read the full consent form and the patient handbook.

What will I be asked to do?

Follow-Up Visits

You will have a follow-up visit at 1 week, 6 weeks, 3 months, and 6 months following the treatment phase and then every six months to have an Oral Glucose Tolerance Test (OGTT). During study visits we will ask questions about your health, diet and activity, and experience as a participant in the study. During study visits we will perform a physical exam and take blood for testing. These tests are done to monitor you for possible development of type 1 diabetes and to monitor your health. Females will also give regular urine samples to be checked for pregnancy.

Other Study Procedures:

- **Oral Glucose Tolerance Test (OGTT):** The OGTT is done in the morning after an overnight fast (not eating during the night). This test is performed to measure the level of glucose (sugar) in the blood after you drink a sweet liquid that contains glucose over a 5-minute period. To make the blood sampling easier, we will place an intravenous needle and plastic tube (IV) in a vein in your arm. This IV will stay in your arm until the end of the test. Blood samples will be drawn through the IV before you drink the liquid and then at several times after you have finished drinking it. A total of about 1 tablespoon of blood will be drawn for the OGTT. The entire test will take about 2 hours.
• EKG: You will have an EKG test when you have completed one year of follow-up in the study. The test is done to check for abnormalities in heart rhythm. It is done by placing sensors on your wrists, ankles, and chest for a few minutes (it does not hurt).

• Monitoring for Possible Diagnosis of Type 1 Diabetes: We will contact you every three months by phone to ask you about any possible symptoms of diabetes (such as weight loss, increased hunger or thirst, or frequent urination). In addition, we will ask you to have a blood test every three months. If you have any of these symptoms or abnormal blood tests, we may ask you to come to the study site for additional testing including an interim OGTT.

Storage of Blood Samples
With the permission of your parent(s), we would like to store any remaining blood samples. Your blood samples could be used to help researchers learn more about what causes type 1 diabetes and how to treat it better.

Are there risks from being in this study?

Common Side Effects:
These side-effects are more likely to occur during the treatment phase and not at follow-up visits. However, it is possible that some of these symptoms could occur following the treatment phase.

Effects on Blood Cells:
Teplizumab can have effects on different types of blood cells. We will test your blood each day prior to each study treatment to monitor for these possible changes. You will not be given the study treatment at a visit if your blood counts are at unsafe levels.

Changes in Liver Function: Your liver function tests will be tested before infusions to make sure that the drug is not given if they are abnormal.

Skin Rash: You may develop a skin rash on your face, neck, body, hands, or feet. This usually resolves quickly, but can result in peeling of the skin.

Less Common Effects:

• Low Platelets (thrombocytopenia): Less than 21% of subjects in previous studies developed low platelet counts (cells that help blood to clot) which could increase your risk of bleeding. Your platelet counts will be reviewed prior to treatment.
Sustained Low White Blood Cells: In one individual (of over 400 who have received the drug) a low white blood cell count lasted a long time - up to two years before returning to normal. However, this person received a dose of teplizumab that is higher than the dose in this study. There were no severe infections when the white cell count was low.

Severe Liver Function Abnormality: Rarely there can be a severe abnormality in liver function tests.

Immunizations:
It is not known what effect teplizumab may have on vaccines. Therefore, any vaccinations with a live virus that you may need should not be given 8 weeks before, or one year after, receiving the study medication because it may not be safe. Any vaccination with a killed virus should not be given 4 weeks before, or 4 weeks after, receiving the study medication because it may not work properly. If you need any vaccinations, be sure to discuss this with your study doctor.

Effects on Immune System:
Even though the drug is given only during the first two weeks of the study for prevention of diabetes, it is possible that the drug may have other effects on the immune system that last longer. In people that receive teplizumab there is a potential risk of more infections. Please refer to the research volunteer handbook about taking precautions to prevent infections especially during the first month of the study. You should contact your physician as soon as possible if you get a fever, nausea/vomiting, sore throat, swollen glands, or cold sores.

Medications like teplizumab that alter responses by the immune system can possibly lead to an increased risk of certain types of cancer. The risk of cancer is unknown but is thought to be very small. An increase in the rate of cancer has not been seen in previous studies of people given teplizumab.

Birth Control and Pregnancy
The safety of teplizumab taken during pregnancy is not known. It is not known whether teplizumab can damage unborn babies. If you are pregnant or are providing breast milk to your baby, you cannot be in the study because we do not know the risks. For this reason it is important that you do not become pregnant for at least 1 year after receiving teplizumab. If you could become pregnant, you must agree to use a reliable form of effective birth control for the two years of the study. Women will need to provide a urine sample for pregnancy testing regularly during the study. If you do become pregnant during the study, you must tell the study doctor right away. It is unknown whether teplizumab affects sperm. It is also unknown whether teplizumab affects the babies of
women who become pregnant from men in the study. If you are a male, you should not impregnate a woman for at least one year after receiving teplizumab. More information about effective birth control options can be found in the research volunteer handbook.

**Intravenous Needle (IV) and Blood Drawing:**
While in the study, you may be at risk for side effects from having your blood taken or an IV placed. The risks of side effects from these procedures are very small. There is sometimes soreness and/or a bruise at the site where the needle goes through the skin. Once in a while, people faint. Rarely, some people may get an infection, a small blood clot, swelling of the vein and the area around it or bleeding where the needle goes through the skin.

**Will this study help me in any way?**
If you decide to take part in this study, there is no guarantee that the drug will delay or prevent type 1 diabetes. It is hoped that the teplizumab will help to maintain the cells that make insulin, but there is no guarantee that this will happen.

We will monitor your health closely and if you do develop type 1 diabetes, it is possible you will be able to start on insulin treatment before you develop symptoms of the disease.

**Do I have to stay in the study?**
You don’t have to be in the study if you don’t want to. You can stop being in this study at any time.

**Can I ask any questions?**
You can ask us questions about the study any time. The staff of the research study will be happy to discuss any questions with you.

**Child’s Printed Name:**

____________________________________________________

**Child’s Signature:**

________________________________________________________

Date: ____________________________

**Witness or Mediator:**

_____________________________________________________

Date: __________________________________
I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study.

Signature of Person Obtaining Assent:

_____________________________________

Date: _________________________________

INVESTIGATOR STATEMENT

I certify that the research study has been explained to the above individual by me or my research staff including the purpose, the procedures, the possible risks and the potential benefits associated with participation in this research study. Any questions raised have been answered to the individual’s satisfaction.

Investigator’s Printed or Typed Name:

_____________________________________

Investigator’s Signature:

_____________________________________

Date: ________________________________