

# Oral Insulin for Prevention of Diabetes in Relatives at Risk for Type 1 Diabetes Mellitus

**This study is currently recruiting participants.**

Verified by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), April 2009

First Received: January 4, 2007 Last Updated: April 16, 2009 [History of Changes](#)

<b>Sponsors and Collaborators:</b>	<a href="#"><u>National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)</u></a> <a href="#"><u>Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)</u></a> <a href="#"><u>National Institute of Allergy and Infectious Diseases (NIAID)</u></a> <a href="#"><u>National Center for Research Resources (NCRR)</u></a> American <b>Diabetes Association</b> <b>Juvenile Diabetes Research Foundation</b>
<b>Information provided by:</b>	National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

ClinicalTrials.gov Identifier:	NCT00419562
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► Purpose

**Type 1 diabetes** (T1D) is an autoimmune disease. This means that the immune system (the part of the body which helps fight infections) mistakenly attacks and destroys the cells that produce insulin (islet cells found in the pancreas). As these cells are destroyed, the body's ability to produce insulin decreases. There is evidence suggesting that repeated oral administration of an autoantigen (the same protein that the immune system is reacting to) may introduce a protective immunity and cause the immune system to stop its attack. An earlier, large scale study was done to see if oral insulin could delay or prevent the development of **Type 1 diabetes** in relatives at risk for developing **Type 1 diabetes**. The overall results showed that for the entire study population, oral insulin did not delay or prevent **Type 1 diabetes**. However, an analysis that was done after the conclusion of the trial suggested a potential beneficial effect in a subgroup of participants. The participants who seemed to benefit from oral insulin had higher levels of insulin autoantibodies which are directed against insulin itself ( called mIAA).

The **Type 1 Diabetes** TrialNet study group will further explore the potential role of oral insulin to delay or prevent **Type 1 diabetes** in a similar group of people. The study will also include a secondary group of individuals at different levels of risk than those in the primary cohort to gather information for future studies.

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
<b>Diabetes Mellitus, Type 1</b>	Drug: Oral Insulin	Phase III

Study Type: Interventional

Study Design: Prevention, Randomized, Double Blind (Subject, Caregiver, Investigator), Parallel Assignment, Efficacy Study

Official Title: Oral Insulin for Prevention of **Diabetes** in Relatives at Risk for **Type 1 Diabetes Mellitus**

**Further study details as provided by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK):**

Primary Outcome Measures:

- Effect of treatment with oral insulin versus placebo in individuals in the primary stratum ( ICA+ confirmed or GAD65 and ICA512 positive on the same sample with confirmation of at least one of these autoantibodies).

[ Time Frame: Metabolic and immunological tests will be conducted every 6 months ] [ Designated as safety issue: No ]

**Secondary Outcome Measures:**

- Secondary analyses will be done to assess the effects of oral insulin versus placebo in other categories of subjects defined using different combinations of autoantibodies and metabolic status. [ Time Frame: Metabolic and immunological testing will be conducted every 6 months ]  
[ Designated as safety issue: No ]

Estimated Enrollment: 400

Study Start Date: February 2007

Estimated Study Completion Date: February 2014

Estimated Primary Completion Date: February 2014 (Final data collection date for primary outcome measure)

<u>Arms</u>	<u>Assigned Interventions</u>
1: Experimental 7.5 mg oral insulin capsules given before breakfast on a daily basis.	Drug: Oral Insulin 7.5 mg oral insulin or placebo given before breakfast on a daily basis.
2: Placebo Comparator	Drug: Oral Insulin 7.5 mg oral insulin or placebo given before breakfast on a daily basis.

**Detailed Description:**

Eligible participants will be randomized to receive either oral insulin (7.5 mg of recombinant human insulin crystals) or placebo daily.

All participants randomized into this study will be seen at a study site for a follow-up evaluation, three and six months after randomization, and every six months thereafter. Participants will be contacted by phone between 6-monthly clinic visits to assess changes in diabetes status, medication compliance and adverse events. These phone contacts will occur approximately 3 months from the date of the participants previous clinic visit.

At the study visits, participants will undergo assessments of their insulin production, immunologic status, and overall health. As the primary outcome measure, subjects will be followed until development of type 1 diabetes or the conclusion of the study.

The trial is expected to last approximately 7-8 years or until the required amount of information is gathered.

## ▶ Eligibility

Ages Eligible for Study: 3 Years to 45 Years

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

1. Have a proband with T1DM. A proband is an individual diagnosed with diabetes before age 40 and started on insulin therapy within 1-year of diagnosis. Proband considered to have type 1 diabetes by their physician who do not meet this definition will be referred to the TrialNet Eligibility Committee.
2. If the proband is a parent, sibling or a child, the study participant must be 3 -45 years of age. If the proband is a second or third degree relative (i.e. niece, nephew, aunt, uncle, grandparent, cousin, or half-sibling), the study participant must be 3-20 years of age.
3. Willing to sign Informed Consent Form.
4. OGTT performed within 7 weeks prior to randomization in which:
  - fasting plasma glucose < 110 mg/dL (6.1 mmol/l), and
  - 2 hour plasma glucose < 140 mg/dL (7.8 mmol/l)
5. mIAA confirmed positive within the previous six months.
6. Two samples with at least one autoantibody other than mIAA positive within the previous six months.

#### Exclusion Criteria:

1. Does not satisfy the above inclusion criteria. Subjects with mIAA positive but no other autoantibodies positive are not eligible for randomization.
2. Has severe active disease, e.g. chronic active hepatitis, severe cardiac, pulmonary, renal, hepatic, immune deficiency and/or disease that is likely to limit life expectancy or lead to therapies such as immunosuppression during the time of the study.
3. Prior participation in a trial for prevention of T1DM, e.g. nicotinamide, insulin, immunosuppressive drugs.
4. History of treatment with insulin or oral hypoglycemic agent.
5. History of therapy with immunosuppressive drugs or glucocorticoids within the past two years for a period of more than three months.
6. Ongoing use of medications known to influence glucose, i.e. sulfonylureas, growth hormone, metformin, anticonvulsants, thiazide or potassium depleting diuretics, beta adrenergic blockers, niacin. Subjects on such medications should be changed to a suitable alternative, if available, and will become eligible one month after medication is discontinued.
7. Pregnant or intends to become pregnant while on study or lactating.

8. Deemed unlikely or unable to comply with the protocol.
9. OGTT that reveals Diabetes, Impaired Glucose Tolerance (IGT), or Impaired Fasting Glucose (IFG).

Diabetes is defined by:

- fasting plasma glucose  $\geq$  126 mg/dL (7 mmol/l), OR
- 2 hour plasma glucose  $\geq$  200 mg/dL (11.1 mmol/l)

IGT is defined by:

- fasting plasma glucose  $<$  126 mg/dL (7 mmol/l), and
- 2 hour plasma glucose 140-199 mg/dL (7.8 - 11mmol/l),

IFG is defined by:

- fasting plasma glucose 110-125 mg/dL (6.1-6.9 mmol/l) AND
- 2 hour plasma glucose  $<$  140 mg/dL (7.8 mmol/l)

10. Subject has HLA DQA1\*0102, DQB1\*0602 haplotype.

## **Contacts and Locations**

Please refer to this study by its ClinicalTrials.gov identifier: NCT00419562

### [Hide Study Locations](#)

#### **Locations**

#### **United States, California**

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Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

National Institute of Allergy and Infectious Diseases (NIAID)

National Center for Research Resources (NCRR)

American **Diabetes** Association

**Juvenile Diabetes** Research Foundation

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**▶ More Information**

Additional Information:

[Type 1 Diabetes TrialNet](#) EXIT

[NIDDK Type 1 Diabetes Clinical Trials](#) EXIT

[American Diabetes Association](#) EXIT

[Juvenile Diabetes Foundation International](#) EXIT

Publications:

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[Lachin JM. Maximum information designs. Clin Trials. 2005;2\(5\):453-64.](#)

Responsible Party: National Institute of Diabetes and Digestive and Kidney Diseases ( Ellen Leschek )

Study ID Numbers: Oral Insulin

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Health Authority: United States: Federal Government

