Brief Title: Comparison of Glargine to Degludec Insulin Transition With or Without a Bridging Glargine Dose (GLIDING)

Official Title: A Randomized Comparison of Transitioning From Insulin GLargine to Insulin Degludec usING a Bridging Dose of Glargine Versus Direct Conversion, in Patients With Type 1 Diabetes Mellitus - a Pilot

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CONSENT FORM

GLIDING study: A randomized comparison of transitioning from insulin **GL**argine to **I**nsulin **D**egludec us**ING** a bridging dose of glargine versus direct conversion, in patients with type 1 diabetes mellitus – a pilot study.

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You can call us at **206-598-4882.** The patient care representative will transfer your call. Your study team will give you a card with their direct number on it. You can contact Arthi Thirumalai by paging 206-314-6080.

24-hour emergency phone number:
Call 206-598-6190. Ask the operator for the Diabetes Care Center doctor on call.

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully. You may ask any questions about the study. Then you can decide whether or not you want to be in the study.

KEY INFORMATION ABOUT THIS STUDY

Insulin degludec (IDeg) is an ultra-long-acting basal insulin. It is increasingly used to treat patients with type 1 diabetes (T1D). Studies of patients switching from long-acting insulins (such as glargine) to IDeg have shown several benefits. These include lower rates of hypoglycemia (low blood sugar), lower fasting blood sugars and needing less basal insulin.

Patients most often stop their current basal insulin and start IDeg at the same dose at their next scheduled time (Routine A). However, this can lead to poor blood sugar control after they switch. This is because IDeg reaches a stable level in the body after the previous basal insulin has stopped acting. Some doctors have their patients take a one-time, partial dose of their current basal insulin when starting their first dose of IDeg (Routine B). The theory is that this "bridging" dose will improve blood sugar control during the time the basal insulin is being changed.

In this research study, everyone will switch from insulin glargine to IDeg for 3-4 days. Half of the participants will use Routine A and half will use Routine B with their first dose of IDeg. Everyone will wear a continuous glucose monitor for at least 48 hours before and at least 48 hours after starting IDeg. There will be 1 visit to the clinic and 5-6 phone calls. You will also go to the study pharmacy to pick up your IDeg and study drug (Routine A or Routine B).

You will not personally benefit from being in this study. You can talk with your own doctor about taking IDeg. You do not need to be in this study to try it. The main risk is that your blood sugar may not be well controlled the first day or two you switch insulin. A rare risk is to have an allergic reaction to IDeg.

PURPOSE OF THE STUDY

The purpose of this pilot study is to test whether Routine B results in better blood sugar control than Routine A. Enough people with T1D taking glargine will be enrolled to have 40 people complete the study. If you are eligible to take part in the study, you will receive IDeg for 3-7 days. You will be randomly assigned (by chance) to receive glargine (Routine B) or placebo (a saline solution with no insulin)(Routine A) with your first dose of IDeg. You have an equal chance of receiving glargine or placebo. Neither you nor the study staff will know which you are taking. The study doctor can access this information if needed for your safety.

STUDY PROCEDURES

This study will last about 3-5 weeks, with 3 clinic visits and 4 to 6 phone visits. Most visits will last about 1 hour. The Visit Schedule below outlines what is done at each visit.

Visit Schedule

Visit	1* (Telemed)	2	3 ☎	4 ☎	5 ☎	6 ☎	7 ☎
Study Day	-28 to -1	0	1	3	4	6-10	11-19
Read & Sign Consent Form	X						
Diabetes & Medical History	X						
Current Medications & Supplements	X						
Vital Signs and Physical Exam		X					
Dispense/Return Log Book and Glucometer		X				X	
Dispense/Return CGM (continuous glucose monitor)		X				X	
Check or Download CGM			X	X		X	
Dispense Study Drug (glargine or placebo)				X			
Dispense IDeg				X			
Review Insulin Dosing		X	X	X	X	X	X
Review Health and Medication Changes		X	X	X	X	X	X

* A blood draw is ordered if recent glycemic control or kidney health test results are unavailable. Women able to have children will have a urine pregnancy test at this visit. These tests will be completed before Visit 2.

The information collected at Visit 1 will show if you are eligible to continue in the study. If you need lab tests, we will schedule the blood draw before Visit 2. If you need a urine pregnancy test, it will be done at the same time as the blood draw or mailed to your home. There may be reasons you cannot be in the study. We will discuss those reasons with you.

At Visit 2 (Day 0), you will be given a glucometer, CGM, and instructions for switching from glargine to IDeg. You will start wearing the CGM. You will be asked to fill in a daily study log. This will be completed online. If you can't complete it online you will need to fill in a paper version of the study log. We will call you the next day (Day 1) to check that your CGM is working and to answer any questions.

We will ask you to download your CGM on Day 3 and review the data. If there is enough data, you will pick up the IDeg and study drug from the study pharmacy and start your first dose of IDeg with the study drug at bedtime of Day 3. If more data is needed, you will continue your glargine and CGM use. CGM data will be re-checked on Day 5.

On Day 4, we will call the morning after your first dose of IDeg with study drug. We will ask about the doses and time taken. If the IDeg and study drug were not started on Day 3 or if the dose or timing was wrong, the Day 4 phone call will be re-scheduled. If Day 4 is rescheduled and you used your single dose of study drug, you will need to pick up a new one at the pharmacy.

Study Days 3 and 4 may be repeated once. If there is not enough CGM data or if starting the IDeg with study drug is missed or wrong a second time, you will be discontinued from the study.

You will continue taking IDeg until Visit 6. At Visit 6, you will be asked to return the CGM by mail in a prepaid envelope provided to you at Visit 2. If you used a paper study log, you will return it in the same envelope. We will give you instructions for switching back to glargine. You will be called 1 week later to see if you have any questions or concerns. You should follow up with your diabetes doctor for any further insulin adjustments you need.

Study Procedures:

During the study, you should use the study glucose meter to check your blood sugar. If you have your own CGM that is calibrated, check your blood sugar at least 2 times daily. Otherwise, you should check your blood sugar 4 times daily.

You will be asked to continue your normal diet, alcohol consumption and exercise routines during the study. Starting at Visit 2, you should not make changes in your routines until Visit 3.

At each visit, we will ask you about your insulin use and about changes in your health and medications.

Blood tests: At Visit 1, if needed, we will order blood tests to be done at a lab. They will collect 1-2 teaspoons of blood if your medical record does not have test results for:

- A1c (glycemic control) in the last 90 days
- eGFR (kidney health) in the last year

Vital signs and Physical exam: We will measure your blood pressure, pulse, weight and height at Visit 2. A focused physical exam will also be done to check your insulin injection sites.

Study Log: You will start filling in a study log at Visit 2. You will be asked to record your daily insulin doses, the times taken, blood sugar tests, carbohydrates and amount of exercise. The log has forms for recording information about low blood sugars. This asks you about your symptoms and, if you needed help, when the symptoms occurred and treatment information. The study log will be completed online. You will get a daily email with a link to your daily log. If needed, we can provide a paper study log.

Continuous Glucose Monitor (CGM): At Visit 2, you will be given a blinded CGM. You will be taught how to use it. You cannot see your blood sugar results on this CGM. If you have your own CGM you can wear it at the same time as the study CGM. You will start wearing the CGM at Visit 2 and wear it at all times until Visit 6. At Visit 6, we will ask you to return the CGM via mail and download the data. You will be given enough CGM supplies to last for about 1 week.

On Day 3, you will be asked to download your CGM. If there is less than 38 hours of usable data, you will be asked to continue wearing the CGM and using your current insulin for another 2 days. The CGM will be downloaded again to check for usable data. If there is not enough, you will be discontinued from the study.

Insulin Dosing and Study Drug:

If you are not taking at least one daily glargine dose at bedtime, you will be switched to bedtime dosing a week before Visit 2.

On Study Day 3, the research pharmacy will give you enough IDeg for 3-4 days and one dose of study drug (glargine or placebo). We will calculate the dose of IDeg and study drug. Your IDeg dose will be 80% of the dose of glargine you were taking. Your dose of study drug will be 50% of your current glargine dose. You will take the study drug with your first dose of IDeg at bedtime on Study Day 3. You will not start the IDeg on Day 3 until the study staff confirms you should start it. You may need to collect more CGM data before starting the IDeg.

If you missed taking the IDeg and study drug at bedtime on Day 3, you will be asked to start them on Day 4. If the wrong dose of IDeg or study drug was taken, or they were taken at the wrong time, we will ask you to switch back to your original glargine for 3 days. After this 3-day "wash-out" period, you will pick up a new dose of study drug if needed and take IDeg and study drug on Day 7 at bedtime.

For 48 hours before and after starting the IDeg, you will be asked to not use any correctional insulin (to lower high blood glucose readings) unless your blood glucose is > 250. This includes correctional insulin at mealtimes and otherwise. This will help us see any differences in blood sugar control between the people who start IDeg with a "bridging" dose of glargine to those who start IDeg alone.

You will continue taking IDeg until Visit 6. At Visit 6 you will be instructed to switch back to glargine. We will calculate your insulin doses as follows:

- If you used glargine once daily: About 24 hours after your last dose of IDeg, you will take 50% of your usual glargine dose at bedtime. At 48 hours after your last dose of IDeg, you will return to your original bedtime dose of glargine.
- If you used glargine twice daily: About 24 hours after your last dose of IDeg, you will take 50% of your usual dose of glargine at bedtime. You will again take 50% of your usual glargine dose about 36 hours after your last dose of IDeg. At 48 hours after your last dose of IDeg, you will return to your original twice daily doses of glargine.

RISKS, STRESS, OR DISCOMFORT

Low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia): These are the most common risks for anyone who needs to use insulin.

Symptoms of low blood sugar can include:		
Early signs: • feeling hungry, very tired, shaky, worried or irritable • feeling of strong or fast heartbeat • pale skin and sweating • finding it hard to think.	Signs during the night: • damp sheets or clothes from sweating • nightmares • feeling tired, irritable or confused when waking up.	Signs of severe low blood sugar: • feeling confused • strange behavior such as slurred speech or being clumsy • problems with your sight • fits or passing out.
Symptoms of high blood sugar can include:		
• being very thirsty • needing to pee more often	• change in vision • weakness, sleepiness or confusion.	

Low blood sugar is more likely to happen if you exercise more than usual, eat too little or miss a meal, or drink alcohol. **If you have any signs of low blood sugar, eat or drink something sweet (juice, soft drinks with real sugar, sweets, glucose tablets). If this does not work, talk to a doctor or the study staff right away.**

IDeg (insulin degludec): Low or high blood sugar is the most common risk for anyone taking insulin. There is a small chance you may have an allergic reaction to IDeg. Serious allergic reaction is a very rare side effect. This may become severe and could lead to death if not treated. **If you have any signs of a serious allergic reaction, stop taking the study medicine and get emergency help right away.**

Allery symptoms can include:	
Signs of mild allergy: • rash, redness, hives • itching • wheezing.	Signs of a serious allergic reaction • swelling of your throat and face, • breathing problems, fast heart-beat, pale and cold skin, • feeling dizzy or weak.

Switching between insulins: When you switch from one insulin to another, there is an increased risk of high or low blood sugars for a few days.

CGM: The CGM sensor is inserted into the skin. Some people find this painful. Rarely, a skin infection can occur where the sensor is inserted. You may have itchiness, redness, bleeding, and bruising where the sensor is inserted. An allergy to the tape that holds the sensor to the skin is possible. Very rarely, the sensor or needle may break under your skin. If this happens, you should contact your study doctor about what to do.

Fingerstick: The fingerstick blood sugar tests may cause pain or bleeding. Some people may get a bruise at the site of the fingerstick. Very rarely, the site of a fingerstick may get infected.

Blood draw: If you have a blood draw at Visit 1, you may feel a little discomfort, bruising, bleeding or swelling where the needle goes in. There is a very small chance of infection where the needle goes in.

Pregnancy: If you learn you are pregnant during the study, please let the study doctor know immediately. We will report any pregnancy to NovoNordisk, as they are providing the IDeg. The study doctor will follow the progress of the pregnancy and may require access to your infant's and/or your medical records for additional follow-up after delivery.

COVID-19: The only visit in which you will interact with study staff directly is visit 2, at which time, staff will take all precautions of masking, physical distancing and hand-washing before interacting with you. During the physical exam the duration of close contact with study staff will also be less than a few minutes, since it is only a focused physical exam.

ALTERNATIVES TO TAKING PART IN THIS STUDY

You do not have to be in this study to change your insulin glargine to insulin degludec. You can ask your diabetes doctor about changing your insulin at your next clinic appointment.

BENEFITS OF THE STUDY

You will not personally benefit from being in this study. You will get to try IDeg for a 3-7 days. This research will help us learn more about whether using a "bridging" dose helps blood sugar control when starting IDeg. Information from this study may help future research into how to best switch from one type of insulin to another.

SOURCE OF FUNDING

The University of Washington is receiving a grant for this Investigator-Initiated study from the University of Washington School of Medicine and funds are supported by NovoNordisk. NovoNordisk is providing the IDeg for this study.

CONFIDENTIALITY OF RESEARCH INFORMATION

Information collected for this study will be confidential. Study data reported to NovoNordisk will be coded, it will not have your name on it. The account we set up for the study CGM will also be coded and not identify you.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

If you have a serious health problem during this study, we may ask your permission to access the medical records related to it. We may need to report your health problem to the government, university staff, and/or NovoNordisk. Your study and medical records may be reviewed. The reviewers will protect your privacy.

Your participation in this study will be noted in your UW medical record. UW Medicine staff and people who have legal access to your medical record will be able to see it. Anything you report to us that is related to your diabetes or current health care may be recorded in your medical record. We do not record other study data in your medical record.

Your identity will not be shared in any reports or publications resulting from this study.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

USE OF INFORMATION AND SPECIMENS

You will not receive individual results from this study. If you are interested in what we learn from this study as a whole, you can opt in to be contacted with results.

□ I am interested in hearing about study results

Information from this study might be used for future studies. Anything that identifies you will be removed. If we do so, that information may be used for future research studies or given to another researcher without getting additional permission from you. It is also possible that in the future we may want to use or share study information that might identify you. If we do, a review board will decide whether or not we need to get additional permission from you.

Commercial Profit

The data we collect as part of this research may be used in the future for commercial profit. There is no plan to share this profit with you.

OTHER INFORMATION

You may refuse to take part in this study. You are free to withdraw from it at any time. Leaving the study will cause no penalty or loss of benefits to which you are otherwise entitled. Leaving the study will not affect your clinical care. We will keep any study data collected before you withdraw from the study. There are no blood or other samples saved as part of this study.

The study will provide you with a glucose meter and tests strips to use during the study. The study will also provide you with the IDeg and the "bridging" dose of glargine or placebo. You will not need to pay for these. You will be asked to return the glucose meter, unused IDeg and study drug containers at your last study visit.

We will pay for your parking when you come to the clinic for study visits. You will receive $50 when you complete the study. You (or your insurance) will not have to pay for any of the visits or tests that are part of this study.

RESEARCH-RELATED INJURY

If you think you have a medical problem or illness related to this research, contact Arthi Thirumalai (pager: 206-314-6080) or Jing Chao (pager: 206-314-2208) right away. If you cannot reach them, call the hospital operator at 206-598-6190 and ask for the diabetes care doctor on call. They will treat you or refer you for treatment at a UW Medicine facility.

The costs of the treatment may be billed to you or your health insurance just like other medical costs, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. The researcher may request HSAP coverage by following established procedures. If you wish to request HSAP coverage yourself, contact the researcher or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. You may also call collect to the UW Human Subjects Division at 206-221-5940 if you do not otherwise have access to a telephone. Ask the researcher if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of compensation for injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form. We will bill your health insurance for treating problems that result from your diabetes or from standard clinical care. If you have no health insurance or your insurance refuses to pay, we will bill you.

Printed name of study staff obtaining consent Signature Date

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject Signature of subject Date

Copies to: Researcher; Subject; Subject's Medical Record (if applicable)