UAB IRB
Approved
29-Jul-2020
until
28-Jul-2021

PILOT PORTION: CONSENT FORM

TITLE OF RESEARCH: **RAD 1502/UAB 1593: Pilot and Phase II Double Blind Placebo Controlled Randomized Trial Examining the Safety and Efficacy of Glyburide as Prophylaxis Against Cerebral Edema in Patients Receiving Radiosurgery for Brain Metastases**

UAB IRB PROTOCOL #: **IRB-160630003**

SPONSOR: **UAB Department of Radiation Oncology**

SPONSOR PROTOCOL #: **RAD 1502/UAB 1593**

PRINCIPAL INVESTIGATOR: **D. Hunter Boggs, MD**

CO-INVESTIGATORS: **Markus Bredel, MD, PhD; Michael C. Dobelbower, MD, PhD; John Fiveash, MD; Barton Guthrie, MD; James Markert, MD; Kristen Riley, MD; Sharon Spencer, MD; Christopher Willey, MD, PhD; Houman Sotoudeh, MD;**

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to see whether glyburide is safe to be used in patients without diabetes who are getting radiosurgery (SRS) for brain metastases.
Duration & Visits	Your participation in the study will last about 3 months, beginning at least 5 days before radiosurgery and ending with your 3 month follow-up MRI scan. We would like to keep in touch with you after that and check on your medical condition if you allow us to. Follow up study visits may be conducted remotely, if necessary.
Overview of Procedures	Over the course of the study, you will receive Glyburide and undergo stereotactic radiosurgery (SRS) treatment. Glyburide is given as a pill that you will start 5-9 days before you start SRS. You will continue to take Glyburide until the evening dose on the day of your 1 month post SRS MRI scan. At 1 week follow-up after SRS treatment, you will return to clinic to see how you are feeling, routine blood work, and check your glucose levels. At 1 month and 3 months after SRS treatment, you will return to clinic to see how you are feeling, routine blood work, and undergo MRI scan.
Risks	The most likely risks are low blood sugar, nausea, fatigue, headaches, dizziness, rash, and edema (swelling of the brain).
Benefits	You may or may not have a direct benefit from being in the study. While researchers hope that glyburide taken by mouth will be safe and reduce side effects from brain swelling, there is no proof of this yet. We do know that the information from this study will help researchers learn more about the treatment of cancer that has spread to the brain.
Alternatives	The alternatives to you participating in this study are: • Getting treatment or care for your cancer without being in a study

	• Receiving treatment with radiosurgery without glyburide • Taking part in another study • Getting no treatment

Purpose of the Research

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have recently been found to have cancer that has spread to the brain (brain metastases).

Your doctor has recommended that you receive stereotactic radiosurgery (SRS, a type of very focused radiation treatment) to the tumor(s) in your brain.

Many patients with cancer that has spread to the brain have side effects caused by swelling around the tumors. A common treatment for this swelling is a medicine called dexamethasone. Dexamethasone is a steroid. Long-term use of steroids has several known side effects.

Recent studies have shown that a drug commonly used in to control high blood sugar in diabetes, called glyburide, can decrease brain swelling in patients with brain damage or stroke. Animal studies have shown that this drug may also reduce swelling from tumors in the brain. Researchers are interested in whether glyburide could treat brain swelling as well as dexamethasone, but with fewer side effects.

This Pilot Portion of the study is being done to see whether glyburide is safe to be used in patients without diabetes who are getting radiosurgery (SRS) for brain metastases.

This information will be used as part of a larger study to find out if glyburide can reduce brain swelling in patients at higher risk for developing swelling after SRS and decrease the need for steroids to control the swelling. The main purpose of this study is to make sure that patients who do not have diabetes can safely tolerate glyburide.

Approximately 10 patients will participate in the pilot portion of the study at UAB.

Study Participation & Procedures

Before you begin the study:
You will need to have the following exams, tests, or procedures. The exams, tests, or procedures listed below are part of regular cancer care. These may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor. Some of these study procedures may be conducted remotely, if necessary.

- History and physical exam that includes a neurological (brain function) exam and a record of your height and weight
- Documentation of your steroid use (if you are taking steroids you may be asked to stop taking them in a safe manner if you wish to participate in this study).
- MRI scan of your brain with contrast (MRI is magnetic response imaging that uses magnets to get detailed pictures inside your head).
- Routine blood tests (about 2-3 teaspoons of blood will be taken from your vein).
- Pregnancy test for women of child-bearing potential

During the study:
If the exams, tests, and procedures show that you can be in the study, and you choose to take part, then you will need the following test and procedures. Some are part of regular cancer care and others are not. Some of these study procedures may be conducted remotely, if necessary. The extra tests and procedures will be outlined below and indicated as research only requirements.

You will need to come to the office 5-9 days before your SRS treatment. The following tests and procedures will be done:

- Documentation of your steroid use.
- *Research Requirement*: You will be given your glyburide pills (the dose is 1.25 mg per pill). You should take one 2 times a day by mouth. Take 1 pill in the morning with breakfast and 1 pill in the evening with dinner. You will be asked to record when you took each dose in a medication administration log, which you will be given at this visit.
    - You should start taking your glyburide at least 5 days prior to your SRS treatment. You will continue to take glyburide until the evening dose on the day of your 1 month post SRS MRI scan. If you miss a dose, please do not make it up at a later time, just omit the dose and record it in your log.
- *Research Requirement*: You will also be given a blood glucose monitor, a blood glucose log, and educational handouts. A detailed list of these instructions is described in Attachment # 1 of this document.
    - You will be trained to test your blood sugar and asked to record it in a blood glucose log, just like a diabetic patient would. We will teach you the symptoms that you need to recognize if you are experiencing low blood sugar, which blood sugar levels are low enough that you should eat or drink something to cause it to go up, and who to call if you need help.

- You will need to record your blood sugar levels 4 times a day (in the morning before breakfast (fasting), before lunch, before dinner, and before bed). This should start on the day you begin glyburide and continue at least until your 1 week follow-up appointment after your SRS procedure. Also, you will be asked to bring your blood glucose log, with your recorded values, to each clinic visit to be reviewed by the study nurse and/or doctor.
- The nurse or a member of the research team will also take a fingerstick glucose reading from you at this visit. This value will be recorded in your blood glucose log by the nurse and/or doctor.

On the day of your SRS treatment the following tests and procedures will be done:

- Documentation of your steroid use.
- *Research Requirement:* You will continue to take glyburide and record your blood sugar levels 4 times a day (in the morning before breakfast (fasting), before lunch, before dinner, and before bed). This blood sugar check should continue until your 1 week follow-up appointment after your SRS procedure. The blood glucose log with your recorded values will be reviewed by the study nurse and/or doctor.

Radiosurgery (SRS) will be done using a Linear Accelerator. You should continue your glyburide at this time. These procedures are considered standard of care at this institution. You will not receive any additional radiation dose by participating in this study.

You will need these tests and procedures in follow-up visits:
At your one week follow-up appointment after SRS treatment, you will come to the radiation oncology department and have the following tests and procedures done:

- Documentation of your steroid use.
- Evaluation of any side effects from treatment you may be having.
- *Research Requirement:* Routine blood tests (about 2-3 teaspoons of blood will be taken from your vein).
- *Research Requirement*: The nurse or a member of the research team will take a fingerstick glucose reading from you at this visit and review your medication administration and blood glucose logs.
  - If there are no problems you will only have to test your blood sugar once a day (in the morning before breakfast (fasting)). You will do this until you finish taking the glyburide.
  - You will continue to take glyburide twice a day until the day of your 1 month follow-up MRI scan. You should take your last dose the evening of this scan. You can stop checking your blood sugar levels then.

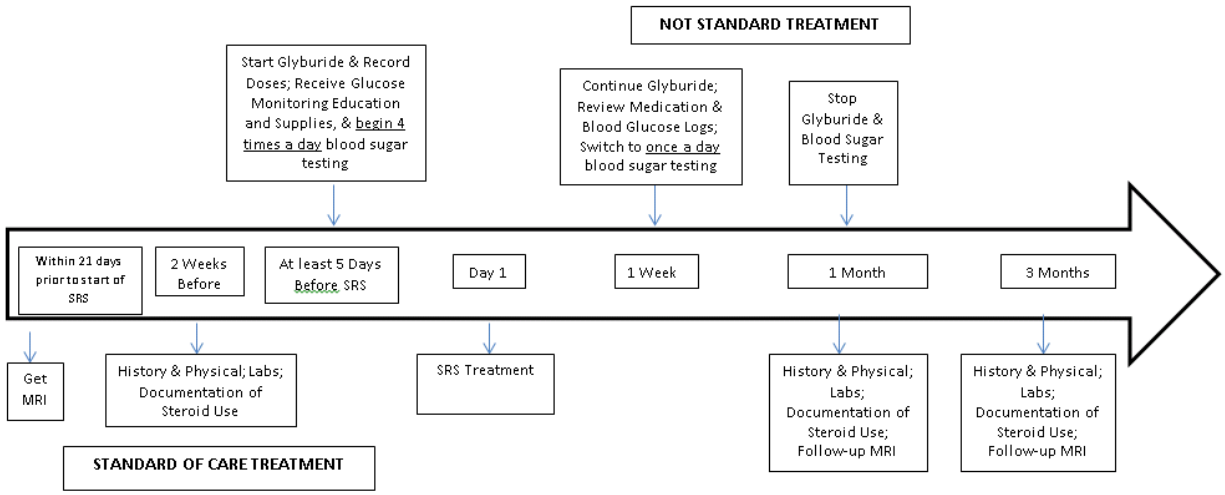
Follow-up appointments 1 month and 3 months after your SRS treatment will be scheduled. Some of these study procedures may be conducted remotely, if necessary. At these appointments the following tests and procedures will be done:

- History and physical exam that includes a neurological (brain function) exam.
- Documentation of your steroid use.
- Routine blood tests (about 2-3 teaspoons of blood will be taken from your vein).
- Evaluation of any side effects from treatment you may be having.
- MRI scan of your brain with contrast.

Research Requirement: On the day of your 1 month post SRS MRI scan, you can stop taking glyburide (after the evening dose) and stop checking your blood sugar. The nurse or a member of the research team will also take a fingerstick glucose reading from you at this visit and collect your medication administration and blood glucose logs.

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading from the left and read to the right, following the lines and arrows.



Length of Study

Your participation in the study will last about 3 months, beginning at least 5 days before radiosurgery and ending with your 3 month follow-up MRI scan. We would like to keep in touch with you after that and check on your medical condition if you allow us to.

Risks and Discomforts

You may have side effects while on the study. Everyone taking part in the study will be monitored for any side effects. However, researchers do not know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop taking the medicine. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects of glyburide include those that are:
One risk is that glyburide will not control symptoms from brain swelling. If you have severe symptoms that glyburide does not control, you will be removed from the study and you will get dexamethasone, the regular treatment for swelling.

Common

- Low blood sugar
- Nausea
- Abdominal discomfort
- Blurred vision
- Weight gain
- Raise in liver enzyme levels
- Rash
- Light sensitivity

Rare, but Serious

- Low blood sugar causing fatigue, seizures, coma, and even death
- Liver damage which may cause yellowing of the skin
- Anemia (low red blood cell count)
- Low white blood cell count
- Allergic reaction (do not take if you are allergic to sulfonamides)
- Damage to your heart

Risks and side effects of stereotactic radiosurgery (SRS) include those that are:

Possible

- Mild discomfort (can include pressure or squeezing sensation) from the frame placement, which usually goes away within a few minutes
- Hair loss, though this will be minimal and dependent on the location of your tumor
- Scalp soreness, numbness or tenderness
- Scarring
- Headaches

- Dizziness
- Nausea
- Seizures
- Fatigue
- Muscle weakness
- Visual deterioration
- Worsening neurological symptoms
- Steroid dependence
- Further surgery to remove scar tissue
- Radiation necrosis (tissue/cell death)
- Injury to surrounding brain tissue
- Edema (swelling of the brain), which is reversible with proper treatment

Reproductive Risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. If you feel you or your partner might be pregnant, even though you practiced birth control, you must notify your study doctor immediately. If you are a woman of child-bearing age, and have not been surgically sterilized (tubal ligation or hysterectomy), you must have a pregnancy test before enrolling in this study.

MRI Scan Risks: A magnetic resonance imaging (MRI) exam is a test that uses magnetic fields and radio waves to generate images of the inside of your body. You will be placed inside a scanner and asked to lie still for approximately 30 minutes. This is a noisy exam; you will be given earplugs to protect your hearing. During the scan, a liquid will be injected into your vein to improve the quality of the scan.

MRI has negligible risks for most people; however, if you have any metal objects in your body MRI may not be safe for you and you will not be allowed to take part in this study.

To prepare you for your MRI exam, a liquid called a “contrast dye” may be injected into your veins to improve the quality of the image. There is a small possibility that you could have a severe allergic reaction to this dye that could cause injury or death. If you have any kidney problems, the dye may cause other medical problems such as a rare disease called Nephrogenic Systemic Fibrosis. If you have any kidney problems or have ever had allergic reactions to contrast dye, you must let the study physician know as soon as possible.

Risk of Loss of Confidentiality: There is also a risk of loss of confidentiality. Efforts will be made to keep personal information confidential. There is no absolute guarantee of confidentiality, but we will work to minimize this risk. The risk of loss of confidentiality will be minimized by storing data in a secure location such as a locked office and locked cabinet. Electronic data will be password-protected.

Risk of Blood Drawing: May include pain, bruising, bleeding, or very rarely, infection at the site of the blood draw.

Risk of Blood Glucose Tests: May include pain, bleeding, infection, and soreness from the fingerstick. You will be taught how to do the testing in a way that minimizes the risk of infection.

There may also be risks in this study, which are not yet known. You will be informed of these, as we are made aware. **For more information about risks and side effects, ask your study doctor.**

Benefits

You may or may not benefit by taking part in this study. While researchers hope that glyburide taken by mouth will be safe and reduce side effects from brain swelling, there is no proof of this yet in humans with cancer. We do know that the information from this study will help researchers learn more about the treatment of cancer that has spread to the brain. This information could help future cancer patients.

Alternatives

The following alternative procedures or treatment are available if you choose not to participate in this study. Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Receiving treatment with radiosurgery without glyburide
- Taking part in another study
- Getting no treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator.

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

Results of research tests or procedures may be placed in your medical record. All information within your medical record can be viewed by individuals authorized to access the record.

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

Who may use and give out information about you?
Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children’s of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children’s of Alabama and its billing agents

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact the study doctor if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

UAB Department of Radiation Oncology will provide Glyburide at no cost to patients enrolled in the Pilot Portion of this study.

You or your insurance company will be responsible for paying for procedures, tests, and possibly medications that are standard treatment for study participants. Some examples of standard procedures include routine laboratory blood tests, x-rays, MRIs, scans, surgeries, and physicians' charges and routine medical care. Examples of other medications you could possibly require in addition to the study medication include antibiotics or other medications to manage side effects of treatment. Your insurance company may not pay for costs associated with research studies like this one. Check with your health plan or insurance company to find out what they will pay for. You are responsible for any charges your insurance company does not pay.

Payment for Participation

You will receive no payment for taking part in this study.

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Significant New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Questions

For more information concerning the research and research related risks or injuries, you can notify Dr. D. Hunter Boggs, the Principal Investigator, at UAB Department of Radiation Oncology, (205) 934-3411. For more information concerning any of the procedures, you may contact the Research Nurse at (205) 975-2880 in the UAB Department of Radiation Oncology.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates you that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____	_____
Signature of Participant	Date
_____	_____
Signature of Investigator or Person Obtaining Consent	Date

ATTACHMENT # 1

GLUCOSE MONITORING INSTRUCTIONS

HOW OFTEN SHOULD I CHECK MY BLOOD SUGAR?

4 Times a Day (the study team will let you know if you can check less often than 4 times a day):

1. Before breakfast (fasting)
2. Before lunch
3. Before dinner
4. At bedtime

More Often:

- When you feel symptoms of low or high sugars, illness, or stress
- When your doctor changes your medicine doses
- If you are more physically active than usual
- If you are pregnant or planning to become pregnant

Please write the results down in your blood glucose log and take it to all your clinic visits.

Why Should I Check My Blood Sugar?
Knowing what your blood sugar is:

- Helps you make decisions about how to eat, exercise, or take my medicine
- Let's you and us know if my any treatment needs to be changed

What Should my Blood Sugar be?
Before Meals: 80-130
2 Hours After Meals: Less than 180
Bedtime: 90-150

Less than 80 is too low.

If you are having symptoms that you think are related to your blood sugar level or if your blood sugar level is below 80, you will be instructed to check your blood glucose level again and to try the items listed on the last page of this document, "How to Manage Blood Sugar". If your blood sugar level does not increase above 80 after drinking or eating, or if your symptoms are not improving or worsening, you need to contact the study team and/or call 911 for emergency services. The UAB Department of Radiation Oncology study team and doctor can be reached at (205) 934-5670. You may reach the on call study doctor, after hours (24 hour paging), by calling (205) 934-3411.

HOW TO CHECK BLOOD GLUCOSE

MONITORING

How to Check Your Blood Glucose

(page 1 of 2 pages)

The only way to know how well your diabetes management plan is working is to check the amount of glucose that is in your blood throughout the day, every day.

Follow these steps when you check your blood glucose.

Step 1. Gather your supplies:

- home blood glucose meter
- testing strips
- **lancing device,** which makes it easier to stick your finger or forearm
- **lancet,** a tiny needle
- **sharps container,** a special plastic bottle in which you dispose of your lancets
- blood glucose record

Step 2. Wash and dry your hands, and the area you are lancing.

Step 3. Make sure you have enough blood in the area you are lancing.

For your finger, hang your hand at your side for a few seconds, or shake your hand several times. You can also squeeze the hand you are using with your other hand – in one motion from the palm of your hand to the fingertip. If you are lancing your forearm, rub it gently.

HOW TO CHECK BLOOD GLUCOSE continued…

MONITORING

How to Check Your Blood Glucose

(page 2 of 2 pages)

Step 4. Set up your meter.
Turn on your meter, if required. Most meters turn on when you insert a testing strip. Insert your testing strip as directed.

Step 5. Lance your finger or forearm.
Use your lancing device to get a drop of blood from your finger or forearm. The side of your finger hurts less than the finger tip. If you are lancing your arm, use the area closer to your elbow than your wrist.

Step 6.
Collect the blood on the testing strip.

Step 7. Read your results.

Step 8. Write the results in your blood glucose record.

There are many different meters available. Not every meter allows you to use your forearm. Use your meter as directed by the manufacturer. If you have questions or concerns, call the toll-free number found directly on the meter.

HOW TO MANAGE LOW BLOOD SUGAR

If you develop any of these symptoms during your time on study, please try:

- Drinking ½ cup of juice or soda
- Eating a few pieces of candy
- Taking 3 or 4 glucose tablets

If it will be more than an hour until meal time, try eating a snack that is high in starch. Snacks that are high in starch include:

- Crackers
- Bread
- Cookies

Symptoms include: