INFORMED CONSENT

PROTOCOL TITLE: Phase II Study of Gamma Knife Radiosurgery and Temozolomide (Temodar) for newly diagnosed brain metastases

INVESTIGATOR: John Fiveash, MD (UAB Department of Radiation Oncology) and Jennifer De Los Santos, MD - (Acton Road Clinic)

SPONSOR: University of Alabama at Birmingham Department of Radiation Oncology

SUB-INVESTIGATORS: Ruby Meredith, MD, PhD, Robert Nordal, MD, Robert Conry, MD, L. Burt Nabors, MD; Sharon Spencer, MD; Bart Guthrie, MD; James Markert MD

EXPLANATION OF PROCEDURES

You have a tumor in the brain that has spread there from another site. Standard treatments for this condition would include radiation to the entire brain and/or a single fraction (dose) of radiation to just the tumor (radiosurgery). Whole brain radiation will decrease the chance that a new tumor in the brain will grow but carries a potential risk of long-term brain injury including memory loss. This study is performed to see if an oral chemotherapy drug (temozolomide, Temodar) can decrease the chance of new brain tumor formation and delay the use of whole brain radiation. The use of this chemotherapy needs to be tested to determine if it is worthwhile. The safety of this chemotherapy has been demonstrated in brain tumor cancer patients who had tumors that started in the brain and did not spread there from another site.

All patients will receive the same treatment. There is no “placebo” or inactive treatment in this study.

If you give your consent for this study by signing this consent form, certain tests will be performed to determine your eligibility for this study. This evaluation will include blood collection (approximately 2 ½ tablespoons) for laboratory studies. If you are a female of childbearing potential, about 1 teaspoon of blood will be drawn to determine if you are pregnant. Your cancer will be assessed by MRI. During follow-up visits you will be asked to complete a short questionnaire that will assess your quality of life.

The total time you will spend in this study will be two years.
There is a slight risk of infection, mild discomfort or bruising associated with obtaining the required blood work.

**BENEFITS**

It is not known whether the radiosurgery and chemotherapy you will be given in this research study will help your condition more than the radiosurgery alone or in combination with whole brain radiation without chemotherapy. It is not possible to predict whether or not any personal benefit will result from the treatment program. The information, which is obtained from this study, may be used scientifically and possibly be helpful to others. The possible benefits of this treatment program are greater shrinkage and control of your tumor, fewer new brain tumors, and prolongation of your life. None of these possible benefits is certain or guaranteed.

You have been told that should your disease become worse, should side effects become very severe, should new scientific developments occur that indicate the treatment is not in your best interest, or should your physician feel that this treatment is no longer in your best interest, the treatment would be stopped. Further treatment options would be discussed.

**ALTERNATIVE TREATMENTS**

Other treatment choices that could be considered with your condition may include the following: (1) radiation therapy to the whole brain; (2) radiosurgery alone; (3) surgery; or (4) no treatment except medications to make you feel better. With this choice, your tumor would continue to grow and your disease would spread.

These options could be given either alone or in combination with each other. If you decide to not participate in this study, radiosurgery alone or a combination of whole brain radiation and radiosurgery could be used. Your doctor can tell you more about your condition and the possible benefits of the different available treatments. You should discuss your condition and the expected outcome with your doctor.

You are encouraged to ask your doctor any questions you have about this research study and the choices of treatment available to you. If you have any questions at all, please ask your doctor.

If your disease becomes worse, if side effects become very severe, or if developments occur that indicate the research study is not in your best interest, the treatment would be stopped. Further treatment options would be discussed at that time.
Treatment:

Radiosurgery will be delivered to the tumor(s) in the brain. This is a one-day outpatient procedure that requires placement of a stereotactic frame (a device that allows for precise measurements of an area in the brain). Within two weeks of the radiosurgery procedure you will start the chemotherapy pills (Temodar) for five days. Cycles will be repeated every 28 days following the first daily dose of Temodar from the previous cycle. This cycle will repeat for one year unless a new tumor develops in the brain or tumor grows elsewhere that would require other chemotherapy. The actual number of pills you take will be dependent on your height and weight. You cannot receive other chemotherapy while you are receiving the Temodar. Blood work is required (approximately 1 teaspoon) before each dosage cycle of Temodar to make sure your blood counts are within acceptable ranges prior to receiving the treatment medication.

RISKS AND DISCOMFORTS

Cancer treatments whether given in a research study or in the ordinary practice of medicine, may often harm you (side effects). The treatment used in this study may cause all, some, or none of the side effects listed. In addition, there is always the risk of very uncommon or previously unknown side effects occurring.

Radiosurgery requires placement of a stereotactic frame. First a local injection of numbing medication is performed at four sites on the head. The frame is then secured to the skull with four pins placed into the outer portion of the bone. This portion of the procedure may be associated with a feeling of pain or tightness for less than five minutes. Afterwards, most patients are very comfortable. There is a slight risk of bleeding or infection with placement of the frame. Radiosurgery may cause headache or nausea, which may sometimes require steroid medication for weeks or months after treatment. Less common complications from further swelling of the brain near the tumor may result in weakness, numbness, difficulty walking, or seizure. Severe swelling may require surgery and may result in death. A follow-up MRI scan may indicate an abnormality that is difficult to distinguish between tumor regrowth and injury to normal tissue or tumor. In this case a biopsy may be recommended.

Temozolomide (Temodar) may lower blood counts making you bruise more easily or lead to an increased risk of infection, weakness, or bleeding complications. Your liver enzymes may also temporarily rise. You may feel tired. You could require hospitalization, treatment with antibiotics, and/or transfusion if these problems are severe. You may also require other medications to treat nausea and vomiting. Less common reactions could include skin rash, headache, loss of appetite, fatigue, constipation, diarrhea, sores in your mouth or hair loss. Your physician will be checking you closely for these side effects. Side effects usually disappear after the treatment is stopped. If capsules are accidentally opened or damaged, inhalation or contact with the skin and mucous membranes should be avoided. Due to the possibility of birth defects, use contraceptive measures.
CONFIDENTIALITY

Records of your progress while on the study will be kept in a confidential form at this institution and in a computer file at the Department of Radiation Oncology at University of Alabama-Birmingham. The confidentiality of the central computer record is carefully guarded. During their required reviews, representatives of the Food and Drug Administration (FDA), qualified representatives of applicable drug manufacturers, the UAB Institutional Review Board (IRB), and other groups or organizations that have a role in this study, may have access to medical records that contain your identity. However, no information by which you can be identified will be released or published.

Information relating to this study, including your name, medical record number, date of birth and social security number may be shared with the billing offices of UAB and UAB Health System-affiliated entities so that claims may be submitted for payment to your insurance company for standard care, non-study related clinical services and procedures provided to you during the course of this study.

If you receive services in University Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at this facility.

WITHDRAWAL WITHOUT PREJUDICE

You are free to withdraw or withhold your consent from taking part in this research study at any time. If you refuse to participate, there will be no penalty or loss of benefits. You may seek care from a physician of your choice at any time. If you do not take part in this study or you withdraw from the study, you will continue to receive care.

NEW FINDINGS

Any significant new findings that develop during the course of the study, which may affect your willingness to continue in the research, will be provided to you by Dr. Fiveash or his staff.

COST OF PARTICIPATION IN RESEARCH

If you choose to be in this study, you or your insurance company or other third party payor must pay for the Temodar, the cost of standard medical care including radiosurgery, office visits, co-payments, any hospital charges, procedures and other treatments. If you do not receive reimbursement for the Temodar, you may apply for assistance through Schering-Plough's Commitment to Care Program (phone number 1-800-521-7157 [8:00am to 7:00pm CT]). Routine blood tests and scans will be done to evaluate the effects of treatment as would be done with alternative treatments normally. The use of medication to help control side effects could result in added costs.
PAYMENT FOR PARTICIPATION IN THIS RESEARCH

You will not be paid for your participation in this research study.

PAYMENTS FOR RESEARCH RELATED INJURIES

The University of Alabama at Birmingham (UAB) and the drug manufacturer, Schering-Plough, have made no provision for monetary compensation in the event of injury resulting from this research. In the event of injury, treatment will be provided, but is not provided free of charge.

QUESTIONS

If you have any questions about the research, you may contact Dr. John Fiveash, the principal investigator at UAB Department of Radiation Oncology at (205) 975-0224 or Dr. Jennifer De Los Santos, the principle investigator at the Acton Road Clinic.

For more information concerning any of the procedures, you may contact Lisa Clemons, R.N., UAB Department of Radiation Oncology at (205) 975-2880 or Teresa Ross, RN at (205) 978-0264 at the Acton Road Clinic.

If you have any questions regarding your rights as a research participant, you may call Ms. Sheila Moore, Director for the Office of the Institutional Review Board for Human Use (IRB). Ms. Moore can be reached at (205) 934-3789 or 1-800-822-8816, press the option for an operator/attendant and ask for extension 4-3789 between the hours of 8:00 a.m. and 5:00 p.m. CT, Monday through Friday.

LEGAL RIGHTS

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

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SIGNATURES

You are deciding whether or not to take part in this study. If you sign, it means that you have decided to volunteer to take part in this study and that you have read or had read to you all the information on this form. You will receive a signed copy of this informed consent.

_________________________________________  __________________________
Signature of Participant or Legally Authorized Representative  Date

_________________________________________  __________________________
Signature of Investigator  Date

_________________________________________  __________________________
Signature of Witness  Date

_________________________________________  __________________________
Signature of Person Obtaining Consent (If other than Investigator)  Date
University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION
FOR RESEARCH

You are being asked to sign this form to serve as authorization for UAB to use and release your health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your health information may be used for the research. Once this information has been disclosed, it may be subject to redisclosure and no longer be protected by federal privacy regulations.

Participant Name: ________________________________  UAB IRB Protocol Number: F020522015
Research Protocol: RAD 0102 - Phase II Study of Gamma Knife Radiosurgery and Temozolomide (Temodar) for Newly Diagnosed Brain Metastases
Principal Investigator: John Fivush, MD
Sponsor: Department of Radiation Oncology

Persons/organizations providing the information (check all that apply):
☒ University Hospital    ☑ UAB Clinics: ______
☒ Kirklin Clinic/Health Services Foundation (“HF”)
☒ The Children’s Hospital of Alabama
☒ Other: HEALTHSOUTH Hospital
☐ Callahan Eye Foundation Hospital (“CEFH”)
☐ Jefferson County Department of Public Health

Description of health information to be provided: All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.

Persons/organizations receiving the information: The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, Children’s, CEFH and the Department of Public Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; and outside regulatory agencies such as the Food and Drug Administration.

Authorization Expiration: Completion of Research Protocol

Authorization Revocation: You or your legally authorized representative must read and initial the following:

Initials: __________________ I understand that I may revoke this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If I revoke this Authorization, it will not have any effect to the extent UAB took action in reliance on the Authorization and any research data generated prior to revocation may still be used by the researcher.

Signature of participant: __________________________________________ Date: __________
OR
Signature of legally authorized representative: ____________________________ Date: __________

Printed name of participant’s representative: ______________________________________

Relationship to the participant: ____________________________________________

Protocol Version: August 12, 2005
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