



**THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER-HOUSTON
INFORMED CONSENT**

**A PHASE II CLINICAL TRIAL OF CISPLATIN, GEMCITABINE HCl
(GEMCITABINE), and LOW-DOSE INTERFERON- α (IFN- α) IN COMBINATIN WITH
FEVER-RANGE WHOLE BODY HYPERTHERMIA
(FR-WBH; 40 °C or 104 °F for 6 hours) IN PATIENTS WITH INOPERABLE OR
METASTATIC PANCREATIC CANCER**

INVITATION TO PARTICIPATE IN A RESEARCH STUDY:

You are invited to participate in this research study to be conducted by the physicians of the University of Texas Health Science Center-Houston and Hermann Hospital. It is important that you read and understand several general guidelines that apply to all persons who take part in this study. This research study, HSC-MS---- has been reviewed and approved by the Committee for the Protection of Human Subjects for the University of Texas Health Science Center-Houston.

You will be one of 50 patients asked to participate in this open treatment study of the efficacy and safety of a combination of two standard chemotherapy agents cisplatin (Platinol), gemcitabine (Gemzar), and a biological agent, low-dose interferon-a (IFN- α) to be given in combination with fever-range whole-body hyperthermia (FR-WBH; 40.0 °C or 104 °F). The cisplatin chemotherapy will be given on day 1, and daily low-dose IFN- α will also begin on day 1. The FR-WBH treatment will be given 36-48 hours after the cisplatin. The gemcitabine chemotherapy will be given to you at the same time as the FR-WBH, two days after the cisplatin. The drugs, cisplatin, gemcitabine, and interferon- α are chemotherapy agents approved by the Food and Drug Administration (FDA) for the treatment of many forms of cancer. Fever-range whole-body hyperthermia (FR-WBH) using the Heckel HT 2000 Infrared WBH unit when combined with chemotherapy is an investigational procedure. This means the treatment is approved for limited testing by the FDA, but is not in general use.

Taking part in this study is voluntary. You may refuse to take part or withdraw your consent at any time without prejudice to further medical care. Your response to treatment determines if you continue to take part in the study.

PURPOSE OF STUDY:

The purposes of this study are: (1) to find out if the heat + chemo-biotherapy treatment is effective in treating pancreatic cancer; (2) which toxicities the treatment causes; (3) whether the treatment improves your well-being; (4) whether the treatment improves your immunological defense against the cancer; (5) whether the treatment allows your cancer to be removed surgically; and (6) whether the treatment increases your survival from pancreatic cancer.

ALTERNATIVE TREATMENT:

You may select other options for treatment than being in this research study. Fever-range whole-body hyperthermia treatment with chemotherapy is one of several options (standard chemotherapy alone, cytokines, surgery, x-ray treatments, local-regional hyperthermia) for therapy undergoing testing that may cause tumors to shrink.

DESCRIPTION OF STUDY:

You will be considered for this study only if at entry, study test requirements are met (blood, urine, CT or MRI exams, heart, breathing tests, and normal mental function). According to the results of these first evaluations, it is possible the doctors may decide against enrolling you in the study. However, if your tests qualify you to be part of this study, you may be included. The treatment will consist of the following: On day one of week one, you will be evaluated with a history, physical examination, blood studies, and fill out a questionnaire asking how you feel. You will then receive hydration prior to, during, and after cisplatin chemotherapy which will be given I.V. over six (6) hours. On day 1, you will be given I.V. fluids, then cisplatin I.V. At approximately 8:00 p.m. on day 1, and every day thereafter, you will take low-dose interferon- α by subcutaneous injection (S.C.). The Oncology nurses will give you the cisplatin and also show you how to self-administer interferon in the Oncology Clinic or on the Oncology hospital floor. On day 3 of week 1, while being lightly sedated, you will be heated to 40.0 °C and maintained at this temperature for 6 hours. You will be given gemcitabine I.V. over 60 minutes when your rectal temperature reaches 39.5- 40.0 °C. One week after the FR-WBH/gemcitabine treatment day, on week 2, day 3, you will receive gemcitabine, alone, without WBH. Every day you will continue daily interferon injections. Week three is a week of rest, with no heat treatment or chemotherapy, however, you will continue the daily interferon injections. The next treatment cycle will begin week four.

Two days before the FR-WBH + gemcitabine, you will be given cisplatin over 6 hours in the clinic with hydration and medicine to prevent nausea. Oncology nurses will give the cisplatin chemotherapy in the Oncology Clinic or on the inpatient Oncology Ward at Hermann Hospital. The chemotherapy drug gemcitabine will be given during the FR-WBH treatment, and the second dose given week two will be given in the Oncology Clinic or by your own Oncologist. During the FR-WBH treatment you will be lying on a standard hospital stretcher or bed, enclosed by a heating tent. Your body temperature will be raised to 40.0 °C (104 °F) over 60-120 minutes and maintained at this temperature for six hours. You will be awake, but sleepy throughout the treatment. You will be able to talk with your nurse, your doctor and her associates throughout the treatment. You will be given medicine for relaxation and sedation that will help keep you comfortable while remaining awake. Your heart function, breathing, and urine function are continuously checked throughout the treatment. You will receive medicine before the chemotherapy to prevent nausea.

In order to be part of this study you must have tests that show your heart and lungs are strong enough to undergo this treatment and a CT or MRI scan of your brain to show that you do not have cancer in the brain. Each patient receives two monthly therapy treatments (two cycles of therapy) followed by evaluation to determine if further treatments will be of benefit. Before each FR-WBH + cisplatin/gemcitabine/IFN- α treatment, blood (less than one ounce) and a 24-hour urine will be collected, an electrocardiogram (heart tracing) and chest x-ray performed, and you will have an examination by the doctor. You will also fill out a questionnaire to determine how you feel. The day after receiving cisplatin and IFN- α , you will have less than 1 ounce of blood taken for analysis. One day

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after treatment you will also have less than 1 ounce of blood taken for analysis. Each week after the chemotherapy treatment (cisplatin and gemcitabine) you must have blood tests (CBC with differential and platelet count, blood creatinine and BUN) to help the doctor evaluate your response to chemotherapy.

TIME COMMITMENT:

On day one, week one, 36-48 hours before the FR-WBH + gemcitabine treatment, you will receive cisplatin I.V. over 6 h with hydration and anti-nausea medication in the clinic or in the hospital. You will give yourself interferon- α with one of Celebrex, Vioxx, or Tylenol that evening and daily, thereafter. You may be required to spend 4-24 hours under observation after the heat treatment. Gemcitabine, alone, (without FR-WBH, or cisplatin) will be given to you on day 3 of week two over 60 minutes in an ambulatory clinic setting. You will continue daily interferon from day 1 throughout the entire treatment.

ORDERLY WITHDRAWAL FROM THE STUDY:

If you should decide to withdraw your consent and participation from the study, you should do so under a doctor's guidance. Failure to follow the physician's instructions in this regard may result in worsening of your overall condition and increase the likelihood of side effects.

TERMINATION OF PARTICIPATION:

You may be removed from this study without your consent, if in the doctor's judgment, it would be for your benefit, or if you fail to follow the study outline for care as explained by the doctor or her associate.

BENEFITS:

While the doctors are using a treatment (cisplatin/interferon- α followed by FR-WBH + gemcitabine) thought to be of benefit to you, actual personal benefit may not result from taking part in the study. However, knowledge gained may be of benefit to others.

RISKS AND SIDE EFFECTS:

Risks involved in participation in this study are relatively low as long as you follow the physician's instructions.

Fever-Range Whole-Body Hyperthermia (FR-WBH):

FR-WBH has been associated with raised anxiety level due to a long duration of treatment. Patients may also experienced fever blisters if they have a history of such disorder, tingling and numbness of fingers and toes, sinus congestion, short term changes in sleep patterns, fatigue, and loss of appetite.

FR-WBH will be performed using the Heckel HT2000 Infrared WBH unit under a Food and Drug Administration (FDA) approved Non-significant risk investigational device exemption (IDE) for establishing the safety and efficacy of simultaneous delivery of mild whole body hyperthermia and chemotherapy.

Cisplatin: This chemotherapy drug can cause nausea and vomiting, and can injure the kidneys (detected by increase in blood creatinine and BUN). Cisplatin can cause nerve damage that is experienced as numbness and tingling of the hands and feet, and it can cause a decrease in hearing. Cisplatin may also cause a decrease in white blood cell count and platelet count, which can increase the possibility of infection and bleeding.

Gemcitabine: This chemotherapy drug is usually well tolerated. Although we give medicine to prevent nausea, some patients may experience mild nausea and cramps in the abdomen. In some patients, their white blood cell count or platelet count may decrease after receiving gemcitabine, which can increase possibility of infection and bleeding.

Interferon- α : This cytokine can cause fever, chills and malaise, much like the flu. These symptoms are very minor to non-existent at the low dose you will receive. Any symptoms from interferon can be largely diminished by administering the drug in the evening prior to sleep and taking Celebrex (celecoxib), Vioxx (rofecoxib), or Tylenol (acetaminophen).

COMPENSATION FOR INJURY:

If you should suffer a physical injury as a result of participation in this study, all necessary medical facilities are available for treatment. However, you cannot expect personal financial compensation for such injuries from the administrators or participants of this study. If you should sustain any injury, you should report it to Dr. Joan M.C. Bull at (713) 500-6820, the Hyperthermia Dept. office at (713) 704-2863, and to the Committee for the Protection of Human Subjects (713) 500-5827.

FINANCIAL COMPENSATION:

Because the heat treatment is an investigational procedure, one approved for limited testing by the Food and Drug Administration (FDA) but not in general use, Dr. Bull will not charge you a professional fee for performing the treatment. However, all costs for hospital observation, tests, sedation, other medications, routine clinical evaluations by the physician will be billed to you and/or your insurance. Although verification of insurance intent to pay for treatment cost has been done before treatment and discussed with you. You have been advised to personally consult with your insurance company as to whether the cost of this treatment is covered. The responsibility for all treatment costs not paid for by insurance is yours.

CONFIDENTIALITY AND ANONYMITY:

Representatives of the Food and Drug Administration (FDA) may review your research and/or medical record for the purpose of verifying data. However, your confidentiality will be preserved within legal limits and the names of patients will not be revealed in any reports or publications resulting from this study.

FOR FURTHER INFORMATION:

Dr. Joan M.C. Bull and her co-investigators will answer questions that may arise during the course of this study to your satisfaction. You may contact her or her associate at (713) 500-6820 or (713) 704-2863.

BEFORE YOU SIGN THIS DOCUMENT:

By signing this consent, you are voluntarily agreeing to participate in this research study. Make sure that questions have been answered to your satisfaction and that you have a clear understanding of the treatment plan. If you have questions regarding your rights as a research subject, call the Committee for the Protection of Human Subjects at (713) 500-5827.

Signature of Patient

DATE

Name of Patient (PLEASE PRINT)

DATE

Signature of Investigator

DATE

Signature of Witness

DATE

Joan M. C. Bull, M.D. (713) 500-6821

Glenna L. Scott, R.N. (713) 704-2437

This study (HSC-MS-02-) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) for the University of Texas Health Science Center. For any inquiries regarding research subject's rights, or to report any research-related injury, call the CPHS at 713-500-5827.

Joan M. C. Bull, M.D. (713) 500-6821

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