GET THE FACTS

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

Frequently Asked Questions About the Mistletoe-Gemcitabine Study

Who is sponsoring this study?

This phase I study is being sponsored and conducted by the National Center for Complementary Medicine and Alternative Medicine (NCCAM) in collaboration with the National Cancer Institute (NCI). Both NCCAM and NCI are components of the National Institutes of Health (NIH), which is part of the U.S. Department of Health and Human Services. NCCAM is the Federal Government's lead agency on scientific research on complementary and alternative medicine (CAM). CAM is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine as practiced in the United States. For more about CAM and NCCAM, see "For More Information."

Clinical studies are research studies in people. Phase I studies try to find out what is the safe dose and how the treatment(s) affect the human body. (To find out more, see the NCCAM fact sheet "About Clinical Trials and Complementary and Alternative Medicine."

Is this study using the same mistletoe that is used as holiday decoration?

This NCCAM study is testing mistletoe, but a different species than the one used to decorate at the holidays. The decorative plant is *American* mistletoe (Latin name *Phoradendron*), and it is not used for medicinal purposes. The plant that does have a history of medicinal use and is being studied by NCCAM is *European* mistletoe (Latin name *Viscum album* L), which is an entirely different plant. Mistletoe is a semi-parasitic plant (it derives many of its nutrients from growing on another plant) that grows on many types of trees, including apple, elm, oak, poplar, and spruce trees. European mistletoe has been used for centuries as a remedy for a wide variety of health problems. Currently, mistletoe extract in an injectable form is widely used in European countries as a treatment for people with certain types of cancer.

Why is NCCAM studying mistletoe as a cancer treatment?

NCCAM

NCCAM is studying mistletoe in combination with a chemotherapy drug as a cancer treatment in people who are at least 18 years old and have certain advanced solid tumors. The study is being done for the following reasons.

First, earlier studies have found mistletoe extracts to contain ingredients that could have a role in cancer treatment. In the laboratory, certain substances in mistletoe (especially two called lectins and viscotoxins) were found to stimulate cells in the body's immune system, such as the white blood cells. When exposed to mistletoe, the white blood cells release messenger substances called cytokines, which in turn may help the body's immune system to fight cancer. Lectins, which bind to the outside of a cell and can initiate changes within a cell, have been shown to kill cancer cells and stimulate cells of the immune system. Second, results from over 30 clinical studies in Europe on mistletoe as a cancer treatment have been published. These studies examined the effect of mistletoe on tumor response, tumor recurrence, quality of life, and survival. Mistletoe was found to be of benefit in most of these studies. However, each study had at least one major weakness (for example, in its design, concentration or schedule of mistletoe extracts used, or reporting of results) that raised doubts about the reliability of its results.

Why is NCCAM studying mistletoe in combination with gemcitabine?

The researchers want to find out more about both mistletoe as a cancer treatment and the effectiveness and safety of combining it with a chemotherapy drug. Mistletoe has been given with chemotherapy in clinical practice, but it is unclear whether that is safe or effective for the treatment of cancer. The drug that appeared to be the best candidate for the NCCAM combination study is gemcitabine. A commercially available drug approved by the Food and Drug Administration, gemcitabine is commonly used as a treatment for patients with pancreatic cancer, non-small cell lung cancer, and gynecological cancers. It is also used as a treatment for patients with advanced breast and colorectal cancer.

The researchers are seeking to find out how patients respond overall to this combination; whether mistletoe affects how the chemotherapy is tolerated (especially in bone marrow functions); and whether mistletoe's previously reported effects on the immune system also occur in this treatment combination.

What are the types of cancer that the researchers are studying this combination for?

The researchers are studying this treatment in persons with pancreatic, colorectal, non-small cell lung, and breast cancer where the cancer is either advanced (unable to be surgically removed), recurrent (has returned), or has metastasized (spread from original cancer site). To find out more about eligibility, see "For More Information."

How is mistletoe prepared?

The mistletoe extract in the NCCAM study is a highly purified standardized whole plant extract, manufactured according to strict guidelines for use in humans. After harvesting the young mistletoe sprouts, the parts are sorted, washed, minced, and then frozen. Batches of the frozen mistletoe plant material are placed in extracting machines where a spinning process separates the bulk from the liquid extract. This extract is then filtered, diluted, and filtered again before being passed through a rigorous quality control process.

How is the treatment in this study being given?

- Gemcitabine is given intravenously (through a vein) on day 1 and day 8 of a 21-day cycle. Gemcitabine is not given during the third week.

- Mistletoe is given daily by injection under the surface of the skin throughout the study, starting on day 8.

- After the participant has completed three cycles (9 weeks) of treatment, the study team will assess her or his response to the study therapy. If the disease appears stable or if there is evidence of tumor response at this evaluation point, the participant may choose to continue to participate in the study.

The mistletoe is given as an injection under the surface of the skin. Participants will be taught to give injections to themselves. The gemcitabine is prescribed as for any cancer patient in an outpatient oncology clinic. It is given intravenously (through a thin plastic tube placed into a person's arm vein) over 30 minutes in the clinic.

Do mistletoe and gemcitabine have side effects?

From previous research and other use, mistletoe is known to be generally well-tolerated. Its side effects, if any, tend to be minor and not life threatening. People might have a temporary reaction, such as itching or redness in the area where they have had an injection. To minimize this, they will be instructed by the study team to vary the places for injections (for example, the abdomen, arms, and upper thighs). Less commonly, participants might have a larger skin reaction or develop low-grade fevers or flu-like symptoms. There have been very rare reports of a more serious allergic reaction to mistletoe extract, such as difficulty breathing.

Gemcitabine has a long and well-established history of use as a chemotherapy drug. Its most common side effect is bone marrow suppression (a condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets). Patients might also experience gastrointestinal symptoms such as nausea, vomiting, or diarrhea.

If someone might be interested in participating, what steps should be taken?

If you are interested in learning more, contact the NIH Clinical Center Patient Recruitment and Public Liaison Office (see "For More Information"). If you appear to be eligible, that office will refer you to the study team for an initial telephone conversation. During this conversation, you will receive further information about the study and be asked some additional screening questions. If it appears that you might be eligible, you will attend a screening visit at NIH located in Bethesda, Maryland. At this visit, you will meet the study team, review your medical history, have a physical examination, and undergo some additional tests.

If you are eligible and would like to join the study, you will go through an "informed consent" process with a member of the study team. This means that you will learn all the details of the study, including any possible side effects, risks, and benefits. If you decide to participate, you will sign an

informed consent form to be officially enrolled. It is important to know that you are free to leave the study at any time if you change your mind about participating. To ensure coordination of your care, the study team will keep your current physician updated on your progress throughout the study.

Are there any costs?

You will need to cover the costs of traveling to the NIH campus in Bethesda, Maryland, for the initial screening visit. If you decide to join the study, there will be no further costs associated with study medications or tests performed at NIH.

For More Information

- To find out more about this study or to inquire about participating, contact the Clinical Center's Patient Recruitment and Public Liaison Office toll-free at 1–800–411–1222. The TTY number (for deaf or hard-of-hearing callers) is 301–594–9774 (local) or 1–866–411–1010 (toll-free).

- For the NIH Clinical Center's description of this trial, including its eligibility criteria, go to clinicalstudies.info.nih.gov/detail/A_2002-AT-0260.html or contact the NCCAM Clearinghouse.

- For a summary of past research on mistletoe extracts as a CAM treatment for cancer, see the National Cancer Institute's summary at www.cancer.gov/cancerinfo/pdq/cam/mistletoe.

NCCAM Clearinghouse

The NCCAM Clearinghouse provides information on CAM and on NCCAM, including publications and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

Toll-free in the U.S.: 1–888–644–6226
TTY (for deaf and hard-of-hearing callers): 1–866–464–3615
Web site: nccam.nih.gov
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NCCAM has provided this material for your information. It is not intended to substitute for the medical expertise and advice of your primary health care provider. We encourage you to discuss any decisions about treatment or care with your health care provider. The mention of any product, service, or therapy in this information is not an endorsement by NCCAM.

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