



## Mesothelioma Articles



### Trial of Cisplatin, Imatinib Mesylate, and Pemetrexed in Malignant Mesothelioma Patients

**This study is currently recruiting patients.**

Verified by M.D. Anderson Cancer Center November 2006

<b>Sponsors and Collaborators:</b>	<b>M.D. Anderson Cancer Center</b> Novartis
<b>Information provided by:</b>	M.D. Anderson Cancer Center
<b>ClinicalTrials.gov Identifier:</b>	NCT00402766

## Purpose

Primary Objective:

1. To determine the maximum tolerated dose of the combination of cisplatin, imatinib mesylate, and pemetrexed in metastatic [malignant mesothelioma](#).

Secondary Objectives:

1. To explore the biologic effects of cisplatin, imatinib mesylate, and pemetrexed on tumor tissue by:
  - a. histologic analysis of biopsy tissue
  - b. by non-invasive assessments of tumor vascularity performed before, during and after treatment
  - c. electron microscopy analysis of endothelial cell architecture after patient treatment with imatinib mesylate
2. To explore the effects of cisplatin, imatinib mesylate, and pemetrexed on surrogate markers in serum.
3. To assess the rate of response to therapy.
4. To determine the doses of the combination regimen of cisplatin, imatinib mesylate, and pemetrexed that enables de-phosphorylation of PDGF-R on malignant mesothelioma tumor cells.
5. To determine the pharmacokinetic interaction between agents in this combination regimen.

Condition	Intervention	Phase
Mesothelioma	Drug: Cisplatin Drug: Imatinib Drug: Pemetrexed	Phase I

MedlinePlus related topics: Mesothelioma

Study Type: Interventional

Study Design: Treatment, Non-Randomized, Open Label, Uncontrolled, Single Group Assignment, Safety/Efficacy Study

Official Title: Phase I Trial of Cisplatin, Pemetrexed, and Imatinib Mesylate in Unresectable or Metastatic Malignant Mesothelioma

Further study details as provided by M.D. Anderson Cancer Center:

Expected Total Enrollment: 42

Study start: August 2006

Cisplatin is used to treat different cancers, including testicular, germ cell, head and neck, bladder, and lung cancer. This drug has an atom-containing platinum, which is designed to poison cancer cells, causing them to die.

Pemetrexed is designed to block enzymes in the body that play a part in tumor growth.

Imatinib mesylate is a drug that blocks certain proteins that play a part in the development of cancer. Imatinib mesylate has also been shown to increase the effect of chemotherapy in tumor cells.

Before you can start treatment on this study, you will have what are called "screening tests." These tests will help the doctor decide if you are eligible to take part in this study. You will have your complete medical history recorded and a physical exam, including measurement of your vital signs (temperature, pulse, breathing rate, and blood pressure) and weight. An ECOG performance status evaluation (a test looking at your ability to perform day-to-day activities) will be done. Blood will be drawn (about 3 to 4 teaspoons) through a needle in your vein for routine tests. You will be asked about any medications you are taking. Women who are able to have children must have a negative blood pregnancy test. Also, your tumor will be evaluated by magnetic resonance imaging (MRI) or computerized tomography (CT) scans before the start of this study.

If you are found to be eligible to take part in this study, you will begin taking imatinib mesylate. Depending on when you begin treatment on this study, you may be asked to take 3, 4, or 6 tablets of imatinib mesylate by mouth once a day. Your doctor will also ask you to take folic acid tablets (or a multivitamin with folic acid) during the week before you receive your first infusion of pemetrexed and then every day while you are on this study. You will also be given an injection of vitamin B12. The vitamin B12 shot will be repeated every 9 weeks during treatment on this study. Folic acid and vitamin B12 will help to decrease the risk of severe side effects from pemetrexed.

After 1 week of imatinib mesylate and folic acid, you will receive cisplatin and pemetrexed by IV infusion. Cisplatin (given over 2 hours) and pemetrexed (given over 40 minutes) will be given on the first day of each treatment cycle for a total of 6 cycles. Each cycle is 28 days long.

Dexamethasone will also be given by vein before you receive pemetrexed. Dexamethasone will help to decrease the risk of rash and nausea that may be caused by pemetrexed. Your doctor will also ask you to take dexamethasone tablets by mouth twice a day (12 hours apart) only on Day 2 of each cycle.

Every 2 weeks while you are on this study, you will have a physical exam, including measurement of your vital signs and weight. An ECOG performance status evaluation will be done. Blood will be drawn (about 3 to 4 teaspoons) through a needle in your vein for routine tests. Also, at every 8 weeks, your tumor will be measured by a CT or an MRI scan.

After you complete 6 treatment cycles of cisplatin and pemetrexed, you will continue to take imatinib mesylate tablets every day up to 1 month after the 6 treatment cycles. If you develop any intolerable side effects or if your disease gets worse, your treatment on this study may be delayed; the dose of the study drugs decreased until your side effects are gone; or you may be taken completely off this study. Your doctor will talk with you about any changes in your dosing schedule or in the doses of your medication after you been evaluated in the clinic.

After you have completed all of your treatment, you will have what is called an end-of-study visit. At this visit, you will have a physical exam, including measurement of your vital signs and weight. You will have an ECOG performance status evaluation. You will have blood drawn (about 3 to 4 teaspoons) through a needle in your vein for routine tests. You will also have your tumor measured by CT or an MRI scan.

This is an investigational study. Both cisplatin and pemetrexed have been approved by the FDA for the treatment of malignant mesothelioma. The FDA has approved imatinib mesylate for the treatment of leukemia and certain sarcomas; however, it has been authorized by the FDA for use in research only in the treatment of malignant mesothelioma. Imatinib mesylate will be provided to you free of charge during this study. Cisplatin and pemetrexed will not be provided free of charge during this study and will be billed to you or your insurance company. Up to 42 patients will take part in this study. All will be enrolled at M. D. Anderson.

## Eligibility

Ages Eligible for Study: 18 Years and above, Genders Eligible for Study: Both

Criteria

**Inclusion Criteria:**

1. A written, voluntary informed consent form must be completed prior to beginning any study procedure.
2. Patients  $\geq$  18 years of age.
3. Histologically documented diagnosis of malignant mesothelioma.
4. Performance status 0-2 (ECOG)
5. Patients must have adequate hepatic, renal, & bone marrow function, defined as the following: (1) total bilirubin  $\leq$  1.5xULN; (2) SGOT & SGPT  $\leq$  2.5xULN; (3) creatinine  $\leq$  1.5xULN; (4) ANC  $\geq$   $1.5 \times 10^9/L$ ; (5) platelets  $\geq$   $100 \times 10^9/L$ . Note: Renal function is only based on serum creatinine level  $\leq$  1.5xULN. The standard Cockcroft & Gault formula or the measured glomerular filtration rate (GFR) using the appropriate radiolabelled method (51-CrEDTA or Tc99m-DTPA) must be used to calculate CrCl for enrollment or dosing. The same method used @ baseline should be used throughout the study. CrCl should be  $\geq$  45mg/dl.
6. Female patients of childbearing potential must have negative pregnancy test within 7 days before initiation of study drug dosing. Postmenopausal women must be amenorrheic for at least 12 months to be considered of non-childbearing potential. Male and female patients of reproductive potential must agree to employ an effective barrier method of birth control throughout the study and for up to 3 months following discontinuation of study drug.
7. Patients who have not received prior chemotherapy for their metastatic or recurrent unresectable malignant mesothelioma; with the exception of patients who have recurrent mesothelioma after induction chemotherapy followed by definitive treatment (surgery +/- radiotherapy). Patients must have had 2 or fewer cycles/doses of induction chemotherapy and must have had tumor response to the induction therapy.
8. Patients must have documented unresectable malignant mesothelioma (pleural or peritoneal).
9. Patients with treated brain metastasis who have stable brain disease (i.e. no steroids at least 4 weeks prior to study enrollment).

**Exclusion Criteria:**

1. Patient has received any other investigational agents within 28 days of first day of study drug dosing.
2. Patient is  $\leq$  5 years free of another primary malignancy except: if the other primary malignancy is not currently clinically significant nor requiring active intervention, or if other primary malignancy is a basal cell skin cancer, squamous skin cancer, or a cervical carcinoma in situ.
3. Patient with Grade III/IV cardiac problems as defined by the New York Heart Association Criteria. (i.e., congestive heart failure)
4. Patients with myocardial infarction within 6 months of study.
5. Female patients who are pregnant or breast-feeding.
6. Patient has a severe and/or uncontrolled medical disease (i.e., uncontrolled diabetes, chronic renal disease, or active uncontrolled infection).
7. Patient has a known untreated or unstable brain metastasis.
8. Patient has known chronic liver disease (i.e., chronic active hepatitis, and cirrhosis).
9. Patient has a known diagnosis of human immunodeficiency virus (HIV) infection. HIV patients are at much greater risk of infection when receiving highly myelosuppressive agents (cisplatin, pemetrexed, and imatinib) and for safety reasons are not eligible for this trial.
10. Patient who received prior chemotherapy for their malignant mesothelioma with the exception listed in inclusion criteria #7.
11. Patient previously received radiotherapy to  $\geq$  25 % of the bone marrow.
12. Patient had a major surgery within 2 weeks prior to study entry.
13. Patient with any significant history of non-compliance to medical regimens or with inability to grant reliable informed consent.
14. Patients must agree not to use herbal remedies or other over-the-counter biologics (i.e. shark cartilage).
15. Prior exposure to imatinib mesylate.
16. Patients taking therapeutic levels of warfarin. However, patients receiving 1 mg daily for catheter related anticoagulation are eligible for the study.

**Location and Contact Information**

Please refer to this study by ClinicalTrials.gov identifier NCT00402766

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## More Information

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