



Clinical Trial Options for Patients with Pleural Mesothelioma at Memorial Sloan Kettering

By [Lee M. Krug, MD](#) | Thursday, June 12, 2014

At Memorial Sloan Kettering, we offer a variety of clinical trials for patients with [mesothelioma](#) at all stages of their disease. These trials focus on a range of topics, from looking for genetic factors that predispose people to mesothelioma to exploring ways to combine chemotherapy, surgery, and radiation to optimize outcomes. We also have studies investigating novel therapeutic options.

The high volume of patients with mesothelioma we see at Memorial Sloan Kettering enables us to be leaders in clinical research for this tumor type.

Genetic Studies

Our researchers are actively working to identify the factors that predispose people to developing mesothelioma. We have found mutations in *BRCA1*-associated protein (*BAP1*) in approximately 20 percent of mesothelioma tumors.⁽¹⁾ There are also rare familial cases of mesothelioma related to germline *BAP1* mutations.

Patients with mesothelioma can take advantage of our clinical studies (protocols [12-235](#) and [12-245](#)) that analyze tumor and blood specimens for *BAP1* and other mutations. Further investigation of these mutations may reveal clues about the causes of mesothelioma and will hopefully lead to the development of improved treatments.

Surgery and Early-Stage Disease

Some patients with pleural mesothelioma are candidates for surgery, which most often involves resection of the lining of the lung (pleurectomy/decortication). However, surgery alone is not adequate, and other treatments, such as chemotherapy and radiation, are required to decrease the risk of recurrence. Our radiation oncologists have developed an innovative technique of administering intensity-modulated radiation therapy (IMRT) to the entire pleura while sparing the lung.⁽²⁾

A trial involving chemotherapy, pleurectomy, and pleural radiation ([protocol 08-053](#)) has just completed enrollment, and we are now analyzing the data. Soon, we plan to conduct a large, multicenter study of pleurectomy followed by chemotherapy, with or without pleural IMRT.

For other patients with early-stage disease, we are exploring a unique approach that involves intrapleural administration of an oncolytic virus ([protocol 12-169](#)). This vaccinia virus has been modified so that it is not pathogenic but does infect and kill cancer cells. The aim of this trial is to demonstrate the safety of the approach; to date, no serious treatment-related toxicities have occurred.

In another study, we are investigating whether a particular vaccine can delay or prevent recurrence of mesothelioma after surgery ([protocol 10-134](#)). The vaccine was developed by Memorial Sloan Kettering researchers to immunize against WT1, a protein that regulates gene expression and cell growth and is

commonly overexpressed in mesothelioma.⁽³⁾

Systemic Treatments

Patients with mesothelioma not amenable to surgery are typically treated with chemotherapy (pemetrexed with cisplatin or carboplatin). For such patients, we are adding LY3023414, a small molecule administered in an oral capsule, to the chemotherapy regimen to determine the safety and efficacy of this combination. LY3023414 blocks growth signals in cancer cells, and a similar drug has already been shown to shrink tumors in patients with mesothelioma. Another group of patients will receive LY3023414 alone. This trial ([protocol 12-286](#)) will open enrollment in August 2014.

In [protocol 13-185](#), we aim to identify a treatment that maintains a response to chemotherapy. The drug being tested is defactinib (otherwise known as VS-6063), which acts by inhibiting focal adhesion kinase, a molecule involved in cell structure and migration. In preclinical models, defactinib is most effective in NF2 mutant tumors. NF2 is aberrant in up to 70 percent of mesotheliomas. In this study, patients with a minimum of stable disease after four cycles of chemotherapy are randomly assigned to receive either defactinib or placebo.

Finally, we are participating in a randomized trial of tremelimumab versus placebo for patients with progression after first-line chemotherapy ([protocol 13-092](#)). Tremelimumab is a monoclonal antibody that blocks CTLA4 (similar to ipilimumab) and has shown activity in patients with mesothelioma.

Find the Appropriate Trial

Identifying the right clinical trial for your patient can be complicated, and many factors need to be considered. Our mesothelioma treatment team is experienced in selecting individuals who are most likely to benefit from a particular therapy, and we can help guide prospective patients and their caregivers through the process of choosing and enrolling in the most appropriate clinical trial.

[Learn more about the eligibility criteria for clinical trials.](#)

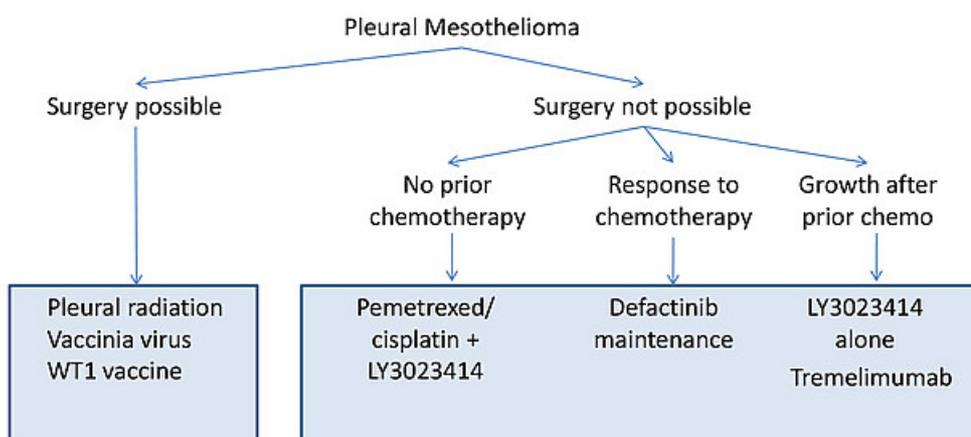


Figure 1

Memorial Sloan Kettering clinical trial flowchart for patients with pleural mesothelioma

1. Bott M, Brevet M, Taylor BS, et al. The nuclear deubiquitinase BAP1 is commonly inactivated by somatic mutations and 3p21.1 losses in malignant pleural mesothelioma. *Nat Genet.* 2011;43:668-72.
2. Rosenzweig KE, Zauderer MG, Laser B, et al. Pleural intensity-modulated radiotherapy for malignant pleural mesothelioma. *Int J Radiat Oncol Biol Phys.* 2012;83:1278-83.
3. Krug LM, Dao T, Brown AB, et al. WT1 peptide vaccinations induce CD4 and CD8 T cell immune responses in patients with mesothelioma and non-small cell lung cancer. *Cancer Immunol Immunother.* 2010;59:1467-79.

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