

Non-Technical Abstract

Phase II, Single Arm, Single Institution Clinical Trial of Docetaxel and Doxorubicin in combination with local administration of Ad5CMV-p53 (RPR/INGN201) in Locally Advanced Breast Cancer

Principal investigator: Massimo Cristofanilli, M.D.

This study will be for patients who have been diagnosed with breast cancer called "Locally Advanced Breast Cancer" (also called LABC here). Patients with LABC will likely not get better when treated by surgery, radiotherapy or both. Eight patients in every ten will die in less than five years even if they get surgery or radiotherapy for LABC.

In the past 15 years, the first line treatment used for LABC has changed from surgery to chemotherapy. How well the patient responds to chemotherapy has been an important indicator of how well the patient will do. The goal of the chemotherapy is to stop the cancer from growing. Many combinations of chemotherapy have been tried, but none is better than the more old-fashioned chemotherapy using a chemical called doxorubicin. Because there has been no improvement in the way chemotherapy is used to treat LABC, possible reasons for LABC have been studied. One of these is the gene for a protein called p53 that is changed in many people with LABC. Five out of 10 patients with LABC have a change in the gene for p53, while early breast cancer patients show this change in only three out of 10 patients. Studies in animals have shown that when the p53 does not work, the cancer is more resistant to traditional chemotherapy and radiation treatment. If the normal p53 protein is put back into cancer cells, the chemotherapy (especially using doxorubicin and docetaxel) works again.

The reason this study is being done is to try to see if injecting the test drug, Ad5CMV-p53 into a tumor can cause the cancer cells in humans to become sensitive to the chemotherapy. This may make it more likely to see complete remission and better survival for patients with LABC. The primary objective is to see if it is safe to administer the chemotherapy with the adenoviral gene therapy. The patient's tumor cells will be evaluated using laboratory tests to see if the combination is making a difference.

To be eligible to participate in the trial, patients must have documented late stage breast cancer and be able to have chemotherapy. The study will be to administer two kinds of chemotherapy (doxorubicin and docetaxel) along with injection of the adenoviral p53 into the tumor. This will be repeated every three weeks for 4 cycles before the patient has surgery.

A maximum of 60 patients will be entered in the trial, which will provide enough information to see if the combination works better than chemotherapy alone.