Non-Technical Abstract

Phase II Study Examining the Biological Efficacy of Intratumoral INGN 241 (Ad-Mda7) Administration in Patients with In Transit Melanoma

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This is a research study to look at the ways in which a treatment called INGN 241 can kill melanoma tumor cells or help the patient's immune system kill melanoma cells. INGN 241 is a type of gene therapy. In this case, the gene codes for the protein MDA-7. Laboratory experiments have shown that when MDA-7 is placed in melanoma cells, the cells stop growing and most of them eventually die; however, when MDA-7 is placed in normal cells, the cells are not harmed. Research has also shown that MDA-7 may help to boost the immune system. To deliver the MDA-7 gene to the cells, it is packaged in a delivery vehicle called a vector. The vector is actually a weakened virus, similar to the common cold virus, which can enter a cell and deliver the gene. This vector cannot divide and cause damage on its own. INGN 241 has been given to cancer patients in a study designed to look at side effects. The drug was injected directly into their tumors. The most common side effects included mild flu-like symptoms, fever, and weakness.

This study is designed for patients with melanoma in transit disease, which is a form of melanoma that spreads across the skin as small tumors in the area where the melanoma first started. Patients in this study must have at least three in transit tumors. Before therapy begins, one tumor will be biopsied and the tissue will be saved for research. On the first day of treatment (day 1) a second tumor will be injected with INGN 241. The same tumor will be injected one week later, and again the following week (days 8 and 15). INGN 241 will be administered using a small needle inserted directly into the tumor. In addition to the blood tests to check for side effects, additional small blood samples will be taken on days 1-4, 8-11, and 17 for research. On day 17, if all tumors can be completely removed, a surgery will be performed; some of the surgical tissue will be used for research. If the tumors cannot be completely removed by surgery, a biopsy of the INGN 241 injected tumor and of another tumor that was not injected will be taken on day 17. Patients who have had their tumors completely removed by surgery will come off the study after day 17. Patients whose tumors cannot be completely removed may remain on the study for up to 24 weeks if their doctor feels that the patient is benefiting from treatment. In this case, injections will continue to be given once a week for three weeks, followed by one week of rest.

The tumor biopsies and blood tests will be used to study the ways in which INGN 241 helps to kill melanoma cells. We will look for MDA-7 protein and for signs of tumor-killing effects both in the injected tumor and in another tumor that was not injected. We will study levels of "cytokines" in the blood. Cytokines are proteins made by the cells of the immune system when they are trying to attack an infection or a tumor. We will look for activation of a certain type of immune cell, the "T cell", which in some cases can kill tumor cells. We will also closely watch any other tumors the patient might have, to see if they are changing in size.