

### **Non-technical Abstract**

In the United States, over 50,000 patients per year develop colon cancer that has spread to the liver (Meta-analysis Group, 1998). Surgery offers patients with liver cancer a one-third chance of cure, but patients with tumors that cannot be surgically removed have few effective treatment options (Fong et al., 1995). The average time to disease progression is 6 to 9 months in these patients, while overall survival is 12 to 18 months (O'Connell et al., 1998).

MediGene, Inc. is currently studying a tumor-killing virus, NV1020, as a potential new treatment for patients with colorectal cancer that has spread to the liver. NV1020 is a weakened herpes virus of the same type that causes cold sores (herpes simplex virus type 1; HSV-1). NV1020 was extensively tested in HSV-sensitive animal models before it was administered to people in clinical studies.

MediGene has tested the safety of NV1020 in 12 patients with colon cancer that has spread to the liver in a study called NR1-001. The virus was injected directly into the main artery leading to the liver via a catheter inserted into the groin. Only a single injection was given but different doses of NV1020 were administered to some patients. In summary, NV1020 was well tolerated by these patients. The most common side effects were short-lived fever, headache, and minor gastrointestinal upset. The highest dose tested ( $1 \times 10^8$  pfu) caused minor changes in blood tests of the liver and blood-clotting systems, but these were not noticed by the patients and did not need any special treatment. The results have been presented at various medical and scientific meetings and will be published shortly (Fong et al., 2002).

MediGene plans to continue evaluating NV1020 as a potential therapy for patients with adenocarcinoma of the colon with metastasis to the liver. A newly proposed study is designed primarily to evaluate the safety of several injections of NV1020, prior to second line chemotherapy, in the same patient population previously studied.

The new study (called CT 1030) will test safety, and the effects of NV1020 on liver tumors, in patient volunteers who have already had chemotherapy but are being considered for more. They must also have some immunity to the herpes simplex virus (which most people have). After patients have enrolled they will have a CT scan and a physical exam before receiving up to four NV1020 injections through a catheter inserted in the groin to a blood vessel leading directly to the liver, or through a side tube of a chemotherapy pump if one has already been placed in the abdomen. Four groups of three study volunteers will each initially receive a dose of NV1020 that has already been tested in humans. If no important side effects occur, each patient receives three further injections of the same dose at weekly intervals. Successive groups of patients will be given larger doses of NV1020, providing no important side effects are seen. (It is also possible that an independent panel of doctors overseeing the safety of this study will request additional patients or dose levels of NV1020 be tested, depending on the results obtained.) After treatment with NV1020 is finished, routine chemotherapy will be started, but the type and duration

will be tailored to the needs of individual patients. Although chemotherapy may last for a number of months, patients will be more intensely monitored for the safety and other effects of NV1020 only until two courses of chemotherapy have been completed. Thereafter they will be seen less frequently, but some contact with the study physicians will be maintained indefinitely.

Once the best dose of NV1020 has been identified, an additional 15 patients will be studied but only 12 will get NV1020 in the same manner as before. The other three (called "control" patients) will be given their intended chemotherapy but no NV1020. All patients, however, will be followed in the clinic the same way that the earlier patients were.

### **References**

Fong et al. *CA Cancer J Clin* **45**:50-62 (1995)

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Meta-Analysis Group. *Cancer J Clin Oncol* **16**:301-308 (1998)

O'Connell et al. *J Clin Oncol* **16**:2528-2533 (1998)