Cantrixil

Cantrixil Program Overview

*A novel chemotherapeutic developed by **CanTx Inc**, a US-based joint venture company between **Novogen** and **Yale University**.*

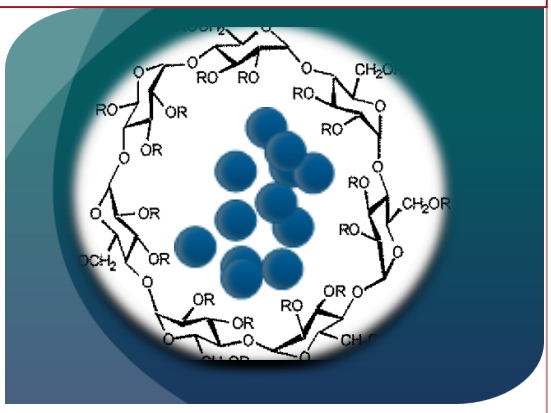
A partnership that has brought together the super-benzopyran drug technology of Novogen with the world-leading position of Yale University Medical School in ovarian cancer stem cell biology.

Cantrixil is a chemotherapy product being brought into the clinic for the treatment of a wide range of cancers, both early-stage and late-stage.

Cantrixil is a construct of the small molecule cytotoxic drug candidate, TRXE-002, contained in a cyclodextrin shell.

It has been designed specifically for injection into the peritoneal and pleural cavities to deliver a cytotoxic effect in a non-irritant and non-toxic manner.

The particular feature of TRXE-002 is its ability to kill the full hierarchy of cells within a tumor including the cancer stem cells, the regular somatic cancer cells, and the various structural components of a tumor.



The cancers in the spotlight

Cantrixil has been designed to treat cancers in the peritoneal (abdominal) and pleural chest cavities.

Peritoneal cancers include cancers that arise in the abdominal cavity and largely remain there such as cancer of the ovary, uterus, stomach, large-bowel and pancreas. Also **cancers** such as breast cancer, mesothelioma, melanoma and lymphoma that arise elsewhere but spread to the abdomen

Pleural cancers include cancers that arise in the chest such as lung cancer and mesothelioma and then spread to involve the pleural cavity. Also **cancers** such as breast cancer, gastric cancer and lymphoma that arise outside of the chest but spread to the lungs to eventually spread into the pleural cavity.

Cantrixil Features

* TRXE-002 contained in a carbohydrate shell
* Carbohydrate shell dissolves on contact with water, releasing TRXE-002
* TRXE-002 seeks out and kills cancer cells **including cancer stem cells**
* Some TRXE-002 also absorbed into the bloodstream to help attack cancer from both sides
* Cantrixil is non-irritant
* Cantrixil is non-toxic to abdominal organs

Inter-Abdominal Chemotherapy

Advantages of an intra-cavity product

* Achieving drug levels in the cancer cell's immediate environment hundreds of times higher than is possible with an intravenous injection.
* Directly acting on cancer stem cells that are spreading within the peritoneal and pleural cavities and which would be little affected by intravenously-administered drugs.

The starting point for clinical testing will be malignant ascites and malignant pleural effusion.

A patient receives chemotherapy injection into the peritoneal cavity

Market Opportunity

Various surveys show that between 15-20% of all cases of malignant cancer end in malignant pleural effusion or malignant ascites. This is a large, unmet clinical need with no approved therapies in the US.

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STRONGER IN PARTNERSHIP

Cantrixil

Inter-Abdominal Chemotherapy

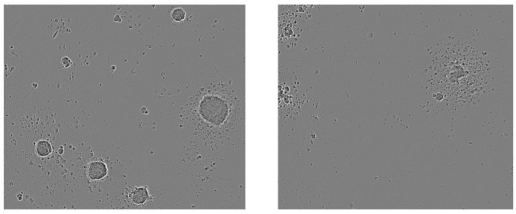
Cantrixil promises to be a breakthrough technology

Researchers at Yale University have demonstrated that Cantrixil can destroy cancer stem cells.

In a highly stringent mouse model of ovarian cancer, Cantrixil was able to inhibit the growth of ovarian cancer stem cells and their daughter cells. No other drug tested in this Yale model of ovarian cancer has been able to effectively kill both the daughter cells and their parent cancer stem cells.

In another highly sophisticated mouse model of recurrent ovarian cancer, Cantrixil can also destroy human ovarian cancer stem cells that have become resistant to standard chemotherapy.

Photos courtesy of Professor Gil Mor, Yale Medical School

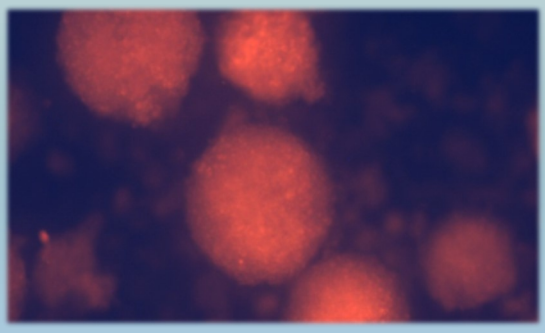


3-dimensional spheroids of human ovarian cancer stem cells are the structures found in the peritoneal cavity of women with ovarian cancer. These are the means by which the cancer spreads throughout the abdomen. Cantrixil efficiently destroys these spheroids.

Proposed Use of Cantrixil

For the treatment of malignant ascites, patients will have a small catheter inserted into their abdomen as a minor surgical procedure. A Cantrixil solution then will be injected into the peritoneal cavity. (The peritoneum is the thin membrane that lines the abdominal walls and all the abdominal organs. The narrow space between the peritoneal membrane sheets is referred to as the peritoneal cavity.) The injection procedure is relatively quick and painless.

Cantrixil originally was developed with ovarian cancer in mind. The objective was to finally develop a product with the potential of producing a generational leap forward in the survival prospects of this aggressive and lethal cancer. Progress in treating this cancer has stalled for the past 30 years. Novogen and Yale believed that the only way to achieve any meaningful increase in survival prospects was to be able to kill the ovarian cancer stem cells. That objective was met with the development of TRXE-002, the first drug to show uniformly high potency against the Yale library of ovarian cancer stem cells collected from tumors that had stopped responding to chemotherapy.



Ovarian cancer spheroids that float within the peritoneal cavity and cause the spread of cancer within the abdominal cavity

Ovarian cancer spreads from the ovary within the peritoneal cavity via the cancer stem cells. These develop into small structures known as spheroids comprising many thousands of stem cells and their daughter cells. The spheroids settle out on abdominal organs where they develop eventually into solid tumors up to many centimetres in diameter.

Cantrixil was developed as a means of ensuring that free-floating ovarian cancer spheroids in the peritoneal cavity along with established tumors were exposed to the highest levels of TRXE-002 that it was possible to achieve.

Ovarian cancer remains a prime indication for Cantrixil. However, the development of Cantrixil as a product that could be injected into the peritoneal cavity opens up the ability to use it to treat all forms of cancer that start in or invade the abdomen. TRXE-002 is active against all forms of human cancer against which it has been treated, so it certainly is not restricted to ovarian cancer. Cancer of the stomach, appendix, large bowel, pancreas, ovary and uterus, as well as invading breast cancer, melanoma and lymphoma are all potential clinical targets.

Equally, the pleural cavity (the space between the outer lining of the lungs and the inner lining of the chest wall) is a cavity in which Cantrixil has significant potential use.

CanTx proposes testing Cantrixil under the following conditions, irrespective of cancer type

1. Early-stage cancer
The best time to kill cancer stem cells and maximize the chances of preventing disease recurrence is early in the disease process when there are fewer cancer cells.
We envisage Cantrixil as a first-line therapy either alone or in combination with standard of care chemotherapies, being administered at the time of diagnosis or following surgery.

2. Late-stage cancer
This is after the patient has had multiple courses of therapy and the tumor is no longer responding to treatment. This is known as refractory cancer.

3. Malignant ascites/malignant pleural effusion
This is the terminal stage of the disease process where there is substantial cancer load in the abdomen or chest to the extent that it is interfering with the movement of fluid in and out of the cavity.
The result is that fluid (ascites in the case of the abdomen; pleural effusion in the case of the chest) builds up causing considerable pain and loss of organ function. There is no effective treatment for this condition and patients generally are made as comfortable as possible. Survival times once malignant ascites or malignant pleural effusion develops are 2-6 months on average.
Our objective is to develop Cantrixil as the first product capable of bringing meaningful survival benefit to the hundreds of thousands of patients worldwide suffering from these conditions of significant unmet clinical need.