



CANTRIXIL

Cantrixil Program Overview



Ovarian Cancer

Ovarian cancer has the lowest survival rate of all gynecological cancers with a five-year survival rate of 43%. Each year, 1400 Australian women are diagnosed; more than 1000 will die from their disease. One of the reasons that the survival rate is so low is that ovarian cancer symptoms can be silent or mistaken for other ailments so many women are diagnosed at late stages of the disease. Also, there is not a screening program to detect the cancer at early stages. The disease most commonly affects women over 50 years old but can affect all ages. The front-line treatment of this disease has not changed significantly in two decades and the disease is notorious for recurring. Targeted therapies for recurrent ovarian cancer have been hit and miss, namely because the disease is heterogeneous. This creates escalating cost burdens for the health care system caring for women requiring palliative care and immeasurable costs to families and friends. Cantrixil offers new hope for women with Ovarian Cancer.



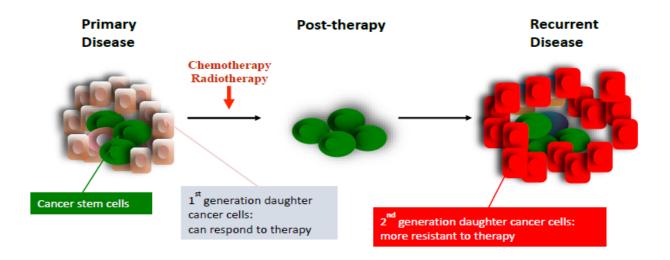
Malignant Ascites

Ascites represents accumulation of peritoneal fluid in the peritoneal cavity. As much as 20 litres of fluid can gather in the abdominal cavity. In healthy people there is a constant move of fluid into and out of the peritoneal cavity. Changes in the flow in and out lead to excess fluid and the formation of ascites. This usually causes compression of organs and tissues and severe pain. Between 15-50% of ALL patients end up with ascites. There is currently NO effective treatment for this condition. As Cantrixil is an intra-peritoneal chemotherapy, Cantrixil will be developed for the treatment of malignant ascites to fulfill this unmet clinical need.

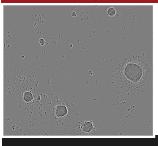
Cancer stem cells are the originating cells that give rise to tumors. They are typically slower-growing than their daughter cells and develop ways to avoid being killed by standard chemotherapy. They survive treatment only to give rise to another generation of cancer cells and a relapse or recurrence of the disease.

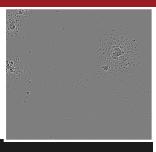
"An obvious strategy is to be more successful in treating primary disease, so that we stop the development of recurrent disease. We need to be able to kill ovarian cancer stem cells before they have the chance to produce a second generation of highly chemo resistance daughter cells".

Professor Gil Mor Yale University



Research

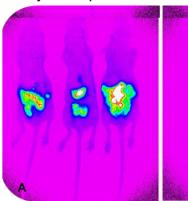


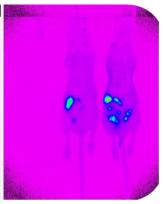


Control

Cantrixil

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.



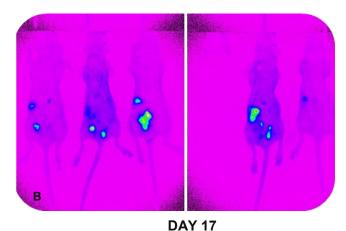


Cantrixil promises to be a breakthrough technology

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

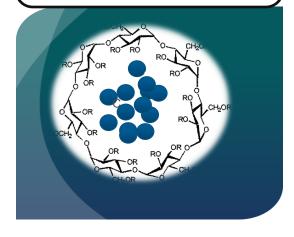
In a very stringent mouse model of ovarian cancer, Cantrixil was able to inhibit the growth of ovarian cancer stem cells and their daughter cells. No other drug tested in this Yale model of ovarian cancer has been able to effectively kill both the daughter cells and the cancer stem cells.

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.



In this mouse study, animals were inoculated with ovarian cancer stem cells labelled with a fluorescent tag and then dosed on day 4 post inoculation with Cantrixil (100 mg/kg, i.p., daily) (A) or vehicle (20% Captisol) (B) and tumours were visualised every 3rd day using a Vivo FX Imaging system. Tumour proliferation was measured by monitoring the fluorescence over time. Terminal tumour burden was assessed by removing and weighing all tumours from both the control and Cantrixil treated animals. Animal mass was measured throughout the study to monitor rodent weight gain/loss as a measure of tolerability of the animals. These data show that daily i.p. delivery of Cantrixil (100 mg/kg; i.p.) retarded the rate of tumour proliferation and significantly reduced the overall tumour burden compared with mice dosed with vehicle alone.

Cantrixil consists of the active molecule, a superbenzopyran names TRX-E-002-1, encapsulated in a sugar ring called Captisol. The Captisol dissolves readily in the body to release the active drug.



Milestones

Clinical Trials estimated to commence Q3 2015

November 2014—Cantrixil Proves Highly Effective in Pre-Clinical Test of Refractory Ovarian Cancer

June 2014—Novogen & CanTx confirm Trx-1 potency in ovarian stem cell Model

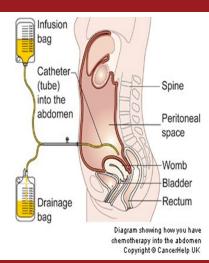
November 2013—Novogen announces joint venture with Yale University dedicated to the development of chemotherapy strategies to fight ovarian cancer

Malignant cancer is largely incurable because the cancer cells resist therapy and produce recurrent disease

Research

Cantrixil lends itself to intra-peritoneal (IP) therapy. This means that the drug is delivered directly to the abdominal cavity. The advantage of treating cancer in the abdominal cavity with this method of administration are:

- * Drugs should stay longer at the site of the cancer
- * Higher drug concentration in the inner core of the tumour
- Lower systemic toxicities since less drug travels throughput the body impacting on other organs
- A recent Cochrane review showed IP-based chemotherapy showed a survival benefit for advanced ovarian cancer patients compared to the traditional intravenous administration of chemotherapy drugs



Clinical Strategy and Market Advantage

- Destroys the cancer stem cells that cause tumor re-growth
- Destroys the cancer cells that have become resistant to chemotherapy
- * Can administer the drug to the site of the tumor

Cost of Ovarian Cancer

The cost of ovarian cancer affects the individual, the individual's family and society as a whole. These costs include medical care, costs of drugs, doctors's costs and the cost such as loss of ability to work and the costs associated with this. The incidence of recurrence of ovarian cancer is high and the costs for women with stage III or IV disease are substantially higher due to the requirement of palliative care.

According to Doyle C, Stockler M, Pintilie M, et al. Resource implications of palliative chemotherapy for ovarian cancer. J Clin Oncol 1997; 15 (3): 1000-7 A retrospective study estimated the costs of palliative care for 40 women with recurring ovarian cancer from the perspective of the provincial healthcare provider. From the start of second- or third-line chemotherapy until the time of death, the mean cost per patient was calculated at \$US53 000 (1994 costs). Approximately 62% of the total costs were due to inpatient admissions, with 58% of inpatient days attributed to symptomatic care.

The intangible costs though are not as easy to quantify although these are often the more significant cost to the patient.

About CanTx Inc.

CanTx Inc is a private biotechnology company based in New Haven, Connecticut, and established as a joint venture between Novogen and Yale University. CanTx is dedicated to the development of anti-cancer drugs for the treatment of ovarian

Projected Clinical Use

The first-in man studies will be conducted in patients with recurrent, late-stage cancers of the abdomen, in particular platinum- and taxane-refractory ovarian cancer, and malignant ascites and peritoneal carcinomatosis associated with colorectal, ovarian, pancreatic and breast cancer. There is no standard of care currently for malignant ascites and peritoneal carcinomatosis and Cantrixil is believed to be the only experimental drug being tested in this area of significant unmet clinical need

Market Opportunity

Market research group GBI Research forecast the global ovarian cancer therapeutics market will grow to US1.9B in 2020 at a CAGR (Compound Annual Growth Rate) of 3.4%

About Novogen Ltd

Novogen has two main drug technology platforms: superbenzopyrans (SBPs) and anti-tropomyosins (ATMs). SBP compounds have been created to kill the full range of cells within a tumor, but particularly the cancer stem cells. The ATM compounds target the microfilament component of the cancer cell and when used in conjunction with standard anti-microtubular drugs, result in comprehensive and fatal destruction of the cancer cell's cytoskeleton. Ovarian cancer, colorectal cancer, malignant ascites, prostate cancer, neural cancers (glioblastoma, neuroblastoma in children) and melanoma are the key clinical indications being pursued, with the ultimate objective of employing both technologies as a unified approach to first-line therapy.