

## **CRC RESEARCH #19**

Sunday, March 16<sup>th</sup> , 2008

### **DRUGS**

#### **1. Davanat Extends survival of Crc Patients Who Have Failed All Other Treatments**

Pro-Pharmaceuticals (Newton, Mass) has compiled data from its Phase II trial which shows that its company's lead product DAVANAT, a carbohydrate polymer made from mannose and galactose, effectively treated end stage crc patients who had been previously treated with standard chemo's and biologics such as avastin and/or erbitux and whose disease had progressed. Davanat was administered in combination with 5FU and data from the ongoing Phase II clinical trial confirmed that 43% of evaluable patients had significant tumor shrinkage with no hematological or gastrointestinal serious adverse events (SAE's). 20 patients completed the mid stage human clinical trial. Of that number, 3 survived more than a year, 2 lived over two years and one patient is still living. [www.cancercompass.com/cancer-news/](http://www.cancercompass.com/cancer-news/)

#### **2. AstraZeneca's Recentin enters Phase III for CRC**

AstraZeneca has announced that its cediranib-based Recentin (AZD2171) product will move into late stage trials for crc. The Horizon Study Programme is evaluating Recentin in patients with first line advanced crc. Recentin is a potent and selective VEGF signaling inhibitor taken once daily, orally, inhibiting all 3 VEGF receptors. Recentin inhibits VEGF signaling by binding to the intracellular domain of all 3 VEGF receptors, in particular VEGFR-2, the predominant receptor through which VEGF exerts its effects on angiogenesis, preventing the growth of new blood vessels, which starves the tumour of oxygen and nutrient supply. Clinical data indicate that Recentin is well tolerated and its profile indicates that it has the potential to be the "best in class" VEGF signaling inhibitor out there. Most common adverse events are diarrhea, hoarseness, headache and hypertension. [www.forbes.com/newsrelease](http://www.forbes.com/newsrelease)

#### **3. CRC Vaccine Oncovax Effectively Prevents Colon Cancer From Recurring**

OncoVAX® is an active specific immunotherapy (ASI) that uses the patient's own cancer cells to block the return of colon cancer following surgery at stage II. OncoVAX® has successfully completed its first Phase III trial in Stage II colon cancer with outstanding, statistically significant, results. This is how OncoVAX® works. Following surgery to remove the Stage II colon cancer, the tumor cells are processed in the company's facility in the Netherlands. The vaccine created in this process is injected into the patient's skin in four doses over the first six months after the surgery. The injections produce a delayed-type hypersensitive response which indicates that the body's own T-cells will respond to tumor antigens. In short, the vaccine unleashes the body's own immune system to fight a cancer that it otherwise would not have recognized.

[www.cancercompass.com/cancer-news](http://www.cancercompass.com/cancer-news)

#### **4. Dendritic Cell Therapy for Stage IV CRC Patients**

Phase I and II trials are currently being performed in respect of crc patients and Dendritic Cell therapy. Dendritic Cell therapy is immunotherapy designed for stage IV crc patients whose CEA levels should ideally be in the 100,000's in order to benefit from the therapy. Dendritic cells are blood cells found in every person's bloodstream in small amounts and are designed to identify foreign entities such as cancer cells. Dendrites are then prompted to alert fighter cells (T cells) who will then attack and kill those foreign entities, which is the basis of an immune response. A heightened immune response is what they are designed to deliver if we had enough of them. Unfortunately, we don't when faced with a situation like cancer. Dendritic cell therapy provides an increased number of dendrites for the purpose of heightening an immune response so that cancer cells can be destroyed. Only stage IV crc patients who have exhausted all therapies may be considered for the trials in the US and abroad. The most promising research is currently taking place at Georgetown with Dr. John Marshall as well as at John Hopkins. [www.dendritic.info](http://www.dendritic.info)

## 5. Magnesium/Calcium Infusions and Folfox Efficacy

The press release last year about the **Concept Trial** indicated that the patients who received calcium/magnesium infusions appeared to have lower response rates than patients in the control group. At a recent GI Symposium, the final efficacy data were presented showing that there is no link between infusions of calcium and magnesium and colorectal cancer progression. An independent panel of radiologists has **not been able to verify** the earlier concern that the use of calcium and magnesium infusions pre and post oxaliplatin to reduce chemotherapy caused neuropathy increased cancer progression. Their reviews of scans from patients who received calcium and magnesium during chemo and those who received a placebo found **no significant relationship** between the infusion and how quickly the cancer got worse. Calcium and magnesium's effectiveness in preventing neurotoxicity will be reported in June at ASCO 2008. And reputable clinicians in the US have commenced using it again such as Dr. Heinz-Josef Lenz from University of Southern California. The article does continue to propose Mag/Cal infusions to reduce oxaliplatin neurotoxicity, in folfox regimens, provided that the compounds are delivered sequentially and not at the same time.

*GI Symposium. Hocster H, et al "Effect of IV calcium and magnesium versus placebo on response to Folfox + bevacizumab in the Concept Trial" ASCO GI 2008; Abstract 280. & Journal of Clinical Oncology, vol 26, No7, March 1, 2008; pp.1188-1189.*

## 6. Evaluation of the Efficacy of Xaliproden in Preventing Oxaliplatin-Induced Neurotoxicity

Phase III clinical trials are underway evaluating the efficacy of Xaliproden (SR57746A) which is designed to prevent the oxaliplatin-induced neuropathy in crc patients. Trial sites are underway in the US, and around the world as well as Canada (Laval) through Sanofi-Aventis.

[www.cancer.gov.NationalCancerInstitute](http://www.cancer.gov.NationalCancerInstitute)

## SURGICAL

### 7. Two Stage Hepatectomy Is Potentially Curative for Patients with Irresectable Liver Mets From CRC – Presented at ASCO-GI on January 29/08

Results of a large single-centre 14 year experience were presented at the GI symposium whereby a two-stage hepatectomy can be a planned strategy based on the concept of regeneration. According to Dr. Adam, with this technique it is possible that 20% more patients initially considered to be non-resectable can be switched to resectability as long as the hepatectomies are performed within one year of each other. Dr. Adam adds that two stage hepatectomies can be considered an established potentially curative strategy in the treatment of selected patients with irresectable multiple colorectal liver mets and can experience a 5-year survival of 39% and are provided with a hope of long term survival. [www.asco.org/Two](http://www.asco.org/Two) Stage Hepatectomy for irresectable colorectal cancer liver metastases: a 14 year experience. R. Adam et al., Abstract No. 283, 2008 GI Symposium

## OTHER

### 8. Advances in Colon Cancer Testing

Response Genetics Inc. is a company that supplies University of Southern California with molecular diagnostic testing which benefit patients with colon cancer. RGI are now offering any oncologists and their respective patients the following tests:

- **KRAS Test:** Test for efficacy of panitumumab/Cetuximab
- **TS Test:** Test for efficacy of fluoropyrimidine based chemo
- **ERCC-1 Test:** Test for efficacy of platinum based chemo (oxaliplatin)

These tests will empower the oncologists to make better treatment decisions, which is the first step into personalized medicine. [www.responsegenetics.com](http://www.responsegenetics.com)

## 9. Early Detection of Recurrence by PET in the Follow-Up of patients with CRC

The benefits of including PET for detecting tumour recurrence in a randomized trial were evaluated. Patients who had undergone curative therapy were randomized to undergo either conventional or PET procedures during follow up. Recurrences were detected after a shorter time in the PET group, in which recurrences were also more frequently (10 vs. 2) cured by surgery. Regular PET monitoring in the follow up of crc patients may permit the earlier detection of recurrence, and influence therapy strategies.

*British Journal of Cancer, Sobhani, E, et al, Early detection of recurrence by FDG-PET in the follow up of patients with colorectal cancer. V 98, Feb. 2008, 875-880.*

## NUTRITION

### 10. Vitamin B6 May Slash CRC Risk

A large Scottish study suggests that increased intake of vitamin B6 from dietary and supplements may reduce the risk of colorectal cancer by over 20%. The new case-control study involved 2,028 hospital based crc patients and 2,722 population based controls. The lead author reported that there was a strong inverse and dose dependent association in the whole sample between crc risk and intake of dietary and total vitamin B6. Furthermore, a meta-analysis of published studies supported these results: High vitamin B6 intakes were reported to reduce the risk of crc by 19%. And another previous study in the Journal of Nutrition found that mild depletion of all four B vitamins was needed to promote the risk of tumour formation as well.

*Cancer Epidemiology Biomarkers & Prevention, Theodoratou, E et al., Dietary Vitamin B6 Intake and the Risk of Colorectal Cancer., Jan 1, 2008, Vol 17, pp 171-182.*

### 11. Omega-3 Fatty Acids Protect Against Colorectal Cancer

Studies including 24 European countries have concluded that consumption of omega 3 fatty acids has shown to protect against the later promotional stages of colorectal cancer. Omega-3s were shown to decrease colon cancer at both the initiation and promotion stages in experiments with animals. Omega 3 fatty acids from fish oil in animal studies have demonstrated positive results to slow the growth of cancer; increase the efficacy of chemotherapy and reduce the side effects of chemotherapy or of the cancer itself. Fish oil works by suppressing the proliferation (rapid growth) of cancer cells; allowing cancer cells to die; and reducing cancer-induced cachexia (extreme loss of weight and muscle mass). Fish oils are also widely recognized for many other health benefits such as improving heart and brain function.

*British J Cancer Jiang WG et al. The Effects of n-6 polyunsaturated fatty acids on the expression of nm-23 in human cancer cells. Mar; 77(5): 731-8*

### 12. Antioxidants & Other Nutrients Do Not Interfere with Chemotherapy or Radiation Therapy and Can Increase Kill & Increase Survival

According to several articles published in early and late 2007 in several popular medical journals, the results of 50 human studies involving 8,521 patients, 5,081 of whom were given nutrients, have consistently shown that they do not interfere with therapeutic modalities for cancer. Furthermore, non-prescription antioxidants and other nutrients enhance the killing of therapeutic modalities for cancer, decrease their side effects, and protect normal tissue. In 15 human studies, 3,738 patients who took non-prescription antioxidants and other nutrients actually had increased survival. The conclusion of the studies: **“A blanket rejection of the concurrent use of antioxidants with chemotherapy is not justified by the preponderance of evidence at this time and serves neither the scientific community nor cancer patients.”**

*J Altern Ther Health Med. Simone CB., et al., Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival. 2007 Oct; 13(5):pp 40-47.*

### 13. Alpha Lipoic Acid Preventing Neuropathy in Clinical Trials at M.D. Anderson

A randomized clinical trial is underway to test alpha-lipoic acid (ALA) to prevent oxaliplatin induced neuropathy at M.D. Anderson. The nutrient is given 3 times/day in pill form. Dr. Ying Guo is the lead investigator and she can be reached at 713 745 2327 or at [yguo@mdanderson.org](mailto:yguo@mdanderson.org). The trial is being conducted at sites throughout the US.

[www.fightcolorectalcaner.org/news/C3News&Events](http://www.fightcolorectalcaner.org/news/C3News&Events)