

# COLORECTAL CANCER ASSOCIATION OF CANADA

## COLORECTAL CANCER RESEARCH Week Ending September 19, 2008

The following colorectal cancer research update extends from September 6 – September 19, 2008 inclusive and is intended for informational purposes only.

### DRUGS

#### 1. Avastin Improves Survival in Colorectal Cancer (Sept 16/08)

Studies presented at the 33<sup>rd</sup> Congress of the European Society for Medical Oncology confirmed avastin's strong position. Avastin remains the only biologic to provide overall survival benefit when used as first-line treatment in combination with chemo for patients with K-ras wild type metastatic crc. It showed that avastin helps patients with crc survive longer. The data was in respect of a cetuximab or erbitux study called the CRYSTAL trial. K-ras wild-type describes the normal gene status seen in approximately 60% of crc patients where the K-ras gene has not mutated. The trial showed that erbitux in combination with chemo failed to deliver a significant overall survival benefit in either the general population or in patients tested for Kras status. In contrast, an earlier analysis of avastin first line in combination with chemo achieved significant overall survival for over 2 years for patients with mcrs with Kras wild type. Avastin therefore remains the best treatment option for patients with mcrs, regardless of gene mutations. The main outcomes from pivotal avastin 2107 study were:

- A statistically significant overall survival advantage in the Kras wild type population
- Statistically significant improvements in the time patients live without their disease worsening for both Kras wild type and mutation
- Statistically significant gain in overall survival in the general population, confirmed in 2 large community based studies, including some 4,000 patients.

[www.roche.com/news](http://www.roche.com/news)

#### 2. Pro-Pharmaceuticals Submits Data with FDA to Support IND Targeting Resistance to Chemo Due to Hypoxia (Sept 10/08)

Pro-Pharmaceuticals Inc, a biopharmaceutical company developing proprietary polysaccharide-based therapeutic compounds in the treatment of cancer, has submitted clinical and pre-clinical data to the FDA for a pre-investigational New Drug (IND) meeting that is scheduled for October 8<sup>th</sup>. The company plans to present the development plan to the FDA for an anti-hypoxia drug to be used in combination with DAVANAT and 5FU to treat advanced solid tumours, including colorectal cancer. The plan is in direct response to current studies indicating tumours' resistance to chemo and radiation are linked to hypoxia, a condition in which there is a decrease in the oxygen supply to a tissue. Many tumours contain a significant fraction of hypoxic cells, due to insufficient vascularization. The reduction in oxygen within tumours confers resistance to both radiotherapy and chemo, and in many cases correlates with a poor prognosis. "Results of end-stage colorectal cancer patients from our completed Phase II trial showed DAVANAT ( a polysaccharide), administered in combination with 5-FU, extended median survival to 6.7 months compared with 4.6 months for the Best Standard of Care", said Eliezer Zomer, Exec VP of Pro-Pharmaceuticals. "This unique combination of drugs offers end stage cancer patients a viable option while improving their quality of life and reducing side effects. This patient population represents a significant market opportunity."

[www.businesswire.com/portal/site](http://www.businesswire.com/portal/site)

### SURGICAL

#### 3. Microsurgery Offers Incisionless Treatment of Colorectal Cancers, Polyps (Sept.15/08)

A novel, less-risky procedure to surgically remove early cancers is now being used by surgeons to remove low rectal to low sigmoid colon polyps and early cancers of the rectum and low sigmoid colon. It's called transanal endoscopic microsurgery or TEM, a technique developed in Germany two decades ago that recently was introduced in the US and in some parts of Canada. Colon and rectal surgeons undergo specialized training to perform the surgery, and hospitals must have advanced equipment to offer TEM. Because of their location, even some early cancer and polyps have required more extensive surgery and possibly a colostomy or temp ileostomy. With TEM, the polyps and cancers are removed with less-invasive, laparoscopic procedures, avoiding longer and more risky surgery, as well as their accompanying pain and complications. TEM has proven to offer the same outcomes and survival benefit that major colon and rectal surgery does for select patients with rectal and low sigmoid tumors and polyps.

Most patients can go home the same day or early the next day after TEM, where standard surgery usually requires up to a 10 day stay. While TEM today is intended for patients with early cancers, some patients with more advanced rectal cancer can be enrolled in national oncology trials that use the less-invasive TEM procedure.

[NB: Dr. Robin Boushey at the Ottawa Hospital specializes in TEM]

[www.st.francisnews.blogspot.com/2008/09/microsurgery-offers-incisionless.html](http://www.st.francisnews.blogspot.com/2008/09/microsurgery-offers-incisionless.html)

#### 4. **New Method Proposed for Determining which Patients Should Get Treatment for Colorectal Cancer** (Sept. 11/08)

A new study shows that outcomes of patients with positive nodes (stage III) in colorectal cancer interact, to a greater extent than previously thought, with how deeply the cancer penetrates the bowel wall. Survival outcomes depend on the thickness of the primary cancer within or beyond the bowel wall in addition to whether nodes are positive or negative. A patient with a node positive “thin” lesion (ie confined to the bowel wall) has a stage III cancer with better survival outcomes than a patient with a stage II node negative “thick” cancer that penetrates beyond the bowel wall. The current standard of practice for colon cancer patients is that all or most stage III patients receive chemo after surgical removal of their cancer but stage II patients do not routinely receive chemo. In a separate National Cancer Data Base analysis, patients with stage III colon cancers confined to the bowel wall who did not receive chemo still had better survival than stage II patients.

*Gunderson, L et al., Cancer. September 11, 2008. Advanced on line edition.*

#### 5. **Hospitals Not Testing Enough Lymph Nodes** (Sept. 10/08)

Removing and testing at least 12 nearby lymph nodes during colorectal cancer surgery improves accurate staging and survival, but most US hospitals are not reaching that goal. In a recent study of nearly 1,300 hospitals, only 38% tested at least 12 nodes in 75% of colorectal cancer surgeries performed in 2004 and 2005. Testing improved from 96-97% when only 15% of hospitals met the 12 node measure. However, during that time, compliance actually went down in 310 hospitals. 980 hospitals improved, and 6 did not change. The lead investigator concluded the following:

“This study provides a national report card of nearly 1300 hospitals showing that more than 60% of institutions failed to achieve a compliance benchmark for the 12-node measure. Considerable improvement is needed in colon cancer nodal evaluation in the United States.”

*Bilimoria et al, Journal of the National Cancer Institute, advance access published online. September 9, 2008*

## **RADIATION**

#### 6. **CT Colonography Accurately Detects Large Colon Cancers** (Sept. 18/08)

The use of computed tomographic colongraphy (CTC) accurately detects 90% of large colon cancers among patients who do not exhibit any symptoms of colon cancer. The standard screening test for colorectal cancer is a colonoscopy, or optical colonoscopy (OC), a procedure in which early cancers and even pre-cancerous areas can be detected and removed. An OC is a procedure in which a lighted tube with an attached camera is inserted into the rectum and moved through the colon. During the colonoscopy the physician is able to view the colon on a screen and is able to remove abnormal-looking areas or growths. Unfortunately, due to the invasive nature of a colonoscopy, as well as the bowel preparation and required sedation, a significant portion of individuals do not undergo the procedure. Researchers have been evaluating ways to achieve accurate colorectal cancer screening coupled with patient compliance. CTC is another screening procedure for crc. CTC uses computed tomography to scan the colon. Results from research have been conflicting about the effectiveness of CTC in detecting crc compared with OC. Because CTC is not as invasive as OC, physicians are optimistic that compliance rates may increase with its use. Researchers from the Mayo Clinic recently conducted a clinical trial to further explore the accuracy of CTC among patients who did not exhibit any signs of crc. This trial included 2500 individuals 50 years or older who underwent CTC followed by standard OC at 15 different medical centers and these are the results:

- CTC accurately identified 90% of cancers measuring 10mm or more
- CTC detected only 78% of smaller cancers (6mm or greater)

*Johnson C, et al., Accuracy of CT Colonography for Detection of Large Adenomas and Cancers. New England Journal of Medicine. 2008; 359:1207-1217*

## 7. Five Year Screening Interval for Colorectal Cancer Safe Following Normal Colonoscopy (Sept 18/08)

Individuals who have normal results on their colonoscopy don't need to undergo another colonoscopy for at least five years. Researchers from Indianapolis recently conducted a clinical trial to evaluate the time interval between repeat colonoscopies among patients with normal results from an initial colonoscopy. This trial included 1256 individuals who underwent rescreening at an average of 5.34 years following their original colonoscopy.

- None of these patients had colorectal cancer identified on their follow-up colonoscopy
- 16% of patients had non-cancerous tumours on repeat colonoscopy, however, advanced non-cancerous tumours were found in only 1.3% of patients.

And the researchers concluded that the findings support a rescreening interval of 5 years or longer after a normal colonoscopic examination.

Imperiale, T, et al., Five year risk of colorectal neoplasia after negative screening colonoscopy. *New England Journal of Medicine*. 2008; 359:1218-1224

## OTHER

### 8. Survival of Hereditary Non-Polyposis Colorectal Cancer patients Compared with Sporadic Colorectal Cancer Patients (Sept. 19/08)

A recent study showed that patients with hereditary non-polyposis colorectal cancer (HNPCC) have better prognosis than sporadic colorectal cancer (crc). A cohort of 40 cases with a hospital series comprising 573 (312 and 261 respectively) were analyzed. Their survival rates were calculated during the period 1970 – 1993. The results showed that overall survival of crc in patients with HNPCC was better than sporadic CRC patients. The different outcome probably relates to the specific tumorigenesis involving DNA mismatch repair dysfunction which appeared more frequently in the sporadic group, reports the lead investigator.

Stigliano, V, et al., *Survival of Hereditary non Polyposis colorectal Cancer Patients Compared With Sporadic Colorectal Cancer patients. Journal of Experimental & Clinical Cancer Research*. 2008. Published online.

## NUTRITION

### 9. Fruits & Vegetables Reduce Colorectal Cancer Risk for Men, Not Women (Sept. 16/08)

In a recent study, eating more fruits and vegetables protected men from crc, but there wasn't a similar benefit for women. Men had about a 25% reduced risk of getting cancer compared to those who ate the least. 86,000 men and 105,000 women filled out food frequency questionnaires at the beginning of the study. Over an average follow-up period of seven years, 1,000 men and 1,000 women were diagnosed with colon or rectal cancer. Using the questionnaires, a research team divided people into five groups (quintiles) ranging from those who ate the most fruits and vegetables to those who ate the least. Men in the highest quintile had a 26% decrease in crc over those in the lowest. Fruit alone boosted chances that men wouldn't get crc by 15%, while vegetables decreased risk 20%. Risks were reduced more for colon than rectal cancer. However, women showed no benefit from high intake. There is some suggestion that the female hormone estrogen and estrogen therapy helps protect against crc. If this is the case, it might help explain why women would derive less benefit from eating fruits and vegetables than men. When the researchers analyzed data from only women who took estrogen therapy, they found no difference in crc risk among those who ate the most fruits and vegetables and those who ate the least.

Nomura et al., *American J of Clinical Nutrition*, Vol 88, #3, Sept, 2008  
Park et al., *Amer J of Epidemiology*, Vol 166, # 2, Jul 15, 2007  
Kouskik et al., *J of the National Cancer Institute*, advance access published online September