CRCColorectal Cancer Resource & Action Network

An Affiliate of the Colorectal Cancer Association of Canada

CRC RESEARCH #23©

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ENCOURAGING

1. Cancer Cases Up But Survival More Than Doubles In Breast & Bowel Cancer (Jul 8/09)

The number of people surviving some of the most common types of cancer for at least five years has doubled since the National Health Service (NHS) was founded 60 years ago in England. Comparisons have shown that survival for colon cancer has risen dramatically from 18% to 47% between 1946 and 1998. Cancer Research UK and the National Cancer Intelligence Network (NCIN) have compared cancer statistics in England and Wales from the inception of the NHS to the present day; survival and mortality statistics are based on recorded data; incidence stats are estimated for England only. Professor David Forman, based at the University of Leeds and NCIN, who helped prepare the figures, said:"We can only estimate the cost of cancer to the NHS because we have been collecting good quality data on incidence, mortality and survival over a long period. Cancer is a substantially more common disease now than in 1948. And the NCIN will help us really understand the effects of improved treatment and earlier diagnosis on better survival." Cancer Research UK said that the improvement in cancer survival over the years is a testament to the world class research that has resulted in earlier diagnosis and better treatments for patients. Hence, bowel cancer death rates have dropped by well over half despite the increase in incidence. *www.accessibility.com.au/news/cancer-cases-up-but-survival-more-than-doubles-in-breast-and-bowel-cancer*

DRUGS

2. Avastin Prolongs Colorectal Cancer Patients Survival – Data Presented in Barcelona, Spain (Jun 30/08)

Data from the randomized, controlled Phase III AVF2107 study involving more than 800 previously untreated metastatic colorectal cancer patients was presented at the World Congress on Gastrointestinal Cancer (WCGC) in Barcelona, Spain. In the study, avastin was combined with folfiri, and showed an 82% increase in the time patients with normal Kras status lived without their disease getting worse compared to chemo alone. It also showed a 57% increase in overall survival vs. chemo alone in the same patient group, while a 60% increase in the response rate was observed, compared to 37% in patients receiving chemo alone. For those patients with Kras gene mutations, there was a 69% increase in the time patients lived without their disease becoming worse compared with chemo alone. Dr. Herbert Hurwitz from Duke University in NC (principal investigator of AVF2107) said: the data demonstrate that the addition of avastin to standard chemo is active for patients with metastatic crc with both Kras wild type and mutant tumours. The high response rate, PFS and OS in the Kras wild type group are impressive and confirm that avastin should be part of the first line management of patients irrespective of Kras status and Kras testing is not needed to initiate avastin treatment. ***Hurwitz et al., Clinical Benefit of Bevacizumab in Metastatic Colorectal Cancer is Independent of Kras Mutation Status, Poster 35, World Congress on GI Cancer, June 2008***

3. Atorvastatin and Celecoxib Synergistic Against Colon Cancer Cells (Jun 25/08)

Atorvastatin and celecoxib synergistically induce cell cycle arrest and cell death in colon cancer cells according to a report in the May 1st *International Journal of Cancer.* "Taking statins and NSAIDS may produce a synergistic beneficial effect in the reduction of risks for colon cancer and other cancer types," said Dr. Chung Yang. "However, this point needs to be studied more extensively in observational epidemiological studies and in future clinical trials. The strong synergy between atorvastin and celecoxib on cell cycle arrest and cell death is of great importance for potential increase of chemoprevention and treatment efficacy by this combination in humans for colorectal cancer. The increased efficacy could also reduce celecoxib dose to minimize possible detrimental side effects while receiving beneficial effect of atorvastin in cardiovascular health." ***Yang, C et al., Combination of Atorvastatin and Celecoxib Synergistically Induces Cell Cycle Arrest and Apoptosis in Colon Cancer Cell. International J of Cancer. 2008; 122. 2115-2124***

4. Researchers See Alternative to Common CRC Drug (Oxaliplatin) (June 22/08)

A compound that accumulates in cells more readily than oxaliplatin may be just as useful in treating crc tumours, but with fewer side effects, according to MIT researchers. The compound is known as cDPCP and may better target crc cells, potentially sparing other body tissues from damage. Oxaliplatin fights tumours by entering the cell nucleus and binding to DNA, damaging it and inducing cell death. cDPCP kills cells in a similar way. However, the key difference is that while oxaliplatin can enter almost any cell, causing harmful side effects, cDPCP requires the assistance of organic cation transporters (OCT's) embedded in the cell membrane. That help is required because cDPCP is a positively charged molecule which is helped by OCT1 and OCT2 which are present in colon cells, thereby specifically targeting colorectal tumours. Researchers hope to launch clinical trails soon. www.sciencedaily.com/releases/2008/06/080617102843.htm

5. Bowel Cancer Patients Live Longer Taking Xeloda (Jun 26/08**)**

Five year follow-up data shows that patients receiving chemo after surgery to treat colon cancer, are more likely to live longer when taking the chemo pill xeloda (capecitabine), compared to those receiving 5FU intravenous chemo. The study compared xeloda to the previous gold-standard iv chemo for colon cancer, 5FU, also known as the Mayo Clinic regimen. The results showed that 5 years after beginning treatment, the percentage of stage III patients who survived was higher in the group taking xeloda adjuvantly than the group receiving 5FU (71.4% for xeloda vs. 68.4% in the 5FU group). Results from the study, known as the X-ACT trial, were presented on June 28 at the World Congress on Gastrointestinal Cancer.
www.presseportal.de/pm/24678/1217590/roche_pharmaceuticals

6. Vaccine Stops Colon Cancer's Spread in Mice (July 3/08)

A new vaccine to treat and prevent metastatic colon cancer appears to work in mice, researchers report. The vaccine has one unique property: It acts on the immune system in the intestine, a separate immune system from the one that protects the body generally. "There are two independent immune systems in our bodies; the central one and one in the gut,' said lead researcher Dr. Scott Waldman, chairman of Pharmacology and Experimental Therapeutics at Jefferson medical College at Thomas Jefferson University in Philadelphia. The theory behind the new vaccine is to take advantage of the immune system in the intestine where colon cancer starts, Waldman said. By targeting this immune system, a vaccine could develop antibodies to the cancer, he explained. The vaccine targets a protein called guanylyl cyclase C (GCC), which is normally made in the intestine. This protein is actually over expressed when cells lining the intestine transform from normal intestinal cells to colorectal cancer cells. Waldman's team engineered a vaccine that expressed GCC, and injected it into mice that had been given colon cancer cells. The vaccine did produce an immune response and it was effective at preventing metastatic colon cancer and actually extended the lives of those animals, for the animals that received the vaccine developed fewer tumours in the liver and lungs compared with unvaccinated mice. And the vaccine also improved survival to an average of 38 days, compared with 29 days in unvaccinated mice. Waldman envisions the vaccine being used in crc patients and in those who are at high risk for the disease.
www.health.usnews.com/articles/health/healthday/2008/06/24/vaccine-stops-colon-cancer's-spread-in-mice

7. Changes in Blood Magnesium Levels Predict Response to Erbitux (Jul 6/08)

Hypomagnesemia, or reduced magnesium levels, is a side effect of erbitux treatment. Patients with colorectal cancer whose blood magnesium dropped the fastest also had the best response to erbitux given with camptosar (irinotecan). Italian researchers measured magnesium levels for 68 patients before treatment began and then 6 hours, 17, 14, 21, 50 and 92 days later. After the 7th day, readings decreased consistently. Magnesium levels fell at least 20% for 25 patients by the third week. More of these patients responded to treatment, they lived longer before their cancer got worse and had longer overall survival. Bruno Vincenzi and colleagues wrote:
Our results confirm that Cetuximab treatment may induce a reduction of Mg circulating levels and offer the first evidence that Mg reduction may represent a new predictive factor of efficacy in advanced colorectal cancer patients treated with Cetuximab plus irinotecan. ***Vincenzi et al.,Changes in Blood Magnesium Levels Predict Response to Cetuximab. Clinical Cancer Research. Volume 14. Volume 14, Number 13. July 1, 2008***

8. Administration of Erbitux Every 2 Weeks in the Treatment of CRC? (Feb 208)

Dr. Josep Tabernero from Vall d'Hebron University Hospital in Barcelona, Spain presented evidence for the administration of erbitux on an every-2-week basis in combination with irinotecan in metastatic colorectal cancer. The currently approved dosing regiment for erbitux is 400 mg/m^2 initial dose followed by 250 mg/m^2 weekly. Many commonly used chemo agents for mcrc (including irinotecan alone or in combo with 5FU/folinic acid {FA}) and oxaliplatin plus 5FU/FA) are administered on an every 2 week basis. An erbitux dose of 500 mg/m^2 every 2 weeks exhibited predictable pharmacokinetics, which were similar to those of the approved weekly dosing regimen (following an initial dose of 400 mg/m^2). ***The data from the study provide early evidence that every 2 week administration of erbitux at a dose of 500 mg/m^2 is as effective and well tolerated as a weekly dose of 250 mg/m^2 and the efficacy data are for the use of treating patients who have progressed on previous treatments***. A number of phase II studies are currently underway investigating the use of erbitux administered every 2 weeks in combination with irinotecan or oxaliplatin based chemo in both the first line and subsequent line treatment of mcrc. ***Tabernero, Josep, et al., Administration of Cetuximab Every 2 Weeks in the Treatment of Metastatic Colorectal Cancer: An Effective, More Convenient Alternative To Weekly Administration? The Oncologist, Vol. 13, No.2, 113-119, Feb 2008***

SURGICAL

8. Similar Outcomes for Patients after Laparoscopic/Open Colorectal Cancer Resection (Jun 16/08)

Laparoscopic colorectal cancer resection and open colectomy provide similar long-term patient outcomes, according to a new report. Dr. Esther Kuhry from Namsos Hospital in Norway and colleagues evaluated the long-term results of laparoscopic and conventional colorectal resection in a systematic review of 12 randomized controlled trials containing 3346 patients. Recurrences at the site of the primary tumor, the occurrence of port-site and wound mets or peritoneal mets, and the development of distant mets did not differ between laparoscopic and open surgery, overall or when colon and rectal cancer were analyzed separately. The investigators concluded that "laparoscopic surgery for **colon** cancer is a safe procedure that is associated with a survival rate equal to survival after open surgery. The procedure can therefore be offered routinely to patients in hospitals where surgeons with sufficient experience in laparoscopic colon surgery are available". "In the case of **recta**l cancer", they add, "data on long term outcome are scarce and the results of large randomized trials have to be awaited". *Cochrane Database of Systematic Reviews 2008; Art.No. CD003432, Reviewed by Ramaz Mitaishvili, MD*

NUTRITION

9. Glycemic Index & Glycemic Load Linked to Risk for Colorectal Cancer (June 17/08)

Glycemic Index and glycemic load are directly linked with an increased risk for colorectal cancer, according to results published in the American J of Clinical Nutrition. Factors linked to glucose metabolism play an important role in the development of cancers, and both glycemic index (**GI**) and glycemic load (**GL**) have been investigated as potential etiologic factors. This comprehensive meta-analysis of GI and GL and cancer risk suggested an overall direct association with colorectal cancer.

Gagnarella, P, et al., Glycemic Index, Glycemic Load, and Cancer Risk: A Meta-Analysis. American Journal of Clinical Nutrition. Vol. 87. No. 6, 1793-1801. June 2008

Glycemic Index: The **glycemic index** of a food is the rate at which the body absorbs the sugars found in that food. Examples of foods with high glycemic indexes are white potatoes and white bread.

Glycemic Load: The **glycemic load** takes into account how much sugar is in a food and can be calculated by multiplying the glycemic index of that food by the number of grams of that same serving of food that is being eaten and then divided by 100. ***GL = GI/100 x #grams of Carb***