

Colorectal Cancer Resource & Action Network

An Affiliate of the Colorectal Cancer Association of Canada

CRC RESEARCH #21©

Sunday, May 25, 2008

DRUGS

1. **Administering Calcium & Magnesium Effectively Reduces Neurological Sensitivity** (May 19/08)

Researchers in the North Central Cancer Treatment Group (NCCTG) have shown that patients who receive intravenous calcium and magnesium before and after the chemotherapy drug oxaliplatin for the treatment of advanced colon cancer experience a significantly reduced incidence and severity of neurological side effects (neurotoxicity). This reduction increases the likelihood that patients are able to complete a full course of treatment. The findings were released as part of the 44th annual meeting of the American Society of Clinical Oncology (ASCO). A double-blind, placebo-controlled study that confirmed the effectiveness of calcium plus magnesium in reducing debilitating neurological sensitivity associated with oxaliplatin was designed. 50 of the 102 patients enrolled received intravenous calcium and magnesium along with oxaliplatin-based chemo, while 52 patients received oxaliplatin-based chemo and an intravenous placebo. Study results showed that the use of calcium and magnesium infusions before and after oxaliplatin was associated with a significant decrease in the incidence and severity of neurotoxicity, and it also delayed the time to the onset of neurotoxicity on oxaliplatin therapy.

www.MedicalNewsToday/ASCOAbstract:4009

2. **Understanding & Treating Peripheral Neuropathy** (May 7/08)

If you have symptoms of peripheral neuropathy that was chemo-induced, recovery is usually slow, but steps can be taken to encourage regeneration of the damaged nerves, according to an article from CancerConsultants.com. Some approaches include

1. **acupuncture** (which uses thin needles inserted in the body at certain points which control pain or numbness);
2. **massage** (which increases blood flow, which may provide pain relief associated with peripheral neuropathy);
3. **physical therapy** (through range of motion and stretching exercise, physical therapy may strengthen muscles that are weak and improve other symptoms of peripheral neuropathy) and
4. **transcutaneous nerve stimulation - TNS** (through the use of a special device that transmits electrical impulses through electrodes attached to your skin, TNS has been shown to provide pain relief and may promote nerve regeneration).

www.cancerconsultants.com/ColonCancerPatients:UnderstandingPeripheralNeuropathy

3. **Studies Point to Benefits of Personalized Chemotherapy Dose Management in CRC** (May 1/08)

A phase III randomized study of 208 mcr patients revealed that mcr patients whose dose of 5FU was personalized based on results of regular blood tests, experienced reduced severe toxicities and nearly doubled response rates, compared to patients who received standard 5FU dosing based on body surface area. The current standard of care in dosing 5FU is based on body surface area (BSA) and is calculated using patients' height and weight. In the study, personalized dosing was based on blood tests to measure the actual level of the drug. The study demonstrated that only 25 percent of crc patients achieved optimal chemo blood levels when dosed by BSA. 17% of the BSA dosed patients received toxic levels of the drug, while 58% were under dosed. Response rates were nearly doubled in the dose adjusted group versus the BSA group and overall survival at 2 years among patients with personalized 5FU dose management improved by 48% compared to the BSA arm.

Gamelin, E, et al: "Individual fluoruracil dose adjustment based on pharmacokinetic follow-up compared with conventional dosage: Results of a multicenter randomized trial of patients with metastatic colorectal cancer." J.Clin Oncol 13:2099-2105, 2008.

4. **Poniard Pharmaceuticals Completes Enrollment of Phase 2 Picoplatin Trial in CRC** (May 6/08)

Poniard Pharmaceuticals will be presenting preliminary phase 2 data and updated phase 1 data at ASCO 2008 in respect of picoplatin, the company's lead product candidate. Picoplatin is a new generation platinum chemo agent and to date has demonstrated good tolerability, with no severe neuropathies when combined with 5FU and leucovorin in the FOLPI regimen. In the phase II trial, a head to head comparison of the efficacy and safety of picoplatin with oxaliplatin

is being performed. The drug was designed to overcome platinum resistance associated with the treatment of solid tumours and has an improved safety profile compared to existing platinum-based chemotherapeutics. www.earthtimes.org/news

5. Health Canada Approves “Personalized Medicine” For MCRC – Vectibix (May 15/08)

Vectibix (panitumumab) received conditional approval from Health Canada for the treatment of mcr. Vectibix (Amgen Canada) is the first and only treatment for mcr to have data in its approved label showing how to predict which patients are most likely not to benefit from treatment by having patients tested for the Kras mutation prior to treatment. Patients with the mutated Kras gene will not benefit from vectibix therapy (which accounts for approximately 40%) and therefore unnecessary treatment can be avoided. The use of Kras biomarker testing is a means to optimize treatment outcomes as it allows healthcare resources to be directed towards those patients who are most likely to benefit from Vectibix, while those who are not can be redirected to other treatment options.

www.amgencanada.com/news/HealthCanadaApprovesPersonalizedMedicineForMetastaticColorectalCancer

SURGICAL

6. Primary Tumor Resection Prolongs Metastatic Colorectal Cancer Survival (April 28/08)

Dr. Alfred Neugut and colleagues from NY, US, reviewed the medical literature from 1996 to 2006 to identify studies that evaluated the management of primary tumours in mcr. The team found 12 relevant studies of which 10 were single-institution retrospective reviews. Approximately 70% of patients diagnosed with mcr in the US undergo primary tumour resection. The team noted that only a minority have this done for tumor-related symptoms or as part of potentially curative resection. Resection of asymptomatic primary tumors was frequently associated with prolonged survival. And Dr. Neugut’s team comments, “**Retrospective data suggest that non-curative resection of asymptomatic colorectal primary tumours may prolong survival.**” They did add the following: “However, selection bias and unaccounted clinical factors may explain this observation” and that “prospective randomized surgical trials are needed to test the role of primary tumour resection in this setting.”

Neugut, Alfred, et al: Primary Tumour Resection Prolongs Metastatic Colorectal Cancer Survival; Int J of Col Dis;2008: 23(6)559-68

NUTRITION

7. Omega-3 Linked to Lower Colorectal Cancer Risk (May 15/08)

Over an impressive 22 years of study, both omega-3 and fish intake were associated with cancer risk reduction in the colon and rectum, according to findings by researchers from Harvard and Columbia University published in the journal *Cancer Epidemiology, Biomarkers & Prevention*. According to a recent meta-analysis by researchers from a university in the Netherlands, the overall body of science indicates that the incidence of crc may be cut by 12% by consuming more fish per week. In addition, for every additional serving of fish consumed per week the risk of developing the cancer could be cut by 4%, stated the meta-analysis in the *American Journal of Epidemiology*. In terms of the Harvard-Columbia University study, Megan Hall and co-workers followed 21,376 men participating in the Physicians’ Health study (PHS) trial (started in 1982) for an average of 22 years. The highest average intake was associated with a 40% reduction in the risk of crc. In addition, this link was relevant for both colon and rectal cancers.

*Hall, M.N., et al. “A 22-year Prospective Study of Fish, n-3 Fatty Acid Intake, and Colorectal Cancer Risk in Men”. *Cancer Epidemiology, Biomarkers & Prevention*. May 2008, Volume 17, p1136-1143.*

OTHER

8. Discovery of a Novel Mechanism for the Development of Colon Cancer (May 7/08)

Recent work from the Finnish Academy Center of Excellence on Cancer Biology at the University of Helsinki, Finland, describe a mechanism by which harmless colon polyps acquire the ability to form malignant tumours. Researchers from the University of Helsinki discovered that PROX1, a protein that in embryos controls formation of normal organs, such as liver or eye, becomes abnormally overproduced at early stages of carcinoma development. PROX1 allows tumour cells to grow even in the absence of stimulating signals from surrounding normal tissues, which leads to dangerous overgrowth and development of advanced tumours. Removal of PROX1 from cancer cells reverses their malignant behavior, suggesting that PROX1 is a promising target for the development of future therapies for colon cancer.

9. Roswell Park Cancer Centre Update (May 16/08)

This is an update on the status of two studies that are becoming available to mcrp patients at Roswell Park Cancer Centre in Buffalo, as provided by clinician and oncologist Dr. Marwan Fakhri.

1. Insulin Growth Factor Receptor Inhibitor (IMC-A12) + Cetuximab: will more than likely be opening at RP the week of May 26. The study is open in 4 centers and accrual is competitive (20 in total – potentially increasing to low 30's). Enrollment requirements are as follows:
 - Patient must have responded/stabilized (min 24 weeks) to erbitux.
 - Eventually, the patient must have failed erbitux therapy as evidenced on CT scans
 - A minimum of 6 weeks needs to go by before enrolling in the IMC-A12 after failing erbitux therapy
 - The patient's tumour needs to be Kras wild type.(ie do not have the gene mutation)

The study supplies both drugs. Testing for the tumour can be done as part of the screening of the study and Dr. Fakhri is looking into the feasibility of performing labs/CT in Canada.

2. High Dose Cetuximab (double) + Irinotecan in Patients Who Previously Responded to Cetuximab: will be opening in approximately 6 months.
 - Cetuximab will be provided by the study.
 - Tumour that is Kras wild type
 - Patient has clinical documentation of disease progression during treatment or within 6 weeks after receiving the last dose of a therapeutic regimen for metastatic disease containing an anti-EGFR-component (erbitux or vectibix).
 - Toxicity or planned treatment break will not be regarded as adequate evidence of disease progression and such patients will not be eligible for this trial.

10. Cancer Experts Issue Seasonal Warning on Grilling – With An Important Research Update (May 1/08)

According to the American Institute for cancer Research (AICR), grilling and what you grill is the most important issue at this time of year. A recently published landmark AICR report on diet and cancer prevention concluded that diets high in red meat (beef, pork and lamb) and especially processed meats (such as hot dogs and sausages) are now a convincing cause of **colorectal cancer**. Based on this report, AICR recommends limiting consumption of red meat to 18 oz (cooked) per week. But the evidence on diets high in processed meat is even more troubling: according to the AICR report's analysis of the available evidence, every 3.5 oz (100g) of processed meat eaten per day increases risk for crc by 42%. Because of this, AICR now advises avoiding hot dogs – along with sausages, bacon, ham, cold cuts and other processed meats.

Also, grilling animal products (both red and white meat) causes potent carcinogens called heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs) to arise within food. These substances have been shown in lab experiments to trigger the cancer process. Hence "people may choose to take precautions that can minimize the production of these carcinogens", such as:

- Select smaller cuts of meat, thereby limiting your portion size
- Select leaner meats to prevent dripping fat from causing flare-ups which deposit carcinogens on the meat
- Reduce flare ups by spreading aluminum foil on the grill. Make small holes in the foil to allow fat to drain
- Try a marinade: marinating meat significantly reduces the formation of HCAs
- Partially pre-cook meat briefly in the microwave before grilling to speed up grilling time
- Flip meat frequently which reduces number of carcinogens that arise