

Colorectal Cancer Resource & Action Network

An Affiliate of the Colorectal Cancer Association of Canada

CRC RESEARCH #22©

Sunday, June 22, 2008

ASCO Highlights

- **Oxaliplatin:** After five years of follow-up, fewer recurrences continue when oxaliplatin is added to 5FU for stage II and III colon cancer. There is a trend toward better overall survival. This study (NSABP C-07) uses bolus 5FU rather than the continuous infusion method in the MOSAIC clinical trial.
- **Avastin:** Adding Avastin (bevacizumab) to folfox for stage II and III colon cancer treatment appears to be safe (NSABP C-08) with no significant increases in serious side effects including GI perforations, bleeding, arterial blood clots, or death. Safety follow-up is continuing, and information about whether the new treatment is more effective will be available in about two years.
- **Follow-up:** Improvements in survival time after a recurrence is detected, have weakened the link between 3 year disease-free survival and 5 year overall survival. We may need to be following up longer to find that statistical improvement.
- **Mismatch Repair:** Patients whose tumors are the result of deficient mismatch repair genes don't benefit from 5FU based treatment for stage II and III colon cancer. In some cases it may actually reduce survival. Testing for mismatch repair status before starting treatment is important for decision making.
- **Mag/Cal Infusions:** Intravenous calcium and magnesium protects against peripheral neuropathy from oxaliplatin treatment and doesn't reduce treatment effectiveness. (ASCO Abstract 4009)
- **Erbix/Avastin:** Adding erbitux (Cetuximab) to folfox and avastin (bevacizumab) for first line colorectal cancer treatment **did not** improve outcomes and, in some situations, actually decreased effectiveness. (CAIRO 2 study – ASCO Abstract 4011)
- **Intermittent Oxaliplatin:** In the CONcePT trial, giving oxaliplatin intermittently increased the time that patients remained on treatment resulting in a trend toward better progression-free survival. Calcium and magnesium infusions reduced neurotoxicity and the number of patients who had to stop treatment because of neuropathy. No reduction in effectiveness was associated with calcium and magnesium. (Mayo Clinic – NCCTG)
- **RFA + Chemo:** Initial safety information from a randomized study of radiofrequency ablation and chemotherapy found no safety problems using the two treatments together.
- **Folfiri Post Surgery:** Adding irinotecan to infused 5FU after surgery for liver metastases did not appear to have an overall advantage.
- **K-ras & Erbitux:** Colorectal cancer patients whose tumours have mutated K-ras genes do not benefit from treatment with erbitux. At the same time, patients with tumours that aren't mutated (wild type) have significantly better results when erbitux is added to either folfiri or folfox chemo. Two randomized trials of initial treatment of chemo with or without erbitux found responses and improved progression-free survival only in patients with wild-type K-ras. The CRYSTAL Phase III study compared folfiri to folfiri with the addition of erbitux. The Phase II OPUS trial used folfox as chemotherapy and compared folfox to folfox plus erbitux. Neither found benefit for patients whose tumour had mutated K-ras gene.

DRUGS

1. **Xelox as Effective as Folfox after Colorectal Cancer Progresses** (Jun 15/08)

Xelox, as second line therapy, was found to be as effective as the more commonly used folfox treatment for patients whose cancer had already gotten worse on treatment with camptosar (irinotecan) Xelox combines an oral drug Xeloda (capecitabine) with Eloxatin (oxaliplatin). Folfox uses an infusional schedule of 5FU and leucovorin. Researchers randomly compared xelox to folfox to treat 627 patients with mcr. Patients had already received initial therapy with irinotecan and either had their cancer progress or were unable to tolerate the treatments. Although outcomes were similar for the 2 regimens, side effects differed, where hand and foot syndrome was more common in the xelox population. Researchers concluded that xelox was noninferior to folfox-4 when administered as second-line therapy in patients with mcr.

Rothenberg et al., Annals of Oncology. Online advance access. June 10, 2008

RADIOTHERAPY

2. Study Suggests Survival Benefit From Radioactive Microsphere Therapy in Patients with Colorectal Cancer Liver Mets Who Have Failed Chemotherapy (Jun 2/08)

Radioactive microspheres appear to be a safe and effective treatment for patients with colorectal cancer that has spread to the liver and who have failed available chemotherapy options, according to the results of a prospective clinical study presented at ASCO. The multicentre phase II study was conducted by the Italian Society of Locoregional Therapies in Oncology (SITILLO) using SIR-spheres, which are tiny resin microspheres labeled with radioactive yttrium-90. The results of the 52 patient study revealed a median overall survival of 13 months. The liver tumours completely disappeared in one patient and 11 patients had partial response involving at least a 30% reduction in tumour size. A further 12 patients had stable disease. The liver tumours shrank sufficiently in two patients to enable potentially curative surgery to be planned. These results demonstrate that sirspheres is a promising therapy for patients with crc liver mets who have failed chemo.

Cosimelli M, et al., Clinical safety and efficacy of yttrium 90 resin microspheres alone in unresectable, heavily pre-treated colorectal liver metastases: results of a phase II trial. ASCO Annual Meeting Proceeding Journal of Clinical Oncology 2008; 26 (May 20 Supplement): Abs. 4078

OTHER

3. DiagnoCure Oncology Labs Introduces Previstage GCC, the First Molecular Colorectal Cancer Staging Test (May 29/08)

DiagnoCure Oncology Labs introduced Previstage GCC, the first molecular diagnostic test for the staging of colorectal cancer at ASCO in Chicago and educated clinicians on the science of guanylyl cyclase C (GCC) which is an enzyme (protein) found in intestinal lining. Because GCC is tissue-specific for intestinal lining, it can be used for exceedingly precise detection of metastatic disease. The presence of GCC mRNA can be detected at a rate of a single cancer cell out of 10,000,000 normal cells, versus one in 200 normal cells with traditional methods. This makes it the most precise staging tool available. When the expression of GCC mRNA is detected outside of the intestine (such as in the lymph nodes), it is a highly sensitive, early indication that colorectal cancer has spread. The Previstage GCC test should provide clinicians a significantly more sensitive tool than traditional histopathology review alone for staging a patient with colorectal cancer and therefore may help the physician determine the most appropriate course of treatment. With the Previstage GCC test, a positive result would be an indication of lymph node metastases and would be consistent with a patient having Stage III disease as opposed to stage I or II.

www.redorbit.com/news/display/?id=Q407851

4. Smokers With Advanced Colon Cancer May Face Higher Odds of Disease Recurrence (May 30/08)

People with advanced colon cancer who have smoked cigarettes or used other tobacco products for many years may have an increased risk that their colon cancer will return, according to research by Dana-Farber Cancer Institute scientists presented at ASCO on June 2/08. Based on data from 965 patients treated for stage III colon cancer, investigators found the chances of recurrence or death up to 22 percent higher in patients with a 20 or more pack year history (calculated by number of years smoking times packs per day) than in those who had never smoked. Smoking history prior to age 30 was particularly harmful for subjects that developed colon cancer years later. *J Clin Oncol 26: 2008 (May 20 suppl: abstract 4039)*

NUTRITION

5. Abdominal Fat & Colon Cancer (June 13/08)

Large amounts of fat around the abdomen increase the risk of colon cancer according to a report from the University of Pittsburg, Penn. Men with waistlines larger than about 36 inches and women with waistlines greater than about 32 inches are at about double the risk of colon cancer when compared to slimmer persons. Earlier studies have shown an association of abdominal fat with increased insulin production. Insulin apparently stimulates the growth of colon cancer. The good news is that visceral fat can be reduced by exercise.

Journal of the National Cancer Institute 91:1147-1154, 1999

6. Selenium to Prevent Recurrence of Colorectal Polyps (June 17/08)

Dr. Peter Lance, of the Arizona Cancer Center at the University of Arizona Health Sciences Center, is running a trial to compare daily selenium supplements with a placebo in patients with non cancerous growths in the rectum and colon. The mineral selenium, found naturally in grains, meat, and other common foods, is being studied to see if it can help prevent several types of cancer. Proteins in the body that incorporate selenium have antioxidant properties and help repair damaged cells, which may reduce the risk of cancer. Although the relationship between selenium in the diet and cancer risk is unclear, some studies of selenium supplementation have yielded promising results. In particular, the Nutritional Prevention of Cancer Trial, designed to see if selenium supplements could prevent nonmelanoma skin cancer, found that the supplements were linked with reduced risks of lung, prostate and colorectal cancer. "That study was a major justification for doing a randomized controlled trial with a colorectal cancer-related endpoint," said Dr. Lance. The investigators plan to follow the patients for 5 years after the end of high dose supplementation.

www.ecancermedicalscience.com/news-insider-news.asp

7. Exercise Improves Quality of Life for Colorectal Survivors (June 18/08)

Colon and rectal cancer survivors who meet Canadian public exercise guidelines have better quality of life and less fatigue. However, only 1 in 4 survivors reported they were actively exercising. Those who were exercising at the level recommended by guidelines reported significantly better quality of life. They also had less fatigue. Carolyn Peddle and her team in Edmonton, Alberta wrote: "Colorectal cancer survivors meeting public health exercise guidelines reported significantly and meaningfully better quality of life and fatigue scores than colorectal cancer survivors who did not meet guidelines. Prospective observational studies and randomized, controlled trials are needed to further assess the causal nature of these relationships".

info@fightcolorectalcancer.org Peddler et al., *Diseases of the Colon and Rectum*, published online June 18, 2008

8. Flavonols May Slash Colorectal Cancer Risk (June 18/08)

An increased intake of antioxidant flavonols from tea, onions, beans, and apples may slash the risk of colorectal cancer by a whopping 76%, suggests a new US study. The researchers led by Gerd Bobe from the National Cancer Institute, used data from the updated flavonoid database from the US Dept of Agriculture to quantify the intake of 29 individual flavonoids, total flavonoids, and six flavonoid subgroups among participants of the Polyp Prevention Trial. And the data suggest that a flavonoid-rich diet may decrease the risk of advanced adenoma recurrence.

Bobe, G. et al., Dietary Flavonoids and Colorectal Adenoma Recurrence in the Polyp Prevention Trial. Cancer Epidemiology Biomarkers & Prevention. June 2008; Volume 17, pp 1344-1353, doi: 10.1158/1055-9965.EPI-07-0747

9. Vitamin D Linked To Colon Cancer Survival (June 20/08)

Patients diagnosed with colon cancer who had abundant vitamin D in their blood were less likely to die during a follow-up period than those who were deficient in the vitamin, according to a new study by scientists at Dana-Farber Cancer Institute. The researchers followed 304 patients until they died or until 2005 (patients diagnosed between 1991-2002), whichever occurred first. During that period, 123 patients died, with 96 of them dying from colon or rectal cancer. The researcher then looked for associations between the patients' previously measured vitamin D blood levels and whether they had died or survived. The results showed that individuals with the vitamin D levels in the highest quartile were 48% less likely to die than those with the lowest vitamin D measurements. The odds of dying from colon cancer specifically were 39% lower, the scientists found. *Ng K. et al. Circulating 25-hydroxyvitamin D levels and survival in patients with colorectal cancer. J Clin Oncol. 2008; 26: 2984-2991*