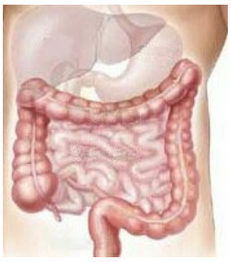
COLORECTAL CANCER RESEARCH
Month Ending May 15, 2009



The following colorectal cancer research update extends from April 18 – May 15, 2009 inclusive and is intended for informational purposes only.

DRUGS

1. **Pralatrexate Shows Anticancer Activity in Colon Cancer Cell Line** (Apr. 19/09)

   Allos Therapeutics, Inc. announced new data demonstrating the anticancer activity of its investigational drug, pralatrexate (an antifolate), in **colon**, ovarian, lung, prostate, and head and neck cancer cell lines. The preclinical research further showed that the antiproliferative effects against these cancer lines were achieved at drug concentrations that are attainable in humans. This data was presented at the American Association for Cancer Research (AACR) Annual Meeting in Denver, CO. Apparently, the killing effects of Pralatrexate are reached rapidly, within 24-72 hours. During this time, cancer cells susceptible to pralatrexate undergo what is called apoptosis, or cell death. Further studies are required and clinical trials on humans are anticipated.

   www.cancercompass.com/cancer-news/1,15598,00.htm

2. **Phase III Trial Comparing Irinotecan with Oxaliplatin, 5FU and Leucovorin in Patients with Advanced CRC Previously Treated With 5FU** (Apr. 22/09)

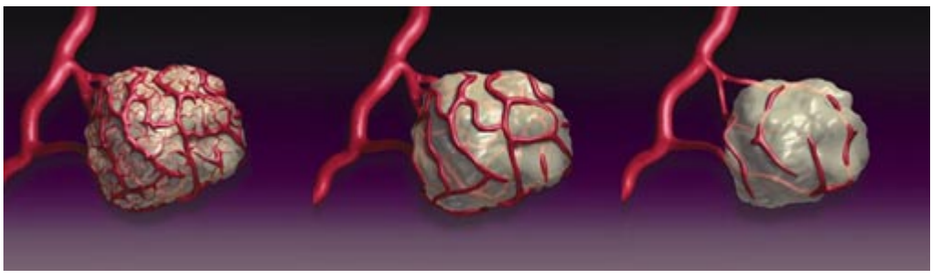
   The primary goal of this multicentre phase III trial was to determine whether overall survival of 5FU resistant patients differed when treated with second line infusional folfox4 vs. irinotecan. Cross-over to the other treatment on disease progression was mandated. Patients who experienced treatment failure with 5FU based therapy and had not received prior irinotecan or oxaliplatin, either for metastatic disease or within 6 months of adjuvant 5FU therapy, were randomly assigned to receive either irinotecan (ARM A) or Folfox4 (ARM B). Response rates and time to progression (time until disease got worse) were significantly better with folfox 4. For patients who crossed over, response rates and time to progression improvements with folfox 4 continued into third-line treatment. Irinotecan therapy was associated with more grade 3 nausea, vomiting, diarrhea, and neutropenia (low white blood counts); folfox 4 was associated with more neuropathies (tingling sensations in the hands and feet).

   Kim, George P, et al., Phase III Noninferiority Trial Comparing Irinotecan With Oxaliplatin, Fluorouracil, and Leucovorin in Patients with Advanced Colorectal Carcinoma previously Treated with Fluorouracil: N9841. J of Clinical Oncology. Early Release, published online ahead of print Apr 20, 2009, 10.1200/JCO.2008.20.4552

3. **Phase III Avastin Trial Didn't Meet Primary Goal** (Apr. 22/09)

   According to the results of a Phase III clinical trial, the addition of the targeted therapy Avastin (bevacizumab) to post-surgery chemotherapy did not reduce the risk of cancer recurrence among patients with **early-stage colon cancer.** Targeted therapies are anticancer drugs that interfere with specific pathways involved in cancer cell growth or survival. Some targeted therapies block growth signals from reaching cancer cells; others reduce the blood supply to cancer cells; and still others stimulate the immune system to recognize and attack the cancer cell. Depending on the specific "target", targeted therapies may slow cancer cell growth or increase cancer cell death.

Avastin is a targeted therapy that blocks a protein known as VEGF. VEGF plays a key role in the development of new blood vessels. Hence, it belongs to the second class described above.



Source: http://www.gene.com/gene/products/information/oncology/avastin/vegf-angiogenesis-cancer.html

By inhibiting the VEGF protein, the blood supply to a tumor may be gradually reduced.

By blocking VEGF, Avastin deprives the cancer of nutrients and oxygen and inhibits its growth. Avastin's effects on blood vessels may also improve the delivery of chemotherapy to the tumor. Multiple studies have shown that the addition of Avastin to standard chemotherapy improves outcomes in the treatment of patients with metastatic colorectal cancer (stage IV). Given these results, researchers have also initiated studies to evaluate Avastin in the adjuvant (post-surgery) treatment of patients with earlier-stage colon cancer (stage II and III). The current results are from a Phase III trial known as NSABP C-08. The study enrolled patients with **Stage II or Stage III colon cancer.** After surgical removal of the cancer, patients were assigned to receive adjuvant chemotherapy alone (mFOLFOX6) or adjuvant chemotherapy plus Avastin. The results of the study indicate that the addition of Avastin to chemotherapy did not reduce the risk of cancer recurrence. Full results from this study are expected to be presented at the annual meeting of the American Society of Clinical Oncology (ASCO), which will be held May 29-June 2, 2009. Results from another Phase III trial of Avastin in early-stage colon cancer (the AVANT study) are expected to be available in 2010.

Roche Media Release. Phase III C-08 Study of Avastin in Early-Stage Colon Cancer Does Not Meet Primary Endpoint. Available at www.roche.com/media/media_releases/med-cor-2009-04-22.htm

4. Hormone Therapy Offers Protective Effect Against Colon cancer in Older Women (Apr. 2309)

In a large study, Mayo Clinic scientists observed that self-reported use of hormone therapy was associated with a significantly lower colorectal cancer risk, though the mechanisms for the apparent protective association are still unclear. Women who used these drugs had a 28% lower incidence rate than women who did not use them. But the lead investigator, David Limsui reports that they still do not know how estrogen compounds work in cancer prevention. Women who reported using other hormone preparations, such as oral contraceptives, did not appear to derive any crc prevention benefits.

www.medicalnewstoday.com/articles/147186.php

5. Micromet Presents Preclinical Data Showing Activity of Erbitux and Vectibix Based BiTE Antibodies Against Kras and Braf CRC Cells (Apr. 23/09)

Micromet, Inc., a biopharmaceutical company developing novel, proprietary antibodies for the treatment of cancer, presented non-clinical data indicating that after developing **BiTE** antibodies from the EGFR-specific monoclonal antibodies Erbitux (cetuximab) and Vectibix (panitumumab), they were highly active against KRAS-and BRAF-mutated human colorectal cancer cell lines. Recent research has shown that the monoclonal antibodies erbitux and vectibix are not active in colorectal cancer patients with tumor cells having mutations in KRAS and BRAF genes. These patients make up more than 40% of the colorectal cancer population. Micromet's researchers converted erbitux and vectibix into novel bispecific antibodies based on Micromet's proprietary **BiTE** technology. Both of Micromet's EGFR BiTE antibodies were able to direct T cells against erbitux/vectibix-resistant human colorectal cancer cells harboring KRAS and BRAF mutations, resulting in the destruction of these cancer cells. In mice, daily EGFR BiTE antibody doses as low as 0.1 microgram/kilogram were sufficient to prevent tumor growth from mutated human colorectal cancer cells. Based on the results, the development of an EGFR-directed BiTE antibody for the treatment of patients with KRAS- and BRAF-mutated colorectal cancer may be possible.

To learn more about BiTE antibodies, please visit http://typo3.micromet-inc.com//?id=69

Lutterbuese, R, et al., Highly efficient lysis of Kras- and Braf-mutated human colon cancer cells by T cell engaging BiTE antibodies cetuximab and panitumumab. AACR Annual Meeting 2009, abstract #3251.

6. Comparing First Line Irinotecan Combinations in Elderly Patients vs. NonElderly Patients with Advanced CRC (Apr. 24/09)

This study attempted to determine the safety and efficacy of irinotecan-based chemotherapy regimens in elderly patients versus non-elderly patients in first line metastatic colorectal cancer. The results demonstrated that elderly colorectal cancer patients treated with irinotecan-based chemo had no more serious side effects than younger patients treated with the same regimens. Patients over 70 years of age also benefited equally from treatment with similar rates of tumor shrinkage, time until cancer got worse (progression free survival), and overall survival time.

Jackson, Nadine, A, et al., Comparing safety and efficacy of first-line irinotecan/fluoropyrimidine combinations in elderly versus nonelderly patients with metastatic colorectal cancer. Cancer. Published online, ahead of print April 20, 2009.

7. Development of Ostarine to Treat Cancer Induced Cachexia (Muscle Loss) (May 2/09)

Cachexia, or cancer induced muscle loss, occurs in about 50% of cancer patients and may lead to loss of protein stores, severe weakness and fatigue, immobility, loss of independence, and an inability to tolerate and respond to cancer treatments. Cancer induced muscle wasting is responsible for at least 20% of cancer deaths. There are currently no drugs approved for the treatment of cancer wasting. ***Ostarine*** is the first of a new drug class called selective androgen receptor modulators (SARMS) and it is designed to increase lean muscle mass in patients with cancer Cachexia. It also helps patients become stronger, as shown by improved performance on a stair climbing task. They did not gain weight because fat tissue was replaced with muscle. Cancer Cachexia or wasting causes significant weight loss and reduced lean muscle leaving patients tired, weak, and with little appetite. Merely eating more – or trying to eat more – doesn't help patients gain weight or strength. In this study nearly 160 patients were randomized to a placebo or 2 different strengths of Ostarine. Before beginning the trial, patients with a number of different cancers had lost an average of almost 10% of their body weight. There was no difference in serious side effects among the 3 groups.

http://www.gtxinc.com/Pipeline/OstarineMK2866.aspx?Sid=4

8. Phase I Study of Vorinostat (SAHA) in Combination with Folfox in Patients with Refractory CRC (May 5/09)

This study sought to determine the maximum tolerated dose of vorinostat in combination with folfox. Vorinostat is an oral agent that was given twice daily for 1 week every 2 weeks. Folfox was given on days 4 and 5 of vorinostat. Vorinostat was started at 100 mg twice daily and escalated. The side effects and toxicity (pharmacokinetics) of vorinostat, FU and oxaliplatin were studied. Thrombocytopenia (low platelet count), neutropenia (low white count), gastrointestinal toxicity (such as diarrhea and vomiting) and fatigue increased in frequency and severity at higher doses of vorinostat. The maximum tolerated dose of vorinostat in combination with folfox is 300 mg orally twice daily per week every 2 weeks.

Fakir, Marwan, et al., A Phase I, pharmacokinetic and pharmocodynamic study on Vorinostat in combination with 5-fluorouracil, leucovorin, and oxaliplatin in patients with refractory colorectal cancer. Clinical Cancer Research. Publisher online First April 21, 2009 doi: 10.1158/1078-0432.CCR-08-2999

9. Looking at Performance Status when Deciding on A Treatment Plan (May 5/09)

Combination therapy with chemo agents or chemo plus a biologic agent is considered standard care for patients with crc. For the most part, the benefit of such therapy has been demonstrated in clinical trials of fit patients with performance status of 1 or 0. Only limited data exist for patients with poor performance status of 2, who constitute less than 10% of phase III study participants. This is relevant to clinical practice because poor performance status (PS) is a predictor of poor survival in patients with advanced crc. Physicians are faced with the dilemma of whether to treat PS 2 patients with more aggressive, but toxic therapy or with a safer alternative that has lower efficacy. Although mortality rates are higher in patients with poor

performance, these patients appear to achieve similar benefits from adjuvant therapy as do fit patients.

This study sought to evaluate the risks and benefits of FU based chemo in patients with crc and PS 2. The results demonstrate that patients with advanced crc who have poor PS derive similar benefits from modern chemo as do fit patients, but with higher rates of toxicity and early death. According to the lead investigator, because there was no increase in toxicity with more intensive therapy, the effect may be attributed to rapid disease progression and comorbidity rather than to treatment-related toxicity. Regardless of the regimen used, (either oxaliplatin or irinotecan), patients with PS 2 require attentive supportive care. It's important to note that regimens incorporating biologic agents were not included in the study.

Sargent, DJ, et al., Pooled safety and efficacy analysis examining the effect of performance status on outcomes in nine first line treatment trials using individual data from patients with metastatic colorectal cancer. J of Clinical Oncology. April 20, 2009; 27 (12): 1948-1955

10. Clinical Trial NSABP C-10 Answering The Question: *Is it Safe and Effective to Leave a Primary Tumor Without Symptoms in the Colon or Rectum and Proceed Directly to Chemo in a Metastatic Setting* (May 7/09)

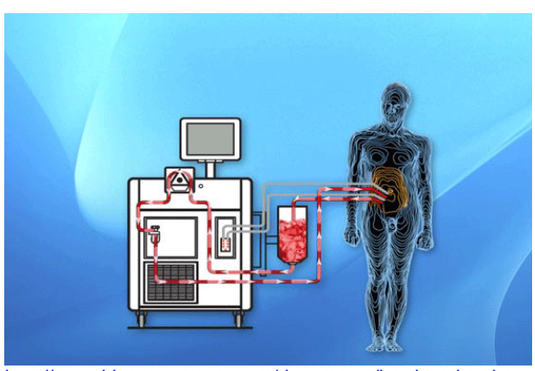
The NSABP C-10 trial is being conducted throughout the US and it is answering the question: Is it safe and effective to leave a primary crc tumor without symptoms in the colon or rectum and proceed directly to chemo in patients with crc that has spread to distant organs where it cannot be surgically removed. Patients in the study will be treated with folfox and avastin every two weeks for as long as their cancer doesn't get worse and they are able to tolerate side effects. The major goal of the study is to measure how often leaving a primary tumor in place causes a major problem that requires surgery or results in the patient dying. In addition, researchers will be looking at serious problems that don't require surgery, side effects from treatment, and overall survival. If treatment with chemo makes it possible to remove mets that were initially unresectable, patients will have both the mets and primary tumor removed surgically.

www.fightcolorectalcancer.org/research_news/2009/05/almost_there_colon_cancer_trial_need_six_more_patietns

SURGERY

11. Significance of Lymph Node Mets in Patients with Colorectal Cancer Peritoneal Carcinomatosis (May 5/09)

Lymph node metastasis is common in patients with colorectal cancer. Its significance in patients at the time of primary colorectal surgery and later in patients who develop crc peritoneal carcinomatosis (mets) is unknown. Lymphatic mets reflects a systemic spread of cancer and its implication on patients who undergo cytoreductive surgery and hyperthermic intraoperative chemo (HIPEC) for carcinomatosis required studies. Patients in this study underwent cytoreductive surgery of their peritoneum as well as HIPEC (heated chemo upon removal of those peritoneal mets) according to a standardized treatment protocol. There was a comparison of survival outcomes performed for patients with and without lymphatic mets. At the time of colorectal surgery, patients with lymph node involvement had similar survival outcomes compared with patients without lymph node involvement. However, when they subsequently develop peritoneal carcinomatosis and underwent treatment with cytoreductive surgery and HIPEC, patients with lymph node involvement did significantly worse. The results of the study suggest that lymph node mets in patients with colorectal cancer peritoneal carcinomatosis is an indicator of a poor prognosis and requires further investigation and recognition.



http://www.hipectreatment.com/documents/howitworks.php

Hyperthermic Intraperitoneal Chemotherapy

Chua, Terence, et al., Significance of Lymph Node Metastasis in Patients with Colorectal Cancer peritoneal Carcinomatosis. World Journal of Surgery. Online Print, May 2, 2009. doi: 10.1007/s00268-009-0059-6

12. Early Surveillance Colonoscopy for Metachronous Colorectal Cancer (May 6/09)

Metachronous colorectal tumours are second primary colorectal tumours that are discovered some time after the diagnosis of the first primary. Some studies recently reported disturbing rates of metachronous colorectal cancer occurring early after curative treatment of the first primary tumour. There are concerns that performing surveillance colonoscopy only 3-5 years after curative surgery may miss a significant proportion of metachronous cancers. This study looked at the rate and timing of metachronous cancer in 2 centers and examined factors which may be associated. Colorectal cancers were identified in 569 patients of whom 15 had metachronous cancers and were included in the study. The median time interval to detection of metachronous cancer was 13 - 36 months. The study showed that a significant proportion (53%) of patients who had metachronous colorectal cancer presented within 13-36 months. Early surveillance colonoscopy may be warranted to detect earlier stage disease relapse.

Hollington, P, et al., Early Surveillance colonoscopy for metachronous colorectal cancer. ANZ J of Surgery. Vol 79, Issue s1, ppA11-A11.

13. Simultaneous vs. Staged Resection for Synchronous Colorectal Cancer Liver Mets (May 8/09)

The aim of this study was to compare postoperative outcomes of patients with synchronous colorectal liver mets treated with either simultaneous or staged colectomy (surgical removal of primary) and hepatectomy (surgical removal of liver mets). 70 patients underwent simultaneous resection of colon primary and liver mets in a single operation. 160 patients underwent staged operations. Simultaneous resections were similar for size and number of liver mets. Major liver resections were similar between staged and simultaneous as was type of colectomy. Patients having simultaneous resection required fewer days in the hospital (10 days vs. 18 days). By avoiding a second surgery (laparotomy), simultaneous colon and hepatic resection reduces overall hospital stay, with no difference in morbidity and mortality rates or in severity of complications, compared with staged resection. Simultaneous resection is an acceptable option in patients with resectable synchronous colorectal mets.

Martin, MD. et al., Simultaneous Vs staged resection for synchronous colorectal cancer liver metastases. J of the American College of Surgeons. Vol 208, Issue 5, May 2009; pp 842-850

RADIATION / INTERVENTIONAL RADIOLOGY

14. Helical Tomotherapy for Limited Cancer Mets (Apr. 23/09)

Colorectal cancer patients who have a few tumours that have spread to other parts of their bodies can be part of a clinical trial in the US to test precisely focused, high-dose radiation treatment called helical **Tomotherapy**. Researchers would like to know if helical tomography, focused on metastatic tumours, can destroy them and keep them from returning in patients whose tumours cannot be removed surgically or who are not willing to have surgery. The trial is being conducted at the NIH campus in Bethesda, MD. Brain mets are considered an exclusion criterion.

www.fightcolorectalcancer.org/Research&TreatmentNews/

15. Stereotactic Body Radiosurgery (SBRS) for the Treatment of Spinal Mets from CRC (May 8/09)

Radiation oncologists at MD Anderson Cancer Center in Houston successfully used stereotactic body radiosurgery (SBRS) to treat cancers that had spread to the spine. SBRS uses computers to precisely focus a narrow beam of high-dose radiation on the tumor. 90% of treated patients had no progression of their spinal mets after six months. 84% were progression free at one year. In addition, there was a substantial decrease in fatigue, pain, sleep disturbance, drowsiness, and distress that lasted at least six months. Lead investigator Chang concluded that SBRS in patients with spinal mets is a safe and effective treatment modality, yielding high 6-month and 1-year PFS (progression free survival) rates and dramatic reductions in pain and symptoms related to the metastatic cancer.

SCREENING

16. Comparison of Guaiac and Immunochemical Faecal Occult Blood Test for the Detection of Colonic Lesions According to Lesion Type and Location (Apr. 17/09)

This study sought to compare the variations in sensitivity between an immunochemical (I-FOBT) and a guaiac (G-FOBT) faecal occult blood test for the detection of colon lesions according to type and location of lesions in an average risk 50 – 74 year olds. Invasive cancers and high risk adenomas were detected. The gain in sensitivity by using I-FOBT increased from invasive cancers to high risk adenomas and was inversely related to the amount of bleeding. Among cancers, the gain in sensitivity was confined to rectal cancer. Among high risk adenomas, the gain in sensitivity was similar whatever the location. This study suggests that the gain in sensitivity by using an I-FOBT instead of a G-FOBT greatly depends on the location of lesions and the amount of bleeding.

Guitter, I, et al., Comparison of guaiac and an immunochemical faecal occult blood test for the detection of colonic lesions according to lesion type and location. British Journal of Cancer. 2009. 100, 1230-1235.

OTHER

17. TP53 Mutation Predicts Erbitux Outcome (Apr. 17/09)

This French study concluded that mutations in the TP53 gene predicted better outcomes from treatment with erbitux. 64 colorectal cancer patients were treated with erbitux. 41 had mutations in the TP53 gene and, as a group, had better disease control with their tumours by having them either shrink or remain stable. Median time before the cancer became worse (time to progression) was 20 weeks in patients with a TP53 mutation vs. 12 weeks in those without the genetic mutation. This study, therefore, suggests that TP53 mutations are predictive of erbitux sensitivity, particularly in patients without Kras mutation, and that TP53 genotyping could have a clinical interest to select patients who should benefit from erbitux-based chemo.

Oden-Gangloff, A, et al., TP53 Mutations Predict Disease Control in Metastatic Colorectal Cancer Treated with Cetuximab-Based Chemotherapy. British Journal of Cancer. (2009) 100, 1330-1335.

18. Gene Mutations May Signal Anti-EGFR Antibody Resistance (Apr. 20/09)

An Italian study demonstrated that mutations in Braf, PIK3CA, and Kras genes and loss of PTEN expression (which controls the rapid division of cells) impaired response to erbitux and vectibix in patients with metastatic colorectal cancer. Previous studies have shown that the Kras gene is a predictive biomarker of resistance to epidermal growth factor receptor targeted therapies, such as erbitux and vectibix, but this is the first study to evaluate the contribution of all four molecular alterations on resistance. Kras mutations apparently account for about 40% of the nonresponsive cases. Researchers wished to know if there were any other biomarkers that could explain the remaining resistant patients. Recent reports indicated that mutations in other genes that affect the EGFR pathway could also drive resistance to anti EGFR therapies (erbitux and vectibix), including Braf mutations and alterations in the PIK3CA and PTEN pathways. This study reviewed gene mutations in tumor samples of 132 patients with mcrc who were being treated with erbitux or vectibix and among the 106 nonresponders, 50 were bearing one genetic alteration, 24 presented more than one altered gene and the remaining 32 were wild type for Kras, Braf, PIK3CA and PTEN. Patients with 2 or more alterations had a significantly worse prognosis compared to patients with zero or one alteration in these four markers.

***American Association for Cancer Research Presentation, April 19, 2009. Federica DiNicolantonio*. LB-93. BRAF, PIK3CA and KRAS Mutations and Loss of PTEN Expression Impair Response to EGFR-targeted Therapies in Metastatic Colorectal Cancer**
http://www.aacr.org/home/public--media/aacr-press-releases.aspx?d=1317

19. Oncotype DX Predicts Risk of Colon Cancer Recurrence (Apr. 16/09)

According to a press release from Genomic Health, the Oncotype DX colon cancer assay—a genomic test similar to one already in use for breast cancer—has been shown to predict the risk of cancer recurrence among patients with Stage II colon cancer. This test may eventually help

guide colon cancer treatment decisions. Gene expression profiling explores the patterns of genes that are active in tumor cells. Studies suggest that gene expression may provide important information about prognosis or likely response to treatment in several types of cancer. For example, among women with early-stage, estrogen receptor-positive breast cancer, the Oncotype DX breast cancer assay has been shown to predict the likelihood of cancer recurrence and the likelihood of benefit from chemotherapy. As a result, the test has been added to medical guidelines for early-stage breast cancer. The test evaluates the activity of 21 genes from a sample of the patient's cancer to determine the patient's Recurrence Score. The Recurrence Score ranges from 0 to 100, with a higher score indicating a greater risk of recurrence.

Research now indicates that a similar test may provide important information for patients with **Stage II colon cancer.** Many patients with this stage of disease have good outcomes with surgery alone, and routine adjuvant (post-surgery) chemotherapy is not currently recommended for Stage II colon cancer. Chemotherapy may, however, be considered for Stage II patients with a higher risk of cancer recurrence. Use of the Oncotype DX colon cancer assay—a gene expression test similar to the Oncotype DX breast cancer assay—may allow for more accurate identification of these higher-risk patients. The genes that are included in the Oncotype DX colon cancer assay were selected from among 760 candidate genes that were tested in more than 1,800 colon cancer patients. After development, the assay was further tested in more than 1,200 patients with Stage II colon cancer. The results indicate that the Oncotype DX colon cancer assay predicted risk of recurrence after surgery for Stage II colon cancer and provided information beyond that of standard markers of risk. Detailed results of this analysis will be presented at the annual meeting of the American Society of Clinical Oncology (ASCO), May 29-June 2, 2009. Genomic Health, the company that developed both the Oncotype DX breast cancer assay and the Oncotype DX colon cancer assay, plans to make the Oncotype DX colon cancer assay available in early 2010.

Genomic Health, Inc. Press Release. Genomic Health Announces Positive Preliminary Results from QUASAR Validation Study of Oncotype DX(R) Colon Cancer Assay. Available at: http://investor.genomichealth.com/releasedetail.cfm?ReleaseID=377186

20. Number of Circulating Tumor Cells (CTCs) can Predict Survival (May 2/09)

The number of circulating tumor cells (CTCs) in the bloodstream can predict both how long it will take for colorectal cancer to get worse (progression free suvival) and overall survival time. Both progression free survival and overall survival (OS) were shorter when three or more CTCs were found in the blood. Those with fewer than three CTCs had median progression free survival of 7.8 months compared to 4.4 months for those with three or more. Overall survival was 20.6 months with fewer than three CTCs compared to 9.4 months for three or more.

Cohen, S.J., et al., prognostic significance of circulating tumor cells in patients with metastatic colorectal cancer. Annals of Oncology. Advance Access published online on March 26, 2009. doi: 10.1093/annonc/mdn786

21. Colorectal Carcinoid Tumors – What are they? (May 11/09)

Carcinoid tumours of the colon are extremely rare tumours and unlike adenocarcinomas, representing approximately 1% of all colonic cancers. Typically, carcinoid tumours of the colon present in the sixth to seventh decade of life during evaluation for anorexia, abdominal pain, and unintentional wieght loss. Research tells us that carcinoid tumours of the colon are diagnosed late in the course of the disease unless of course they have been discovered through regular screening, such as a colonoscopy. The average size of these tumours if discovered late is 5cm at diagnosis, and local nodal involvement or disant mets (liver) are therefore likely resulting in an overall 5 year survival rate of 25-41%. Rectal carcinoids < 2cm rarely metastasize, directing the conclusion that for these smaller lesions local excision, through a colonoscopy for example, is sufficient. For lesions > 2 cm, a low anterior resection or abdominal perineal resection should be performed provided distant mets are absent. For more info on carcinoid tumours, please visit: http://www.carcinoid.org/pcf/specialists.shtml

www.humpath.com/colonic-carcinoid-tumor

22. Risk of Dying from Colorectal Cancer in Bowel Disease is Down (May 12/09)

According to this Swedish study, the incidence of colorectal cancer in people with inflammatory bowel disease (IBD) has not significantly changed in recent decades, but the risk of CRC death has dropped substantially. Researchers assembled data on a large group of 7,607 patients with IBD, diagnosed between 1954 and 1989. They then tracked the group looking for the incidence of CRC and resulting mortality through 2004. In follow-up, the researchers noted that there were 188 cases of CRC and 92 CRC deaths among the 7,607 IBD patients. CRC risk remained relatively consistent in the IBD group over the decades; however, CRC mortality risk dramatically decreased over the time period. "Over the past 35 years, the risk of diagnosis of CRC in patients with IBD has not declined significantly, but the risk of dying of CRC has decreased substantially," the authors concluded.

Soderlund, Sverre, et al., Decreasing time-Trends of Colorectal Cancer in a Large Cohort of Patients with Inflammatory Bowel Disease. Gastroenterology. Vol 136, Issue 5; pp 1561-1567.

NUTRITION

23. High Consumption of Fruit & Vegetables is Associated with a Reduced Risk of Colorectal Cancer (Apr. 27/09)

According to this Norwegian study, a high consumption of fruit and vegetables is possibly associated with a decreased risk of colorectal cancer. Researchers examined the relation between self-reported usual consumption of fruit and vegetables and the incidence of colorectal cancer. After completing a dietary questionnaire, patients were followed up for cancer incidence and mortality until 2006. After an average follow-up of 9 years, 2,819 incident colorectal cases were reported. Consumption of fruit and vegetables was inversely associated with colorectal cancer in a comparison of the highest with the lowest consumption, particularly with colon cancer risk. The research team noted that the association between fruit and vegetable consumption and colorectal cancer risk was inverse in never and former smokers, but positive in current smokers. The team observed that this modifying effect was found for fruit and vegetables combined and for vegetables alone. Lead investigator concluded that these findings suggest that a high consumption of fruit and vegetables is associated with a reduced risk of colorectal cancer, especially of colon cancer and that this effect may depend on smoking status.

Van Duijnhoven, Franzel, et al., Consumption of Fruit and Vegetables is Associated with a Reduced Risk of Colorectal Cancer. American J of Clin Nutrition. 2009: 89 (5): 1441-1452

24. Researchers Examine Vitamin D Levels in Colorectal Cancer Patients (Apr. 23/09)

According to scientists at Roswell Park Cancer Institute in Buffalo, NY, genetic changes may predict the response of vitamin D based chemoprevention and therapy. Studies indicate that a vitamin D deficiency is associated with an increased risk of developing colorectal polyps and cancer. In this study, vitamin D levels were measured in 50 colorectal cancer patients receiving 2000 IU of vitamin D supplements daily, before and at various times during a one year study. Genes that could potentially modify vitamin metabolism were also monitored. Researchers found widespread vitamin D deficiency in colorectal cancer patients and substantial variations of vitamin D levels at the beginning of the study and in follow-up tests after supplementation. They also identified a genetic change in the vitamin D binding protein which may explain some of the variations of vitamin D deficiency among crc patients. While vitamin D supplements increased levels in all patients, the rate of increase was slower in patients on active cancer chemo when compared to patients not on chemo. And genetic changes in the vitamin D metabolizing proteins may help to explain, in part, vitamin D deficiency in colorectal cancer patients. The hope is that an understanding in the genes that regulate vitamin D absorption, patients' response to vitamin D based prevention program and treatment regimens will be improved upon.

www.medicalnewstoday.com/articles/147090.php

25. Vitamin B6 Cuts Men's Colorectal Cancer Risk (Apr. 30/09)

Getting enough vitamin B6 each day from supplements or foods such as fortified cereals can cut a man's risk of developing colorectal cancer, according to this study. Vitamin B6 is a crucial ingredient in DNA production. Low levels of this vitamin have been linked to the DNA changes that can lead to colorectal cancer, as well as other types of cancer. Vitamin B6 deficiency is also associated with inflammatory markers that are related to cancer development. Previous research has indicated that vitamin B6 may lower colorectal cancer risk, but it hasn't been clear whether this risk reduction is influenced by other B vitamins, inflammatory processes, or other factors. The researchers in this study measured levels of pyridoxal 5'-phosphate (PLP), the active form of vitamin B6, in the participants' blood. They also measured blood levels of folate

(another B vitamin) and vitamin B12, as well as markers of inflammation, and they controlled for known colorectal cancer risk factors such as body mass index (BMI), exercise, and consumption of red meat and alcohol. Men with high PLP levels had a 53% lower risk of colorectal cancer than those with low PLP levels. The effect of plasma PLP on colorectal cancer was independent of other B vitamins related to DNA modification or production, or inflammation, which indicates that vitamin B may reduce colorectal cancer risk by another mechanism, for example by blocking the spread of cancer cells, reducing the oxidative stress that can cause cells to turn cancerous, or inhibiting the formation of blood vessels that feed cancerous tumors (angiogenesis). The recommended amount of B6 every day in the diet is 1.3 mg for adults under age 50, and up to 1.7 mg for those aged 51 and over.

Lee JE, et al., . Prospective study of plasma vitamin B6 and risk of colorectal cancer in men. Cancer Epidemiol Biomarkers Prev. 2009;18(4).

26. Coffee is Questioned to Decrease Risk of CRC (May 4/09)

Researchers from the Harvard School of Public Health have reported that, contrary to the results of several previous studies, coffee consumption does not appear to reduce the risk of colorectal cancer. Some studies have indicated that coffee may have a protective effect against colon cancer; however, researchers continue to evaluate this link in an effort to establish more direct evidence. In order to examine the relationship between coffee consumption and colorectal cancer, researchers from Harvard conducted a review of 12 studies that included 646,848 participants and 5,403 cases of colorectal cancer. They evaluated high versus low coffee consumption and found no significant effect of coffee consumption on colorectal cancer risk. The review included four studies in the United States, five in Europe, and three in Japan. The data from each country was very similar. There were no significant differences by gender or site of cancer; however, there was a slight inverse relationship between coffee consumption and colon cancer for women, which was even more pronounced among Japanese women (21% for total study, 38% for Japanese women). The researchers observed that inverse associations between coffee consumption and colorectal cancer "were slightly stronger in studies that controlled for smoking and alcohol and in studies with shorter follow-up times."

They concluded that coffee is "unlikely to have a strong protective effect on colorectal cancer risk"; however, they also note that it does not appear to increase the risk of colorectal cancer either.

** The relationship between coffee drinking and cancer incidence is likely complex, and the best that can probably be said at present, based on the literature, is that coffee drinking may not increase the risk of developing cancer.

Je Y, et al., Coffee consumption and risk of colorectal cancer: A systematic review and meta-analysis of prospective cohort studies. International Journal of Cancer. 2009; 124: 1662-1668.

27. Diet & Rectal Cancer Risk: A Difference Exists Between Races (May 11/09)

Associations between individual foods and nutrients and colorectal cancer have been inconsistent, and few studies have examined associations between food, nutrients, dietary patterns, and rectal cancer. This study examined the relationship between food groups and dietary patterns and risk for rectal cancer in non Hispanic Whites and African Americans. Among whites, nonwhole grains and white potatoes were associated with elevated risk for rectal cancer whereas fruit, vegetables, dairy, fish, and poultry were associated with reduced risk. In African Americans, high consumption of other fruit and added sugar suggested elevated risk. Three major dietary patterns were identified in whites and African Americans:

- While both groups ate foods in the high fat/meat/potatoes group, only whites had elevated risk for rectal cancer when high amounts of these foods were eaten. Risk was almost doubled for whites who ate mostly high fat foods, meat, and potatoes.
- For whites eating mostly vegetables, fish, and poultry, there was a reduced risk of getting rectal cancer, as did fruit, whole grains, and dairy foods.
- African Americans had higher risk from legumes and dairy products and lower risk from fruits and vegetables.

Researchers concluded that associations of certain food groups and overall dietary patterns with rectal cancer risk differ between Whites and African Americans, highlighting the importance of examining diet and cancer relationships in racially diverse populations.

Williams, Christina Dawn, et al., dietary Patterns, Food Groups and Rectal Cancer Risk in Whites and African-Americans. Cancer Epidemiology, Biomarkers and Prevention. May 1, 2009: 18; 1552