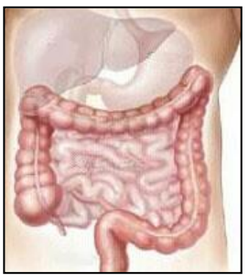
COLORECTAL CANCER RESEARCH UPDATES

Month Ending June 21st, 2013



The following colorectal cancer research update extends from May 25th, 2013 – June 21st, 2013 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Panitumumab Added to Irinotecan Does Not Improve Overall Survival of Patients (May 29/13)

The goal of this study was to assess the addition of panitumumab (Vectibix) to irinotecan in pretreated advanced colorectal cancer. Between Dec 4, 2006, and Aug 31, 2010, 1198 patients were enrolled, of whom 460 were included in the primary population of patients with KRAS wild-type tumours and no previous EGFR targeted therapy. 230 patients were randomly allocated to irinotecan and 230 to Irinotecan + Panitumumab. There was no difference in overall survival between groups, but individuals in the second group had longer progression-free survival and a greater number of responses (79 [34%] patients vs 27 [12%];) than did individuals in the irinotecan only group. Investigators concluded that adding panitumumab to irinotecan did not improve the overall survival of patients with wild-type KRAS tumours.

Seymour, Matthew, et al., panitumumab and irinotecan versus irinotecan alone for patients with kras wild type, fluorouracil-resistant advanced colorectal cancer (PICCOLO): a prospectively stratified randomized trial. The Lancet Oncology. Early Online edition. May 29, 2013.

2. Erbitux Beats Avastin in Colorectal Cancer Trial (Jun.1/13)

Erbitux was shown to be more effective at prolonging the lives of colorectal cancer patients than Roche's Avastin, according to the results of a new study. In a drug trial, the two drugs were each given in combination with Folfiri chemotherapy to patients whose colorectal cancer had started spreading to other organs. The results showed the Erbitux group survived on average nearly four months longer than the Avastin group. Only patients whose tumors contain the normal, or wild-type, version of a gene called KRAS took part in the trial. Erbitux is only approved in this patient subgroup, which accounts for approximately 60% of colorectal cancer cases. The trial data presented at the American Society of Clinical Oncology in Chicago showed that overall survival was a median 28.7 months in the Erbitux arm and 25 months in the Avastin arm. There was little difference, however, between the two groups in how long it took before the disease got worse, so-called progression-free survival, which was about 10 months for both. The study's principal investigator said the results suggest that Erbitux should be given preference over Avastin for the patient group in question while Avastin should be given to patients who could not be helped by Erbitux.

Heinemann, V, et al., Randomized comparison of folfiri plus cetuximab versus folfiri plus bevacizumab as first line treatment of kras wild type metastatic colorectal cancer. German AIO study krk-0303 (FIRE-3) LBA3506

3. New Option for Some Patients with Treatment-Resistant Colorectal Cancers (Jun.2/13)

A subset of colorectal cancers responds to anti-epidermal growth factor receptor (anti-EGFR) therapies (such as erbitux and vectibix), but develops resistance within months. Among cancers that develop resistance to anti-EGFR therapy, some showed overexpression of a gene called **MET**. Preliminary data published in this study showed human tumors with MET amplification, grown in mice, responded to MET inhibitor drugs. The MET gene is known to be amplified in about 10% of colorectal cancers, and is associated with worse prognosis. The paper was also presented as part of an oral session at the 2013 American Society of Clinical Oncology Annual Meeting. "Our studies provide evidence that colorectal cancer resistance to anti-EGFR therapies can be driven by MET gene amplification," said lead investigator Alberto Bardelli. "But what is more exciting is that we were able to detect these amplifications in the blood." A subset of metastatic colorectal cancers responds to the anti-EGFR drugs cetuximab (erbitux) and panitumumab (vectibix), but almost always develops resistance within several months of the initiation of therapy. Mutations in genes related to EGFR signaling, including KRAS, BRAF and NRAS, account for about 60% of the cases that develop resistance; the cause of resistance in tumors without these mutations is unknown. Unfortunately, patients whose tumors recur after anti-EGFR therapy are out of further options currently. "The possibility that we can identify those who have MET amplification using a blood test is exciting because they might be treated with MET inhibitors" Bardelli maintains. Researchers analyzed tumors from seven patients who developed resistance subsequent to anti-EGFR therapy, and identified three who did not have the previously known mutations. Using next-generation sequencing, they demonstrated amplification of the MET gene in these three tumor samples. Blood samples collected at regular intervals during treatment with anti-EGFR therapy until relapse were available for two of the three patients. The researchers were able to detect MET amplification in the blood, and they demonstrated it occurred prior to relapse. The ability to detect MET amplification in blood provides a noninvasive, highly sensitive method for monitoring and predicting drug resistance and tumor recurrence, according to Bardelli. Using "xenopatients" -- patient-derived, drug-resistant colorectal cancers grafted and grown in mice -- the researchers identified a novel, biologically distinct subset of tumors that were resistant to anti-EGFR drugs and did not have alterations in KRAS, BRAF or NRAS but carried MET amplification. The researchers further confirmed the overexpression of the MET gene and MET protein in these tumors using special techniques called fluorescent in situ hybridization and immunohistochemistry. As a next step, the researchers tested the efficacy of the clinically approved MET inhibitor ***crizotinib*** in two xenopatients. According to Bardelli, a MET inhibitor in combination with an anti-EGFR drug caused maximum antitumor activity and sustained response in both xenopatients. He added

that this provided proof of concept that MET inhibitors, alone or in combination with anti-EGFR therapies, offer novel therapeutic opportunities.

Bardelli, A, et al., Amplification of the MET Receptor Drives Resistance to Anti-EGFR Therapies in Colorectal Cancer. **Cancer Discovery*, 2013; 3 (6): 658 DOI: 10.1158/2159-8290.CD-12-0558***

4. Results for Tivantinib in Combination with Erbitux and Irinotecan for mCRC (Jun.2/13)

This Phase 2 clinical trial administered **tivantinib** in combination with cetuximab and irinotecan in patients with relapsed or refractory KRAS wild-type metastatic colorectal cancer (CRC). The data was presented at the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO) (abstract number 3508). The clinical benefit observed in this trial include consistent trends in improved

- progression free survival (PFS),
- overall response rate (ORR) and
- overall survival (OS) in patients who received tivantinib in combination with cetuximab and irinotecan.

Data analyses showed that the median PFS in the treatment arm (patients treated with tivantinib plus irinotecan and cetuximab) was 8.3 months, compared with 7.3 months in the control arm (patients treated with placebo plus irinotecan and cetuximab). Median OS in the treatment arm was 19.8 months, compared with 16.9 months in the control arm. ORR in the treatment arm was 45% versus 33% in the control arm. The PFS and ORR results obtained in both the treatment and control arms were substantially greater than expected compared to previously published papers. Patients pre-treated with oxaliplatin in the treatment arm experienced favorable PFS and OS results. Among these patients, median PFS was 8.3 months compared with 7.2 months in the oxaliplatin-treated control arm, and median OS was 22.3 months compared with 14.1 months. ORR in oxaliplatin pre-treated patients who received tivantinib was 42.6%, compared with 27.1% in the placebo arm. Efficacy observations in a small MET-high sub-group were inconclusive and would require further assessment with a larger sample size. The 122 patients in the trial (US n=67; Russia n=39; Western Europe n=16) had unresectable CRC and disease progression after first-line therapy. Patients were randomized to receive tivantinib twice daily in combination with cetuximab every 14 days and irinotecan every 14 days or placebo twice daily with the same regimen of cetuximab and irinotecan.

About MET and Tivantinib (ARQ 197)

Tivantinib is an orally administered, selective inhibitor of MET, a receptor tyrosine kinase, which is currently in Phase 2 and Phase 3 clinical trials. In certain healthy adult cells, MET is present in low to normal levels to support natural cellular function, but in some cancer cells, MET is inappropriately and continuously activated. When abnormally activated, c-Met plays multiple roles in aspects of human cancer, including cancer cell growth, survival, angiogenesis, invasion and metastasis. The activation of certain cell signaling pathways, including MET, has also been associated with the development of resistance to EGFR (epidermal growth factor receptor) inhibitors such as cetuximab. Pre-clinical data have demonstrated that tivantinib inhibits MET activation in a range of human tumor cell lines and shows anti-tumor activity against several human tumor xenografts. In clinical trials to date, treatment with tivantinib has been generally well tolerated and has shown clinical activity in the tumors studied. Tivantinib has not yet been approved for any indication in any country.

http://www.dailyfinance.com/2013/06/01/phase-2-study-results-for-tivantinib-in-combinatio/

5. Calcium/Magnesium Not Helpful for Oxaliplatin-Induced Neuropathy (Jun.5/13)

For patients getting the common FOLFOX chemotherapy for colorectal cancer, many oncologists add intravenous calcium and magnesium, hoping to decrease the neuropathy (nerve damage) associated with oxaliplatin-based therapy. But experts at the 2013 ASCO meeting (American Society of Clinical Oncology), announced strong evidence that the calcium/magnesium does no good in either preventing or decreasing neuropathy—and it should no longer be part of routine treatment. Oxaliplatin-based chemotherapy (e.g. FOLFOX, with Eloxatin®) is one of the most commonly used drugs for people having high-risk stage II, or stages III or IV colorectal cancer. But far too often after patients have had many doses of FOLFOX over months, they have to stop this effective treatment because of increasing neuropathy—burning or numbness especially in hands and feet that becomes chronic, even permanent. Based on two earlier preliminary studies (and biological reasoning), many oncologists began giving calcium and magnesium intravenously a half-hour before and/or after the chemotherapy, in an effort to prevent the nerve damage. But in results from the first large, randomized trial announced at the ASCO meeting, researchers found absolutely no effect from the calcium/magnesium. A multisite trial randomly assigned 350 colon cancer patients receiving FOLFOX into three groups—one receiving the calcium/magnesium before and after chemo; a second receiving a look-alike placebo; and the third group

getting calcium/magnesium before chemo and a placebo afterwards. The symptoms of nerve damage—measured in multiple ways—were no different in any of the three groups of patients. Also, there were no differences in the average number of days until symptoms became significant, or in the number of patients who had to stop the chemotherapy. "This study did not demonstrate any activity of IV CaMg [calcium magnesium]…" said lead author Charles Loprinzi from the Mayo Clinic. He noted that when he has asked medical meeting audiences how many use intravenous Ca/Mg, more than half the clinicians present say they do.

"Phase III randomized, placebo-controlled, double-blind study of intravenous calcium/magnesium…" 2013 ASCO meeting and Journal of Clinical Oncology 31, 2013 (suppl; abstract 3501)

http://fightcolorectalcancer.org/research_news/2013/06/experts_issue_practice-changing_advice_stop_giving_calciummagnesium_for_oxaliplatin-caused_neuropathy

6. Aspirin May Help Reduce Colon Cancer (Jun.13/13)

Aspirin appears to help destroy genetically unstable cells and prevent them from developing into cancer cells. A team of researchers from Thomas Jefferson University in Philadelphia and the University of Regensburg in Germany studied the effects of aspirin on a specific type of colon cancer. Hereditary nonpolyposis colorectal cancer strikes about 20,000 Americans every year, often before the age of 50. In test tube studies, researchers say aspirin suppressed genetic mutations that can lead to tumors. Now the American and German researchers are enrolling people who are at high risk for this hereditary colon cancer in a five-year international study to see if aspirin can protect them. Researchers also say people concerned about colon cancer should not take aspirin without consulting a physician. Aspirin can cause stomach ulcers and the proper dosage needed to create this preventive effect is not yet known.

http://www.newsfix.ca/2013/06/13/aspirin-may-help-reduce-colon-cancer-risk/

SURGICAL THERAPIES

7. Benefit from HIPEC in Advanced Abdominal Cancers (Jun.14/13)

Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CS/HIPEC) appears to be safe and effective for select patients with advanced abdominal cancers, according to the results of this study. There has been much discussion as to whether there is a benefit with this procedure, and historically it has been associated with a lot of risk. However, reviewing the data in patients treated with CS/HIPEC over the last decade showed a statistically significant benefit in terms of survival, with low morbidity and low mortality. It is thought that candidates for CS/HIPEC are patients with appendiceal, **colorectal**, or mesothelioma tumors that are refractory to standard chemotherapy and/or previous surgery. With this approach, all visible metastases to the peritoneum (the lining covering the abdominal organs) are removed surgically and then high doses of heated chemotherapeutic agents are perfused throughout the abdomen to eradicate any remaining cancer cells. To limit systemic toxicity, the chemotherapy is administered only to the targeted area and is washed out after 90 minutes. The entire procedure takes 8 to 18 hours. "HIPEC is an extremely invasive procedure that an increasing number of cancer centers across the United States offer," Dr. Skitzki said. "Our research shows that when it's used for appropriate candidates as part of a multidisciplinary treatment approach in an experienced setting, outcomes will be favorable, compared with standard combination therapy, with the added benefit of shorter-term side effects." Because most reports of CS/HIPEC use in the United States come from a very few high-volume centers, "the applicability of CS/HIPEC among a broader spectrum of providers has been questioned," said Jan Franko, MD, PhD, from Mercy Medical Center in Des Moines, Iowa. The study "provides increasing support of the technical safety of CS/HIPEC in proper settings". The data demonstrate that CS/HIPEC can be safely implemented outside of traditional high-volume centers."

Haslinger, Michelle, et al., A contemporary analysis of morbidity and outcomes in cytoreduction/hyperthermic intraperitoneal chemoperfusion. Cancer Medicine. Vol 2, Issue 3: pp.334-342

8. PET Helpful in Ablated Colorectal Liver Mets (Jun.13/13)

Early positron emission tomography and computed tomography (PET/CT) imaging is effective at identifying local-site recurrences of colorectal liver metastases after radiofrequency ablation. Although there are no guidelines for the timing or interpretation of images, they are best used 3 to 12 months after radiofrequency ablation, according to this new study. Liver metastases are common in patients with colorectal cancer. In some cases, the lesions can be effectively treated with radiofrequency ablation. If local-site recurrences are caught early enough, they can also be treated with radiofrequency ablation. Most physicians use contrast-enhanced CT or MRI to do follow-up on these patients, although there is

literature that suggests a beneficial role for PET/CT because of the added metabolism factor that you have with PET. The sensitivity and specificity between normal CT and PET/CT differs by 10% to 15%, so a significant number of local-site recurrences may be missed. When seen in follow-up scans, they could be too large for repeated treatment. The researchers set out to develop criteria for PET/CT image interpretation after radiofrequency ablation and to determine a timetable for follow-up analyses. The study involved patients who underwent radiofrequency ablation for colorectal liver metastases and then underwent PET/CT in the 12 months after treatment. They defined local-site recurrences as increased fluorodeoxyglucose uptake in the ablated region or adjacent to it. Researchers analyzed 170 scans from 79 patients with 179 ablated regions. Of those patients, 72.2% were scanned in the 6 months after treatment. Of the 30 patients who developed a local-site recurrence, 90.0% occurred in the 9 months after treatment and 96.7% occurred in the 12 months after treatment. The problem of incomplete ablation is notorious; that's why follow-up is so important after that treatment," maintain the researchers. "PET is absolutely important in the first year after ablation, but not before 3 months," they added. Just 2% of lesions smaller than 1 cm and 4% of lesions smaller than 2 cm showed a local-site recurrence.

Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2013 Annual Meeting: Abstract 67. Presented June 9, 2013.

SCREENING

9. Long Term Colon Screening Reduces Mortality (May 29/13)

People with more than ten years of screening show reduced rates of death from colon cancer, according to Danish scientists. The faecal occult blood test (FOBT) is a proven method of detecting early colon cancer. Researchers from Odense University Hospital in Denmark show the value of this screen done over a long time period. They had more than 60,000 individuals have either the FOBT or no test every two years. When they went into the seventh screening round, there was no difference in rates of colon cancer between the two groups – with over 11,000 people having had each of the seven tests. But the mortality rates were different. Those having the screen had a 0.66 relative chance of dying from colorectal cancer compared to those who had no screening. This is an eight per cent lower chance of death in the lower colon and rectum and a 28 per cent lower chance of cancer elsewhere in the colon. The findings strongly suggest that a long time screening program for colon cancer can be a lifesaver.

http://www.newsfix.ca/2013/05/29/long-term-colon-screening-reduces-mortality/

10. New Innovative Test for Colorectal Cancer Announced (Jun.19/13)

The July issue of The Journal of Molecular Diagnostics has good news regarding colorectal cancer diagnosis. It concerns a new, non-invasive test to pick up early signs of colorectal cancer (CRC). It could provide an alternative or an accompanying option to standard tests such as colonoscopy, besides monitoring cancer progression and treatment. Like most types of cancer, early detection is crucial to improve chances of surviving the disease, which in the case of CRC increases to 90 per cent if diagnosed before metastasis. The researchers used tissues from primary tumors and non-tumor tissues from 12 CRC patients to perform DNA analysis coupled with enriched methylated DNA. The investigation led the scientists to find a set of genes that were highly methylated (methylation is the removal of a hydrogen atom in a molecule and replaced with a methyl group) in all of the CRC tumors they were analyzing. Eventually they were able to identify one gene called **SDC2**, which encodes the membrane syndecan-2 protein, one that is active in cell proliferation, cell migration, and is expressed in colon cells. “The SDC2 methylation test was able to detect 92% for detection of stage I cancer patients indicating that SDC2 is suitable for early detection of CRC where therapeutic interventions have the greatest likelihood of curing the patient from the disease," researchers concluded.

http://www.justmeans.com/New-Innovative-Test-for-Colorectal-Cancer-Announced/59722.html

11. Diagnosis of Colon Cancer Via Colonoscopy Improves Surgery Outcomes (Jun. 19/13)

Patients who underwent surgery to treat colon cancer had significantly better outcomes and a lower disease stage at presentation than patients diagnosed through other means in a recent study. Researchers performed a retrospective review of 1,071 patients who underwent surgery for colon cancer between January 2004 and December 2011 at Massachusetts General Hospital. Two hundred seventeen patients were diagnosed via screening colonoscopy, and postoperative staging, survival and disease-free interval were compared between them and patients diagnosed using other methods. “Screening colonoscopy is believed to be a major contributor to the consistent decline in the number of colorectal cancer diagnoses in the U.S. over the last decade,” the researchers wrote. “The current screening program … also contributes to earlier detection of malignant neoplasms, leading to significantly lower staging and perhaps better long-term outcome.” The risk for a high-stage tumor was significantly greater among patients who were not diagnosed through screening colonoscopy. They also were at greater risk for nodal disease and metastatic disease at presentation. Risks for death and recurrence were elevated without a screening-based diagnosis, and both disease-free intervals (mean 109 weeks vs. 150 weeks) and survival duration (mean 157.4 vs. 196.1 weeks) were shorter in this group. The results indicated that patients diagnosed through screening colonoscopy continued to have longer survival and lower mortality rates than patients diagnosed via other means. “Patients with colon cancer identified on screening

colonoscopy are shown to have considerably better staging and outcomes than those with tumors identified through other means," the researchers concluded. "Considering the tremendous effect early diagnosis through screening has for the prognosis of patients, this further emphasizes the important role compliance to screening colonoscopy guidelines can play in prolonging longevity, improving quality of life and reducing health care costs through early detection of colon cancer."

Amri, Ramzi et al., Impact of Screening Colonoscopy on Outcomes in Colon Cancer Surgery.* JAMA Surg. *2013;doi:10.1001/jamasurg.2013.8.

PSYCHOSOCIAL

12. Phone Support Leads to Healthier Lifestyle (May 28/13)

Telephone-delivered health coaching is effective in improving physical activity, diet and BMI in colorectal cancer survivors, Australian researchers say. Participants in the CanChange program – comprising 11 phone coaching sessions focusing on a range of health issues – reported an extra 30 minutes of physical activity per week at 12 months compared to those assigned to usual care. They also dropped almost a kilo in BMI and consumed less total and saturated fat than those in usual care. However, the randomized trial of over 400 bowel cancer patients showed no significant group differences in cancer-related fatigue, alcohol intake or smoking. The researchers concluded that the intervention was effective for improving physical activity, dietary habits, and body mass index in colorectal cancer survivors. The intervention is translatable through existing telephone cancer support and information services in Australia and other countries.

Hawkes, Anna, et al., Effects of a telephone delivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial. JCO. Published online ahead of print May 20, 2013.

NUTRITION & HEALTHY LIFESTYLE

13. Fibre Linked to Reduced Colon Cancer (May 25/13)

A high fiber intake appears to reduce the risk of colon cancer, but had no impact on rectal cancer. Previous research on the link between high fiber intake and colorectal cancer has been controversial – some studies show a protective effect and others do not. Researchers from the US National Cancer Institute now report on a comparison between 3,600 people with at least one adenoma in the bowel – a polyp which often precedes cancer – and 34,000 individuals with no polyps. Those in the top 20% of dietary fiber intake had a 25% reduced risk of adenoma compared to those in the bottom 20%. The difference in intake was about 24 grams a day and the protective effect most significant for fiber was from grains, cereals and fruits. There was no link between fiber intake and rectal cancer. Meanwhile, a European study reveals similar results. A study of over half a million individuals showed that those eating 35 grams a day of fiber, on average, had a 25% reduced risk of colorectal cancer, compared to those eating 10 grams a day or less. A more detailed analysis showed that the greatest reduction in risk was in left-sided colon cancer.

http://www.newsfix.ca/2013/05/25/fiber-linked-to-reduced-colon-cancer-risk/

14. Exercise Lowers Risk of Colorectal Cancer Among Middle Aged Men (May 29/13)

New research conducted by researchers at the University of Vermont reveals that middle-aged men who engage in a lot of cardiovascular exercise are at a reduced risk of suffering from lung and colorectal cancer. In addition, those who exercise are less likely to die from prostate cancer (although their risk of contracting the disease remained the same). *While poor fitness is already known to predict future cardiovascular disease, this is the first study to explore fitness as a marker of future cancer risk prognosis. This finding makes it clear that patients should be advised that they need to achieve a certain fitness level, and not just be told that they need to exercise. And unlike exercise behavior, which relies on patient self-reporting, fitness can be objectively and accurately measured in a clinical setting.* A total of 17,049 men participated in the study. They each received a cardiovascular fitness assessment from the Cooper Institute at a median age of 50. The test involved walking on a treadmill with a variation of different speeds and elevations. They recorded the men's performance with the ratio of metabolic rate (the rate of energy consumption), known as metabolic equivalents or METs. The team divided the participants into different groups based on their level of fitness. The researchers then analyzed their medical histories to determine whether they had developed either lung, colorectal, or prostate cancer. In this study, men who were in their 40s who achieved 13.5 minutes in the fitness test belonged to the lowest quintile for fitness as well as men in their 50s who achieved less than 11 minutes. During the follow-up period of 20 to 25 years, a total of 2,332 men were diagnosed with prostate cancer, 277 were diagnosed with lung cancer and 276 were diagnosed with colorectal cancer. They adjusted the results of the study for factors such as BMI, smoking habits and age. **The risk of lung or colorectal cancer decreased by 68 and 38 percent among men who were the most physically fit and active compared to those who were not active at all.** The researchers found that physical activity did not have any effect on the rate of prostate cancer diagnosis. However, previous research has indicated that men with prostate cancer who exercise vigorously have a notably reduced risk of dying from the disease compared to other diagnosed men. Men who were physically fit at the time they developed cancer had a much higher survival rate and lower risk of dying from the cancers compared to men who were not fit. In

fact, **a 1MET increase in fitness was associated with a 14 percent reduced risk of dying from the cancer**, as well as a 23 percent reduced risk of dying from cardiovascular disease. In addition, the researchers noted that patients who weren't fit, yet not obese, were still at an increased risk of cardiovascular disease (CVD), suggesting that people should be aware that fitness also impacts risk. Exercise has been shown to have huge beneficial effects on people diagnosed with cancer and it has also been found to help minimize the risk of recurrence, or another cancer developing.

http://www.medicalnewstoday.com/articles/260652.php

15. **Drinking Alcohol Boosts Cancer Risk** (Jun.1/13)

Alcoholic beverages are carcinogens, according to the US National Toxicology program. A new observational study confirms that alcohol consumption increases the risk of a number of cancers. The study shows that high alcohol consumption was associated with increased risk of total cancer, upper aerodigestive tract cancer, cancers in the oral cavity, throat, larynx, esophagus, colorectum and liver. Researchers found that consumption of equal to or greater than 140 grams of alcohol per week was associated with 36% increased risk for total cancer, compared with consumption of 0.1 to 10 grams per week. The higher alcohol consumption increased the risk for upper aerodigestive tract cancer by 179% and alcohol-related cancers including cancers of the oral cavity, throat, larynx, esophagus, colorectal cancer, and liver cancer by 88%. Drinking alcohol 2-7 times per week, compared to drinking a few times per year, was associated with 45% increased risk for total cancer, 83% increased risk for alcohol related cancer and 35% increased risk for other cancers.

Everatt, R. et al., Consumption of alcohol and risk of cancer among men: a 30 year cohort study in Lithuania. European J of Epidemiology. May 2013, Vol 28, Issue 5: pp. 383-392

16. Vitamin B6 Reduces Men's Risk of Colorectal Cancer (Jun.12/13)

A study suggests that vitamin B6 helps reduce the risk of colorectal cancer. Blood levels of the vitamin were measured and those with the highest levels had a 53% reduced risk. Moreover, the protection is independent of levels of other B vitamins and may work through reducing oxidative stress or some other mechanism still to be discovered. The role of vitamins in cancer prevention is controversial, with some studies showing a protective effect from fruit and vegetables or supplements and others contradicting the findings. There is already some evidence that vitamin B6 may protect from colorectal cancer but research has not, so far, been able to establish whether other B vitamins are also involved. Vitamin B6 is known to be vital for DNA production and its lack might lead to the kind of DNA damage that is associated with cancer. Researchers at Brigham and Women's Hospital and Harvard Medical School looked at data from the long-running Physicians' Health Study, which involves more than 22,000 male doctors and aims to look at many factors influencing long term health. In the current study, blood samples from 197 men with colorectal cancer were compared with those from 371 matched cancer-free controls. The researchers measured levels of pyridoxal 5′-phosphate (PLP) which is the active form of vitamin B6. Folate, another B vitamin, was also measured along with vitamin B12, markers for inflammation, and other colorectal cancer risk factors like consumption of red meat and body mass index. Men with high PLP levels had a 53% lower risk of colorectal cancer compared to those with low PLP levels. The effect of plasma PLP on colorectal cancer risk stood independent of other B vitamins that are involved in DNA modification or production, and also of inflammation. The mechanism by which vitamin B6 reduces colorectal cancer risk may not be related to DNA damage. Some ideas put forward by the researchers are that vitamin B6 might block the spread of cancer cells or of the formation of blood vessels that can feed a tumor. It may also reduce oxidative stress. Many people have low levels of vitamin B6 and thus may be putting themselves at risk, according to researchers. Fortified cereals or supplements could help boost intake – but high dose supplements of B6 should only be taken under the direction of a qualified practitioner.

http://www.newsfix.ca/2013/06/12/vitamin-b6-reduces-mens-risk-of-colorectal-cancer/

17. Obesity Linked to Higher Risk of Colorectal Cancer in Men (Jun.14/13)

Obesity is associated with significantly increased risks for incidence of colorectal adenoma and colorectal cancer in middle-aged and older men who are screened with sigmoidoscopy, according to research published. Researchers evaluated the association between baseline body mass index (BMI) and risks for incidence of distal (left sided) adenoma, recurrence of adenoma, and incidence of colorectal cancer. Among men and women, aged 55 to 74 years, who were screened with flexible sigmoidoscopy as part of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, 1,213 cases of incident distal adenoma, 752 cases of recurrent adenoma, and 966 cases of incident colorectal cancer were detected. The researchers found that the risks of incident adenoma and incident colorectal cancer were significantly higher in obese men (BMI, ≥30 kg/m²) compared with normal-weight men (BMI, 18.5 to 24.9 kg/m²). A non-significant positive association was found between obesity and recurrent adenoma in men. No significant associations were found between obesity and either colorectal adenoma (incident or recurrent) or incident colorectal cancer in women. "Data from this large prospective study suggest that obesity is important throughout the natural history of colorectal cancer, at least in men, and colorectal cancer prevention efforts should encourage the achievement and maintenance of a healthy body weight in addition to regular screenings," the authors write.

Kitahara, Cari, et al., Prospective Investigation of Body Mass Index, Colorectal Adenoma, and Colorectal Cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. JCO. Published online before print May 28, 2013.

18. Healthy Grilling Tips to Avoid Cancer-Causing Agents (Jun.15/13)

Adults can avoid cancer-causing agents when they barbecue by using the healthy grilling tips in the new *infographic*, "How to fill a healthy barbecue plate," created by experts at The University of Texas MD Anderson Cancer Center (please see below). "Summer is a popular season for outdoor grilling," said Mary Ellen Herndon, an MD Anderson wellness dietitian. "But before you fire up the grill, take the right precautions to make sure you serve healthy barbecue dishes that won't expose your family to increased cancer risks." Research shows that common meats served at barbecues, like hot dogs and hamburgers, can increase colorectal cancer risk. Even some 'safer' meats can expose people to cancer-causing agents if they're cooked improperly. Herndon suggests using the tips in the infographic to give grilling a healthy makeover. Grab the embed code to place this infographic on your website. Or, grab the infographic link. To learn more about red meat and colorectal cancer risks, watch MD Anderson's "limit red meat" video and grab the YouTube embed code under the "share" tab. This infographic is part of MD Anderson's Healthy Bites 2013 challenge, which encourages adults to make healthier food choices to lower cancer risk. Participants take on a different nutrition challenge every month. "Maintaining a healthy diet can be difficult," Herndon said. "That's why we created the Healthy Bites program, which encourages small dietary changes and each one supports a cancer prevention message." People who join Healthy Bites will have access to additional MD Anderson nutrition materials, food journals, healthy recipes and expert tips.

How to fill a Healthy BBQ Plate!

86% of U.S. households own an outdoor barbecue grill or smoker.[1]

Most popular grilling holidays:[1]

1. Fourth of July 77%
2. Memorial Day 62%
3. Labor Day 60%

Don't let your health go up in flames

BBQ Do's:

- ☑ Marinate meat for 30 min. to reduce heterocyclic amines (HCAs). It damages genes.
- ☑ Grill chicken, fish, fruits and veggies.
- ☑ Eat no more than 4-6 oz. of beef or pork per meal

BBQ Dont's:

- ☒ Burn meat. Charred meat is covered in HCAs.
- ☒ Overeat hot dogs. It's processed meat and can damage DNA.

Too much red meat can cause colorectal cancer.[3]

The lifetime risk of developing colorectal cancer is 1 in 20.[4]

Pick items on this list that fit your target calorie range:[2]

Men: **500** calories per meal

Women: **400** calories per meal

- BBQ pork spareribs, 3 ribs or ½ oz. ..... 134 calories
- Grilled steak, 6 oz. ..... 483 calories
- Hamburger, ¼ lb. or 4 oz. ..... 294 calories
- Chicken breast, 3 oz. ..... 251 calories
- Fresh green salad, 1 cup with 1 tbsp. light ranch dressing ..... 48 calories
- Ambrosia fruit salad, 1 cup ..... 135 calories
- German style potato salad, ½ cup ..... 77 calories
- Coleslaw with raisins and low-calorie dressing, ½ cup ..... 71 calories
- Baked beans, ½ cup ..... 195 calories

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