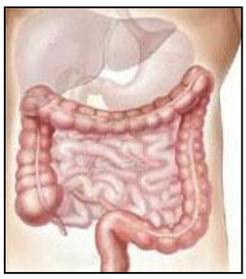
COLORECTAL CANCER RESEARCH

Month Ending July 17th , 2011



The following colorectal cancer research update extends from June 25th, 2011 – July 17th, 2011 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Superna Launches Pilot Usage Program for New Oral Mucositis Treatment (Jun. 20/11)

Superna Life Sciences has begun the pilot program for Caphosol, an oral rinse used to treat and prevent oral mucositis, or mouth sores that occur as a side effect of chemotherapy and/or radiotherapy. Superna Life Sciences is offering the pilot program to cancer patients in Canada who are receiving cancer therapy and need a solution to the side effects of oral mucositis. For more information about the pilot program, please go to the Caphosol Canada website at www.caphosol.ca/about/pilot/ or contact them directly at 1-877-469-1254 or by email at pilot@supernapharma.com. Treatment-related mouth sores occur in over 90% of patients receiving radiation and chemotherapy to treat head & neck cancer. Up to 40% of patients being treated for breast cancer, **colorectal cancer** and other solid tumours may also experience mouth sores. In some cases mucositis becomes more problematic as patients receive additional cycles of chemotherapy. Superna Life Sciences Inc. is a Vancouver-based pharmaceutical company that specializes in commercializing oncology related products in the Canadian market.

http://www.cbcn.ca/index.php?pageaction=content.page&id=7239&lang=en

2. Imprime PGG Improves Survival in KRAS Mutant Colorectal Cancer Patients (Jun. 20/11)

Biothera presented data from its Phase II clinical trial in stage IV KRAS mutant colorectal cancer at the European Society for Medical Oncology (ESMO) 13th World Congress on Gastrointestinal Cancer June 22-25. In a heavily pretreated patient population that is known not to respond to cetuximab (Erbitux) because of a mutation in a gene known as kras, Biothera's Imprime PGG has provided important improvements in key patient outcomes compared to historical data based on the average of three published studies for Erbitux alone.

- A 40% increase in median survival to 28 weeks.
- A 115% increase in one-year survival. Five of 18 subjects (28%) survived at least one year while two subjects are still alive ~2 years after enrollment.
- An objective response (tumor burden decrease of >30%) in one subject.
- An approximately 75% improvement in disease control to 39%.
- A well-tolerated safety profile.

"These data represent compelling clinical proof of concept support for the potential of Imprime PGG to provide significant clinical benefits to this unserved patient population," said Daniel Conners, Biothera Pharmaceutical Group president. "We are currently evaluating next steps in the continued clinical development for this indication." Biothera's ESMO presentation abstract is entitled, "Imprime PGG Plus Cetuximab Therapy for Advanced KRAS Mutant Colorectal Cancer." Biothera is conducting multiple clinical trials in various cancers to evaluate the therapeutic efficacy of its developmental drug Imprime PGG, which induces a neutrophil killing mechanism normally used against antibody targeted pathogens, and redirects this mechanism against antibody targeted tumor cells. Previous clinical research has suggested synergistic efficacy in subjects with KRAS wild type colorectal cancer when Imprime PGG is added to a regimen containing cetuximab. Although tumor cells in subjects with KRAS mutant colorectal cancer express the receptor for cetuximab and bind the antibody, in these cells, cetuximab does not inhibit the signals that promote tumor cell proliferation due to constitutive signal transduction induced by the KRAS mutation. Since Imprime PGG-activated neutrophils will still recognize cetuximab-targeted cancer cells, researchers hypothesized that this therapeutic regimen would also be effective against mutant KRAS colorectal cancer.

Imprime PGG is a novel immunomodulatory drug in development as a cancer therapy. Neutrophils are the most abundant immune cell in the body and normally responsible for pathogen killing, but not anti-tumor activity. In preclinical cancer models, however, Imprime PGG has been shown to bind to neutrophils and harness their killing ability to reduce tumor growth and enhance long-term survival. This targeted mechanism is synergistic with multiple anti-tumor monoclonal antibodies, demonstrating the potential to improve patient outcomes in a wide range of cancer indications. Imprime PGG is currently being evaluated in a Phase III trial in KRAS wild type colorectal cancer and multiple Phase II clinical trials in non-small cell lung cancer and chronic lymphocytic leukemia. For more information, visit http://www.biothera.com/pharmaceutical/pipeline.html .

http://www.marketwatch.com/story/imprime-pggr-improves-survival-in-kras-mutant-colorectal-cancer-patients-2011-06-22

3. Researchers Test Benefit of Fish Oil in Colorectal Cancer Spread (Jul. 4/11)

Researchers from the University of Leeds will carry out a series of experiments to see whether fish oil can prevent or treat the spread of colorectal cancer to the liver. The cancer scientists will test the effectiveness of pure Eicosapentaenoic Acid (EPA) - a naturally occurring omega-3 fish oil component which is widely available in mixed fish oil preparations in health stores and supermarkets nationwide. Investigators will use results from the initial experiments to design a future clinical trial to test the effect of pure EPA in humans at risk of or with metastatic colorectal cancer. The research is being funded by Yorkshire Cancer Research and it will hopefully back up existing evidence from a previous clinical trial from Leeds that showed that EPA may prevent large bowel polyps, the benign precursors of large bowel cancer. "We and others have already demonstrated that EPA might have beneficial effects at a later stage after development of malignancy," said Professor Hull. "These new tests will help us establish whether EPA can prevent the spread of large bowel cancer to the liver, the commonest site of spread and eventual cancer-related death which we call metastasis. The tests will also help us establish how EPA reduces growth of established liver metastases in an experimental system prior to design of the clinical trial." The trial published last year, which involved 55 patients with the rare inherited condition Familial Adenomatous Polyposis (FAP) thought to be responsible for about one in every 100 bowel cancers, saw a significant reduction in the size and number of pre-cancerous growths, known as polyps, in those patients who took a two gram daily dose of EPA in the free fatty acid form over a six month period. Another promising study currently being led by the Leeds team involving nearly 1000 patients, is investigating whether taking EPA alone, or together with aspirin, can help stop pre-cancerous growths from developing in the bowel.

http://medicalxpress.com/news/2011-07-benefit-fish-oil-bowel-cancer.html

4. Cost Analysis of Xelox v.s. Folfox for Treatment of Colorectal Cancer To Assist Decision Making (July 11/11)

XELOX (capecitabine + oxaliplatin) and FOLFOX 4 (5-FU + folinic acid + oxaliplatin) have shown similar improvements in survival in patients with metastatic colorectal cancer (MCRC). A US cost-minimization study found that the two regimens had similar costs from a healthcare provider perspective but XELOX had lower costs than FOLFOX4 from a societal perspective, while a Japanese cost-effectiveness study found XELOX had superior cost-effectiveness. This study compared the costs of XELOX and FOLFOX4 in patients with MCRC recently treated in two oncology departments in Hong Kong. Cost data were collected from the medical records of 60 consecutive patients (30 received XELOX and 30 FOLFOX4) from two hospitals. Drug costs, outpatient visits, hospital days and investigations were recorded and expressed as cost per patient from the healthcare provider perspective. Estimated travel and time costs were included in a societal perspective analysis. All costs were classed as either scheduled (associated with planned chemotherapy and follow-up) or unscheduled (unplanned visits or admissions and associated tests and medicines). Costs were based on government and hospital sources and expressed in US dollars (US$). XELOX patients received an average of 7.3 chemotherapy cycles (of the 8 planned cycles) and FOLFOX4 patients received 9.2 cycles (of the 12 planned cycles). The scheduled cost per patient per cycle was $2,046 for XELOX and $2,152 for FOLFOX4, while the unscheduled cost was $240 and $421, respectively. Total treatment cost per patient was $16,609 for XELOX and $23,672 for FOLFOX4; the total cost for FOLFOX4 was 37% greater than that of XELOX. The addition of the societal costs increased the total treatment cost per patient to $17,836 for XELOX and $27,455 for FOLFOX4. Sensitivity analyses showed XELOX was still less costly than FOLFOX4 when using full drug regimen costs, incorporating data from a US model with costs and adverse event data from their clinical trial and with the removal of oxaliplatin from both treatment arms. Capecitabine would have to cost around four times its present price in Hong Kong for the total resource cost of treatment with XELOX to equal that of FOLFOX4. Researchers concluded that XELOX costs less than FOLFOX4 for this patient group with MCRC from both the healthcare provider and societal perspectives.

Tse, Vicki, et al., Cost analysis of xelox and folfox4 for treatment of colorectal cancer to assist decision-making on reimbursement. BMC Cancer. 2011. 11:288.

5. Adjuvant Chemo For Stage II and Stage III Colorectal Cancer – Updated Practice Guidelines (Jul. 13/11)

The standard adjuvant therapy (therapy administered after surgical removal of the primary tumour in the colon) for resected stage III colon cancer has been intravenous 5-fluorouracil (5FU). However, newer chemotherapy agents, such as capecitabine (xeloda), oxaliplatin and irinotecan, have been investigated in clinical trials since the publication of the original guidelines. The Gastrointestinal Cancer Disease Site Group (DSG) conducted a systematic review of the evidence for the use of adjuvant systemic chemotherapy for patients with resected ***stage II and III colon cancer*** and developed an updated practice guideline based on that evidence and expert consensus. The following research questions were addressed:

- *Should patients with stage II or III colon cancer receive adjuvant systemic chemotherapy?*
- *What are the preferred adjuvant systemic chemotherapy options for patients with completely resected stage II or III colon cancer?*

Outcomes of interest were:

- disease-free survival,
- overall survival,
- adverse effects and
- quality of life.

A systematic search of published studies was conducted for the time period following the publication of the original guidelines to identify relevant randomized trials and syntheses of evidence in the form of meta-analyses (a review of published studies). Recommendations were based on that evidence, evidence contained in the original guidelines and consensus of the Gastrointestinal Cancer DSG. The systematic review and practice guideline were externally reviewed through a mailed survey of practitioners in **Ontario, Canada**. Recommendations were drafted based on the available evidence and expert consensus. ***The routine use of adjuvant chemotherapy for all patients with stage II colon cancer is not recommended.*** However, a subset of patients with high risk stage II disease should be considered for adjuvant therapy. ***Patients with completely resected stage III colon cancer should be offered adjuvant chemotherapy***. **Treatment should depend on factors such as patient suitability and preference, and patients and clinicians must work together to determine the optimal course of treatment.**

Jonker, Derek, et al., Adjuvant Systemic chemotherapy for stage ii and iii colon cancer after complete resection: an updated practice guideline. Clin. Oncol. 2011. Jun 2011. 23(5): 314-322.

6. Genetic Marker May Help with Rectal Cancer Treatment (Jul. 14/11)

A team of researchers have identified a genetic marker that may predict which patients with rectal cancer can be cured by certain chemotherapies when combined with surgery. They analyzed the DNA of European patients with locally advanced rectal cancer who were treated with cetuximab (marketed as Erbitux) prior to surgery. Cetuximab is usually used for metastatic colon cancer, for which it is effective. They asked if it

could be effective for **locally** advanced rectal cancer. The retrospective analysis found that 45% of patients with a particular genetic combination ***(EGF 61 G/G)*** emerged disease-free when treated with cetuximab before surgery, compared to 21% and 2% of patient groups who did not have the same genotype. This is the first study to suggest that the genetic variation -- detectable by blood test -- can be used to predict whether a patient with locally advanced rectal cancer will respond to cetuximab before surgery. Cetuximab is a drug that is typically used to treat head and neck cancer and colorectal cancer that has spread to other parts of the body. It blocks epidermal growth factor receptors (EGFR) from binding with epidermal growth factor (EGF) proteins found in the body, which have been linked to increased risk for cancer. For tumors that are difficult to cut out but have not yet spread to other parts of the body, the standard treatment is a combination of capecitabine (Xeloda), fluorouracil (5-FU) and radiation. The patients in the study received intravenous doses of cetuximab in addition to standard care. Additional data is required to validate the results, Lenz said. His lab is participating in another trial looking at a larger sample size in the United States. The study was performed in the Sharon A. Carpenter Laboratory at the USC Norris Comprehensive Cancer Center and Hospital.

Lenz. H-J, et al., EGF61 polymorphism predicts complete pathologic response to cetuximab-based chemoradiation independent of KRAS status in locally advanced rectal cancer patients*. Clinical Cancer Research*, 2011; DOI: 10.1158/1078-0432.CCR-10-2666

SURGICAL THERAPIES

7. Chewing Gum Helpful After Surgery (Jun. 26/11)

Doctors at a leading London hospital are advising bowel cancer patients to chew sugar-free gum after their operations, in order to get their digestive systems back to normal so they can get better faster. Studies have found that patients undergoing surgery likely to affect their bowel function were fit enough to go home as much as two days earlier than other patients if they chewed gum. Chewing gum has helped new mothers recovering from caesarean sections, as well as patients undergoing stomach surgery, who can suffer from painful cramps until digestion returns to normal. Surgeons at University College London Hospital are asking patients booked for bowel cancer surgery to bring supplies of sugar-free gum with them, to be chewed three times a day, for an hour, after their operation. Consultant colorectal surgeon Alastair Windsor said the trial is part of a program to find new ways to help patients recover from treatment. He said many patients undergoing many types of surgery likely to affect their digestive system could benefit from bringing gum to hospital - but advised them to ask their own doctor first. Dr Windsor said: "One of the things that delays people recovering from surgery is that they get what is called an ileas - where the bowel goes to sleep. It seems that chewing gum can stimulate the saliva, which starts enzyme production in the pancreas, and that then stimulates gastro-intestinal activity." The trial, which began six months ago, has yet to publish results, but the surgeon said so far patients were responding well to it. He said: "Patients seem to like it and in particular to like the fact they are doing something to aid the recovery. We don't yet know how far it is speeding up their recovery, but there doesn't seem to be a downside to it." The surgeon added: "If I was a patient going into hospital for surgery, I would say talk to your medical team first, but from all the research done, it seems that chewing gum is something that can help patients and for most people, it is certainly unlikely to do any harm." Different studies from across the world have shown faster recovery when patients are asked to chew gum, but it is not known whether the act works as a placebo, improving patients' sense of well-being, and reducing stress - which could in itself improve bowel function - or whether the impact is physical.

http://www.telegraph.co.uk/health/healthnews/8598457/Cancer-patients-prescribed-chewing-gum-to-get-better-quicker.html

SCREENING

8. Targeted Contrast Agent Reveals Colon Cancer (Jul.1/11)

Colon cancer could become easier to detect, thanks to a newly developed medical contrast agent and advanced optics that illuminate dangerous, invisible polyps. The Norwegian subsidiary of international medical giant GE Healthcare is conducting pioneering research on new medical procedures based on targeted contrast agents. A new product now under development could play an important role in diagnosing colon cancer. "There are strong indications that we can now make it far easier to not only find but also remove the most dangerous cancerous polyps in the colon." Colon cancer was thought to be relatively simple to detect through colonoscopy, a procedure using a camera mounted on the end of a flexible tube to enable doctors to see the mushroom-shaped growths called polyps. An instrument in the same tube is used to excise the polyps. It has become clear, however, that these easily visible polyps are not the only danger. Japanese doctors discovered that there are also flat polyps in the colon that are far more difficult to detect visually. The new contrast agent will be valuable for detecting those. The contrast agent for detecting colon cancer is called **GE-137**. It is a targeted agent, meaning that once it is injected by needle in the patient's arm, it seeks out the cancer. After roughly 90 minutes the substance has been absorbed in areas where cancer is present. This is where the other part of the cancer research project comes in: locating the substance is the next step in the procedure. GE Healthcare AS in Norway has drawn on parent company General Electric (GE) -- one of the world's largest conglomerates and a developer of both pharmaceuticals and medical equipment -- to refine the colonoscopy system and camera apparatus used in the project. GE Global Research provided substantial help with the new instrument. It works in much the same way as previous

models, but also shines a strong red light. The contrast agent changes the colour of this light so it can be detected by the new camera equipment and compared against regular-colour images. In a prototype of a colon containing nearly invisible malignant polyps, these dangerous growths are easy to see when the red light is directed on them. The contrast agent and medical equipment could greatly ease the task of the surgeons wielding the camera and monitor at the operating table. The contrast agent has now been fully tested on animal subjects, and researchers have launched a phase-1 clinical trial on people. GE Healthcare has already examined the substance's effect on healthy volunteers and so far has found no side effects whatsoever. Trials such as these are time-consuming, however, and must be carried out meticulously, so much work remains to be done.

http://www.forskningsradet.no/no/Forsiden/1173185591033

9. Overuse of Screening in the Elderly (Jul. 13/11)

Among Medicare beneficiaries, a large portion of colonoscopies for screening purposes are performed more frequently than recommended intervals. But among older patients treated at Veterans Affairs facilities, warranted follow-up colonoscopies for patients with positive fecal blood tests often do not occur, or cause burden when they do. These findings are from two reports posted online that will appear in the August 8 print issue of *Archives of Internal Medicine*. Colonoscopy, a screening test used for the detection of colorectal cancer, may be overused as a screening tool, the authors suggest as part of the *Less Is More* series in the journal, with potential negative consequences including adverse effects without sufficient benefit, unnecessary expense, and use of limited medical resources. At first screening, most patients have no signs of cancer and clinical guidelines recommend that the next screening colonoscopy not take place for another ten years. "Identifying and decreasing overuse of screening colonoscopy should free up resources to increase appropriate colonoscopy in inadequately screened populations," write the authors. James S. Goodwin, M.D., and colleagues analyzed a national sample of 5% of persons enrolled in Medicare from 2000 through 2008. They identified patients at average risk for colon cancer who received an initial screening colonoscopy between 2001 and 2003. The researchers determined that 24,071 patients in the sample had a negative screening examination result and calculated the time before the procedure was repeated. Of the group of 24,071, nearly one-fourth (23.5%) received a follow-up colonoscopy within seven years with no clear indication for the early repeated examination. Repeat screening rates were relatively high among older patients (45.6% in ages 75 to 79 years, and 32.9% in patients ages 80 years and older). Researchers also found that men, patients with more health conditions, those screened in high-volume colonoscopy settings, and those in certain geographic areas were more likely to be tested. The authors recommend that closer attention be paid to colonoscopy screening rates so that this procedure is reserved for those who can really benefit from it. "Early repeated colonoscopies without clear indication compose a substantial proportion of the present endoscopist workload and also represents substantial Medicare expenditures," they state. "Given the increasing public interest in and ownership of cancer screening, public information campaigns that emphasize both the necessity for colorectal cancer screening as well as the dangers of overuse may prove beneficial in reducing overuse." In another article, Christine E. Kistler, M.D., M.A.Sc. from the University of North Carolina at Chapel Hill, and colleagues, found that some patients who should receive colonoscopies did not receive the procedure, and some who did experienced a burden from screening. The authors studied 212 patients receiving care through Veterans Affairs facilities, and who were age 70 or older and had a positive result on a fecal occult blood test (FOBT). The study participants were followed-up for seven years to determine what other interventions occurred and what the outcomes for patients were. More than half of the patients (118 of 212, or 56%) received a follow-up colonoscopy, which found 34 significant adenomas and six cases of cancer. Among this group, ten percent developed complications from the procedure or from cancer therapy. Of those (94 of 212, or 44%) who did not have a follow-up colonoscopy, three died of colorectal cancer within a five-year period and 43 died from other causes. The authors also estimated the relative benefits and burdens of the procedure against patients' life expectancies. The findings point to the need to better determine which patients are good candidates for FOBT in the first place. "As with all screening tests, FOBT does not benefit most patients because most do not have cancer or significant adenomas," write the authors. Still, the proportion of those who had cancer or significant adenomas detected by the test and successfully treated (15.6%) "suggests that a significant minority received net benefit from current practices." Noting that those with the best life expectancies were the most likely to benefit from the test, the authors conclude, "Our study supports guidelines that recommend using life expectancy to guide colorectal cancer screening decisions in older adults and argues against one-size-fits-all interventions that simply aim to increase overall screening and follow-up rates."

Goodwin, James s, et al., Overuse of Screening Colonoscopy in the Medicare Population. Archives of Internal Medicine, 2011; DOI: 10.1001/archinternmed.2011.212

Kistler, Christine, et al., Long-term Outcomes Following Positive Fecal Occult Blood Test Results in Older Adults: Benefits and Burdens*. Archives of Internal Medicine, *2011; DOI: 10.1001/archinternmed.2011.206

OTHER

10. Cancer Survivors Lag in Care for Comorbid Conditions (Jun. 7/11)

The quality of care that older cancer survivors receive for comorbid conditions such as diabetes and heart failure varies by tumor type, according to a retrospective, cross-sectional analysis of database records for more than 25,000 people. Colorectal cancer survivors fared the **worst** of three tumor cohorts studied

(breast, prostate and colorectal). Compared with a control group of cancer-free patients, they were more likely to receive acute and chronic care that was subpar on a variety of measures. Breast cancer survivors fared best, receiving equivalent acute and better chronic care than did cancer-free controls. Prostate cancer survivors came out somewhere in the middle, receiving worse acute care but better chronic care. The study does not explain why care was or was not provided, listing its limitations. Investigators hope to explore why survivor care varies by tumor type as well as possible relationships with cost. The issue of comorbid-condition care in cancer survivors has been understudied. As treatments improve and survivors live longer with a history of a cancer diagnosis, quality care for comorbid conditions takes on greater importance. Cancer survivors' health care needs include surveillance for recurrence and monitoring for the physical and psychosocial long-term and late effects of the disease and its treatment. Their needs also include general primary and preventive care, and often care for comorbid conditions. Additional studies are required.

http://www.labome.org/grant/r01/ca/comorbid/conditions/comorbid-conditions-in-cancer-survivors--costs-and-quality-of-care-8005311.html

11. Lower Lip Holds Clue to Hereditary Colon Cancer Syndrome (Jun. 7/11)

Abnormally dense blood vessel growth in the mouth appears to be associated with familial adenomatous polyposis (FAP), an autosomal dominant disease that causes hundreds of colorectal adenomas in teenagers and progresses to colorectal cancer if colectomy (surgical removal of the colon) is not performed. FAP is normally diagnosed with costly DNA tests and colonoscopies, and sometimes goes unnoticed until cancer develops. In 2003, Italian researchers reported that a similar genetic condition—hereditary nonpolyposis colorectal cancer (HNPCC)—was linked to a greater complexity of blood vessels in the oral mucosa. Acting on this information, a team at Johns Hopkins School of Medicine in Baltimore, Maryland, and The Catholic University of America in Washington, DC, developed a device that allowed a direct and relatively automated measurement of this vascular density. Measures of oral mucosal vascular density (OMVD)—the density of visible blood vessels in the lower lip—were significantly higher in 33 FAP patients than in 50 healthy controls, according to investigator Francis Giardiello, MD, director of the Johns Hopkins Hereditary Colorectal Cancer Program, part of the Johns Hopkins Kimmel Cancer Center in Baltimore, Maryland. "About 90% of controls were below that threshold, so in principle, we could use that threshold for screening purposes," observed Giardiello in a statement describing his group's findings. An additional five patients with multiple adenomas but no detectable mutation for FAP or HNPCC on genetic tests underwent the OMVD test, ultimately scoring above the high-risk threshold. The results suggest that this high-OMVD condition may be an alternative marker for colon cancer risk, even when researchers can't find a gene mutation.

Gardiello, Francis, et al., A new phenotypic manifestation of familial adenomatous polyposis. Familial Cancer. Vol. 10, Number 2: pp. 309-313.

NUTRITION & HEALTHY LIFESTYLE

12. Folic Acid to Decrease Risk of Colorectal Cancer (Jun. 28/11)

It has been known for some time that optimal amounts of folic acid decrease the risk of colorectal adenomas. However, nobody had defined the minimum amount of folic acid needed to achieve that beneficial effect. Nor had anyone definitively shown that the decreased risk of colorectal adenoma also leads to a decreased risk of colorectal cancer. And the question became even less clear a year or two ago when a couple of studies suggested that folic acid supplementation might even increase the risk of colorectal cancer. Fortunately, that question has been put to rest by a recent American Cancer Society study with over 100,000 participants that definitively showed that increased intake of folic acid from fortified foods and supplements does not increase the risk of colon cancer (Gastroenterology, doi:10.1053/j.gastro.2011.04.004) as reported in last month's updates. In this study, Dr. Fujimori and colleagues looked at 458 patients (258 men and 200 female), ages 40-75, who underwent a routine colonoscopy at the Cibu Hokusou Hospital of Nippon Medical School in Japan. A blood sample was drawn before the colonoscopies and serum levels of folate (a mixture of folic acid and its metabolites) was measured. Of the patients examined, 287 had adenomas and 171 did not. The study showed that a serum folate level of around 8.0 ng/ml was the minimum needed to decrease the risk of colorectal adenomas. There were no statistically significant differences in the incidence of colorectal adenomas in patients with serum folate levels above 8.0 ng/ml. ***However, patients with serum folate levels below 8.0 ng/ml were significantly more likely to develop colorectal adenomas***. For men, the increased risk was 50%, while for women it was 23%. One of the study's limitations was the fact that it did not define the amount of dietary folic acid required to get your serum folate levels above 8.0 ng/. Hence, additional studies are required as recommended by the study authors.

Fujimori, Shunji, et al., Determination of the minimal essential serum folate concentration for reduced risk of colorectal adenoma. Clinical Nutrition. Doi: 10.1016/j.clnu.2011.04.007